Episode 98 Transcript

Jaclyn (00:01.186)
Dr. Mohit Khera earned his undergraduate degree from Vanderbilt, an MBA and Master's in Public Health from Boston University, and his medical degree from the University of Texas Medical School at San Antonio. He completed his urology residency and male reproductive medicine fellowship at Baylor College of Medicine. And he holds the F. Brantley Scott Chair in Urology at Baylor today. Now Dr. Khera has specialized in sexual dysfunction.

Men's Health in Hormone Replacement Therapy. And he's also the director of the Laboratory for Andrology Research, the medical director for the Baylor Executive Health Program, and president of the Sexual Medicine Society of North America. So we're really lucky to have you here today, Dr. Khera. Thanks for joining me. So I'm really excited to talk a lot about men's health with you today. You're one of the nation's leading experts in men's health. And I want to start at the top with the topic that's getting the most discussion.

Mohit Khera (00:41.413)
Thank for the invitation.

Jaclyn (00:53.752)
that I see across the country, which is testosterone in men. So can you talk a little bit about why testosterone is such an important hormone for men? And then what have we seen? You you hear about this trend towards low testosterone in men and all these things that can cause it. And there's a lot of worry. So I'd love you to kind of break down what's real and what's hype.

Mohit Khera (01:12.335)
Okay, Jaclyn, there's a lot to talk about here and this is a great topic. So it's one of my favorite topics to talk about. I've been doing this now for 25 years and just testosterone. So let's go back at history. So how long has testosterone been around? People say, look, has it been 10 years, 20 years? It was first synthesized in 1935. 1935. And there's documents of using testosterone in men since 1935, even in testosterone in women. So I treat a lot of women with testosterone. We may get into that. And we've been using it since 1939.

Jaclyn (01:14.04)
There's so much.

Mohit Khera (01:42.007)
Initially, what we started using testosterone for was to help with symptoms. Low energy, low libido, erectile dysfunction, decreased muscle mass, increased fat deposition, depression, poor sleep. And as a patient comes in with these symptoms, testosterone therapy has been shown to improve or mitigate many of these symptoms. So that's been

great. But as we're getting into this new era of testosterone, we're finding out that testosterone is also important for your...comorbid conditions and there's five of them. We know that men with low testosterone are much more likely to have a heart attack Non-negotiable that's fixed right? No, low testosterone much more likely to have bone fractures osteopenia osteoporosis low testosterone is associated with Diabetes and obesity we know that those are conditions. We know that low testosterone is also associated with depression. We published a large paper on that and we know that there's an association. can't say causation, but lower testosterone levels are associated with Men with more likely having prostate cancer. So let's think about that for a second I can't think of another hormone another blood test that's associated with more comorbid conditions than testosterone It is the best barometer of a man's overall health. No question So if you're check one blood test in a man to predict his health today and what it will be in the future, check his testosterone level. And I think that every man over age of 40, every man over the age of 40 should have a testosterone level checked every single year.

Jaclyn (03:12.79)
It's so interesting because I've actually, I mean, I've done a lot of work in the fertility space myself and there's similar studies around like all-cause mortality and then several different conditions in men's sperm health, which is, you know, this one article that was published suggested that we should maybe even consider semen analysis as part of a wellness screening for men in their 30s and 40s. And I think that goes along with what you're saying because, of course, testosterone is a big part of sperm production as well as oxidative stress, mitochondrial health. There's a lot of other factors there, but, you know, it's...really interesting to me to talk about testosterone. think almost because the wellness space has adopted it so heavily and maybe over adopted it in some cases, then we see this pushback from conventional medicine. But what you're describing to me, when you look at safety, as long as you're staying within a good treatment parameter and you look at all the positive impacts, you know, when you're weighing an SSRI versus testosterone or, you know, when you're weighing a brand new medication out, for metabolic health versus testosterone, it seems like optimizing testosterone would be a very natural first step.

Mohit Khera (04:17.541)
Yep, I want to give you an example. let's talk about depression for a second. So back in 2011, I published a very large paper, 850 patients, multi-site throughout the country, looking at low testosterone and its effect on depression. And we gave all these 849 men a PHQ-9 questionnaire to look for depression. We found that 92 % of men who had low T had some degree of depression, whether it be mild, moderate, or severe.

Jaclyn (04:22.062)
Hmm.

Mohit Khera (04:45.359)
but 17 % of these men actually had severe depression. We treated them for one year with testosterone supplementation and we dropped severe depression down from 17 % down to 2%. But what was interesting is if a man was already on an SSRI, they also saw significant improvements in PHQ-9 questionnaire symptoms, suggesting that maybe there may be some synergy between SSRI and testosterone. Now, I am not advocating to treat major depressive disorder with testosterone.

But what I am advocating for is to at least check a testosterone in men who present with depression. And so when I give a talk to my psychiatry colleagues, I say to them, are you checking testosterone levels? And they say, no, you know, but I say you should because checking testosterone levels and replacing testosterone could help this man with depression. Now, they flip it on me and they say, okay, Kara, when these patients walk in with low energy, low libido and ED, do you ever screen them for depression?

