PCOS

Logan, PCOS Firsthand: Hi, my name's Logan. I'm a transgender man. I use he/him pronouns, and I have PCOS. My symptoms first started really appearing when I hit puberty. My periods would last a week on average, and they were very heavy. The cramps would be so bad that I couldn't walk. I couldn't sleep. I would just lay awake at night in agony, despite taking pain medications. I also had very severe acne, and I had a lot of excess body and facial hair. If I didn't shave or pluck my hair, I could actually grow like this scraggly little chin beard, which was very affirming to me as a young transmasculine person. That was probably the only benefit of having PCOS was the masculizing features. By the time I was 19, my periods became even more painful, if that was possible, and even more irregular.

At one point, I went 10 months without a period. December, 2018 is when I first experienced a cyst bursting. I was sitting in a college math final at the time, and I remember being in so much pain from my abdomen that I could barely breathe. I managed to finish the final, but I could hardly walk because of the pain, so I was rushed to the ER. When we got there, I was not treated well. They started off by accusing me of faking my pain to get opioids, uh, but soon after they thought that it could be appendicitis. I had to get blood drawn and a CAT scan. They actually ended up bursting one of the veins in my arm, like trying to do the dye for the CAT scans, and that was also, um, not, not a fun experience. When the doctor finally came in, uh, to give me a diagnosis or so, I thought, all he really told me was, your appendix is fine, but you have multiple cysts on both your ovaries, so just go on birth control. And then I was dismissed right after with no diagnosis.

The next year that followed, I had to get a lot of blood work and scans done, but no one seemed to understand what was wrong with me. I started birth control, but immediately became extremely depressed and suicidal. My body reacted so poorly that I had to quit after like a month. Um, it was actually very terrifying, um, how it changed my mental state. Um, and once I stopped the birth control, I really wasn't given any other options for treatment. At some point, a doctor pulled me to the side and said, "I looked at your records and I'm gonna formally diagnose you with PCOS. You have elevated testosterone, facial hair, irregular periods, and multiple cysts on both ovaries." I'll never forget her telling me that I was lucky that I had lean PCOS, which basically meant you have PCOS, but at least you're skinny. Once again, I was told my only options for treatment were birth control, uh, which did not work before, or to get pregnant, uh, much to my horror. By this time, I was aware that I was transgender, and I told her birth control makes me suicidal. So she said in that case, I should just go to therapy

and go on a diet. I was 20 years old and 125 pounds at the time. Needless to say, the diet didn't help. I lived in chronic pain for the next few years with both my physical and emotional states causing me a lot of harm. It wasn't until I decided to start testosterone for my gender dysphoria that I actually felt like myself again. As a result of taking testosterone, my period stopped, my mental state stabilized, and I was happy and pain-free for the first time in a very long time. I remember bringing this up to my new doctor and her telling me, "some bodies just function better on different hormones."

I've now been living without PCOS symptoms for the past three years, and the quality of my life has greatly improved. I'm a bioengineer, and it really breaks my heart that this is the state of medical care for people who menstruate. I experienced a lot of sexism and a lot of transphobia throughout the whole process. All the assumptions doctors made about me at the time were made through these heterosexual, cisgender lenses. They assumed that I didn't wanna look masculine, that I'd eventually get pregnant, and that only birth control and estrogen-based pills would work for my body. But this was never the case, and I suffered so much as a result. Transgender people are often left out of these conversations, and I think it's important for people to know just how distressing it can be to have your pain and your identity dismissed by the medical field.

EW: Logan, thank you so much for sharing your story with us. It, it really is so meaningful and important to like, get to hear these stories of like what it is actually like to live with PCOS. I think it really, It, really helps so much.

EAU: it it [00:05:00] really provides so much context for us, for everyone listening, and thank you so much for, for, sharing your story with us.

EW: Hi, I'm Erin Welsh

EAU: and I'm Erin Allmann Updyke.

EW: And this is, This Podcast Will Kill You.

EAU: Welcome to PCOS. Long awaited, I feel like

EW: So long awaited, I mean, I wonder, I didn't do this search, but I wonder if you like searched our email what the first suggestion for PCOS would

EAU: it had to be years ago and probably probably even before we did endometriosis, which was how many years ago now? Long time.

EW: 2019? Was that, no, no,

EAU: I don't remember. I have no idea,

EW: I don't remember either. That's fine

EAU: but it's been a minute. Um, and PCOS has been on our radar since then and before. Um, and I am thrilled for this episode and also. Honestly embarrassed by how little I knew when I thought that I knew I, I was diagnosed with PCOS in 2013.

EW: I remember.

EAU: Yeah. And I went through all of med school and all of residency, so I thought that I had a pretty good handle on PCOS. I learned so much, Erin.

EW: Yeah, I, same, same. I mean, I do not have PCOS as far as I know, but I thought, I thought, I was like, oh yeah, I know what this is.

EAU: Yeah.

EW: Oh my gosh. so like, I'm just, so, i, I think that this was a moment where I, was so, I'm so grateful that we get to do this podcast where, because part of it selfishly is like, oh, I feel like I know more about now. Like, I, there were, I had all these misconceptions. There were that I finally realized. But I think also, like this is, so many people have similar misconceptions.

EAU: Exactly. Like it's never just us. Yeah, so we're really excited.

EW: Yeah.

EAU: Maybe sometimes it is just us,

EW: just us but in any case

EAU: any case,

EW: I'm excited. Um, but before we get into the full picture of PCOS, it's quarantini time. What are we drinking?

EAU: We're drinking [Under Revision]. Those were bracket

EW: case, Yeah, I was gonna say in case you're not watching this Yes. [Under Revision] because truly, like, I feel like our, our perception of this is constantly changing and needs to change in many ways to deliver better care and better empathy and awareness. So there

EAU: We'll get into

EW: go.

EAU: on it, but tell us first, Erin, what's in [Under Revision].

EW: It's, it's, um, it's a placeborita version and it's so good. It's, um, lavender syrup and lemon juice and club soda, and it's

EAU: a little lavender lemonade situation.

EW: And relaxing. Love it.

EAU: We'll post the full recipe on our website. This podcast will kill you.com. We'll post a video of Erin Welsh making it. Are we still gonna do that?

EW: Yeah. We're gonna try.

EAU: Okay, on our social medias like, uh, Instagram and the TikTok and the Facebook, et cetera, um, we're on blue sky as well. So if you're not following us, you should consider doing that. If you haven't yet rated and reviewed and subscribed to our podcast on your favorite podcaster, iHeart podcast, apple Podcasts, Spotify, we'd love it if you do that. If you're not yet subscribed to the exactly right youTube network channel, consider doing that. Um, we're there

EW: a gentle recommendation, a nudge

EAU: a nudge in the right direction? Um, and we have a

EW: exactly right direction. Sorry.

EAU: Oh, that was good.

EW: Thank you. Thank you.

EAU: Um, and finally, we have a website. It's called, this podcast will kill you.com and on it you can find merch. You can find Patreon, you can find bookshop.org affiliate accounts, and a good reads list and Blood Mobile, who does our music and all of our sources and so much more.

EW: so much more.

EAU: I

EW: That was great. And I think, um, there's nothing else to cover except PCOS, so let's take a break and begin.

EAU: Okay. I can't wait.

EAU: PCOS stands for polycystic ovarian syndrome, which really makes it sound like it's a disease where you have cysts on your ovaries. It should be pretty straightforward. It's not that, Erin,

EW: not that.

EAU: it's not that,

EW: That was my misconception, number one. I was like, surely the name must be a clue as to what's going on here.

EAU: not not even really a good clue at all. Actually. What PCOS really is, is an endocrine disorder, which means it's a disorder of our hormones and not just like one or two of our hormones. No, no. Today we're gonna get to talk about almost all of the hormones that we use and have in our bodies [00:10:00] and their effect on all of our body systems. Okay. Yeah. There is not a single test that we can do to diagnose PCOS, but rather there are a list of criteria

EW: Okay.

