

## **Sawbones 240: The Placebo Effect**

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**Intro (Clint McElroy):** *Sawbones* is a show about medical history, and nothing the hosts say should be taken as medical advice or opinion. It's for fun. Can't you just have fun for an hour, and not try to diagnose your mystery boil? We think you've earned it. Just sit back, relax, and enjoy a moment of distraction from that weird growth. You're worth it.

[theme music, "Medicines" by The Taxpayers, plays]

**Justin:** Hello, everybody, and welcome to *Sawbones*, a marital tour of misguided medicine. I am your cohost, Justin McElroy.

**Sydnee:** And I'm Sydnee McElroy.

**Justin:** We used to be on this great... this great string, the great combo of, I believe, 2017, when we chained a bunch of episodes together. Do you remember this?

**Sydnee:** Oh, yeah!

**Justin:** Our ideas for episodes kept chaining to other ideas, from each one would spring anew.

**Sydnee:** And we broke that chain.

**Justin:** We broke the chain, but in a sense, we are—we're taking a run, unintentionally, at an unplanned new chain.

**Sydnee:** Uh-huh.

**Justin:** I guess you can't really plan the chain; otherwise, it's like...

**Sydnee:** And it has to be organic.

**Justin:** It's just, you plan ahead.

**Sydnee:** Do you know, though, that – and we'll get to this in this episode – I already know next week's topic, because I found it accidentally while researching this episode.

**Justin:** Combo!

**Sydnee:** So the chain continues.

**Justin:** The chain continues. But this week, we're gonna talk about something that came up a lot during our discussion of uh, CBD oil. If you didn't listen to that, go check that out. And um, it is something that I think everybody is sort of familiar with, but it comes up so frequently in, I mean, nearly every episode of *Sawbones*. I mean, in some sense it's about it, so it's cool that we're finally gonna talk about the placebo effect!

**Sydnee:** That's right, Justin. The placebo effect, or the placebo response, depends on if you're talking about—

**Justin:** Effect!

**Sydnee:** Well, it depends on if you're talking about—

**Justin:** You say to-may-to, I say to-mah-to!

**Sydnee:** No.

**Justin:** You say response, I say effect!

**Sydnee:** Well, no.

**Justin:** Let's call the whole thing off.

**Sydnee:** It depends on if you're talking about groups or individuals.

**Justin:** You say po-tay-to, I say po-tah-to!

**Sydnee:** It's the same—okay. Are you good there?

**Justin:** They're the same thing.

**Sydnee:** Are you good with that? Are you good there?

**Justin:** Yeah.

**Sydnee:** Okay. A lot of people have asked us to talk about this, and I mean, it makes sense, because this topic does relate to almost every single episode of *Sawbones*.

**Justin:** Yeah, in a sense.

**Sydnee:** So for all the emails we've gotten suggesting this...

**Justin:** Maybe not vaccines.

**Sydnee:** Yeah. Not that. But... although, placebo controlled trials have been used to... show whether or not vaccines have worked through history.

But anyway, thank you to Thaddeus and Adrian and Jennifer and Elizabeth and John and Ethan and Drew and Janie and Marie and Noah and Isaac and Emily and Guybrush and Aria and Riz.

**Justin:** Guybrush?

**Sydnee:** That was the name!

**Justin:** Fantastic.

**Sydnee:** Lots of people have recommended this, and they are right, because uh, placebos, the use of placebos, especially in double-blind trials and drug trials where you don't know if what you're getting is real or not, have become necessary to evidence-based medicine.

**Justin:** How so?

**Sydnee:** Because you... because if you're gonna test two people to see, like, "Does this medicine work?" and you give one person the medicine, and then you don't give the other person anything, that's a problem, right?

**Justin:** Right.

**Sydnee:** 'Cause you can't control for the concept of placebo. 'Cause one person got a pill, the other person didn't; the person who got the pill might be responding just 'cause they got a pill, right?

**Justin:** Right.

**Sydnee:** So you have to give the other person a pill, too.

**Justin:** What kinda pill?

**Sydnee:** A sugar pill. Anyway, so placebo has become necessary to do science.

**Justin:** I wanna say, I was um, when I was a kid and I first found out placebo—I heard they were called—they were sugar pills, and I uh, I always really wanted some placebos. They sounded like... kind of like they were candy, and I wanted to try some, 'cause I heard they were sugar pills.

Anyway.

**Sydnee:** Well...

**Justin:** Just my sidebar. Never ate any placebos.

**Sydnee:** As someone who took birth control for a while, and if you—many birth control pills do have sugar pills for the week that you're supposed to be on your period.

**Justin:** Yeah.

**Sydnee:** Uh, they don't taste like anything.

**Justin:** Am I allowed to—are you gonna talk about sugar pills a lot more?

**Sydnee:** I mean, I'm—I'll mention them.

**Justin:** Okay. I wanna continue my sidebar here.

**Sydnee:** [laughs]

**Justin:** If you're gonna give me something, and you're gonna sneak me in something... why can't it be... why does it have to be sugar? If I'm gonna consume sugar, I wanna know how I'm doing it. It's, like, a big deal if I'm gonna eat sugar. I wanna know that I'm eating the sugar. Why can't it be, like, I don't know, math pill, or something, right?