Why do you assume it's low T? And I said, you're right. My colleagues in urology are guilty for not screening for depression. We just hand them the T. So it works both ways. If you're a psychiatrist, you see someone with these symptoms, check the testosterone. If you're urologist, primary care, and you see someone with these symptoms, not only should you check for low T, but screen them for depression. I think that's very important. Because everything you're describing today is synergy. In other words, T helps, I think, with depression. T helps with

Jaclyn (06:05.486)
Mm.

Mohit Khera (06:13.815)
obesity. helps, I believe, with cardiovascular disease. So it's synergy. And why not have that extra tool to help you with the comorbid condition you're trying to take care of?

Jaclyn (06:23.308)
Yeah, it's almost like optimizing thyroid hormone. mean, you're looking at like, are there root causes that could be contributing factors, even if they're not the sole contributing factor? I mean, I think it makes perfect sense. Yeah.

Mohit Khera (06:32.43)
I agree. And I do want to make one more comment about fertility, because you said something very important. You're absolutely correct. we know that Dr. Eisenberg showed a

wonderful study at UCSF showing that a semen analysis, if a man has a poor semen analysis today, is a predictor of cardiovascular events and morbidity in the future.

And even Tom Walsh at a Washington show that you know, it's also predictor of cancer You can predict someone with property get tested testicular cancer or prostate cancer So a semen analysis has a lot of predictive value of your current and future health as well So I think that's very important. Let's think about this healthier people are more fertile period I tell my patients that it's it's Darwinism survival of the fittest healthier people are more fertile. If you want to become more fertile, I want you to become more healthy. And if you are unhealthy, then it's going to make it more difficult. again, I think a semen analysis is a great other predictor of men's health.

Jaclyn (07:40.268)
Yeah, it's a really interesting concept and you know, really fertility is kind of the canary in the coal mines. It's one of the first areas that we see chronic illness show up functionally, you know, when people are trying to conceive and can't because they're in their thirties. Most other chronic illnesses don't present in a meaningful way until decades later. So it is, it's a really opportunity if that's identified to try to improve the underlying health parameters. So I want to start with like, cause you mentioned low T.

Mohit Khera (08:05.359)
Yeah.

Jaclyn (08:09.368)
How do you define low T for men? Because when we look at the metrics for labs, typically normal is considered the bottom fifth percentile for healthy men. But of course, some men don't feel their best, even if they're in the normal range. So functionally, how do you look at that concept?

Mohit Khera (08:25.251)
Yeah, so remember that the number of 300 nanogram per deciliter was arbitrarily chosen, right? There was just an arbitrary number to say, this is the number, we had to pick a number. Now, the reality is that every single person, men and women, we have our own number. You cannot assume that at 290 everyone feels bad and at 310 everyone feels good. That makes no sense. And I would say that the number 300 is actually quite low. And I was the head of an international consensus guideline.

In Spain and we raised ours to 350 and many other guidelines have raised theirs to 350. So I do think that many men who are symptomatic, who are at 350, even 360, I would give them a trial to see if they have improvement. Because a lot of it's based on our genetics. So we published a paper and we still do this today. When someone comes into my clinic, I take

their blood, I send it to a lab, I started a basic science lab in 2007 and we look at something called the CAG repeats. The CAG repeats are the sensitivity of the androgen receptor. And we show that those men with more sensitive receptors need less testosterone. Those men with more insensitive receptors need more testosterone to feel better. We're all very different, right? So I'm just not big on this one number fits all, and if someone has a level higher than 300 and is borderline, obviously look at the free tea, because maybe the free tea is low and that's a better predictor than total tea, but it doesn't hurt them to have a trial of the medication to see if they have improvement.

Jaclyn (10:01.432)
That's a really – I I love that you're bringing that up and receptor function and receptor number is so critical. I think people misunderstand even what a blood test measures, right? So when you look at testosterone in the blood, you're looking at total testosterone. Most of that's bound so you can measure free testosterone as well and all those two represent is the available fraction to cells. But it doesn't all act on cells. There's processes between being in the bloodstream and having and effect and maybe you can describe that a little bit more for people. Like what happens at the receptor, you know?

Mohit Khera (10:32.388)
That's very important. Let's talk about it. So what I'm referring to when I talk about the sensitivity of the receptor is that if we measure something called the CAG repeat and we count them, if the CAG repeat is greater than 27, that patient has an insensitive receptor. But all of us have different degrees of sensitivity. It's not like an on-off. Maybe yours is 30%, maybe yours is 80%. So the sensitivities can vary. And that's very important. Now, I'll tell you the answer to your question in the context of a story, and this will really help.

There was a medication called Natesto that was out for many years. And this was the intranasal testosterone. And when I looked at the PK curves on this drug, I said to myself, this is never gonna work because it shoots up quickly in the body and then it comes down very quickly. And it was probably in the body for an hour or two hours, in the bloodstream is what I could see. And I said to myself, if it's only there for two hours, comes down, you do it three times a day, that is not gonna work. But patients were coming in feeling better.

Jaclyn (11:20.95)
Yeah.

