Ben Colagiuri – 'The Placebo Effect: Something From Nothing'

Moderator: Welcome to the podcast series of *Raising The Bar Sydney*. Raising The Bar in 2016 saw 20 University of Sydney academics take their research out of the lecture theatre and into 20 bars across Sydney, all on one night. In this podcast, you will hear Ben Colagiuri's talk, *The Placebo Effect - Something From Nothing*. Enjoy the talk.

Ben Colagiuri: Okay. Tonight I'm going to talk about the placebo effect and how something can come from nothing. I'll start with a very simple question of, what's a placebo? I don't know about you guys, but anytime I have a serious question that I need an answer to I like to refer to TV Morning Show hosts as they're fountains of knowledge. In this, case we'll ask David Reyne, who's the former host of David & Kim, what he thinks a placebo is.

(Video Playing)

David Reyne: ... understand what a placebo is, but it seems to have saved them and it wouldn't make sense that every time a trial like this takes place that there is a placebo on hand.

Female Speaker: David was talking about the English clinical drug trial that went terribly wrong. Six men suffered multiple organ failure and nearly died. Doctors are still baffled, but not quite as baffled as David Reyne.

Male Speaker: A placebo is just an inactive agent. So it's a …

Female Speaker: … it's a pretend drug.

Male Speaker: … sterile saline, for example; with no active agent in it.

David Reyne: I was thinking it was a cure, of some sort.

Ben Colagiuri: Okay. He got there in the end.

A placebo is just a fake treatment; like a sugar pill or, a saline injection that doesn't have any active ingredients. Despite the fact that it doesn't have any active ingredients and have quite powerful effects. One of the first examples of the placebo effect comes from the Second World War. When a physician, named Henry Beecher, was working in a small battle-filled hospital. There were lots of soldiers coming in who were injured. He would treat them for their injuries and at one point, he realised that the hospital had run out of morphine. He didn't have any more morphine to give these wounded soldiers but instead of telling the soldiers that he didn't have any more morphine to give them, he decided to give them saline and tell them that they were getting morphine; in the hope that the knowledge that they were getting a treatment would help to relieve their pain.

Quite remarkably, it worked. For 30% of the patients that he gave these saline injections to, that he had told them that was actually morphine, they had significant reductions in their pain. The simple belief that they're receiving an active treatment was enough to reduce their pain.

Since Beecher's study, there's been quite a lot of interest in the placebo effect and how we can get these placebo effects or, this massive improvement from these fake treatments.

A more recent and I think very fascinating example comes from a comparison of real surgery versus placebo surgery. In this case, the surgery was for osteoarthritis of the knee. Osteoarthritis of the knee is a condition that affects people, particularly as they get older. It's very painful condition. It can influence how functional people are, whether they can walk the shops, or not. It's a pretty significant and uncomfortable condition to experience.

In this particular surgery, patients go in and they get put under general anaesthetic. They have incisions made in their knees. Then they have the knee joint cleaned out. Their surgeons go into the knee joint and they clean out the knee and that's because there's believed to be debris in the knee joint and fluids that have built up, that can contribute to the osteoarthritis and that cause the arthritic pain. This is a very common surgery. About a million people each year have this in the United States alone. It costs about $5,000 per operation. We're talking about five billion dollars in money spent on this operation each year. For most people, it seems to work or, for the majority of people. Over half of the people that have this treatment experience significant improvement after the surgery. It seems to be quite a good surgery but for obvious reasons, surgeries are very rarely compared to placebos because who in their right mind is going to put someone on general aesthetic, cut them open and do absolutely nothing?

In fact, a surgeon, named Bruce Moseley, decided to do exactly that. About ten years ago, he decided to get 200 patients with osteoarthritis of the knee and randomise them either to the real surgery or, to the placebo surgery. They didn't know which one they were going to get. He decided whether. He randomly allocated them; either to the real surgery or, the placebo surgery. Real surgery, the patients get put under general anaesthetic, have these incisions made in the knee and have their knee joint cleaned out. Okay? Which is believed to be the active component.