**Sydnee:** It's just a not-dangerous substance in tiny amounts that—I mean, I don't know.

**Justin:** Overlong *New Yorker* article pills. Like, at least—if I'm gonna ingest something, like, let it be something that's like, supposed to help me in some way.

**Sydnee:** It used to be bread pills. We'll get into that.

**Justin:** Oh, excellent.

**Sydnee:** Uh, the origin of the word "placebo" comes from the Latin for "I shall please."

**Justin:** Okay.

**Sydnee:** But you can find that in scripture. I believe it is Psalm 1:16 where they say "Placebo Domino, I shall please the Lord."

**Justin:** Alright!

**Sydnee:** But although—although I read one author claiming that this is a mistranslation.

**Justin:** Okay.

**Sydnee:** That when it was translated from Greek into Latin, that it should've been "ambulabo coram Dominon."

**Justin:** Ambulabo?

**Sydnee:** "I shall *walk* before the Lord." So the word placebo is, like, a... mistake.

I don't know. Anyway, it doesn't matter. Placebo means "I shall please," and that makes sense, because it's a medicine that pleases you.

**Justin:** Because it makes you think you're taking medicine.

**Sydnee:** Whether or not it works. [laughs] It pleases you; that's the concept.

The word placebo, in a sense, was used first in the 14th century in reference to hired mourners at funerals.

**Justin:** ... Okay...

**Sydnee:** So you would get people to come and mourn to make someone, I guess, look more...

**Justin:** Beloved?

**Sydnee:** Yeah? [laughs] And uh, along the—and they would begin—it would begin like, openly sobbing and wailing...

**Justin:** [laughs]

**Sydnee:** ... around the ninth first of Psalm 1:14, "Placebo Domino, I shall please the Lord." And so they were called uh, placebos. And a singer of placebo was someone who would claim that they knew the person who had passed away, even though they didn't really, to try to get, like, in on the big dinner...

**Justin:** [laughs]

**Sydnee:** ... maybe? Like, at the wake or whatever?

**Justin:** Yeah.

**Sydnee:** Or maybe even to try to get money.

**Justin:** [laughs]

**Sydnee:** So it was—so it was tied to deception.

**Justin:** Okay.

**Sydnee:** The concept of placebo even then was tied to deception, although it was not a deception of medicine, it was, "Hey, I'm your long-lost nephew."

**Justin:** Right.

**Sydnee:** "Can I have some dough?"

**Justin:** [laughs]

**Sydnee:** "Please."

The Catholic church famously used placebo, and this is probably the closest we see in the early uses of—I mean, 'cause this will echo the way that it is used in medicinal trials later, people in the 16th century who were claiming possession, the Catholic church wanted to try to figure out if they were really possessed or not, because there were people who were going around and making a lot of money off of fake exorcisms.

They basically, they were people who had no affiliation necessarily with the Catholic church, and would go when someone was claiming possession, and be like, "Oh, yep, yep, yep, definitely possessed!" and then do these fake exorcisms for a lot of money, and cure, heal, save...

**Justin:** Right.

**Sydnee:** ... whatever you wanna say, the person, and then go about their business. And so the Catholic church started to say, "Listen, one, that exorcism was fake, and two, I don't think that person was ever actually possessed.

**Justin:** Burn.

**Sydnee:** And so one of the ways they sought to prove that was by giving them fake holy relics. The concept being that in a case of – and again, you have to actually believe in possession for this whole situation that I am describing to you to work – you believe that possession can happen, and then, in that case, a person who is possessed by a demon or the devil would be harmed by a holy relic. If it was truly a holy... whatever, a rosary or a cross or whatever...

**Justin:** Right.

**Sydnee:** ... if it was truly that, then touching it would burn their skin or cause them pain, or whatever. Cause them great distress. And so the Catholic church would send people out with these fake relics to hand them to people who were possessed, and then see if they reacted.

**Justin:** Huh. [reluctantly] Yeah. Yeah, okay.

**Sydnee:** And if they did, then you could say, "Listen, you're not really possessed; this is something else."

**Justin:** [reluctantly] Yeah.

**Sydnee:** "Because that was fake."

**Justin:** Okay. There's kind of a few levels there... [laughs] going at once.

**Sydnee:** That's—I think that happens in *The Exorcist*, if I don't—if I'm remembering correctly.



**Justin:** I don't remember.

**Sydnee:** I think he uses fake holy water. And I think she says it burned.

**Justin:** So wait, it—is it a twist in *The Exorcist* that she was just faking it the whole time?

**Sydnee:** Well, I think, if you've seen *The Exorcist*, that's...

**Justin:** No, right?

**Sydnee:** Like, her head goes all the way around.

**Justin:** Everybody can do that, but...

**Sydnee:** No, but I mean, I think it was based on stories of possession that were questionable and unclear.

**Justin:** So they would throw, like, a placebo chocolate cross at them, and then, "Psych!"

**Sydnee:** I don't think it was a chocolate cross, necessarily.

**Justin:** "Psych, look at the wrapper! It's chocolate, the whole time, idiot."

**Sydnee:** [laughs]

**Justin:** "It's not magic at all." Do they say magic? [laughs]

**Sydnee:** No. [laughs]

**Justin:** Holy. Spiritually magical. [laughs]

**Sydnee:** So uh, obviously, we are not experts on the issue—on anything related to religion.

Uh, the idea grew from there, began to circulate through the medical community as well, the idea of using something that was um, not necessarily

active in a way that we—like, that we attended to, using a substance that, as far as we knew, was either inert or whatever it did, it had nothing to do with the problem, but nevertheless had some sort of positive effects on a patient.