Mohit Khera (11:30.187)
and I would check the blood and the levels were low, but they were feeling better. And so I quickly reached out to one of my colleagues who's really amazing, Dr. Dinsa, who's done a lot of basic science work in this. said, what do you think? He said, look, Mo, all that matters

is the activity that's going on in the receptor level. So if I have a bunch of testosterone, it binds to the receptor and the testosterone in the blood goes down. It doesn't mean that the receptor is not working. It's continuing to do its action and work despite the fact that the level in the blood has come down and that made a lot of sense to me. So we always assume if the blood level comes down, nothing's happening at the receptor level, but that's not true. It's already been bound, it's already been activated, it's doing its thing, right? So there are patients that you may see a discrepancy between the way they feel and what the level is, and I think that's a very important point.

Jaclyn (12:18.81)
Now, do you find that there's – so above 350 – well, 350 is kind where you think about diagnosis of low testosterone. But of course, we see people who are, let's say, quote, unquote, optimizing testosterone. I see it up like 600, 800, 1,000.

Mohit Khera (12:33.189)
Absolutely. So remember, everyone has their own number. Maybe that patient's number is 600. Maybe it's 700. And if you take a patient from 350 to 500 and he's not feeling what he needs to feel, take him higher. Right? And I typically take everyone to the upper quartile of normal. 800. Still normal, but 800. Why? Because I know that I will cover almost everybody's set point. Right? So if I take it higher,

Jaclyn (12:57.774)
Mm.

Mohit Khera (13:00.357)
I should be fine. Now look, if someone comes in and he says, at 550, I feel amazing, I'm gonna leave him alone. You feel amazing? Great, that was our goal. But if you're not feeling amazing, or what you're supposed to feel, I think the biggest mistake is, well, Mr. Smith, you're at 450, your levels are normal, so unfortunately, it has to be something else. No, I think you can salvage 30 % of patients who say they're not responding to make them responders, by raising their levels into the normal range. Now, let's be fair, know, low T has very nonspecific symptoms.

Jaclyn (13:29.016)
Mm-hmm.

Mohit Khera (13:29.565)
and maybe they are suffering from something else, but I wouldn't give up on tea until they least took them to the upper quartile of normal and then look for other symptoms if they're not feeling better.

Jaclyn (13:40.716)
Yeah, I love that you described that because the normal range is so broad for testosterone. you know, if they're just in the very bottom of it, they might not feel great. It'd be like taking a man with a size 12 foot and putting him in like a 9.5 sneaker. It might not be a fit even though a 9.5 is the normal range, right? So I love that you're, you know, describing that so clearly because I think there is a range. Is there like an upper limit where you start to get concerned or are you concerned, are men getting too much testosterone these days in some of the means of prescribing?

Mohit Khera (14:12.133)
Yeah, let's talk about it. Because some of the medications, the way they work, inherently take you super physiologic at the beginning, right? So if I use an injectable or if I use a pellet at the beginning, you will be somewhat super physiologic, but then you come down into the normal range and you're riding that peak and trough. And so you have to go high in order to keep that level normal for that period of time. And so slightly physiologic, makes sense particularly at the peak. You don't want to be something superficial logic You don't be superficial logic at the trough that would be a problem, right? So at the peak I accept a superficial logic So I think that's very important now There's one interesting concept you should think about if you look at the guidelines and the guidelines say that you should be between our guidelines in American your logic say 450 to 600 that is the optimal range you want to put someone in and then the second paragraph will talk about the

Jaclyn (14:47.325)
Mm-hmm.

Mohit Khera (15:09.573)
It has to be less than 300 to make the diagnosis. So I'll give you a really interesting example that happened to me the other day with the patient that came in. He said, what am I shooting for? I said, you really want to be between 450 and 600 according to the AUA guidelines. And I said, he said, well, what's my level? I said, well, you're 370. I said, okay, well, can I get treatment? I said, well, you that's considered normal, so you can't get treatment. He's like, well, wait a minute. So I'm supposed to be 450 to 600, but I am, sorry, but you're not going to put me there because you're saying that I'm normal.

You choose. You gotta choose one way the other. And I thought to myself, he's right. you know, if we're telling everyone the normal range is four, we wanna get you to 450 to 600, but we won't treat you between 350 and 450, 300 and 450, what is that man supposed to do? What is he to do? Right, right, but what is that man supposed to do? He's like, you're telling me should be 450 to 600 to be optimal, but you won't treat me because I'm too good, not, you know, so never made sense.

Jaclyn (15:42.734)
Hmm. Right, that's a tricky one. It's a difference between like normal and optimal, ultimately. Right?

Mohit Khera (16:08.165)
So really, I will take patients even up to 450 and give them a trial for three months. Again, that's off-label, that's not what the guidelines say, but I do find that if they're symptomatic and you're trying to put them between 450 and 600, let's see what happens when you put them to 450 and 600 for three months. If they don't respond, if they don't have symptomatic improvement, then I stop. I I say, look, the goal is not really so much the number per se, the goal is to have you feel better. There's an exception.

If someone's really low, like less than 200, I get worried about bone, cardiovascular process. So there is an exception to my rule. If you're really low, I am worried about you.