In the placebo surgery, the get put under general anaesthetic, have incisions in their knees made but, don't actually get any of the cleaning out of the knee joint. They don't get the active component of the treatment. Even in the placebo group, you're under general anaesthetic and you actually wake-up with this pain in your knee because you've had incisions made there. You actually get scars from the surgery. You just simply don't get the cleaning out of the knee and the results are pretty fascinating. Two weeks after the real surgery, the patients that had had the real surgery had a 31% reduction in their pain symptoms. Whatever pain they came in with, on average there were 31% better after the surgery.

In the placebo group, the patients were 33% better after they'd come in. In fact, the placebo was just as effective as the real surgery; if not more. Of course that’s only two weeks after the surgery. One might argue that maybe this is just some acute effect. If you go into hospital, you've got your friends and family around you. You're getting lots of attention from the health professionals are there. That could really make you better in the short term. Surely after longer periods, we can't have placebo surgery working just as well as real surgery.

Well in fact, after six months the real surgery had improved their treatment outcomes, their pain by 30%. The placebo had, also improved it by 30%. Even two years later, the real surgery had improved symptoms by 27% and the placebo had improved it by 28%.

For this surgery that a million people have each year that costs five billion dollars to US citizens alone, the real surgery appears to be just as effective as the placebo surgery. Simply just anesthetising people, making incisions in their knee and not cleaning out their knee joint is just as effective as giving the real surgery. Another pretty remarkable finding comes from studies on deep brain simulation. Deep brain simulation is a fairly new technique in which, we insert electrodes into specific parts of the brain and we give them electrical simulation.

One of the more common diseases that's being used to treat, is Parkinson's disease. In Parkinson's disease there are various symptoms that affects, obviously. One of the most common, is the interference with motor performance and motor control. You see people with Parkinson's can have quite significant tremors and can't engage with their environment; in terms of their motor performance, very well. Deep brain simulation has been used for Parkinson's disease. It's a pretty invasive procedure, as you can imagine. It's a pretty fascinating procedure, as well. What happens is, the patients go in and they have a local anaesthetic on their skull. They're not under general anaesthetic. It's only a local anaesthetic on their skull. They have holes drilled into their skull so they can actually hear the drilling of their skull. Then they have these electrodes implanted into specific regions of their brain.

The reason that they're awake and not under general anaesthetic is they have to be very careful to make sure that the electrodes go into the right spot. If you were to affect the vision of the brain, you could see that in the patient straight away. They would be able to report, "Something's going wrong with my vision." So in the case of deep brain simulation for Parkinson's disease, the electrodes are implanted into an area called the subthalamic nucleus. The idea here, is that stimulating the subthalamic nucleus by providing these electrical currents there after this surgery can interfere with the subthalamic nucleus; which his responsible for creating this disorders of motor performance.

I should point out that obviously given that this is such an invasive treatment, it's reserved for people at that extreme end of symptoms. Okay. If you have Parkinson's disease, you're not immediately offered this type of treatment. You're only offered this type of treatment if you've failed to respond to other medications. Seeing any improvement in patients that are at that extreme end of the spectrum, in terms of their Parkinson's symptoms, is pretty impressive. The results seem fairly promising. If you give this operation to patients with Parkinson's, you see these pretty remarkable effects where only a few days later they've got much better motor control than they've previously had before.

It seems like it's quite an effective surgery; however, the really interesting part is, if you do the same operation but, you simply tell the patients that you've turned on the electrodes afterwards but, you don't actually switch them on, you see the same level of improvement. If you do this operation and you just keep the electrodes inactive afterwards.

They’re not actually getting any electrical simulation; you see just as much improvement in the patients, as if you were stimulating their subthalamic nucleus. The placebo deep brain simulation is also, just as effective as the real deep brain simulation.

How is it that these fake treatments elicit improvement? Hopefully those examples that highlight the really simple, but important point. That's that medical treatment does not occur in a vacuum. Every time we take treatment, there's a rich context that goes along with it. It's not like when we need some medical treatment that it spontaneously is transferred into our body. There's some context that goes with it. For example, if we were to take a medical treatment, there's usually some root of administration. It might be something that we take as an oral capsule. It might be something that's in an injection or, it might be something that we need to have an IV for. Similarly, there's almost always some information that goes along with the treatment. Whether it's what's written on the information package, what the health professional tells us or, what we've heard from our friends and family or, right from the media. Of course, there's always the setting. We might take the treatment at home. It might be something we go to the GP's office for or, it might be something that we actually have to stay in hospital for.