EAU: and you have to fulfill two of three of these criteria to earn, I guess, the diagnosis of PCOS. And this list underscores some though not all of the possible. And I'm gonna put this in quotes, symptoms, um, 'cause we're gonna get into it, but some of the possible symptoms of PCOS. And so I thought that that's where we would start, is how we actually diagnose PCOS. And then we'll talk about what we know about what PCOS means in terms of the risks of various chronic diseases. And then we can get as deep or stay as shallow as you

want in terms of what we know about the, like nitty gritty pathophysiology of what's causing this.

EW: How much do we actually know about the nitty gritty of the pathophysiology that's causing this?

EAU: We know both a lot and so little

EW: I mean, that's, that's typical.

EAU: It is, isn't it? Um, and then we'll talk about how we treat it. And my goal is to do this in 20 minutes, so we'll see if that's gonna happen. Okay. it won't.

EW: It's quite a lofty goal.

EAU: I know you should see all the words on my page. Um, so there has been fluctuation over the years over these diagnostic criteria, but at this point there's pretty well established guidelines on how we diagnose PCOS. So to make this diagnosis, you need two out of three of the following criteria. One is hyperandrogenism, and we'll talk about what that means. And this can be either clinical, so symptoms that you can see on a person or biochemical. So looking at lab tests, you have to have oligomenorrhea or a amenorrhea, so few periods, or not having any periods at all.

EW: Mm-hmm.

EAU: And polycystic ovarian morphology. So you need two out of three of those. So let's talk about what those actually mean. Like what they would look like, right in English. So hyperandrogenism means an elevated amount of androgens, which are steroid hormones. We often think of testosterone, and testosterone is one of the androgens, but there's a lot of others. Uh, DHEA, androsterone, there's a whole bunch. Okay? And so you can determine whether a person has what is considered hyperandrogenism by measuring the levels of those hormones in a person and comparing that to what we see in typical females. And this is, again, we're talking about people with ovaries here, and that is entirely the focus of PCOS at this point. Asterisk, abound.

EW: Uh, quick question. When you are, let's say you, you are being tested for these hormone levels, what does that test involve?

EAU: Uh, those are, if you're testing for hormone levels, it's gonna be blood tests. What exact hormones people are going to test for can vary depending on

who is doing that test. One of the important things is to make sure that you're doing enough testing to rule out other androgenic disorders because your adrenals produce androgens. There's other like known disorders where we know like, oh, you have a deficiency in, say this enzyme that produces a specific clinical syndrome that's different than PCOS. And so you have to do enough of the blood tests to make sure that you're ruling out these other things. And then if you see still an increase in androgens, and again, this is already where we can get some variation because you might have an increase, you might not have an increase, but this is just one possible criteria and you can look at a number of different androgens. So that's one

EW: I already have so many questions. Okay. So the, like where it, where, what is the source of the excess androgens?

EAU: you're jumping so far ahead. Okay. We'll get there. We'll get there.

EW: get there.

EAU: Um, ultimately the main source of the excess androgens is the ovary, but the question of why is is at the heart of it.

EW: Is that, yeah.

EAU: but ultimately, the ovaries are producing excess androgens.

EW: I, I just, I swear, two more quick questions just 'cause I'm trying to get a sense of what elevated means. Um, so is this, how, how much do hormones fluctuate during the day, during the month, during the year, et cetera. And so then how much is excess, how is excess determined? Or like how is greater than average determined? What's, is there a standard deviation? Like what's the vibe?

EAU: This is a great question, Erin. There's not like a, a number cutoff necessarily. So every lab, uh, that you do a a lab test at is going to have their, what is called like normal range or typical range. Um, and for hormones like testosterone or DHEA or estrogen or progesterone or any of those they're gonna have a normal range for females and they're gonna have a normal range for males. And so if it is higher than that normal range for [00:15:00] females, then that would be considered hyperandrogenism. And that could be if you're looking at free or total testosterone or it could be one of these other hormones. Um, I don't have like exact numbers, and you're right that it can vary, uh, day to day. It can vary during the time of day as well. Um, So again, this can get quite complicated.

EW: Okay. Sorry.

EAU: doesn't have to be bio. It's okay. Don't apologize. I love your questions. Um, it. does not have to be biochemical evidence though. We also can see what's considered clinical evidence of uh, hyperandrogenism and that usually there's three main things that we think of, um, acne, usually more severe acne, sometimes cystic acne, but not necessarily androgenic alopecia, AKA scalpel like male pattern hair, hair loss, and hirsutism, which I always have to look up how to pronounce

EW: I'm glad that you said it first 'cause I would've gotten it wrong.

EAU: Hrm, which is, uh, hair growth, like coarse thick hair growth that specifically grows to longer than five millimeters. So not just tiny, tiny little hairs, um, in androgen dependent areas. So that means places like the underarms, the pubic area, the face. And this is a kind of tricky one because there's a grading scale that in theory one should use to determine how much would be considered excess or like hirsutism, truly. Um, and there's also going to be like racial and ethnic variation in hair patterns to begin with. But, but that is also one of the possible clinical criteria. So that's all just hyperandrogenism. That's one thing that someone might have to put them on this list of possible PCOS. The second is ovulatory dysfunction which means people either aren't ovulating at all and then therefore They're not having any menses

EW: Mm-hmm.

EAU: or they're ovulating infrequently or irregularly. and So they're having very infrequent or irregular menstrual cycles. Exactly how infrequent or like how far apart they have to be or how irregular depends in part On how far you are from menarche or that first menstrual period because it's quite typical in the first few years to have irregular menstrual cycles. Um, but if you are more than three years after your first menstrual cycle, then anything less than eight per year or greater than 35 days apart would be considered oligomenorrhea or having few menstrual cycles. Um, but that's again, so that's, that's one. So ovulatory dysfunction. And then the third and final is polycystic ovarian morphology, which does not really mean that you have a bunch of cysts on your ovaries, but means that if you look on ultrasound in the ovaries, you see a bunch of, and by a bunch, I mean 20 or more visible follicles that are arrested In an early stage of development. So we're born in With all, if you have ovaries, your ovaries have as many eggs in there as they're going to have. And typically in response to these hormonal cycles, every month, one, like multiple follicles start

to mature, but then one takes over, matures completely, and then is released during ovulation.

EAU: And what happens in PCOS is that. multiple follicles start to grow And then grow to a certain point, but then are arrested in their development without ever having one that takes over and is released, which is why you have uh, oligo or a amenorrhea because you're not ovulating. And then it's also why You have so many of these kind of follicles that are. Arrested at a stage in development that is before they get to ovulation

EW: So you've got a bunch of these, like not fully, uh,

EAU: developed follicles

EW: follicles just hanging out at the ovary

EAU: Exactly.

EW: Like little grape clusters

EAU: they look like little grape clusters. Sometimes on ultrasound you might not see specific follicles, but. you would have an overall larger volume, like greater than 10 milliliters volume without having One dominant follicle. 'cause if you have just one that's burst or ready for ovulation, they can get quite large,

EW: Okay. Okay.

EAU: Now, one thing that's new in the most recent guidelines from 2023 is that you don't necessarily have to do an ultrasound to look for those polycystic ovaries. you also could diagnose polycystic ovarian morphology by looking at AMH, which is another hormone that you would check via a blood test that we've talked about, I think in our infertility episodes or, and menopause, I know, I know we mentioned it in menopause as well. Um, but this is a hormone that relates to like how many follicles are still in existence in your ovary ki kind of a thing. Um, And having an elevated level of AMH is suggestive of PCOS, but again, here, there's not like an exact cutoff value yet for this which is interesting in and of itself. So that's how we diagnose it. You gotta have two out of those three.

EW: Okay. So either you have this [00:20:00] hyperandrogenism, um, infrequent or no periods. Oh, and cyst, yeah, cysts

EAU: morphology.

EW: The, in the name? Yeah,

EAU: In the name.

EW: I was like, what's the third?