The question, even from the early uses of it, was, "Is that okay?" And we're gonna kind of go through the turn of opinion on that. Because when it was first used, a lot of people just found it very practical. "I will give you this pill, and you feel better, so..."

**Justin:** Great.

**Sydnee:** "... case closed." But now, with our common—with our current concept of medical ethics, that doesn't—it's not that simple.

So placebo used to be just a standard part of medical practice. In part, this was because we didn't really know what worked or didn't work anyway, right?

**Justin:** Right.

**Sydnee:** So a lot of times, a doctor might be employing placebo without even... knowing... that the placebo effect was all that was working.

**Justin:** Okay.

**Sydnee:** You were giving a patient something that you honestly believed might help them, but it had absolutely no effect whatsoever.

**Justin:** Right.

**Sydnee:** So a true believer, if they didn't necessarily know they were using a placebo, and you saw that a lot more before evidence-based medicine, because nobody knew what they were doing.

**Justin:** What if a placebo—if you're controlling for placebos, wouldn't it be—wouldn't the person giving the treatment have to be unaware as well?

**Sydnee:** Yeah. Yeah, if you're talking about a double-blind study. But I'm talking about a time when medicine inherently was placebo, because it was...

**Justin:** Right, right, right. I'm with you.

**Sydnee:** You know, it was like a tonic, with like, some opium in it or a bunch of sugar...

**Justin:** Yeah, I'm with you.

**Sydnee:** ... or some weeds, you know?

**Justin:** Yeah.

**Sydnee:** Or weed.

**Justin:** Or weed!

**Sydnee:** Um, there—and many people had, like, religious or magical beliefs as to why disease happens, so if that's the kind of the perspective you're coming from, it's easy to see how your faith in a treatment, your perception of the treatment, could influence your response to it. I mean, if you already have some sort of magical belief, you know, as to why the disease happened in the first place. Does that make sense?

**Justin:** Yeah.

**Sydnee:** And physicians, whether knowingly or unknowingly, throughout history have been taking advantage of that. You know, whether they intended to be deceiving the patient, or just—they didn't—they thought the medicine worked too, or they had no idea and were doing their best.

We've talked a lot about Paré, who was groundbreaking in many ways, Ambroise Paré, in the surgical field. But he also said in the 1500s that a physician's duty was to cure occasionally, relieve often, console always. And placebo is just a part of that. If you can't do anything else, you console your

patient, giving them something that maybe doesn't work, but makes them feel better. Is that not providing consolation? Is that not—

**Justin:** I go back and forth on this, honestly. I don't know.

**Sydnee:** [laughs]

**Justin:** I don't know. You and I have talked about this enough times that I don't think I know. I don't think I have a strong feeling anymore. I used to; you've worn me down.

**Sydnee:** There are two realms that we're gonna continue to talk about placebo in, in this way that I'm kind of referencing already that physicians were giving patients medicine that either they did or didn't know—either they didn't know if they worked at all, or they absolutely knew they didn't work at all, and letting them just have whatever effect from it, you know, because that was their job, to help the patient out even if they couldn't, really.

**Justin:** Mm-hm.

**Sydnee:** And then there's also the use of placebo in a study to, you know, to have a control group, right? Placebo's used in a control group. The ones who don't get the medication, or don't get the treatment. But you don't want them to know they didn't, 'cause you're trying to control for placebo effect. And where did that come from? That's the whole other use of placebo.

In 1752, James Lind, who I think we talked about when we did the scurvy episode, I'm sure we did...

**Justin:** Yeah.

**Sydnee:** ... um, he published the—*A Treatise of Scurvy* after performing what was probably one of the first placebo-controlled experiments. Although he didn't call it that, that's probably what it was.

So he—and I think, again, we may have talked about this in our scurvy episode, but he picked 12 sailors who already had scurvy, he divided them into groups of two, and um, each group had one of six different treatments for 15 days. One group got cider, another got sulfuric acid, another got vinegar, another got seawater, another got lemons and oranges, and the last one got garlic, mustard, and horseradish.

**Justin:** [sarcastically] Yum! Sounds good. Potent.

**Sydnee:** Kind of an odd one at the end there. Just throw everything else that has any effect.

**Justin:** [laughs]

**Sydnee:** If you were in the fifth group and you got lemons and oranges, you got better. Cider also seemed to make people a little bit better. Everybody else was not doing well, and they were in placebo groups, if you can call them that.

**Justin:** Huh.

**Sydnee:** But that demonstrated, kind of, the, "Even if you think one thing works, you give everybody something" concept.

**Justin:** Okay. Right. Right.

**Sydnee:** You don't just, like, "You don't get any medicine; let's see what happens to you." Give everybody something.

Jefferson, Thomas Jefferson, spoke of the rampant use of placebo in 1807. He talked about doctors as pious frauds.