Jaclyn (16:40.718)
Yeah, I've only seen one case of like, it was actually osteopenia, not osteoporosis in a man, but he had undiagnosed low T probably since his 20s or teens. I mean, think it's just, it's problematic.

Mohit Khera (16:53.509)
Yeah, yeah, yeah, low bone fracture. In the instance of a low impact bone fracture, you are obligated to check a T-level in those patients because they have a higher risk of being hypogonadal.

Jaclyn (17:06.126)
So what are some of underlying causes that like why are we seeing so many men with low testosterone these days? Has this always been a problem? Is it getting worse?

Mohit Khera (17:13.455)
Yeah, decade by decade we're going down in terms of T levels, right? And I always put this graph, I show a graph of the T levels coming down decade by decade in men, and I superimpose that graph decade by decade on obesity and diabetes and metabolic syndrome. And they mimic each other. Because remember, there are comorbid conditions that shut down our T. And the biggest comorbid condition is obesity. So obesity, fat cells aromatize, the T from testosterone to estradiol, obesity causes an increase in leptin, increases in increase in cortisol, and that all shuts down our testosterone level. So as we become more obese decade by decade, it is not surprising that our T levels will fall. As we also become aware that diabetes is a risk factor for hypogonadism as well. And what's sad is the fastest growing sector of obesity in the US is the adolescent, which is growing at 4X. So we see younger and younger men.

Jaclyn (18:06.638)
Hmm.

Mohit Khera (18:11.011)
If it's an older man and the T goes down, okay, I get that. But the younger man, that results in infertility, right? Because they're trapped kids, right? And so we see that every decade. What are other risk factors for hypogonadism? Stress. So stress will shut you down and shut down the T levels. We know that sleep, you you need to sleep. Lack of sleep, poor sleep will shut down the production. And we know that diet and exercise can have an impact as well. So as the population becomes more and more unhealthy, remember,

Jaclyn (18:16.75)
Mm. Right.

Mohit Khera (18:39.567)
Testosterone is the best barometer of a man's overall health. If the population is becoming more unhealthy, it is not surprising that the T-level will come down every decade. Not surprising, you know?

Jaclyn (18:48.11)
That's interesting. Now has the normal range changed over time as the populations change? Like you think about that if the normal, what are the, you said the normal was above 200, 250?

Mohit Khera (18:59.814)
Well, 300 to 1,000 is the normal range, right? And that's been established for a long period of time.

Jaclyn (19:02.85)
Okay. So they haven't modified that because I think about the population of people they test to determine reference ranges is probably less healthy now than 50 years ago.

Mohit Khera (19:09.455)
Yeah. The only one is that the endocrine society has dropped the normal range on the cutoff to 264. So it is a little bit lower. All the other societies still use roughly 300 to 1,000. But it's unfortunate because when you drop the normal range, the cutoff, then what happens is if someone comes in at 270, which we know is low, they'll say, no, you're normal, so we can't treat you.

Jaclyn (19:26.71)
Yeah.

Mohit Khera (19:41.419)
And so you're excluding more and more men that would benefit from testosterone therapy.

Jaclyn (19:46.7)
Yeah, so it's really a challenging, a challenging enundrum to be kind of caught in the middle. So let's talk a little bit about the main symptoms that men come in with presenting that they've maybe read about that are low testosterone. Like erectile dysfunction is a big one that I know you treat quite a bit. Let's maybe start there.

Mohit Khera (20:02.415)
Yeah. So let's start there. So the symptoms are the following. So ED, erectile dysfunction, low libido, increased fat deposition, decreased muscle mass, poor sleep, some depression. Those are kind of the most common symptoms that you're going to see in men. And many men, when they come in, they say, you know, I think this is a natural part of aging because it sounds like I'm just getting older, but no, it's actually the exact same signs and symptoms of low T in men. And replacing the testosterone can help. I don't want them to think that

Jaclyn (20:25.422)
Mm.

Mohit Khera (20:31.481)
You take the tea and the world is great, right? That's very important. Some patients say, look, I took your testosterone, my libido's still low, I'm still tired, I feel terrible. I say, well, tell me about your diet, exercise, sleep, stress reduction. What are you doing to help me in combination? I call this Meet Me Halfway. I will optimize you medically. You will help me with diet, exercise, sleep, and stress, and then we're on fire. Everything's working. But for you to take the testosterone, continue to eat potato chips, not exercise, and expect everything perfect is really gonna be a struggle. So it helped meet me halfway. So those are the main signs and symptoms, but I do put everyone on a very intense diet, exercise, sleep, and stress reduction program. So, Jathlyn, I don't have a pill on the planet stronger than diet, exercise, sleep, and stress reduction. I don't. Yeah, I mean, think about it. And if you and I, and anybody who decided to focus on just one of those, just one, would have a profound impact on your quality of life.

Jaclyn (21:16.96)
No, can you come up with one? It'd be so helpful. Yeah.

Mohit Khera (21:30.029)
Now let's imagine if you did all four, right? If you did all four, and we've published on this, we've shown a lot of publications on exercise alone as monotherapy for reversing ED. Sleep

improves at T levels in sexual function in men and women. Diets, particularly the Mediterranean diet, but there's other diets as well, that can reverse ED and sexual dysfunction in men and women with no pills, right? So these are the true cures. Everyone is looking for the magic but that is not, these are the two cures in my mind.