All of those contextual factors influence what an individual expects from their treatment. As a very simple demonstration of those types of expectancies. If I told you that these two treatments were painkillers and asked you which of these do you expect to be the most powerful painkiller, most people would choose a needle over a pill and that's without knowing any of the ingredients whatsoever. It's exactly those types of expectancies that drive the placebo effect. That's all well and good. It's nice enough to say that we have these expectancies due to their context and that's what produces health improvement but how is that expectancies actually translate to real changes in people's health? One of the main mechanisms of the placebo effect is called classical or, Pavlovian conditioning. Classical conditioning is a very general phenomenon, which is how humans and other animals learn to predict and to respond to different stimuli in their environments.

I'll run through a simple example of this from an early study by Pavlov, which you may have heard about. Which is Pavlov's showing that you can get dogs to salivate in response to a bell after you pair that bell with food. The procedure goes that before any conditioning, before any learning, you have this food. You present food to a dog and it will start to salivate. That's just a complete reflex. You do that to any dog, present food to any dog and it'll start salivate. Then what we want to do is condition something but we have to condition something that's neutral originally. In this case, the bell is a neutral. If you ring a bell without any conditioning, a dog won't salivate. Okay? It might orientate to it because it can hear it but it won't salivate. It's completely neutral with respect to salivation. The bell's a neutral stimulus in this scenario. If we pair the bell with the delivery of food, so we pair the bell with this active stimulus, the food, then we do that a number of times, the dog will be salivating because the food's present. It's learning this association between the bell, food and salivation. Eventually, if after that conditioning we present the bell alone, the dog will start to salivate in response to the bell as if it was the food. The bell through its previous pairings with the food becomes an active stimulus, in-and-of-itself and a real life example of classical conditioning comes from this video.

(Video Playing)

Male Speaker: Hey Psych 101 class! I'm David and I'm going to be testing Pavlov's theory of classical conditioning on my roommate Brian. The condition stimulus will be the sound effect, "That was easy." Then I'm going to shoot him with this airsoft gun. He will soon learn the relationship between the sound effect and the shot before he gets too hurt.

"That was easy." "That was easy."

Brian: Ah!

"That was easy."

Brian: Punch.

"That was easy." "That was easy."

All right guys. Looks like Pavlov's theory works.

Ben Colagiuri: Okay. A nice example of classical conditioning in practice. T

The idea and terms of the placebo effect is that, as I mentioned before, when we take active treatments like morphine, of course these active treatments work and they create pain relief but the morphine's not spontaneously transferring into our bodies. It always comes with a context. It might be the side of the nurse, if it's something you're taking in a hospital. It's literally my mum and dad. It's embarrassing.

Audience: Take it, no take it. We want to hear what they have to say.

Ben Colagiuri: Sorry, guys. Can someone take my ... can he look after that? I would crucify any of my students that had their mobile phone going to talk.

We have these active agents, like morphine that produce pain relief. Of course, morphine is not transferred into our body magically. It comes with the context. Let's say a nurse is delivering it. We're in a hospital. We've got the side of the nurse. We've got the smell of the hospital. We've got the feel of the injection as it goes in. Every time I get morphine, it's paired with that context. The association between the morphine and the context builds, such that eventually if we get exposed to a placebo, so if we switch that morphine injection with saline, let's say to salt water, then that placebo and the context can elicit placebo-induced pain relief. Why this classical conditioning?

We know even more than that now, these days in terms of the neurobiological processes that underlay these expectancy-induced placebo effects. We have these verbal, contextual, social cues, in terms of verbal cues, what information the patient is told. Contextual cues, the hospital, the side of the hospital, the smell of the hospital and social cues, what we've seen or, heard from other people that elicit these expectancies. We start to expect something as a result of our treatment.