**Justin:** [laughs] That's nice.

**Sydnee:** And he talked about a doctor who said that he prescribed—more than anything else he prescribed, he gave out bread pills that were dyed various colors and powders made of hickory ash.

**Justin:** What on Earth could a bread pill be?

**Sydnee:** A pill made of bread... ?

**Justin:** Like, do you just like, squeeze real tight?

**Sydnee:** That's kind of what I was envisioning, like—

**Justin:** Like, you take a scroll roll, and you like, squish the insides into, like, a little—I'd rather have that one. I don't care what medicine you got; give me a scroll roll any day.

**Sydnee:** Even after it's been squished?

**Justin:** Uh, especially after it's been squished. It's returned to its dough-like state, and it's ready. Oh, it's perfect.

**Sydnee:** Charlie likes to do—Charlie always saves me her toast crust.

**Justin:** Uh-huh.

**Sydnee:** But first, she likes to kind of, if she gets to them to give to me, she balls them up. [laughs]

**Justin:** [laughs]

**Sydnee:** So not only is it just the crust of the toast, it's balled up, squished crust. I'll take it.

**Justin:** But you said things were—things changed.

**Sydnee:** Yeah. So things are gonna change. This idea that giving somebody a bread pill could still be considered pious, even in its fraudulence, is about to change.

**Justin:** Okay. Well, what happened?

**Sydnee:** Well, I'm gonna tell you about that, Justin, but let's go to the Billing Department!

**Justin:** You're kidding me. Let's go!

[theme music, "Medicines" by The Taxpayers, plays]

**Justin:** Folks, our first sponsor this week is Casper. It's a sleep brand that continues to revolutionize its line of products to create an exceptionally comfortable sleep experience one night at a time. They offer affordable prices 'cause Casper cuts out the middle man and sells directly to the consumer. We have a Casper mattress in our own home, and you know, folks, we wouldn't let our guests sleep on just anything.

**Sydnee:** No, only the best.

**Justin:** Only the finest.

**Sydnee:** Only the best for our McElroy guests.

**Justin:** The McElroy guests?

**Sydnee:** That's our motto. [laughs]

**Justin:** That—we say, "Only the best for our McElroy guests." We have it carved in wood...

**Sydnee:** Over our door.

**Justin:** ... right above our door, on every door and window in our home. 'Cause we wanna be [laughs] sure that everybody knows.

**Sydnee:** We all wear t-shirts that say that every day.

**Justin:** We have it tattooed on our necks. Casper brand [laughs] mattresses combine multiple supportive memory foams for a quality sleep surface with the right amount of both sink and bounce. Be sure of... [laughs] your purchase...

**Sydnee:** Please don't say it like that.

**Justin:** ... with Casper. Just—I said it 'reglear', just the way I always say [stressed] bounce. 100-night risk-free sleep-on-it trial. Get 50 dollars towards selected mattresses by visiting [Casper.com/Sawbones](https://Casper.com/Sawbones) and using promo code "Sawbones" at checkout. Terms and conditions apply. Go to [Casper.com/Sawbones](https://Casper.com/Sawbones), and use promo code "Sawbones" at checkout.

**Sydnee:** Hey, Justin.

**Justin:** Yeah, Syd?

**Sydnee:** Do you like meat?

**Justin:** Who's got the meat?

**Sydnee:** ... Us?

**Justin:** We do! It's in our freezer, and it's already ready to take out, defrost, and have some truly delicious meat. We're sponsored this week by ButcherBox. That's not related to my earlier point, though.

**Sydnee:** [laughs]

**Justin:** It absolutely is, because ButcherBox is delivering healthy 100-percent grass-fed, grass-finished beef, free-range organic chicken, and heritage-breed pork directly to your door. ButcherBox meats come from humanely-raised open-pasture animals that are never fed antibiotics, hormones, or fatty fillers. The meat is frozen at peak freshness in individual, vacuum-packed biodegradable packaging.

**Sydnee:** And it's delicious.

**Justin:** And it's delicious, and you'll be shocked that this meat was ever frozen, because... I grew up with a sort of an anti-frozen meat bias. You watch a lot of fast food commercials where they're like, "And the other guys



freeze them! Can you believe these buttheads?" But uh, this meat is frozen—it comes frozen, and it is delicious, so uh...

You can get free bacon, and—I wish every place just offered that.

**Sydnee:** [laughs]

**Justin:** Free bacon and 20 dollars off your first box. Go to [ButcherBox.com/Sawbones](https://ButcherBox.com/Sawbones), and enter code "Sawbones" at checkout. That's [ButcherBox.com/Sawbones](https://ButcherBox.com/Sawbones), and promo code "Sawbones" at checkout.

[pause]

**Sydnee:** So.

**Justin:** Things change.

**Sydnee:** As I mentioned—yeah, things are about to change. So placebo, at this point in history, is a term that is being used almost for any, like, common medication.

**Justin:** Really?

**Sydnee:** Yeah. Like, and it was—and it referenced, in part, what I already mentioned: the fact that we really didn't know what worked and what didn't. So there was a lot of stuff that people used a lot, a lot of tonics and elixirs and soothing syrups and things like that.