Jaclyn (22:02.776)
Well, I love that because you really, you know, there's a path to getting well and the testosterone supplementation or replacement really is a supportive tool. If you're doing those lifestyle factors, I mean, how can you work out if your energy is really poor, right? So it's like if you can temporarily raise it through medical support and it can, you know, influence your ability to tackle it at the root, that's medicine at its finest.

Mohit Khera (22:16.986)
Right. That's medicine and I think that we can use patients who come in with low T to motivate them to consider changing their lifestyle modification. We have the opportunity, right? It's a window, right? So someone comes in and they say, I have low T, I say, okay, I'm not gonna just give you the pill. This is my window to change your lifestyle modification, which will not only improve your T levels, but it'll improve your health span and your lifespan as well. We didn't talk about this, but this is very important.

Jaclyn (22:39.694)
Mm-hmm.

Mohit Khera (22:56.449)
Everyone in what you talk about is talking about lifespan and healthspan. You've heard of this over and over again. Jaclyn, you and I, I assume we want our healthspan to last as long as our lifespan. Like I don't want to live till 80, but be healthy only till 60. Right? That is not what I want. That is... Right. I want my healthspan to last as long as my lifespan. But there's a new concept that I came up with and I want to introduce it. It's called sexspan, right? So the sexspan...

Jaclyn (23:06.787)
That's right.

Jaclyn (23:10.432)
Right. It's the opposite of what we want.

Mohit Khera (23:24.163)
is the portion of your life where you'll have the ability and the desire to engage in sexual activity, right? Well, I'm gonna assume most people want their sex ban to last as long as their lifespan. Yes, particularly in men, they say, look, it is unacceptable for me to have my sex ban at 50 and my lifespan at 80, and that is not gonna work, right? So everyone wants

our sex ban and our health span to last as long as our lifespan. And how do you do that? You do that.

Jaclyn (23:34.158)
Mm-hmm.

Mohit Khera (23:51.023)
by diet, exercise, sleep, and stress reduction, and you do that today because if you decide to do it later on when the problem already occurred, it's too late, right? What you do today will dictate your health span and sex span lasting as long as your lifespan. That's a really good point.

Jaclyn (24:06.306)
I know, it's like how can you motivate people to start earlier before they're symptomatic? That's one of the toughest things is.

Mohit Khera (24:13.509)
Right, right, how do you motive them earlier? And in my business, particularly younger patients, if a man is 18 to 40 years old, and I remember when I was 30 years old, there's no way I was gonna go in for an annual blood pressure check. There's no way at 30 I was gonna say, let me go screen my hemoglobin A1c today and see if I have pre-diabetes. But you know that there's a good portion of men in that population that have diabetes, that have a cold cardiovascular disease, and actually have hypertension.

Jaclyn (24:27.778)
Mm-hmm.

Mohit Khera (24:42.533)
But they're still not coming in to get screened and unfortunately that 30 year old man will probably come in at 40 when he's symptomatic. So I call that 10 years of damage. I call that area under the curve. Wouldn't it be amazing if I met him at 30 and changed the course of his life as opposed to 40 and I saved the 10 years of damage? Well, it's possible. And the reason why it's possible is because they're gonna come in for sex. If a man has ED, he will be at my front door tomorrow morning.

Jaclyn (24:47.224)
Mm.

Mohit Khera (25:11.549)
He will not wait a minute longer to get that treated. And if he comes in for ED, we know that 15 % of them could have a cold cardiovascular disease. We know they're two times more likely to have diabetes. Screen and treat immediately. if you do that, you're actually doing a

great service. The mistake is to hand the Viagra or hand the testosterone and say, I'll see you later in 10 years when you have the cardiovascular event. You have a window now because they will come in for sex. They were out.

Jaclyn (25:41.806)
I'm so glad. I'm like so, glad you bring this up. So I was going to ask that question because with erectile dysfunction, you have hormonal contributors, but sometimes it's more of a cardiovascular contributor. I was going to ask you about that. I'm so glad you brought that up because again, it's like that canary in the coal mine, that early opportunity that comes your way to really help people see that. Are you seeing men, younger men coming in with erectile dysfunction? Like has that changed in your practice?

Mohit Khera (25:53.53)
Yeah, the study-and it's more common. used to think that younger men are more likely to come in because of psychogenic ED, but now it's coming in for organic ED because the population is becoming more and more unhealthy. And so I do see more organic true causes. The study that made the biggest impact on me was Ian Thompson's study. Ian Thompson ran a trial called the Prostate Cancer Prevention Trial, and he looked at roughly over 4,000 men, healthy men, and they came in and he followed them over time. And what he found was that if a man gets ED today, he just develops ED today,

Jaclyn (26:10.424)
Right.

