THIS TALK MAY CAUSE SIDE EFFECTS | KATE FAASSE

PODCAST TRANSCRIPT

Ann Mossop: Welcome to the UNSW Centre for Ideas podcast. A place to hear ideas from the world's leading thinkers and UNSW Sydney's brightest minds. I'm Ann Mossop, Director of the UNSW Centre for Ideas. The talk you're about to hear, *This Talk May Cause Side Effects*, features UNSW Sydney's Kate Faasse, and was recorded live at the Festival of Dangerous Ideas.

Kate Faasse: I'd like to tell you the story of Mr. A, a young man who enrolled in a clinical trial for a new antidepressant medication. One day, after a huge fight with his girlfriend, Mr. A took all of the remaining 29 pills he'd been given for that study. Knowing he made a mistake, he got himself to hospital where he said, help me, I took all my pills, before collapsing. The hospital staff raced into action. Mr. A was drowsy, pale, sweating, breathing rapidly, and when they got him on monitoring equipment, it became clear that his heart rate was extremely high, and his blood pressure was very low. He was showing concerning signs of a drug overdose. When the physician from the clinical trial arrived, everyone expected to be told that Mr. A had taken 29 antidepressant pills. What she revealed instead, was that he taken 29 placebo pills, sugar pills, containing no active ingredient at all. So everyone in that room was relieved, but a little surprised at this information. But sure enough, within 15 minutes, Mr. A was alert, sitting up, chatting to everyone in the room, and his blood pressure and heart rate had gone back to normal. So rather than a drug overdose, Mr. A had taken a placebo overdose. Now, most people are familiar with the placebo effect, where taking a sugar pill can cause healing or health improvement. What Mr. A experienced was a dramatic example of the nocebo effect, the dark side of placebo, where that same sugar pill can cause unpleasant and sometimes very serious side effects.

This is what we study in my lab, the nocebo effect. We give people sugar pills, we warn them about possible side effects. And we watch what happens. We don't do this just because we

like making people sick. But because we really want to understand how nocebo effects are formed and what we can do to prevent them. This is particularly important because while you can get nocebo effects from taking sugar pills, like Mr. Ray, you can also get nocebo effects from taking real medications. And lots of people take medications, and lots of people get nocebo effects from them. Anyone can experience a nocebo effect, given the right circumstances.

I want you to imagine tiny bugs, like lice crawling all through your hair, down your neck and down your back across your arms and over your legs. Perhaps you have an itch on your face, maybe you need to scratch your leg. Now I want you to focus on how tired you are, how sleepy, how fatigued. Maybe your eyelids are starting to get heavy. Perhaps you're just stifling that urge to yawn. Just paying attention to symptoms like this can actually cause them to happen. And yes, it is all happening in your head. But those symptoms are also very real. If we looked at your brain activity, while you're imagining those tiny bugs, it would have looked remarkably similar to somebody really experiencing that situation, those same edge brain regions would have been active.

So this is at least part of the explanation for why we experienced nocebo effects. Just thinking about symptoms can make us experience them. And now imagine you've been prescribed a new medication. What's one of the first questions you might ask, what are the side effects? And so you pay just a little bit more attention to those side effects expecting that you might experience them. So the nocebo effect is really driven by the power of negative expectations. Expecting side effects can actually cause them to happen.

So how common is the nocebo effect? In one huge study involving more than half a million people, 76% of people taking a range of active medications reported side effects. But 73% of people taking placebos reported remarkably similar side effects. Which means that overall, only 4% of all those drugs' side effects are actually caused by the drug itself. Most side effects were not. Now, some of those that people reported were common everyday symptoms that all of us experience, but up to 60% are caused by the nocebo effect. Most side effects, more than half, are likely to be caused by nocebo effects. So nocebo effects are common. They can

be serious, and they can be caused really easily, just by warning people about possible side effects of a drug.