The medical—on some level, I think doctors knew it didn't really do anything.

**Justin:** Right.

**Sydnee:** And so they would call it a placebo, but you didn't know it to be fake, but you kinda did.

**Justin:** You had it in your gut.

**Sydnee:** Right.

**Justin:** Your gut feeling.

**Sydnee:** And that was—that was all the way up until double-blind studies to prove this stuff became a thing, and then we start to see the word placebo being used in that context. And this shift that starts to happen, I think it's important to understand what is happening in medicine in this moment that changes this.

So initially, doctors were very patient-driven. They focused—they catered to each patient's needs. You would go see somebody, take a long time, probably at their home, right?

**Justin:** Yeah.

**Sydnee:** Like, do a house call. Take a long time to take their history, do an exam, get to know them. You would forge a bond with them, like a real trust.

**Justin:** Okay.

**Sydnee:** You're *their* doctor. They are *your* patient. This is a sacred bond that you are forming. And so you are committed to making them feel better, to making them better. Whatever that looks like, you're committed to doing that through any means necessary. And that relationship, and the trust, was almost as comforting as just about anything that doctors had to offer at this point in time.

**Justin:** Right.

**Sydnee:** Because a lot of their therapeutic options were flawed.

**Justin:** Yeah. Less than ideal.

**Sydnee:** Right, like bloodletting or mercury.

**Justin:** Or [???].

**Sydnee:** Yes.

**Justin:** We in fact—we have—

**Sydnee:** There's a whole podcast [laughs].

**Justin:** Two episodes.

**Sydnee:** Now, over time, this relationship, while, I think you could say beautiful in many ways, and the idea of a healer and they're heal-y...

**Justin:** They're heal—heal-ish.

**Sydnee:** Yeah.

**Justin:** They're healies. If the healies wore Heelies... it's the story of a doctor, Patch Adams Jr., when they wear Heelies everywhere in the hospital and they inspire the kids to get better.

**Sydnee:** That's a great movie. Over time, this inevitably had to change. As doctors began to cater to more and more patients, and as medicine became institutionalized. So...

**Justin:** A lot of people—a lot more people going to doctors when they started being able to fix things. [laughs]

**Sydnee:** That's fair. And also, the hospital began to become the dominant institution, you know? That that was where medicine happened, and your—and your doctors were trained there, and so they began to lean less on like, a patient-focused—patient-first kind of theory of medicine, and more of like a laboratory-focused theory of medicine. We learned what works in a lab, and then we apply it to patients, as opposed to learning what works based on your individual patient and their response to a medicine.

And this is good, in a sense. 'Cause this is evidence-based medicine. You don't treat Patient A this way and Patient B that way. You treat *hypertension* this way, and you treat diabetes that way.

**Justin:** Right.

**Sydnee:** Does that make sense?

**Justin:** Absolutely.

**Sydnee:** And that needed to happen, because there were a lot of people who were doing a lot of dangerous stuff, and it needed to happen so that everybody knew about the newest advances in medicine and was trained to use them so that all patients, no matter where they lived or what doctors they were seeing, got appropriate treatment.

**Justin:** Right.

**Sydnee:** But it also kind of eroded that bond. You no longer had that deep connection, necessarily, to your physician. I'm not saying you can't, but it wasn't a given. You didn't have that faith and trust in them, and so the idea of just any old therapy...

**Justin:** 'Cause they were just reading out of a book, like any creep could.

**Sydnee:** Well, they weren't individualizing that treatment to you as much, and so the idea, that faith that it's going to work as well, starts to go away too, you know?

**Justin:** That makes perfect sense.

**Sydnee:** A medicine worked now if science said it worked, not because the patient said they felt better after they took it. And so the more distance between the patient and the doctor, the harder it is for just trust and comfort to heal the patient.

Richard Cabot, who was a physician who did some groundbreaking work in the field of hematology...

**Justin:** Study of blood.

**Sydnee:** Yes. Very good, very good. ... uh, also helped to shift things. He was trained to use placebo as part of his practice, but by the time he was on his own, writing influential papers, he said, "Listen, deception is wrong. It doesn't matter the outcome, it doesn't matter if it works or not. Lying to your patient is always wrong. Stop. Even though I was trained to use placebo, I would advise against it."

And this sounds like, "Well, who cares?" This is a big deal. To say this out loud and write it in a paper and send it out to other doctors...

**Justin:** Really?

**Sydnee:** ... was a big deal at the time. Because everybody kind of accepted that you did that, and you also don't say it, because... you don't want the patients...

**Justin:** Hey, you're messing up the placebo effect!

**Sydnee:** ... to know. Um, there was a big—there was also a big, groundbreaking investigation on something called Perkins's Tractors.

**Justin:** I have not heard of this.

**Sydnee:** These were the tractors—these metal prongs that were supposed to cure disease. And then there was this big trial with a—or this big test with a placebo done at the time that proved that they didn't work. I don't wanna say too much more about them, other than that this helped to shift the balance on placebo, because this is our episode for next week.