Mohit Khera (26:35.205)
15 % of them will have a heart attack or stroke within seven years. I said wow 15 % will have a heart attack or stroke within seven years and then Montorsi out of Italy said found the same thing men with who have cardiovascular vent typically have ED three years prior now people will say why what is the mechanism for this and there's two main mechanisms and there's the first one called the arterial diameter theory and if you remember from physiology from medical school 50 % occlusion of a vessel, 50%, starts causing end organ damage. So we know that the penile arteries are one to two millimeters. The coronaries are three to four millimeters. The carotid are five to six, the peripheral seven to eight. So if you're going to start occluding an artery first, you occlude the penile first. Then you're much more likely to get ED before heart attack, more likely to have a heart attack before a stroke, more likely to have a stroke before peripheral vascular disease. It follows the order because of the occlusion.

Jaclyn (27:25.367)
Hmm.

Mohit Khera (27:34.309)
So it is telling you something when someone has ED that they're having an increased risk. Another great study out of Greece, they were looking at echocardiograms and coronary cathing these patients who came in with ED. 20 % of men who walked in, 20 % on coronary cath, just walking for ED, had some degree of one vessel, two vessel, three vessel occlusion. So I think to myself, one out of every five guys I'm just handing the Viagra to, actually have a cardiovascular event that is just looming. And what am I doing by just hitting the viagra and letting them go? So ED is the sentinel marker of a cardiovascular event. A man gets ED, they should be screened for cardiovascular events.

Jaclyn (28:06.734)
You...Well, it really brings to light the risk of some of the online, know, send a text message, get a prescription in the mail like HIMS and services like that that are aimed at convenience that are, you know, driven by VC funding and all their great business opportunities. But I think about how many of those men never see a physician and actually get screened.

Mohit Khera (28:23.684)
Yes.

Mohit Khera (28:39.299)
Yes, I agree. Listen, there are advantages of online. Online do have advantages of it's discreet, they have access, they can get the medication. Remember that people who have sexual dysfunction, I call it suffer in silence. They just live with it and then have this ability to get the medication is great. But the downside is exactly what you said. It's typically done in what we call an asynchronous manner. So it's not done like you and I talking like this. It's I feel something out, someone reads it, they approve it.

Jaclyn (28:51.214)
Mm-hmm.

Mohit Khera (29:07.161)
and then they send the medication, right? So it's not the ability to even see the patient. And so there are some disadvantages. And one of the disadvantages is not capitalizing on the fact that we should screen for cardiovascular events, we should be able to screen for diabetes, we should have a discussion on lifestyle modification. I do think that these online HIMS enrollment are trying to do a better job. They're understanding and realizing that. But you can't substitute sometimes the interaction, the personal interaction for these types of things that we're talking about.

Jaclyn (29:25.454)
Yeah, absolutely. Well, I want to shift gears a little bit and talk for a few minutes because a lot of our listeners are female about testosterone in women. Can you talk a little bit about the importance of testosterone in women?

Mohit Khera (29:44.004)
Yes, Yes, first of all, we've been using testosterone in women since 1939. And if you look at some of the earlier studies, even published by Goldblatt, many of these physicians who wrote about giving testosterone to they talk about significant improvement in quality of life and libido. Currently, you and I can walk into Walgreens and we're gonna say, show me all the testosterone for men, FDA approved, and they'll put a dozen or more on the counter. You'll say, show me all the testosterone for women, and they have nothing not a single FDA approved testosterone product for women that is terrible I that is not fair and I just got back from Australia last week You can walk into Australia and you can ask for testosterone for women from their Walgreens and it exists You pay your copay and she walks in and she gets it's called androfem. No issue, but in the u.s We still to this day. I cannot believe do not have an FDA approved product for women. Let me tell you something very interesting women make way more testosterone than estrogen

Jaclyn (30:22.798)
Hmm.

Mohit Khera (30:46.829)
in their body. They make up four to five times more testosterone than estrogen. why can I, let me backtrack. Any hormone that a woman doesn't make, I am allowed to give it to her with no controversy. She has less thyroid, I can give it to her. Less estrogen, most people say yes, now you can give it to her. Progesterone, cortisol, any hormone she makes, I'm allowed to give it to her. But for some reason, if she has low testosterone, there's a stigma that you can't give it to her because it's going to be dangerous, right?

Jaclyn (30:47.598)
Mm-hmm.

Mohit Khera (31:16.517)
understand that. She makes it, she makes it one of the most, hormones she makes, now she's not making it, but for some reason I can't give it back to her? That makes no sense.

Jaclyn (31:25.07)
It doesn't make any, it really doesn't make any sense. And it's been, what year was the first FDA approved indication for testosterone women? It wasn't very long ago.

Mohit Khera (31:33.253)
Yeah, so well in the US we still don't have one, that's scary, and it was in 2002 when Intrinza, which is a patch, was almost about to get through the FDA and they had some very good data. They even had some cardiovascular data in their phase four trial. They very good data showing that not only was safe but effective. But you and I know exactly what was happening at that same time. That was when the WHO published that same year that estrogen and progesterone caused cardiovascular events and breast cancer.

And immediately that year, the FDA cut it. They're like, we're not gonna approve it. And so even later on, there were medications that tried to get approved for testosterone for women through the FDA that actually got shot down. And there's some now data to suggest or information to suggest that we're gonna, I know another company that's gonna try again. So we gotta get it through. My daughter, I was having dinner with her the other night she said, so let me get this straight. Men can go to the Walgreens and pay a $10 copay and get it.