EAU: And so, because there are these three different criteria, and you only need two out of three to have a diagnosis, it leads to four different, what are called phenotypes of PCOS. So one of the options is that you have all three, you meet all three of these criteria, and that would be called phenotype A. the second option is that, you have evidence of hyperandrogenism and evidence of ovulatory dysfunction without having polycystic ovaries. We'll call them polycystic ovaries. They're not cysts. And that would be phenotype B. And those two together are called classic PCOS, and they account for an estimated two-thirds of people with PCOS. So two thirds of people with PCOS, will have evidence of hyperandrogenism, either clinical or on lab tests, um, and they'll have ovulatory dysfunction with or without having polycystic ovarian morphology on ultrasound. The third phenotype phenotype C, someone will have hyperandrogenism and on ultrasound, polycystic ovarian morphology, but without necessarily having any issues in terms of their ovulation, so not having oligomenorrhea. And then phenotype D is ovulatory dysfunction and polycystic ovarian morphology, but no evidence of hyperandrogenism.

EW: Hmm. All right.

EAU: Okay. Why is a great question. Okay,

EW: Yeah.

EAU: so just looking at all of those, like, there's a, there's a why question and then there's a huge part that's missing already. Okay. In these diagnostic criteria, because those criteria give us a lot of insight into some of the symptoms as well as some of the consequences of PCOS.

EW: Right.

EAU: So anovulation, which can happen very commonly in PCOS can result in infertility or reduced fertility. And PCOS is the major cause is estimated to be like the number one cause of anovulatory infertility. So if you're not ovulating

and you can't get pregnant when you want to be pregnant, PCOS is the number one cause of that

EW: Mm-hmm.

EAU: In addition this, an ovulation also leads to an increased risk of endometrial cancer down the line. And that's because your uterus, because of the hormones that are floating around, is out here, like getting ready to have an egg implant. It's getting ready, it's getting ready, it's getting ready. That egg never comes. You never menstruate. Your uterus lining is proliferating this whole time, and that proliferation increases the risk of cancer in this continually proliferating tissue.

EW: Okay.

EAU: The hyperandrogenism that we see in PCOS that we can see may or may not be associated with symptoms that are undesirable, right? It depends on someone's perception of what those symptoms are. Male pattern hair growth or hair loss may or may not be something that is distressing to someone. Acne, most people are not a fan of acne. Um, but. This, all of these definitions are missing one of the huge, very clear, well-defined major factors of PCOS and that is its relationship to insulin resistance. So insulin resistance leads to glucose intolerance and that puts people at risk for type two diabetes as well as a whole bunch of other metabolic complications, hyperlipidemia. So having elevated cholesterol levels that puts you at risk for cardiovascular disease, it puts you at risk for hypertension and so much more. And PCOS also gets quite a lot of attention as it relates to obesity, which I always put in quotes. Um, because obesity is, it's considered a disease in medicine that is defined entirely based on BMI and BMI is not an indicator of health.

EW: Right.

EAU: Elevated BMI is associated with PCOS, but whether this is cause or consequence is very much still up for debate.

EW: I feel like is a lot of some of the symptoms associated or the pre that are prevalent with PCOS, is it

EAU: all.

EW: Or consequence? Yeah,

EAU: Yeah, but all of these, and, and here's what's really important about that, is that all these other symptoms, and there are a lot, so like increased risk of insulin resistance, risk for type two diabetes, risk for hyperlipidemia. Even people who have P-C-O-P-C-O-S are also at an increased risk for obstructive sleep apnea. We don't know the mechanism there, but all of those risks increase regardless of BMI. They [00:25:00] exist regardless of BMI. We know that, or we think at least from the data that we have so far, which is mostly in mouse models that PCOS might be related to changes in adipose tissue, like the way that your adipose tissue responds to insulin or things like that, and how, how it like uptakes glucose and things like that. But all of the other complications and metabolic complications in PCOS are prevalent regardless of BMI. And in like BMI matched case control studies, they are elevated in PCOS regardless of BMI. Just like in people without PCOS, in some cases an elevated BMI can also put you at higher risk for some of these other me metabolic complications. So again, what is the cause and what is the consequence? We don't know. What we do know and what is prevalent enough that it has made it into the 2023 guidelines is the very real problem of fat shaming that happens in PCOS and weight stigma. Like enough so that the awareness of this fat shaming and stigma is in the PCOS guidelines of like, you need to be aware of this if you're a clinician and not do it.

EW: Yeah.

EAU: Um, but like you said, we do not know exactly how this metabolic dysfunction happens at the beginning. Like what are the core causes of it?

EW: And how does, how do other hormones. Play into this.

EAU: My gosh, erin,

EW: What's, what's, what's the, the timeline, the sequence, the cascade,

EAU: if I, if I could tell you a step-by-step cascade, I would have a lot more clarity as to what the heck is going on. Um, but I can give you some more detail. Okay. To kind of understand a lot of what's going on in PCOS, we can first understand what's called our HPO axis. This is our hypothalamic pituitary ovarian axis or gonadal axis, because you have one if you have test testes too. So in your hypothalamus, you are releasing hormones. This is a part in your brain. You're releasing hormones. The one that is important in PCOS is called gonadotropin releasing hormone, and it is being pulsed out. It is normal. It is typical in our brains that it's not being released all the time, but we pulse it out in phases. Your brain is like, yep, give a little bit. Yep, give a little bit. It's job is

to travel to our pituitary and tell our pituitary, which is another part of our brain, to secrete other hormones, luteinizing hormone LH, and follicle stimulating hormone. FSH. We've talked about these in our infertility or pregnancy episodes. These two hormones job is to travel through our blood bloodstream, go to our ovaries, and modulate the production of estrogen and progesterone, and make our ovaries mature. One follicle, release it, and ovulate right.

EW: Mm-hmm.

EAU: This whole system, our HPO axis works on a system of both positive and negative feedback loops, right? So one part of our brain tells, another part of our brain, tells our ovaries and those hormones go back to our brain and they're like, Hey, we're here. So calm down.

EW: Yeah, yeah, yeah, yeah.

EAU: In PCOS, there is a wrench in this system.

EW: Mm-hmm.

EAU: What exactly the first wrench is we don't know. So we know that. The pulsatility of this gonadotropin releasing hormone, GNRH in PCOS is increased. So we see more and more frequent pulsatility of GNRH from our hypothalamus. What that does is it tells our pituitary, Ooh, keep going, keep going, keep going, and actually leads to a disruption in the LH versus FSH ratios.

EW: and so instead of like it being okay now ovulate, it's like, oh, maybe, maybe, maybe, maybe

EAU: it's like,

EW: of a strong message,

EAU: yeah. And the message is like, mature, mature, mature, mature, mature, mature. A bunch of follicles. A bunch of follicles. But, but no, there's no ovulate

EW: there's no release.

EAU: There's no release signal. Right? And that, because that LH is then going to our ovaries and it's being like, make, make, make androgens, make

androgens, make androgens. Then there's also something else going on because that hyper androgen secretion should negative feedback onto our hypothalamus and be like, Hey, stop. But that negative feedback is impaired. We don't exactly know why.

EW: Hmm.

EAU: Then, okay, here's where it gets even more complicated, erin, where does insulin resistance play into

EW: That's what I'm trying to figure out

EAU: We know that insulin resistance, tissue level insulin resistance leads to an increase in insulin production, [00:30:00] right? Because if your body is trying to regulate glucose, uh, insulin is in charge of that. And if your tissues aren't responding to insulin, insulin is binding through the receptors. It's supposed to, but it's not doing its job. So you can't collect that glucose, then your body's gonna make more insulin. 'cause it's like, Hey, there's too much glucose floating around. We need more insulin, more insulin, more insulin. That Hyperinsulinemia feeds back onto the ovaries and tells them by a reason, I don't understand to make more androgens. Okay.

EW: I mean, Okay. But no, I

EAU: No, exactly. No, we don't know why. So in short, we know that all of these feedback loops are sort of not working the way that they would typically,

EW: in some way. Yeah.

EAU: there's more and more evidence. 'cause we used to think like, oh, it's just the ovaries and there's some evidence in like mice and rats that like disruption at the level of the ovary, just like a tendency to excess androgen secretion to begin with can produce things like polycystic ovarian morphology. But it again, doesn't account for the lack of this negative feedback loop. It doesn't necessarily account for this insulin resistance piece of it. So there's more evidence that these other groups of hormones that act more in our brains. Called kisspeptins and other like other types of hormones as well are likely involved. So I guess the point of all of this is to say a number one, it's complicated,

EW: Yeah.