**Justin:** Oh, alright!

**Sydnee:** Here's your sneak peek, 'cause this is a great story. Next week, you'll learn more about Perkins's Tractors.

And then we first see the term, not just placebo, but "placebo effect" used in 1920 in a paper in *The Lancet* by TC Graves, talking about some psychiatric medications that didn't seem to be biologically active, but nevertheless he

was seeing an effect in his patients, and he began to talk about the concept of the placebo effect.

**Justin:** Okay.

**Sydnee:** And not just a placebo, but...

**Justin:** A whole effect.

**Sydnee:** ... an actual effect that might occur from taking a medication, even if it didn't, you know, essentially do anything.

So now, even as doctors are questioning the use of intentional placebo, evidence-based medicine was creating this growing demand for researchers to actually prove what did work, right?

Okay, so now you're saying we can't just use fake medicine. Well, how the heck do we know what works? Well, we gotta do trials. And so there were a lot of researchers arguing, "We need to do things where we give some patients medicine and we don't give other patients medicine, and we see what happens."

**Justin:** Right.

**Sydnee:** And doctors were very reluctant to do that, because that sounded unethical.

**Justin:** Yes.

**Sydnee:** So you have a medicine that you think might work. Let's give it to everybody.

**Justin:** Yes, I get it.

**Sydnee:** That makes sense, right? You think it might work. What if you— what if somebody who doesn't get it dies, and it did work? You harmed them.

**Justin:** But the problem is, we don't know what works.

**Sydnee:** Yeah, but what if it does?

**Justin:** But what if it doesn't?

**Sydnee:** But what if it does?

**Justin:** What if it doesn't?

**Sydnee:** You see the—

**Justin:** What if you give it to these people, and it kills 'em?

**Sydnee:** You see the issue here. So there was a lot of debate as to whether or not this was okay, and the other argument that they were making was, do you really think this placebo effect is such a big—everybody's talking about this placebo effect; is that a real thing? Because if it's not real, it shouldn't matter!

You should be able to—like, I should be able to say, "Hey, Justin, I'm gonna give you a pill, I'm not gonna give you a pill to your buddy, and we'll see if it works for the same disease you have. And we'll just trust whether or not you get better, right?" If there's no placebo effect, you don't need a control. You just—that's it.

**Justin:** Right.

**Sydnee:** Right? It works, or it doesn't. You get the medicine, or you don't even have to do a trial. You just give the medicine to everybody, and see if they get better. So the placebo effect had to be real for doctors to be okay with this.

**Justin:** Yeah. Understandable.

**Sydnee:** Okay. In comes Henry Beecher. He was a Harvard anesthesiologist and an ethicist, and he, in 1955, gathered data from 15 different studies of 1,082 patients with all these different kinds of pain, and

from analyzing all these studies, he stated that a placebo analgesic, a fake pain pill, is effective, on average, in 35.2 percent of cases. And depending on the patient and the pain, that could range anywhere from as little as 4 percent of the patients to 86 percent of some patients are going to respond to a placebo.

**Justin:** Okay. I—I'm sure Hank did some great work in his time. You can't say that a st—you can't say that some—[through laughter] can't breathe. Between 4 percent and 86 percent.

**Sydnee:** Well...

**Justin:** [through laughter] You might as well say, "I have absolutely no idea!"

**Sydnee:** No, they were very—they were very—varying causes of pain in patients and...

**Justin:** [through laughter] Sometimes, it was 4 percent. Other times it was 86!

**Sydnee:** 4 percent was this pain, 86 percent with that pain.

**Justin:** [through laughter] I learned—that fact you just told me made me dumber.

**Sydnee:** No—okay.

**Justin:** I know less after hearing it.

**Sydnee:** You—there were some things—um, pain that was the least intense did not show as much of a response to placebo.

**Justin:** Okay.

**Sydnee:** Whereas extremely intense pain, like angina, like heart pain, heart muscle pain, that happens when your heart's not getting enough oxygen, that was very sensitive to placebo.



**Justin:** Okay.

**Sydnee:** Um, if—if you thought a placebo would work, you were more likely for it to work.

**Justin:** Okay.

**Sydnee:** If you didn't think it was gonna work, it's less likely for it to work. And there were—anyway, he wrote all this out, and there were a lot of different reasons for it, but this was very compelling. After he published this, a lot of doctors said, "Well, heck, if the placebo effect is really as big as Dr. Beecher is saying that it is, we gotta do these studies."

**Justin:** Yeah, we have to.

**Sydnee:** We have to do double-blind studies. So this was revolutionary. This study, which demonstrated the breadth and depth of the placebo effect, is why so many people adopted the double-blind studies, and why we have them probably as rampantly as we do today, is that they're the gold standard, right?

He also published a study in 1961, I thought this was interesting, that suggested that surgeons that he called "enthusiasts" relieve their patients' chest pain and heart problems more than surgeons who were "skeptics."

**Justin:** Surgeons that were, like, pumped to be there?

**Sydnee:** Yeah. Surgeons who were just like, really like, "This is gonna work! This is gonna work! Don't worry, we got you!" Their patients did better. And uh, this uh, there was also the same year, Walter Kennedy coined the term "nocebo." I'd just like to mention this. This is like a bad placebo.

**Justin:** That's weird. You mentioned that to me while you were researching a few days ago. This morning, I watched an episode of Legion that opened with some Jon Hamm narration about those.