We now know that these expectancies can actually trigger the release of certain neurotransmitters within our central nervous system. For example, expecting pain relief can trigger the release of endogenous opioids. Endogenous just means from within the body. Opioid is similar to morphine, in the sense that it's something that relieves pain. We have these endogenous or, internal opioids that are essentially the bodies own painkillers. When we come across verbal, contextual or, social cues that trigger our expectancies for pain relief, we then have our central nervous system releasing these neurotransmitters that actually reduce pain. That's how we get from the expectancies to actually placebo effect.

Does that mean that the placebo effect is all powerful, then? Can the placebo effect influence any outcome? Well, no. There's definitely limits to the placebo effect. I wouldn't recommend that you took a placebo in order to fix a broken leg. It may, potentially help with the pain associated with the broken leg, as you're recovering. It's not going to influence how quickly you heal from a broken leg. Similarly, if somebody had insulin dependent diabetes, I wouldn't recommend that they replace their insulin injections with saline and hope for the best. Most likely outcome would be that they'd end up in hospital in a coma.

What we do know that the placebo effect works for are things like depression, anxiety, pain, nausea, sleep, learning, memory, Parkinson's disease, attention deficit hyperactivity disorder and chronic fatigue. They're probably lots of other things that I haven't got space to include in there and other things that we might discover in the future. It's quite a range of conditions.

I want to highlight the fact that a lot of these conditions do involve some level of subjectivity. Certain things we support, like pain are things that we report; like pain and anxiety and nausea. Also, you can measure some of these things objectively. For things like sleep, we can measure via measuring brain waves, how long somebody sleeps for and obviously, we can test learning and memory via computerised tests. We still see placebo effects when we assess these outcomes objectively. Including and even in Parkinson's disease, when we assess people's motor performance. It's not the case that this is just something that is all in people's head. We see real changes and real outcomes, as well.

You might be thinking what, then actually affects whether somebody experiences a placebo effect, or not? I have to apologise to the gents in the audience, that unfortunately size does matter in the case of the placebo effect. A larger placebo will produce a larger placebo effect. A placebo capsule will produce a larger placebo effect than a pill. Two placebo capsules will produce a larger placebo effect than one placebo capsule. An injection will produce a larger placebo effect than a capsule.

Together, what this suggests is, that the more invasive the placebo is, the bigger the placebo effect. If we think about a pill that's not so invasive to take, we can just have some water and swallow that. An injection that might be something. We've got to stick something into ourselves or, we might even need to go to hospital for it. As you guys noted before when I showed you the injection versus the pill, your natural instinct was to expect more improvement from the injection compared with the pill. The more invasive the placebo, the larger the placebo effect is. That may well explain why we get such large placebo effects in response to things like surgery. Surgery's a very invasive treatment.

You're put under general anaesthetic, have scars on your knee from being cut open. It's probably triggering quite strong beliefs, in terms of the improvement.

Another thing that you might be wondering is, is it the case that just some people are gullible? Gullible people respond to placebos and other people won't. Right?
I would argue that definitely lots of people are gullible, primarily the people that voted for this abhorrent human being. In terms of the placebo effect, there doesn't appear to be any set of placebo responders. It's not the case that there's just one group of people that will always respond to placebos and another group of people that won't respond.

What seems more important is that it's the interaction between individuals' particular beliefs and the treatment context that they're exposed to. To give you a more concrete example of that, if we were to take two people: one person that believed in Western medicine and another person that believed in Eastern medicine and we told them that we're going to give them a couple of different types of painkillers. One of the painkillers was a capsule that we told them was Paracetamol, let's say. The other painkiller was acupuncture. Actually, they're both placebos. This is just a pill and we administer placebo acupuncture. What we would predict is, that the person that believes in Western medicine will have the stronger placebo effect to the placebo pills and to what they think is Paracetamol; all that they're getting. Whereas the person that believes in Eastern medicine, is more likely to have a placebo effect in response to the placebo acupuncture. That's more consistent with their beliefs.