EAU: and B, number one, while we know a lot,

EW: two or be number one.

EAU: Whatever. A number one, it's complicated. B. Number two, we know a lot about the features of these disruptions. Increased GnRH pulsatility, increased androgens, insulin resistance leading to more increased androgens. We also see like a decrease in sex hormone binding globulin because of these androgens. So like there's all these feedback loops that are very well documented and drawn in all these papers, but we do not know what the first underlying issue really is,

EW: right.

EAU: which means that all of our treatments that we have are addressing individual parts of the issue, but not coming close to like curing anything or really getting to like one drug or one mechanism fixing this cascade.

EW: So do we think that it is one mechanism?

EAU: That is an excellent question, Erin. No idea. Especially because when you think of all of these different phenotypes, right? I said that there are four different phenotypes. They also are associated with like differential risk in things like insulin resistance. So types A and B, that like classic. Um, PCOS picture, something like 80% of people with this phenotype will have evidence of insulin resistance and therefore might be at higher risk of things like diabetes. Phenotype C we see still a significantly increased insulin resistance, but like 60% compared to 80%. And in phenotype D, which is the one where people have no clinical hyperandrogenism, about 40% of them we see insulin resistance. But in all of these, the incidence of type two diabetes and is like four times higher in people with PCOS compared to people without PCOS, regardless of bMI, though that incidence does increase with increasing BMI.

EW: Okay. And so basically the. The outcome of this, like domino, like the, the, the path that the dominoes take might be different just, but we don't know why it might be different, but that's what results in these different phenotypes. But the end result for the most part, is similar in terms of health consequences,

EAU: I mean, it is similar. It is not exactly the same. It is similar and then it, it's also like not exactly the same in terms of even those initial dominoes, right? Because in some people we see this hyperandrogenism, and in some we don't, but we still call it PCOS is, that really the same disease or not?

EW: Yeah. Is yeah.

EAU: It? We don't know Right. now. We, we really don't know. Um, we don't, 'cause we also don't know like what actually causes PCOS right there. It's very strongly genetic. There is a big heritability component.

EW: 70% heritable.

EAU: Yeah. And that's not necessarily all strictly genetic. There's like at least 20 different gene loci in different populations. There's not one single gene. But there's also evidence of like epigenetic changes that we don't really know what is the, trigger for these changes. But there's likely some epigenetic things that are involved in the, like increased risk of pCOS. Um, and then there's likely other environmental factors [00:35:00] at play that we don't really understand. Right. Like, what are all of these other triggers?

EW: I, I'm gonna say it here 'cause I didn't put any of this in my notes, but I didn't wanna get into the evolutionary. There are like a lot of different papers I read about the evolutionary origins, uh, of PCOS as proposed by certain researchers. And it is, and I was like, ultimately we don't understand what PCOS is, and so how can we really talk about what. How can we test these hypotheses if we don't know what it's caused by? And, um, Yeah. So that I didn't, I don't have anything about that.

EAU: I mean, yeah. 'cause we don't, I feel like we don't even have a good, we have a clinical definition, right? We can diagnose this, but are all, are all of these phenotypes, are all PCOS the same? I don't know. We don't know.

EW: We don't know.

EAU: In terms of what we do about it and how we treat it, um, it really depends on what we're worried about, what the symptoms are that a patient or a person is worried about. Because a lot of these symptoms of PCOS are related to these androgenic hormones and related to this hPO axis, A lot of times we rely on birth control as one of the first line treatments for PCOS, especially combination birth control like estrogen containing birth control. Because what that does is it helps kind of override a lot of this HPO axis. It's gonna negate any of these ovulatory dysfunctions, it's gonna decrease your risk of endometrial cancer. And the, estrogen effect especially can help to alleviate a lot of the, symptoms of excess androgens if those symptoms are unwanted, like acne and hirsutism, because the estrogen, what it does is, it de it. It helps to address this decrease in sex hormone binding globulin, which then helps to decrease the amount of free testosterone that's circulating. Sometimes though, we might use anti-androgen specific medications like, spiron, lactone, or other medicines if

we're targeting some of those hyper androgen symptoms as a concern. But none of those are going to address the metabolic effects. Right? Birth control is not gonna change insulin resistance if that's present. By the way, we don't have a test for insulin resistance. There's no test. We don't have a test. We don't have a way to test for insulin resistance.

EW: Huh?

EAU: We can test for risk of diabetes, but diabetes is not just insulin resistance. It's. It's, we see our diabetes episodes, there's other ways that? you can get diabetes besides just insulin resistance. But insulin resistance can lead to diabetes if you then have impaired glucose tolerance. But insulin resistance Is like a first step if that's the pathway and we can only like see it if it's come to the point of, okay, you have an increase in your A1C or you have an increase in your fasting glucose, but that's not directly a marker for insulin resistance itself. And we don't have a test for that. That's easy to do.

EW: I just

EAU: I know. Nope, we don't. Um, but.

EW: Why it's not part of the clinical picture.

EAU: Cause you can't test for it. Right. You cannot test for it. Um, so, but if there is evidence especially of like glucose intolerance, right? Like, uh, increased A1C or something like that, then you can address that with metformin is usually the first line. And that's a drug that we use for diabetes. It helps to increase insulin sensitivity in our tissues. Um, it sometimes can also Cause weight loss, which may or may not be desired depending on the situation. What's very, very interesting about Metformin is that it also has data that it helps to regulate ovulation. and what exactly is the mechanism there? Like does that give us any insight into what is going on here? I don't know that it does, but I just still think it's so interesting

EW: Right. Is there a, does that, is that, does that help shine a light on the link between this whole process?

EAU: It helps shine a light on the, because when you look at these, uh, graph, we should post one of these like graphs of, of what these feedback loops look like and how they're disrupted. um, in PCOS, there is a strong link between insulin resistance and hyperinsulinemia and androgen production in the ovaries. So we know that that's like an inward arrow. There's just no backward arrow

that that goes. Like then why does the insulin resistance come up in the first place? That is what we

EW: the dots in that first, yeah. Yeah.

EAU: Like, is insulin resistance actually the primary mechanism? Uh, I don't know. But then why do we see Anyways? It's, it's much. Um, but for people who maybe want to get pregnant and are struggling with infertility, sometimes metformin can then be used to help alleviate the anovulation. It is not first line if the goal is pregnancy though, um, usually first line what we use is a medicine called Letrozole, or another similar medicine that triggers ovulation [00:40:00] that's more directly triggering ovulation. But metformin can, and it has good data that it can, it like normalize ovulation to a regular degree, which can help with infertility if that's a goal. And then there's also, uh, interest of course in using newer medicines like gLP ones, uh, which are the ozempic of the world, um, or other combination medicines. But we'll get there later in this episode. Erin,

EW: Um, quick questions. A menopause.

EAU: Ah, yes.

EW: Yeah.

EAU: What's the question?

EW: Well, the question is like, are, I guess the question is a very vague unformed question, but just like for people who have PCOS, is their menopause experience any different?

EAU: This is such a great question. No idea.

EW: Okay. No, no one has examined it.

EAU: All of these papers are like, Hey. Yeah. So a lot of what we know about PCOS we think of as a reproductive disorder, and so it's primary effects are in the reproductive years, so we don't have a lot of data on post-menopausal pCOS. is the insulin resistance still a thing? Are you at higher risk for cardiovascular disease and type two diabetes post-menopausal compared to someone who has, like, does your PCOS still exist post menopause?

EW: right. That's what I was trying to, that's what I was trying to ask. And

EAU: a great question.