**Sydnee:** Really?

**Justin:** So that's strange.

**Sydnee:** That is strange.

**Justin:** They actually—I thought this was kind of interesting. They actually drew a connection between the idea of nocebos and stuff like the dancing [microphone cuts out]. And other mass delusion.

**Sydnee:** Hmm. That's interesting.

**Justin:** You can kind of—

**Sydnee:** Yeah.

**Justin:** It's something that you think caused you harm and your mind manifesting that harm...

**Sydnee:** Even though that doesn't—

**Justin:** ... despite that—even though it doesn't exist. Technically, I think it's kind of the flip side of...

**Sydnee:** In essence, it is what the Catholic church was doing with the fake holy relics. Because people were reacting as if they caused them pain, even when they didn't. So a nocebo is something that shouldn't cause you pain, but you react as if it does.

**Justin:** Mm-hm.

**Sydnee:** For a while, the word Obecalp was used to sell placebo medicine.

**Justin:** Backwards? Placebo backwards?

**Sydnee:** That's placebo backwards. But you'll find a lot of medicines that were called that. Even into the '90s, it was usually just a sugar pill.

**Justin:** It could be a little bit [microphone cuts out, indecipherable mumbling].

**Sydnee:** In my own practice, and this is not something that I certainly have done or that I know people doing now, but I have heard, doctors like to tell tale of the old days, things that used to happen in the old days.

**Justin:** Yeah. Things they all used to be able to get away with?

**Sydnee:** Right. So I've heard tale of NaCl being used. You know what NaCl is?

**Justin:** Uh, NaCl is... a tables—is it a—

**Sydnee:** It's sodium chloride. It's saline solution, like that you—like a fluid, IV fluids. Giving somebody a shot of NaCl.

**Justin:** Somebody give me some NaCl?

**Sydnee:** Yeah. Um, or like, just giving somebody a saline flush to flush their IV, which you need to do, so it's not like, a harmful thing to do, but like, saying that it's a medicine, and the patient saying their pain was better, even though you didn't give them anything.

Or like, switching something to IV. Like somebody keeps asking for an IV pain medicine, so you give them IV Tylenol, and they say that they're all good, "I got that stuff I needed." I've heard these things. We are not allowed to do this. This is not something that we do now. We get in big trouble if we do it.

**Justin:** House does it.

**Sydnee:** Yeah. We don't do that. Um, I'm not saying there is no doctor anywhere who ever does it; I don't know, I can't vouch for everybody. All I know is, we don't do it, we're certainly not trained to do that.

There's some general rules with placebo, supposedly. Shots are more effective than pills for pain, if you're gonna use placebo.

**Justin:** Yeah. Seems very...

**Sydnee:** People tend to think a shot works better.

**Justin:** That's very legit.

**Sydnee:** But pills are more effective for sedation. For like, sleeping pills and that kind of thing. Blue pills work better for sleeping; red pills work better for pain.

**Justin:** I know it.

**Sydnee:** If a medicine is expensive, brand-name, hard to get, it tends to have more effect. If your doctor's really excited about it, it tends to have more of an effect.

**Justin:** Of course. Yeah.

**Sydnee:** Now, this all sounds like it makes sense, right? At this point, we've accepted all this. So now we know this is how placebo happened, and this is why we use double-blind studies, and the placebo effect is real, blah-blah-blah. Here's the problem with all of this. Beecher lied.

**Justin:** What do you mean?

**Sydnee:** That big study that I cited was um, reevaluated in, like, '97 by some German scientist and found that most of his results were inaccurate, and some of his conclusions were just straight-up...

**Justin:** Oh, no!

**Sydnee:** ... like, they conflicted with the data he presented.

**Justin:** Oh, no!

**Sydnee:** It's unclear if he misinterpreted—I mean, he was a good scientist. He was a good doctor, a good scientist, so it's unlikely that he just didn't get

it. So it's unclear if he misinterpreted things, or if he was trying to maybe exaggerate findings to push science in the direction of placebo controlled double-blind studies. Like, he knew something like this was necessary to sway doctors, and so he published it, even though maybe it wasn't... quite that real.

**Justin:** Aww, boo!

**Sydnee:** A 2001 systematic review of a bunch of different clinical trials showed that essentially, there is no placebo effect, except occasionally with some subjective symptoms, like pain. Subjectively, someone might report that it's better. But it's only to the extent that, like, if you're in pain and I give you a placebo, there's a chance that you might say your pain is less.

**Justin:** Mm-hm.

**Sydnee:** But it doesn't eliminate pain, it doesn't cure things. The placebo effect, I'm not saying it doesn't exist, but it is not *nearly* what science thought it was for many decades.

**Justin:** Wow.

**Sydnee:** Yeah. A lot of what we think—yes, it can happen, but it is not the problem that we used to think it was. There are studies that have looked into brain activity and receptors to try to figure out why there might be some placebo effect and some causes, and they've seen some things like endorphin release and dopamine release that could explain why you feel better, even if nothing chemically should've made you feel better.

But it is not nearly the—the influencer that we thought it was. And as I said, it is now considered unethical to give a patient a placebo knowingly, and lie to them, 'cause it violates the uh...