So it's about the interaction between the specific individual and their beliefs and the treatment they end up getting. Also interestingly, it's not all good news. There's also a dark side to the placebo effect. We can also get expectancies for negative outcomes that do go on to produce negative outcomes. It's not so hard to imagine situations in which treatment context can lead to negative expectancies. So if I ask you guys to predict which of these types of pills is likely to have more side effects, most people would pick the red pills, rather than the white pills. So it's those types of expectancies that produce what's called the nocebo effect.

Placebo means I shall please in Latin. Nocebo means I shall harm. The nocebo effect is when negative expectancies produce negative health outcome. Going back to that example that I talked about, nocebo effect has been studied much less, so far than the placebo effect. The conditions that we know that there are nocebo effects for are things like: headaches, pain, nausea, poor sleep, appetite loss and anxiety.

Going back to the example I gave you earlier on, in terms of deep brain simulation for Parkinson's disease, we can also get evidence of nocebo effects there. If we have a patient that's undergoing deep brain simulation and we've turned on the electrodes in them. They're actually getting the real simulation. If we tell them a few days after the surgery, "We just want to check how it's going now that it's truly working. We're going to turn off the simulation now, for a little bit. Just to see what goes on." We actually don't turn it off. Just told them we're turning off the simulation but we actually keep it on. What we see is, that those symptoms of Parkinson's, like the hand tremors, very quickly re-emerge. They're getting exactly the same treatment. They've just now, been told and they've come to expect that they're not getting treatment anymore and that their symptoms are going to return. Sure enough they do.

Another interesting example of nocebo effects is side effects. Every time we get a treatment, we're worried about side effects; most times, anyway. Obviously, that's for legal reasons.

When I first started my PhD, I was really interested. Now ten years ago, I was very interested in warnings about side effects. This whole idea you that you can get nocebo effects. If you warn somebody about side effects, surely they're going to expect them and that may well, then go on to cause side effects.

In a study that I ran, I tried to look at this. I got a bunch of people that had difficulty sleeping. I told them that I was running a trial of a new sleep medication. That I would either give this sleep medication or, no treatment, so I could test whether the sleep medication was working. In fact, all of the patients that got treatment were given placebos, of course; given my interest. Of course, I wouldn't tell them that at the time. Within the group of people that were getting placebo treatment, I warned half of them about a side effect and the other half I didn't say anything about side effects. Half of the people that got placebo treatment, I said, "Umm. By the way, this sleep medication might cause side effects. The most common side effects that we're seeing in the past, is a loss of appetite. You might experience a loss of appetite as a result of taking this treatment." The other group, I didn't say anything about side effects whatsoever. There was a nice placebo effect, in the sense that the group that I had given placebo treatment to, had much better sleep, both on subjective and objective outcome. The placebo was effective for improving their sleep quality.

Even more interestingly, the warning influenced the side effects that people reported. The group that was warned about loss in appetite, were much more likely to report a loss of appetite. I thought my phone was going off again. The group that didn't get any warning didn't have any. They very rarely would report a loss of appetite. Just by warning people about side effects, even when we gave them a placebo treatment with no active ingredient, we're getting influence on the type of side effects that people experience.

Of course, hopefully that's interesting in its own rights. Something that I think is very interesting, in terms of what level of information we should give patients when we're prescribing them drugs. Also, there are some even broader and more general implications for public health and public policy. One of the examples that you guys are probably familiar with is wind turbines. There's been a lot of debate in Australia about wind turbines; that whether they cause negative health outcomes. Obviously, wind turbines are reflecting, I think an interesting opportunity for more renewable energy, given that climate change, at least in my opinion, seems to be a real phenomenon. If we want to, want our future generations to enjoy the things that we've enjoyed, then we need to come up with more ways of generating energy. Wind turbines seem to be good opportunities to do that; however, there's been this big debate about whether they cause adverse outcomes.

The idea is that the people that argue that wind turbines cause negative outcomes have noted the fact that wind turbines emit something called infrasound. It's an inaudible sound. We can't hear infrasound but it's still present in the environment. There's no debate about that. They do emit infrasound.