So the first study to tell us about this happened, kind of by a lucky mistake. For me, at least. There was a mix up with the consent forms. And some people were warned that they might experience indigestion, nausea, vomiting, and diarrhea from the drugs they were taking. And some people didn't get this information. Despite all taking the same pills, the people who got these warnings were three times more likely to experience those side effects. And six times more likely to quit that study because they were so unpleasant. Warnings have also caused some problems for statins. So statins are drugs that are prescribed to reduce cholesterol, and more importantly, to reduce people's risk of having a heart attack or a stroke. And if you've heard of statins, you've probably heard that statins cause muscle pain. It's been on the news. On television, it's one of the first things to pop up in an internet search. Except that's not what the data says. What the data says is that people who take statins are just as likely to experience muscle pain as people who take a placebo. Despite this, people taking statins are still warned about muscle pain as a possible side effect. And up to 30% of them experience it not because of the statins, but because of the nocebo effect. And some of them stopped taking their statins because of that muscle pain. Statins that were prescribed to reduce their risk of having a heart attack or a stroke.

So why are things like muscle pain still listed as drug side effects when there's actually really good evidence that they're not? What happens is that all symptoms that are reported by people in a clinical trial end up in that long list that you see. The catch is that it doesn't matter whether they're reported by people taking the real drug or people taking the placebo, they end up on that list regardless. So we end up in a vicious cycle. People in clinical trials report symptoms, these symptoms end up listed as side effects whether or not they have anything to do with the drug. And for the most part, they don't. Then other people get that drug, they're warned about the side effects. And these warnings cause nocebo effects. To break this cycle. And to prevent nocebo effects, we need to stop warning people about things that aren't actually drug side effects. But to do that, we need to know what things are actually drug side effects and what things aren't.

So we use clinical trials already to test whether a treatment is effective, we compare people taking the drug to people taking a placebo. And drugs are only approved if they work better than the placebo. We can and should be using these same clinical trials to test what side effects these drugs cause, by assessing and comparing the symptoms reported by people taking the drug, to people taking the placebo. Only symptoms that occur more in people taking the drug should end up on that list. Please know that if I was in charge, we would already be doing this. But the current system was designed by lawyers, not by doctors, and certainly not by nocebo researchers. And it's going to take a while to change. So in the meantime, we've been looking for other strategies to help tackle the nocebo effect. And I'm going to tell you about three.

The first is to change the way we talk about side effects. So often we see information like this drug might cause headache, or 30% of people who take this drug experience headache. But what if we flipped the script? That means that 70% of people who take this drug don't experience headache? It certainly sounds better. And it turns out that this focus on the positive on the proportion of people who remain side effect free can reduce the nocebo effect. So we've seen this with sugar pills, but also with things like flu vaccines and pain-relieving medications. The second strategy is to make people happy. Now this is still very new research. But it looks like having people watch funny videos, putting them in a positive mood before they take a treatment can actually stop nocebo effects from forming. The third strategy is teaching people about nocebo effects, much like we've been doing here for the past 10 minutes. So as well as causing side effects, this talk might also prevent them, because people who have been taught about the nocebo effect are less likely to experience them in the future.

Now, there are also some real medication side effects. And it's important to know what they are so that we can all make good decisions, informed decisions about our medical care. But there aren't anywhere near as many as we've been led to believe. But when you're in the position of being a patient, you probably feel like your doctor or your pharmacist is doing the right thing by warning you about possible side effects. And you're doing the right thing. By paying attention to that information. We've been taught to see these warnings as cautious, sensible and prudent. But when that list of side effects is an unscientific mess that we know is causing nocebo effects, we need to be extremely careful. Now, I'm not popular with some

of my colleagues when I say this, but there's a really simple way forward. We need good scientific evidence of what the real side effects of drugs are. And we need to stop warning people about things that are not actually side effects, because all those warnings are doing, is causing us harm.

Ann Mossop: Thanks for listening. This talk was part of the event 'Unthinkable', presented by the UNSW Centre for Ideas and The Festival of Dangerous Ideas. For more information visit centreforideas.com, and don't forget to subscribe wherever you get your podcasts.