EW: I guess the, the other question. Then is, okay, so, and this maybe kind of gets into what I'm gonna talk about a little bit, but like, you get a diagnosis of PCOS, you are not interested in becoming pregnant. You maybe are not interested in, uh, addressing any of of the other symptoms of PCOS. Is there anything in your medical care that is like, we should have increased screening for cardiovascular disease, we should have this and that? Is that something that physicians

EAU: do. Does anyone do it, is a question I can't answer. That is the guidelines though, that those are the guidelines, especially from the 2023, uh, update. You should be screened for potentially for sleep apnea, uh, which not everyone is necessarily needs to be screened for sleep apnea. But if you have PCOS you probably should at least be screened with like some of the questionnaires. Um, you should be screened for diabetes, so checking in A1C, you should be screened for hyperlipidemia. Even if you don't want to address any of the symptoms of hyperandrogenism, and it does not matter to you whether like you don't want to get pregnant. and so it doesn't matter to you if you're not ovulating on a regular schedule. You do need to think about endometrial protection. You have to do something to reduce that risk of endometrial cancer. So that is something that you have to think about. Um, and yeah, that those, I mean those are the main things. There's, there's probably more that, that i'm forgetting off the top of my head. Um, also, depression and anxiety are higher in people with PCOS. Why we don't know. Is that just because of how people are treated with PCOS by the medical system? Uh, how long it can take to get a diagnosis, how much they're like ignored by the medical system? We don't know. Is it just because, is it, does it actually have anything to do with PCOS and the like pathology there or is it all just our medical system? We dunno, but it's an important thing to keep in mind as well as Yes. Society. Exactly.

EW: Uh.

EAU: Um, Erin, that was only twice as long as I anticipated. So tell me, how did we get to here? What do we know? Um, you know,

EW: Those are some great questions. Let's, um, let's get into it.

EAU: Okay.

EW: For all that we still don't know about the biology of PCOS, this condition can teach us so much when it comes to the power of societal expectations, the

inadequacy of a name, our failure to provide care to all who need it, and how silence, stigma, and shame can profoundly deepen the impact of a medical condition. At least it can teach us those things if we are willing to listen.

EAU: Yeah. Can we learn those

EW: Can we learn those things? Prevalence estimates of PCOS vary. The most common numbers I've seen are six to 20% of people assigned female at birth. Others say, you know, one in 10, a huge, huge prevalence, and yet PCOS receives less funding for research compared to other similarly prevalent conditions. There is less awareness both in the medical community as well as within the general public. We still lag behind in terms of treatment options and medical knowledge about PCOS. Clearly not enough of us are listening. [00:45:00] Hopefully that will change thanks to the incredible advocacy work by some groups and individuals and thanks to the internet, which I never thought I'd say. But truly thanks to the internet where people with PCOS can find the support and community that is so often lacking in their everyday lives or in interactions with their healthcare provider. Before I go any further, I wanna shout out one advocate in particular, and that is Dr. Stacey l Williams, a social health psychologist at East Tennessee State University, and author of an incredible book that I read for this episode titled The Psychology of PCOS, building the Science and Breaking The Silence. As someone who does not have PCOS, but thought they knew a thing or two about it, which turned out to be true in the literal sense, I found this book to be incredibly eye-opening and perspective shifting, truly, and almost everything that I'm gonna talk about when it comes to PCOS today and some of the issues that we see comes from this wonderful book. But before we get into today and the today's landscape, let's go back in time to get a sense of the lengthy history of this condition.

EW: So, PCOS is likely an ancient disease in humans, and it's probably not limited to our species. One of the challenges with understanding the root causes of PCOS is not having a naturally occurring animal model, but I did come across a paper that described rhesus monkeys that had naturally occurring high levels of testosterone and seemed to exhibit some of the clinical picture of PCOS. It's still like, it's not clear, you know? Yeah. The first likely descriptions of the condition in humans come from ancient Greece in Hippocrates diseases of women text written in the fourth century, b, CE

EAU: Oh gosh. Can't wait for this.

EW: Quote. "But those women whose menstruation is less than three days or is meager, are robust with a healthy complexion and a masculine appearance. Yet

they are not concerned about bearing children, nor do they become pregnant." End quote.

EAU: Okay.

EW: Uh, other ancient texts mention hirsutism or hirsutism in combination with changes in menses as a condition. And another Greek physician Soranus of Ephesus wrote around the second century CE quote. " Sometimes it is also natural not to menstruate at all. It is natural too, in persons whose bodies are of a masculine type. We observe that the majority of those not menstruating are rather robust like mannish and sterile women." End quote.

EAU: Geez.

EW: I know language is not great here. Um, but what these descriptions show is that PCOS was likely an ancient disorder and common enough that it was mentioned in several old medical texts, and that it has always been described as violating expectations of femininity. The next description that historians point out comes from 1721 when an Italian physician Valisneri, uh, described a married quote unquote infertile woman who died young at 21 years, and upon autopsy was found to have "shiny ovaries with a white surface and the size of ovaries as pigeon eggs or ovaries the size of pigeon eggs".

EW: Mm-hmm.

EAU: I have no idea like how big a pi pigeon egg is.

EW: I'm not sure either. I

EAU: I imagine they're small, though, like pigeons aren't very big birds. Okay.

EW: Mm, I don't know.

EAU: All right.

EW: Uh, additional mentions of what was likely PCOS popped up throughout the 18th and 19th centuries, including from Rokitansky, the famous pathologist I mentioned before on the podcast, who did like tens of thousands of autopsies. And this period, especially in like the late 19th century, early 20th century, was crucial time for building a foundation of knowledge, for understanding the role of different hormones in our physiology and what could happen when things do not go as expected. This was also when the testosterone equals male,

EAU: Mm,

EW: estrogen equals female false dichotomy was established.

EAU: Oh, love that.

EW: Yeah, still unlearning that, I

EAU: Yeah.

EW: And so while that piece of the puzzle, like the hormone piece of the puzzle wouldn't get slotted into PCOS until the 1960s when researchers demonstrated the ovary's role in producing androgens, a complete clinical picture of the condition was formed by 1935, more or less complete. Yeah. That year, two physicians, Irving Freiler Stein and Michael Leo Leventhal published a paper titled A Amenorrhea Associated with Bilateral Polycystic Ovaries. There you go. And in it, they described the case reports that they had collected over the previous few years while investigating factors underlying difficulty getting pregnant.

EW: They followed [00:50:00] these patients for long periods of time and like truly got to know them, got to know their histories, got to know like just everything about them. It was sort of this like, you know what, let's just cast a wide net and see what what comes out. And by doing this, which is not a very common thing done today, they were able to draw out patterns that otherwise might have been missed. A subset of their patients had started menstruating years before, but their periods since had been unpredictable or just lacking

EAU: Mm-hmm.

EW: They tended to have more hair growth than average and enlarged cystic ovaries, often larger than the uterus even. One, at least a few. And they performed surgeries on a few of their patients to remove the cysts and part of the ovaries, both for diagnostic as well as therapeutic purposes. And a couple of people actually delivered children after the surgery.

EAU: Okay.

EW: So what was different about Stein and Leventhal's clinical picture? Like why is this the one that put PCOS on the medical map, so to

EAU: Mm-hmm.

EW: They were the first to describe the triad of polycystic ovarian morphology, hirsutism, and infrequent, irregular periods. And of course, this is not a perfect clinical picture, which over the decades has evolved to account for more diverse symptoms and still maybe as one could describe it as incomplete. Mm-hmm. And their focus on ovarian cysts, ultimately leading to the name polycystic ovary syndrome, was misleading. Since cysts are not always present or like Yeah, it's not, it's not quite accurate, you could say,

EAU: I mean, if you a cyst just a fluid filled thing, then sure, sure. We'll, we'll

EW: sure.

EAU: Yeah. it Doesn't have to be present.

EW: Yeah. Doesn't have to be present.

EAU: Yeah.

EW: But what they did was provide a starting point and drive interest in this condition. And in the decades since researchers have added detail and depth to what we know about PCOS, from diagnosis to possible treatments, but not nearly enough. To quote Dr. Stacey Williams, who's the author of the Psychology of PCOS quote, "it is unfathomable that in the 21st century, we are still grappling with diagnosis and treatment for PCOS. After more than 85 years, since PCOS was formally identified, doctors still lack knowledge of the syndrome, combine that reality with a continued lack of cultural sensitivity of providers towards their patients, and we have a recipe for continued delays in diagnosis, biased interactions, and increased risk of worse health outcomes."

EAU: Yeah.

EW: The resulting cost of this is huge on the economic side, $8 billion annually in the US alone. That was estimated in 2022. That's

EAU: for PCOS.