The people that argue that wind turbines are bad argue that that infrasound actually causes a range of symptoms; including headaches, depression, anxiety, nausea, dizziness and anxiety and whole raft of things. That's, as you're probably seeing in the media, been this big debate. It actually caused our beloved former Prime Minister to come on air and say that he didn't particularly think wind turbines were that good; based on no evidence whatsoever, of course, unlike his other policies. That part of it was because he just didn't like the look of them, as well.

Interestingly our peak medical body, the National Health and Medical Research Council, did a big review on this. Actually before Tony Abbott had said that and he clearly hadn't read or, chose to ignore it. Our peak medical body did this massive review of all the evidence available for the effects of infrasound and found no evidence that suggests that being exposed to infrasound was actually associated with negative outcomes. In fact, what they concluded was it was most likely the case of the nocebo effect. It was most likely the case that people had developed these negative beliefs and that was what was triggering their symptoms.

I thought that was a really interesting conclusion so, I decided to run a study recently, testing that. In the study that I ran, we randomly allocated healthy volunteers to get exposed to infrasound or, to placebo simulation. In both conditions, they obviously didn't know what we were exposing them to. We said they're either going to get infrasound or, no infrasound but, we won't tell you what you're getting. They put those headphones on and we gave them this infrasound simulation or, we put the headphones on, we didn't give them any simulation whatsoever. Then we measured the types of symptoms that they reported. There was absolutely no difference in the symptoms reported by people exposed to the real infrasound or, the placebo infrasound. It didn't seem like there was any genuine effect as a result of being exposed to infrasound.

Most interestingly, we actually measured people's prior beliefs and concerns about infrasound before they went into the study. We found that that perfectly predicted whether somebody would report adverse symptoms from their simulation, or not. If someone came into the study believing that infrasound was bad for you, they were much more likely to report negative symptoms afterwards. Completely independently of whether they got the real simulation, or the fake simulation. It all came down to the negative expectancies.

Hopefully that's a good example of why the placebo effect and nocebo effect can be quite important in the context of Australia. I should point out that these debates aren't necessarily happening in other countries. It seems to be something about infrasound that's particular to Australia. It's a case where we may have this quite significant and broad nocebo effect that's actually influencing our public policy and our ability to reduce greenhouse gases and develop more sustainable energy.

There are also, other reasons that the placebo effect is pretty interesting. Probably one of the ones that you're most familiar with is in terms of what's called evidence-based medicine. Placebos are essential for determining whether a drug or, treatment is truly effective. A good example of that, it comes from complementary medicine. Complementary medicine is gaining popularity in Australia, in other Western countries. Complementary medicine is now used much, much more than it previously was in Australia and other countries.

If we take acupuncture, as an example, the idea in acupuncture is that needling specific acupoints along energy meridians can help to heal patients by correcting energy imbalances in their bodies. The idea is that we have this energy flowing through our body and that illness is caused by disturbances in that energy flow. The idea is that we can put needles in particular points that will correct that imbalance. There are lots of studies that show that acupuncture works better than no treatment. If you give somebody acupuncture, they will experience less pain and less anxiety and less depression and other improvements; compared with no treatment. That's undeniable. Getting acupuncture compared with no treatment. Getting acupuncture is better than getting no treatment. That type of evidence, naturally I think, leads many people to believe that acupuncture is an effective treatment. The manipulating energy therefore, can actually heal people. Of course, it's missing a critical condition. That's a placebo control group. We need to compare acupuncture, real acupuncture to placebo acupuncture to really test this idea. If it's about a manipulation of energy channels.

It sounds bizarre but you can actually give placebo acupuncture. Placebo acupuncture, basically involves these needles that retract into themselves, like stage daggers. It's a blunt needle. You feel the prick on your skin, as if a needle's going in and you can see it going down but, it's just like a stage dagger. It's actually just retracting into itself. Okay? Even more than that. We've got that, the actual placebo needle itself. Of course, we don't need to put it on the meridians. We can put it somewhere else, as a placebo. We can have it far away from the meridians and this sensation of being needled. It's quite a nice and convincing. People can't tell the difference between the placebo and the real acupuncture.

When you look at the evidence comparing placebo acupuncture and real acupuncture, both of those types of treatments are better than no treatment. Okay? If you get real acupuncture, you're better than no treatment. If you get placebo acupuncture, you're better than no treatment. There's absolutely no difference between real acupuncture and placebo acupuncture. Placebo acupuncture is just as effective as real acupuncture.