Jaclyn (32:05.879)
Hmm.

Mohit Khera (32:31.717)
but a woman has to go to Walgreens and pay $400 because there's nothing covered and she has to pay the cash price. I said, yep, that's So I took my wallet I was like, that's exactly right. Currently that is the case in the US. And she said to me, she said, it's not fair. And I said, you're right, it's not fair. Yeah.

Jaclyn (32:37.614)
Flash will get me started. Yeah.

Jaclyn (32:44.974)
Now the thing that's so interesting about it is now, I I can understand that there could be ethical considerations for like safety studies for testosterone in females, but now we have gender affirming care where the intent is to increase androgen effect. And so we have organically grown the body of data that shows exactly when most women begin to get androgenic side effects and safety data around that process too. it is interesting because we talk about that a lot. We look at that data a lot because it really can inform provider's care to know what a safe dose might be for a woman.

Mohit Khera (33:26.021)
And we use 10X, right? So I use 10X. If we're doing transgender care, we use 10X. We don't see an increased risk in cancer in that population. We don't see any major adverse, and we've been doing this now for many years, right? So we don't see an increased risk. But let's take it back to the root. Why don't we have research in women for low testosterone? I

mean, that's a bigger fundamental question. I mean, we should. If a woman makes this hormone, now she's deficient. That's something she makes.

Jaclyn (33:48.579)
Mm-hmm.

Mohit Khera (33:55.909)
and I want to give it back to her, wouldn't you think that we would spend a lot of time, since we started in 1939, investing in research in testosterone for women. Now let's look, many of us off label have been doing this for many years. We give a lot of women testosterone. I've been doing it for 17 years, giving women testosterone. They benefit. They tremendously benefit. It's not just libido. It's energy, muscle mass, sleep, some depression. We know that studies looking at estrogen plus testosterone tend to be more effective than estrogen alone when it comes to building mineral density. So yes, we do need more research, but I can tell you anecdotally what we see clinically, these women definitely benefit.

Jaclyn (34:35.694)
So for women with hypoactive sexual desire disorder, that is one of the reasons why testosterone can be prescribed. It's the only reason, right, that it can be prescribed.

Mohit Khera (34:43.311)
Well, for two societies, right. Yeah, so the ISHWISH has put out their consensus statement, and so did the global testosterone consensus statement. And the global consensus statement is adopted by many other international societies. And in those statements, if you read it, the only indication now is for HSDD, hypoactive sexual desire disorder. So if a woman is low libido, you can use the medication now. Why do I believe that other indications were not in there? It's because we don't have the studies.

And if you don't the studies, you can't promote it. But again, the lack of research sometimes is not enough for me to say then you can't give it. And I would say that, look, I'm a big proponent on safety. Don't get me wrong. I think something should be safe. And I think it has to be effective. But I think that what we've seen for decades in providers that have prescribed this medication is exactly that.

Jaclyn (35:12.782)
Hmm.

Jaclyn (35:23.106)
Mm-hmm.

Mohit Khera (35:42.041)
We've seen it to be safe and effective.

Jaclyn (35:44.93)
What other indications have you seen smaller studies in that suggest that in the future, 10 years from now maybe, there may be other approved indications for testosterone in women?

Mohit Khera (35:52.529)
depression. I've seen, because you know, as I mentioned to you earlier, we have seen significant improvements in men with depression. I've seen some studies with women as well. Men and women are not that different when it comes to certain conditions. Like I don't have, I can't say well SSRIs are meant for women but not for men. Like there's some biology that is very similar between men and women, you know, and when we talk about neuro steroids and transmitters in the brain for depression, the mechanism seems to be the same.

Right? And so the medications and the benefits seem to be the Muscle mass seems to be somewhat the same. If you give a man or a woman testosterone, they will see an increase in their muscle mass. Right? I think that's fair. But there's certain conditions that I think that, you know, do make a difference. I do think that testosterone helps with decreasing fat deposition, obesity, increasing muscle mass, depression. I do see improvement in sleep in men and women who take it. That means it needs more literature and more research. But these are some areas that, you know, I really feel that we have to invest in testosterone for women. We just finished the Traverse Trial. We have to talk about it. I was one of the nine that ran that trial. I was on the steering committee. I did it for six years. And this trial is the largest trial ever published in men receiving testosterone. The reason this trial came up was in 2015, 2014, there was some concern that testosterone may increase the risk of a heart attack. Okay.

So the FDA in 2015 said, okay, if there's some signal, we would like to have a large randomized placebo control trial showing that testosterone does not increase the risk for heart attack. And it was called the Traverse Trial. 5,246 men randomized testosterone gel placebo. We followed these men for four years and what did we find? No increased risk in cardiovascular events. It was 7 % in both arms.

Jaclyn (37:44.182)
Hmm.