EW: Mm-hmm. And that's split about equally between reproductive issues and metabolic vascular issues and is likely an underestimate. Erin, you took us through some of the physical costs associated with PCOS, some of which can be substantial, but the psychological costs of this condition can be immeasurable and mostly go unacknowledged, at least in the medical literature.

EW: PCOS, like many chronic conditions, reveals a divide between how society expects you to act, look and feel, and how you actually act, look and feel. The price for not meeting those expectations can be steep. Whether it results from medical gaslighting, bullying, or internalized stigma. People with PCOS are at a higher risk of depression and anxiety, like you said, and it's difficult to disentangle whether these mental health impacts are a direct or indirect consequence of PCOS. Is it hormone dysregulation? Is it the medications someone has prescribed? Is it the stigma you face with PCOS? Is it not just one thing, but many, like we don't have a good answer, but if we want to find one, what we need is more information, not just about the biological underpinnings of PCOS, but especially the lived experiences. What is it like to live with a condition whose symptoms mark you visibly or invisibly as not conforming to societal norms or medical expectations? How does our society or our medical establishment treat someone with PCOS and how is that wrapped up in ingrained notions of gender and sexuality? Let's get into it,

EAU: Okay.

EW: and I'm roughly breaking it down between outside of clinic and inside clinic.

EAU: Okay.

EW: As you described, Erin, PCOS is associated with a broad array of signs and symptoms, some of [00:55:00] which are visible, like you know, what is called male pattern body hair or baldness, uh, weight gain, others which aren't visible such as irregular periods, difficulty getting pregnant, but many of which challenge gender norms. Our society has hammered into us that women should not be hairy. That in fact, any body hair or facial hair is shameful and disgusting, and we should take steps to conceal it

EAU: and avoid it. Laser it away.

EW: I mean, bearded ladies, were a staple of circuses, for goodness sake. Our society equates fatness with a moral failing, believing that it demonstrates a lack of self-control. And women especially should be delicate, slender

EAU: Mm-hmm.

EW: Our society tells us we become women when we get our first period, and that our monthly bleeding is a powerful reminder of our womanhood.

EAU: God. Sorry. It makes me nauseous.

EW: Mm-hmm. Our society assumes that every woman will want to give birth. Our society expects that every person assigned female at birth should look a certain way, act a certain way, and want certain things, and PCOS can throw a wrench into society's expectations. Sometimes because we are raised in this society and these expectations are deeply ingrained in us, this can lead to intense feelings of stigma that come from within. If you don't menstruate regularly. And menstruation though itself is stigmatized, is associated with womanhood. Does that mean that you are less of a woman? Of course not. But that is a difficult thing to unlearn.

EAU: Right.

EW: The author of the Psychology of PCOS interviewed 50 people with the condition for the book and included snippets of the interviews, which were so insightful. Like I loved that approach so much. I think it's so important, and I wanna share a few throughout the rest of this. So Jo, late twenties, genderqueer non-binary, described being bullied for having male pattern facial hair when they were younger and said that they quote, " spent a lot of time trying to get rid of my body hair to the extent that nobody would even be able to know I even had it. So I feel that it's a cultural mandate for people who are trying to pass as women, that you can't have even stubble in places that you're not supposed to have hair, which is pretty much everywhere except your head. It's a lot of time and a lot of paranoia to try and maintain that appearance if that's not what your body is actually doing. And that was a big source of feeling invalidated as a woman for a long time." End quote. And like, okay, I don't have PCOS as far as I know, but I do have a lot of body hair. Thanks, genetics. And it has been and continues to be a cont, a source of shame and like embarrassment and anxiety in my life. And it was just like, it still to this day.

EW: Ugh. Anyway,

EAU: Yeah. No, it's very real.

EW: It is very real. Um, and then there's another firsthand account or another like snippet I wanna share from Kim, mid thirties cisgender who said quote, "before I was diagnosed with PCOS, I really just felt like my body was broken. And I think I had a lot of shame around not understanding why I was having trouble with periods and what this pain was that other people in my life who menstruate don't have. So what was going on for me? Why was I weird? And I think that shame made me feel isolated because I couldn't talk about it or I didn't

know I could talk about it." end quote, stigma can also arise from other people. One person interviewed in the book describes getting facial hair shavers for Christmas from their mom.

EAU: Oh,

EW: yeah, I mean, I was bullied all throughout middle school and high school for body hair. Um, yeah,

EAU: Why? Oh my gosh. Why body hair? Like.

EW: I mean there, we could do a whole episode on that, but I think we, maybe we should. I think part of it too is like, razor companies were like, oh, we're missing half the population. You're disgusting.

EAU: You're disgusting. Your hair is disgusting.

EW: Unhealthy. It's unhygienic. Oh, it makes me so upset. Um, and then Meg, early twenties, cisgender talks about a college field trip for her geography major involving canoeing. Quote, "the professor was concerned about my ability to canoe because I'm overweight. Therefore, I might not have enough stamina, even though I've been kayaking all my life and I'm very good at canoeing and kayaking." End quote.

EAU: Yeah. I mean, that's Ah, Mm-hmm.

EW: Another person interviewed, described how her parents don't really quote unquote believe in PCOS and think that the weight is completely a matter of self-control.

EAU: the amount of fat shaming

EW: It's, it's ridiculous. It's [01:00:00] over, it's it's overwhelming. Yeah,

EAU: Yeah,

EW: yeah, Yeah. There is, there is nothing inherently shameful about any part of PCOS, but because we are exposed to societal expectations from the minute we are born, and multiple symptoms of PCOS do not align with those expectations, stigma remains a huge issue. Whether that comes from within or from without,

EAU: Yeah,

EW: But not everyone experiences PCOS in the same way. For instance, some cisgender women may feel self-conscious about their facial hair. Others may be done performing femininity by removing that hair, and they're like, no, I'm, I'm growing it out. I don't

EAU: Doesn't bother me.

EW: And other people that don't identify as women may welcome that facial hair feeling that it more closely aligns with their gender identity. Along those lines, infrequent or unpredictable periods might be a painful reminder to cisgender women who are trying to become pregnant or a source of anxiety for those who do not want to be pregnant. While absent periods might be the desired outcome for people who find them distressing, since they do not align with their gender

EAU: Mm-hmm.

EW: And then there's, there's everything in between. People can feel a million different ways about these different symptoms. Kendall, uh, late twenties non-binary describes the mixed feelings that can arise. Quote, "but the gender dysphoria, like, I feel like PCOS actually helps a little bit, but it also kind of makes it worse because I'm having all these problems that revolve around my female anatomy. So it's kind of like a push and pull of two differing emotions. And before I felt as though I was ready to identify as transgender, it definitely made me feel terrible about my body, very much like I was unlikable, unattractive to other people. But now I feel the opposite. I feel like it makes me more attractive because I'm transgender now and I present masculinely, but at the same time the health aspects. And if I don't watch myself, I could gain weight, then I will feel even worse about myself." End quote.

EAU: Yeah.

EW: There hasn't been very much research on gender identity in PCOS, but one study looking at the experience of transgender men with PCOS found less gender dysphoria and less negative body image in those with PCOS compared to those without, there is No hard and fast rule for how someone will experience PCOS. Maybe there's shame or stigma. Maybe there's confidence and power. Maybe there's discomfort or sadness. Maybe there's empathy and understanding. And maybe there's everything all at once or at different stages of your life. Each experience is unique and influenced by a person's inner and outer world. Do

they have someone or a community of someones that supports, understands and listens to them? Part of what perpetuates stigma in PCOS is a lack of awareness surrounding this condition. People don't know what it is, and since it affects those assigned female at birth, there's a tendency to assume that it's a gynecological disorder. And well, we don't talk about anything down there,

EAU: down there, it's off limits in polite

EW: for polite company. Yeah. And this unwillingness to engage with PCOS because it's seen as a unquote "women's disease", shrouds it in silence, leading to less understanding and less interest in both the general public as well as the medical community. Just as society has its expectations of what a woman should be, medicine has their own notion of what PCOS looks like and how it should be managed.

EAU: they do.