What that tell us, is that it can't be the simulation of these energy meridians that's causing the improvement in these real acupuncture conditions. It has to be something else. Most likely, it's expectancy or, some other type of psychological mechanism. Placebos are really important for being able to test the mechanism, or the supposed mechanisms of how some treatments work. Of course, I don't want to only pick on complementary medicine because we know very well that there are some very good examples of problems with evidence-based medicine. Only by using a placebo control, could we discover that arthroscopic lavage is actually no more effective than a placebo.

In the case of this knee surgery, by doing this placebo-controlled study, we found out that actually cleaning out the knee joint of debris and any fluids that built up, doesn't have any effect beyond the placebo effect or, these other factors. Placebos are a cornerstone of evidence-based medicine. We need to use placebos in order to pick apart theories of how treatments work and to show that these treatments work better than placebos, in order to incorporate them into medical practice. That's one important role of placebos.

Another, I think, potentially more interesting or, exciting role, at least for me, is whether we can actually use the placebo effect to improve patient outcomes. Can we use what we know about the placebo effect in a clinical setting, to improve patient outcomes? One possibility on the extreme end is, maybe we just take the Beecher approach. We tell patients that they're getting morphine and actually give them saline. After all, we get these placebo effects. Of course, that's a ridiculous suggestion. It would completely undermine our patient autonomy. We can't go around lying to patients about what their getting, or telling them that in the hope that they're going to get better.

There are some interesting ways that we might be able to use placebos without any deception. One example is that we … I mentioned before that if you use two capsules, compared to one capsule, you get a larger placebo effect. It could be possible. Let's say we want to give somebody 500 milligrams of Paracetamol, all for a headache. We could actually give them that 500 milligrams as a single tablet or, we could also give them two 250 milligram tablets. The idea here is that we're giving exactly the same dose or Paracetamol or, both patients are getting 500 milligrams but, in the case of the two capsules, we're capitalising on what we know about the placebo effect. We're bolstering their expectancies and we should see stronger pain relief in the participants, or the patients that get the two 250 milligrams; even though, they're actually given the same little effective dose. There's no deception whatsoever. We're just using our knowledge about the placebo effect.

Similarly, we could use what we know about conditioning to try and bolster expectancies. In a standard treatment regiment, let's say we need to give somebody Paracetamol of 500 milligrams for five days. We can just give them five, five capsules; one each day. We could also, do something to try and increase their expectancies in the placebo effect. That would be, imagine if we gave them 1,000 milligrams on the first day. We give them a big dose and they have a big improvement. That's going to lead them to believe, "Yeah. This treatment really works." Then on the second day, we give them 500 milligrams when we've built up their expectancies. We may then be able to actually reduce the amount of active dose that we give them. We could get them down to 250 milligrams and getting just as much improvement because we've bolstered their expectancies with those big doses at the start. Again, no deception required at all.

Perhaps most interestingly, there's recent evidence to suggest that you can even get placebo effects when the patient knows that they're being given a placebo. A study that was done about five years ago was looking at irritable bowel syndrome and the researchers gave. At randomly allocated patients with IBS either to the placebo treatment, or to no treatment. The critical part was, in the placebo treatment they told them, "This is a placebo. It's just a sugar pill but we think it may help you based on mind-body mechanisms and as a result of conditioning." "We believe this may help you but, be assured there's no active ingredient in this treatment."

Quite remarkably, four weeks later the group that had received the placebos had significant reductions in their IBS symptoms compared with the group that got no treatment; even though, they knew that it was a placebo.

It's exactly those types of findings that led Thomas Jefferson over 200 years ago, to note that one of the most successful physicians I have ever known, has assured me that he used more of bread pills, drops of coloured water and powders of hickory ashes than of all other medicines put together. It certainly was a pious fraud.

Thank you.

Moderator: Thank you for listening to the podcast series of *Raising the Bar Sydney*. If you want to hear more Raising the Bar talks, head to raisingthebarsydney.com.au.

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