Mohit Khera (37:47.597)
Now there were two urologists on that team, myself and Dr. Ian Thompson, and we actually put in prostate cancer in there also. We actually had six other sub-studies. Prostate cancer, BPH, no increased risk of prostate cancer, no worsening of urinary symptoms,

improvement in libido in men, that was fantastic. So we were able to get this large trial. It was unbelievably expensive, and it took a long time, but we got it done. Now, I'm not, I don't, I would love to have a very similar study in women, like I would, but I don't think that this was funded by industry and that's how the money came from. But we should have larger studies in women, at least some studies, because I think that the studies will be positive and I do think the studies will show that it will be safe and effective.

Jaclyn (38:23.886)
Hmm.

Jaclyn (38:35.052)
Yeah, and interestingly, I think that consumer awareness for even in women around testosterone has increased so much that, you know, I'm putting this out there for anyone. Maybe we can get that funded for you. But I think the market is getting there where this could be something, you know, if it proves to be effective for women that they'd be very interested in.

Mohit Khera (38:45.444)
Yeah.

Mohit Khera (38:52.504)
Yeah. Yeah, Jacqueline, think about this. When I look at post-menopausal women and they come in, you know, they're 55, I say, man, what are you suffering from? Tell me your symptoms. And she said, well, I have low energy. I'm a little depressed. I'm not sure on my nose, increased fat, truncal fat. I'm looking at decreased muscle. I'm not sleeping as well. I say, well, yes, those could be signs of menopause. That's true. They are but they're the exact same signs and symptoms of low T in women. It's identical. So the problem is that most clinicians will only focus on estrogen and progesterone, but I call it the triangle. The triangle is testosterone, estrogen, and progesterone, T, E, and P, TEP. And I said, you're not focusing on the T, you're missing one third of the triangle in her treatment algorithm because she's telling you these symptoms.

Jaclyn (39:23.69)
Exactly.

Mohit Khera (39:49.433)
and they're the exact same symptoms of low T, and she has low T, replacing it will help.

Jaclyn (39:54.83)
Yeah, I can't disagree with your statement at all on that. And we do see some providers, particularly in the pellet space, that do testosterone first for women because, of course, testosterone converts into estradiol as well. you know, there's – I mean, that's

controversial, but there are a cohort where they say, well, you're going to make estrogen from testosterone and similarly, you're going to help with a lot of that – symptom picture.

Mohit Khera (40:18.277)
Right, but remember the conversion is 0.3%, so it's a small amount. And so if you are going to need that, you're going to have to have a very high level in most women of T to get the conversion to E. Why not just give her the E? If you're just, I don't get it. if you, if you, I mean, just give it to her. If you're, if you're hoping she's going to convert it to have enough, great. But if she doesn't convert enough, then you can supplement it. Right. And remember, she has a uterus, you got to give her progesterone anyway. Right. And if you give her...

Jaclyn (40:20.748)
Right, very small. Right, many do.

Mohit Khera (40:47.845)
back. It's such a simple concept. She now is low in testosterone, estrogen, progesterone, and I will give it back to her in the normal range. Nothing fancy. Nothing fancy about what I just said. It's the same concept. She's low in thyroid today. I'm going to give it back to her. She's low in cortisol today. I'm going give it back to her. Same I use in men. Any kind of hormone. He's low in X. I'm going to give it back to him. Same concept. And guess what? They feel better.

Jaclyn (40:58.648)
Hmm. Yeah.

Jaclyn (41:14.52)
Mm-hmm, that's right. Now with women due to, you know, insurance coverage and things like that, do you ever use DHEA as an alternative?

Mohit Khera (41:22.691)
I do in younger women because DHEA actually works fantastic in women, not in men. It works much better in women. And I compound it and I'll use 10 milligrams and they'll have them convert their own. So in younger women, I say, look, you're premenopausal. Let's sort of see if we can make it naturally and kind of use a 10 milligram. And we can always adjust. It works. DHEA will convert to T and you can get a very good level in these women if you need to. So I use DHEA quite a bit in younger women.

Jaclyn (41:48.686)
Great. Well, this has been a really awesome eye-opening conversation. I'm so glad we had the chance to get you on the podcast today. So thank you so much for joining me. If people want to learn more about you, get more education, learn about your practice, what's the best place for them to do that?

Mohit Khera (41:55.365)
Thank you. I have a website and I try to put out a lot of information. put out newsletters, so it's drmohitkira.com. You can get information there. Instagram, put a lot of information as well on social media, Dr. Mohitkira. That's, think, the best way to get the information. And also, there's a society that I want everyone to know about. It's called the Sexual Medicine Society of North America, SMSNA. It's incredible. The resources, smsna.org, the resources on that are ridiculous. Just information, testosterone, sexual dysfunction. Ishwish is another fantastic society as well.

Jaclyn (42:38.35)
Great, we'll make sure we drop those in the show notes for everyone. if you guys enjoyed today's podcast, please make sure you subscribe to our channel. Follow us on social media at DutchTest on Instagram and tune in next Tuesday. I hope you join us every Tuesday. We get great conversations like this. Today was really super interesting. So again, thanks Dr. Kara for joining us.

Mohit Khera (42:58.309)
Thank you, Jaclyn.

Jaclyn (43:02.252)
That was awesome. I learned a lot. was great. I loved talking with you. I know you've done some work with us before, but I've never had the chance to actually have a conversation with you. So I really appreciated it.

Mohit Khera (43:03.371)
Thank you.