EW: And often this leads to a much narrower view of this condition that excludes people who might not fit the, you know, quote unquote "typical" clinical

EAU: Right, which is phenotype A and B or classic PCOS. Mm-hmm.

EW: And this results in delays in diagnosis and inappropriate

EAU: Mm-hmm.

EW: because of its impact on fertility, PCOS is often seen primarily as a condition of heterosexual women who are struggling to become pregnant, and treatment is prescribed accordingly.

EAU: Yep.

EW: This erases the experience of so many people who do not fit that description. Oh, you've got irregular periods, let's get you on some birth control so you'll bleed monthly. Which doesn't take into consideration that someone might not want to have periods at all.

EAU: Yeah.

EW: Maybe

EAU: I, sorry. Just like this is my personal opinion, like why would we wanna have periods every month? But no, some people do. Some people it's important and some people definitely don't.

EW: uhhuh. Absolutely. People feel different ways about

EAU: Oh, it's shocking.

EW: one way. Yeah. Or maybe your doctor says "it's, you know that facial hair. It's from your hormone imbalance. You're a good candidate for electrolysis. Let's set up an appointment for you." Again, pointing out ways that you don't conform to gender expectations and pressuring you [01:05:00] into performing femininity and making you feel othered and rejected. Whether or not it's well intentioned. And then there's, "you really need to try harder to lose weight. It's not healthy. Are you exercising at all? You should eat less processed foods."

EAU: " You are doing it to yourself."

EW: " You're doing it to yourself." Assuming that someone's weight is solely due to poor diet or poor health behaviors not related to PCOS, and that someone's weight is entirely responsible for all their symptoms. "Oh, you have pain, you should try to lose some weight."

EAU: Also assuming that their weight is the problem at all,

EW: Yes,

EAU: like assuming that their weight, that their BMI is a problem because obesity is a quote unquote disease. Like, ugh, it drives me up the wall.

EW: And this, this weight bias in medicine can lead to disordered eating. Or maybe the doctor will say something like, okay, you're sure you don't wanna become pregnant. Well then there's not really anything you need to worry about

EAU: Oh gosh. That one gives me palpitations,

EW: a hundred percent. And this is, you know, as you described. PCOS is associated with other health outcomes, not related to fertility, diabetes, cardiovascular disease, high cholesterol, high blood pressure, fatty liver disease, endometrial cancer, metabolic syndrome. I mean, there's like

EAU: Yeah. Sleep apnea.

EW: Sleep apnea.

EAU: Yeah.

EW: um, the author of the Psychology of PCOS, who has the condition herself said that in the 30 years since her diagnosis, no doctor has ever told her about these other health consequences. And I get, you know, n of one anecdote, but still that is not a unique experience.

EAU: I, and I just have to say, this is where like I honestly was, so I'm a primary care provider. I care for people with PCOS all the time. I was so embarrassed by how little I knew about the extent of the metabolic complications and how important they are. First of all, regardless of BMI, second of all, like to at least screen for, despite how flawed our screening tools might be and in, in everyone, like I, it just, it, it is not as well known as it should be despite efforts to standardize these guidelines and get this information out there, and despite the fact that it is much better today than it was like prior to 2018.

EW: Yeah, I mean that's, it's very true. Um, and I, I have a, a study that, uh, was reported on, it was back in 2007, so prior to 2018, but it was testing US medical residents knowledge of PCOS.

EAU: I bet it was bad.

EW: Oh, they found that they scored on average 50%

EAU: Ooh,

EW: and that only a subset scored higher than 70%, like who were specializing in women's health. I think Uhhuh Uhhuh. That is abysmal for a condition that affects one in 10 people conservatively assigned female at birth. It's inexcusable. And that's also an underestimate, right? Like one estimate I saw suggested that 70% of cases go undiagnosed.

EAU: Wow.

EW: Yeah. Yeah. If you don't fit the classical clinical picture phenotype A and B, your doctor might dismiss you. They'll point out your weight and say, uh, but you're not obese. I don't think it's PCOS. You're thin, or, well, you're older.

Maybe your periods are just slowing down, even if they've been quote unquote "slow" your whole life. Delays in diagnosis for PCOS are exacerbated by race, by socioeconomic status, and by gender identity.

EW: The term "women's health", along with all the other gendered language surrounding PCOS illustrates this. But of course, this doesn't apply to all healthcare providers, and some people have really great experiences with their individual providers, but even for them, even for those providers, an overall lack of knowledge about PCOS is limiting. What might the trans non-binary experience be like for someone with PCOS? What do we know about hormone replacement therapy and PCOS? Is a healthcare provider equipped to answer those questions or willing to look for the answers? Do the answers even exist? There needs to be a shift in the way that we diagnose, treat, study, and talk about PCOS.

EW: We need to incorporate mental healthcare, do a better job educating healthcare providers, raise awareness with the general public, improve treatment options, conduct more research into every aspect of this, and have more compassion and self-compassion. Unfortunately, these changes won't happen overnight, but progress is being made by advocacy groups, by online communities where people can learn and share, and by some researchers who are trying to better understand this condition. And so, speaking of which, I'll turn it over to you, Erin, to tell us where we stand today when it comes to PCOS.

EAU: I can't wait. I have a huge surprise for you,

EW: Ooh, okay.

EAU: Take [01:10:00] this whole thing in these last 10 minutes and turn it on its head, and then drop the mic and walk away. Ready?

EW: Okay. Yes, please.

EAU: You said already most papers cite an estimated prevalence anywhere between five or six and 20%. Most of the newer papers, like the newest 2023 guidelines said maybe 10 to 13%, but, but we don't know. The prevalence is thought to be relatively homogenous across the globe with maybe slightly higher prevalence in people of Southeast Asian descent and Eastern mediterranean descent. What underlying that we don't know,

EW: Right.

EAU: and there's maybe some data that it's increasing in the recent decades, but it's very unclear to me whether this is related to any true increases in incidence or just increasing awareness and diagnosis or things like that. So when it comes to current research, you laid it out for us really nicely, Erin. There's a lot to be desired. For me, I kind of just was like, what do I wanna know about PCOS? Um, we know how much insulin resistance is a major factor, but we don't have any assays that can really measure insulin resistance. So I'd love, I'd love more research on that. and there's certainly people doing that and there are ways to measure it. It's just that they're not easy to do clinically. They're like very time intensive, labor intensive, expensive, so they can't be used. So then people are trying to come up with like, okay, what is something that we can use that, that like measures up to these gold standard versions. There's also a lot of work that needs to be done that is being done on like understanding some of this kind of higher level. What is this underlying cause? What is linking insulin resistance and this hyperandrogenism? Are these kisspeptins and other like peptides and receptors in our brain, in our hypothalamus, are those involved? Do we have a master regulator switch that we can find? That we could target? We don't know. Um, but a lot of people are working on potentially looking at other targets for medications. I mentioned GLPs. These are all the rage right now.

EW: Mm-hmm.

EAU: Um, GLP-1 receptor agonists. We need to do, uh, an episode on these. They, I know they, what would they would be targeting is in part this insulin resistance because what they help do is kind of regulate insulin release from our pancreas. And so there was a, study that came out recently that looked at GLP-1s alone plus really interesting combinations of GLP plus other medicines, including estrogen, um, for pCOS. And they found that in some, at least in this study, which was on mice and rats, I actually don't remember if it was mice or rats. Um, but they found a better treatment like alleviation of all of the various things that that they look at in mice and rats with PCOS, uh, then compared to metformin, um, which is very interesting, the GLP plus estrogen combination,

EW: Yeah, GLP, they, the effects are so broad. It's really fascinating and it goes like way beyond. It's like, you know, weight loss from GLP ones versus, uh, weight loss from not GLP ones. And it's like there are extra effects still. Like it's just like what's happening?

EAU: Well, and like the the cardio, the cardiologists are so stoked on them. The cardiovascular effects are so good. the kidney protection, the nephrologists love them.

EW: Advances in Care episode on GLP ones and cardiovascular disease and heart failure especially. So if you are interested,

EAU: Yeah. it's uh, it's pretty major. They're also still very expensive and any new drugs that have come out will gonna be even more expensive. Uh, so that's another thing to know. But here's where I wanna take this whole table and flip it over.