**Justin:** Outside of, like, a research scenario.

**Sydnee:** Yeah. Outside of a research setting. Outside of a research setting.

When you enter a research setting, you sign papers that say, "I know I might be getting a placebo."

**Justin:** "Yeah. It's fine. Just let me know, so I can chew it up."

**Sydnee:** Well, no. [laughs]

**Justin:** Get that good good sugar.

**Sydnee:** But no, like, if I were to walk into a patient's room, and try to give him a medicine that I said was real and wasn't, that would be—I mean, that's unethical. That violates the principle of autonomy, which means you have the right to information about your body and to everything I'm gonna do to it and to consent to it or not. And you wouldn't consent if I told you, "I'm gonna give you something fake. Is that cool with you?"

**Justin:** [laughs]

**Sydnee:** Probably would not be okay with that. So obviously, we don't do that. But some have offered this, and this is my final parting thought on this: if placebo effect is real sometimes, and a placebo, let's say it's a sugar pill, something harmless, if it could help a patient, is not giving it harming?

**Justin:** I don't know.

**Sydnee:** If we could take advantage of placebo effect, especially in situations of like...

**Justin:** But you're saying if it doesn't...

**Sydnee:** ... chronic pain, where maybe there isn't a great solution right now, if there's something that would help them that wouldn't harm them, but wasn't really supposed to work... ?

**Justin:** No.

**Sydnee:** I'm not proposing—I'm not saying that I believe this.

**Justin:** No. You don't—

**Sydnee:** I'm just telling you that these are the ethical arguments.

**Justin:** Do you wanna know why? Do you want me to actually tell you why, I think? My point that I'm trying to make...

**Sydnee:** Sure. And I agree with you. Let me say, I—straight-up, I agree with you. I think the patient should always know what we are doing to their bodies. I don't think we should ever be trying to deceive someone about their healthcare.

**Justin:** I have a different reason.

**Sydnee:** Okay.

**Justin:** I think that we are, all of us, not just ourselves, but we are members of this great human race of ours, and I think that if I get something that I think worked for me, and I start telling people that this thing works, then I am actually, like, not advancing human knowledge. And like, the cause of the species. Look at the stuff we do, and it is—like the stuff that we talk about, and it is millennia of people saying, like, "Well, this thing works for me. It must work." And, like, that is exactly what you're talking about. And I don't wanna be party to that.

And I think that even if I—whether I do or don't want to be party to it, I think you owe me the option of just deciding whether or not I want to be party to it. But the irony, of course, there is in a lot of situations, if you give me that option, you'll have actually removed it for the placebo effect. 'Cause if you say, like, "Want this?" then like... no. Like, unless you've got one of those *Men in Black* lasers that erase my memory, then that ship has sailed.

But that is my thing. I don't wanna be—I don't wanna believe in the fake here, even if it helps.

**Sydnee:** You're not a fan of goop, then?

**Justin:** Not a fan of goop. I heard they're hiring their own, you know, truth-seeker.

**Sydnee:** Their fact-checker.

**Justin:** Yeah. Great.

**Sydnee:** Yeah. Good luck.

**Justin:** It might be kinda cool, they got their own... Vitamins, but whatever.

**Sydnee:** Good luck, and godspeed to whoever winds up in that position.

Yeah, so—doctors don't do this. It's not good anymore, except for in studies. That's it.

**Justin:** You got any sugar pills, though, you can toss em to us.

**Sydnee:** Honey, if you just want sugar, like, we have sugar.

**Justin:** Not in pills!

**Sydnee:** But we have a bag. [laughs]

**Justin:** Thank you for listening to our podcast. We hope you've enjoyed yourself. Thank you to our sponsors, and thank you to you for listening. If you get a second, and you could tweet about the show, we are @Sawbones on Twitter. I'm @JustinMcElroy, M-C-E-L-R-O-Y, and she is @SydneeMcElroy, S-Y-D-N-E-E. And uh, follow us there...

**Sydnee:** We have an email, too.

**Justin:** We have an email. Sawbones@MaximumFun.org.

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**Sydnee:** I'm gonna—

**Justin:** Or with *Bubble*, a fiction series that's just wrapped that you would love. It's kind of like a post-apocalyptic *Buffy* [microphone cuts out] vibe. It's great.

**Sydnee:** I'm gonna be on a show next week.

**Justin:** What?

**Sydnee:** *Court Appointed*.

**Justin:** Oh, yeah, that's right!

**Sydnee:** That's right. So my dad and my uncle, Michael, do like a, it's sort of like a legal *Sawbones*.

**Justin:** Legal *Sawbones*.

**Sydnee:** Like *Sawbones*, except for law, 'cause he's a lawyer. My dad's not.

**Justin:** Yeah.

**Sydnee:** But my uncle is. And anyway, so *Court Appointed*, and I'll be on there to talk about medical malpractice.

**Justin:** Awesome. Well, make sure to check that out.

**Sydnee:** Yeah. Comes out Monday.

**Justin:** And thank you for checking us out. That's gonna do it for us, folks. So until next week, my name is Justin McElroy.

**Sydnee:** I'm Sydnee McElroy.

**Justin:** And as always, don't drill a hole in your head!

[theme music, "Medicines" by The Taxpayers, plays and ends]

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