EW: Ooh,

EAU: Ready for this. We have talked so far exclusively about PCOS, polycystic ovarian morphology as a disease of people assigned female at birth, as in people with ovaries. However, polycystic ovarian morphology is not necessary to the definition, right, and in fact, the presence of ovaries themselves may not be necessary in the metabolic phenotype of PCOS. That's a quote from one of the papers because we see very similar metabolic abnormalities and very similar hormonal disruptions in terms of free testosterone, DHEAS, sex hormone binding globulin, looking at all of these hormones in both people assigned female at birth with ovaries and in people with testicles.

EW: All right, so

EAU: Aha.

EW: what's happening?

EAU: Happening, Erin? I dug deep into this because [01:15:00] there is a male equivalent that likely exists. However, It does not have a clinical definition. It does not have any clinical criteria. there are plenty of papers on it. Let's get into

EW: yeah.

EAU: We see in family members like male family members of people with PCOS, either siblings of, or children of people with pCOS, increased incidence in things like early onset androgenic alopecia, so male pattern hair loss before age 35. we also see increases in metabolic syndromes including insulin resistance, type two diabetes, dyslipidemia, hypertension, cardiovascular disease. And in studies that, have actually looked at this, we see a similar angiogenic hormone profile. We can see increases in things like D-H-E-A-S. We can see increases in anti-Mullerian hormone. Yes. Males also make it and LH and fSH and sometimes we see a, sometimes we see a decrease in free testosterone, but then, uh, an increase in these other types of testosterones and

things. So. Anyways, it is hypothesized based on all of this, that first of all, there is in fact a similar metabolic and hormonal profile that is essentially a male equivalent, a person with testes equivalent to PCOS, and that early onset male pattern hair loss is possibly one like physical visual marker for this syndrome, except that about 30% of people assigned male at birth have early onset androgenic alopecia. So does that mean that it's just not as specific as a marker? Does it mean that the incidence is higher? What? What does that mean? We

EW: are multiple causes of it that Yeah. Are not related to the syndrome. Yeah.

EAU: And when we look at like the actual gene loci that we know are associated with PCOS, we see those gene loci in these males that have these other symptoms. And yet when I for example, went on up to date, which is where I often go as a clinician, but also when I'm like, does this and did I just miss this? it is nowhere mentioned on the PCOS page when I, tried to look up like male equivalent PCOS. It does not, it's not a thing, Erin, because we don't have any test for it.

EW: or presumably very many treatments if somebody wants

EAU: It would be the same things in terms of like the, metabolic sym symptoms, right? so we'd be talking about, we'd be talking about metformin, we'd be talking about it'd be these other things. What would we need to do to treat the male pattern hair loss? Maybe, we do the, the same kinds of things that we would do in females, but yeah, we don't we don't have Erin we don't. We do not, this is not recognized as a clinical condition. I wanna make that very clear. but it is recognized in the, literature dating back a couple decades, at least a decade. Um, and I feel like this highlights, so PCOS for me, like the biggest takeaways that, I have from PCOS, aside from just like how much we don't know

EW: Yeah.

EAU: is first of all. How much what we think of as binaries in medicine are spectrums, right? And where we put our cutoff markers. What is abnormally high testosterone for a female? What is abnormally low free testosterone for a male? All of this is somewhat arbitrary, right? And we've known this for a long time, but it becomes so much more important when we're looking at a condition like PCOS, right?

EW: I find it very interesting, like this is, I think that yes, this is very revealing of, of the way that medicine considers bodies and binaries. Um, and I'm just like thinking about this, like the, the male version of PCOS. What does that like, that should be able to tell us more about the root cause of

EAU: should. Right? it should. If we started looking at it,

EW: looking at why, why aren't we looking

EAU: I mean, there are people who are right, 'cause these papers exist,

EW: but you said that this is mul, this is two decades older. People started

EAU: two might have been a, it's more than 10 years old, so two decades might have been a, an exaggeration. I don't remember when the first paper was.

EW: Okay. Okay. Um, because I feel like in this case then, the, the thing that really struck me about PCOS is that we are failing to capture people. We are failing to meet the needs that they have in many different ways. Sometimes that means we're not giving them the treatments that they want. We're not diagnosing them. Sometimes it means that we are. Giving them treatments they don't want and that, oh, the birth control actually is worsens your symptoms of anxiety and depression. Um, and also, I don't want periods so I don't need to bleed monthly. But we also, it's just like, [01:20:00] it shows our narrow view of this and how difficult it is to change these, to change these perspectives and to like broad and actually broaden a clinical picture of

EW: something

EAU: It also for me, highlights how stigmatized "women's health" is.

EW: A hundred percent.

EAU: Because If you label a disease polycystic ovarian syndrome, inherently, you assume it only affects people with ovaries, which means that we're ignoring it, we're dismissing it. We're not funding. Its research, which means that everyone's health is compromised because women's health affects men's health too.

EW: women's health is health. It's human health.

EAU: It is human health. Okay? And whether you have ovaries or whether you have testes, we should be looking at

EW: Mm-hmm. Mm-hmm.

EAU: So that's like my big rant.

EW: I feel like I have learned so, so much about everything, about medicine, about PCOS, but also about medicine and society and perspectives and, yeah.

EAU: I know, and it just, yeah, I, there's so much, there's so much still that we don't know, especially like you were saying about the, like long-term potential for complications post-menopausal P-C-O-S. P-C-O-S in testes, you can't call it PCOS. There's a paper that isn't yet published, actually it's, uh, printed as a pre-print. Um, so presumably it will be published soon, but I do have a link to it. That's about how we need to rename PCOS 'cause it's such a false. Name, like, it's such a, a misnomer. Um, and so we'll see what, what changes. Maybe, maybe it will change soon. What will we call it? I don't know.

EW: Someone was like this. I, I feel like I read something somewhere and I wish I had kept the quote in, but it was like the, this name is so ingrained in medicine that it was, it's going to be as as easy to change the name and get people to accept it as it is to find the ultimate cause, which will then force a name, rechanging or something like that, or a name change.

EAU: Oh yeah, I know.

EW: Yeah.

EAU: Well, if you wanna read so much more, uh, we can tell you so much about it or where to find it rather, uh, on our website.

EW: Yep. Um, okay. I, once again, the book, the Psychology of PCOS by Dr. Stacey Williams. Great book. Check it out. And then for like the overall history kind of part of it, there was a paper, I have a few, but there was a paper by Azziz and Adashi from 2016 called Stein and Leventhal, 80 years on.

EAU: I've got links to both the 2023 and the 2018 guidelines on the recommendations, like evidence-based recommendations for assessment and management. So those are both there. Um, two papers that I loved that were just overviews of PCOS. One was from the Lancet Diabetes and Endocrinology from 2022 just titled Polycystic Ovarian Syndrome. Ah. Uh, and the other one is

from BMJ Medicine from 2023 titled Polycystic Ovary Syndrome, pathophysiology and Therapeutic Opportunities. Um, and then those couple of papers that I loved about the male equivalent of PCOS, um, one was titled Male Equivalent, polycystic Ovarian Syndrome, hormonal, metabolic, and Clinical Aspects. And that was by DiGuardo uh, at all from 2020. And there's another one too from 2018. Um, so you can find the list of sources from this episode and all of our episodes on our website. Thispodcastwillkillyou.com under the episode, tap.

EW: Yep. You can. Thank you again to Logan for providing the firsthand account. We, we cannot, we don't have the words to thank you, but it means so much. Thank you. Thank you.

EAU: It does. Thank you so much.

EW: Thank you to Blood Mobile for providing the music for this episode and all of our episodes,

EAU: Thank you to Lianna and Tom and Brent, and Pete and Mike and Jess and everyone else at Exactly right for making all of this possible.

EW: Yes. Thank you. Uh, and thank you to you listeners. Uh, we hope that you also learned something from this, or I don't know. Yeah. Tell us. Tell us what you think.

EAU: if you knew all of this already. Wow. If that's impressive, teach us something. Please. And thank you as always to our patrons, your support means the absolute world to us. Thank you.

EW: Thank you. Well, until next time, wash your hands.

EAU: You filthy animals.