If you think about pregnancy and reproductive life from infertility to preeclampsia to maternal mortality, we have a lot of problems in kind of that period of time during the lifespan. And then you think about midlife and the onset of menopause and its association with everything from an increase in cardiovascular disease to a decrease in cognitive function.

And so really across this lifespan, for women, there are many disorders and conditions that we just haven't attended to.

Stephen Calabria: Why haven't we attended to them? Why are they so challenging to treat?

Michal Elovitz: The same reason you asked me what women's health is, right? It is an understudied, unfocused, and it all really, without sounding too trite, stems from this misogynistic view that we have of the world.

And so, women are not centered. Women's science is not centered. It is understudied. It is underfocused.

Stephen Calabria: You've said, both in your research and today that so much of the research that doctors have collected has been disproportionately done on and about men. How does the gap in data collection affect treatment, especially of chronic diseases affecting women?

Michal Elovitz: So, there's a lot out there about cardiovascular disease, right? Number one killer of men and women, depending on what age group we're talking about. For years, the idea was that women should take aspirin, right?

Low dose aspirin to prevent cardiac events, because that's what the study showed. It's kind of changed now, but let's go a few decades ago. If you look back at those trials, though, they were almost exclusively done in men. So our assumption was that women react the same way to men, but we know that's not true.

We know there's sex-specific biology. We know there's so many difference in the physiology of a female versus a male. And yet, we expected the treatment to have the same preventive effect, and it turns out it absolutely doesn't.

Stephen Calabria: Who would ever have made that determination without actually looking at the data and studying it?
Michal Elovitz: I could tell you so many stories. There was a story, which I won't get into about a drug, um, I'll get into a little bit, but about a drug that there was a question about whether it would cross the placenta. So I went to the people who invented the drug and I said, well, first just tell me, what, did it go to the ovary?

How was it, how did it reach the uterus? At what time span does, et cetera, et cetera. And with a complete straight face, they said, well, we've only done the study in male mice. And I was like, alrighty then. So, again, patriarchal misogyny, I mean, people like to throw these buzzwords out, like, they're just kind of comments and a political stance, but it really has formed how we think about healthcare for women.

Stephen Calabria: That's the, the research side. On the patient side, are there any patient stories that come to mind when someone came in and they were not able to get the care they needed, perhaps because the research wasn't there, the, the treatment wasn't there? Does anything

Michal Elovitz: Every single patient I've ever seen, I've had this with. So, I ran for a number of years a prematurity prevention clinic and over doing it for over a decade, there were women I saw twice and they would come in and say, so Dr. Elovitz, tell me what's different this time. How are you going to prevent me from having a 24 week baby? And the answer would be, I'm trying, but I don't know.

I don't know, there's not enough out there, there's not enough being studied in the right way, so there, there are some things being studied, but unfortunately they're not, some of the clinical trials, some of the therapeutics that we use to improve care for women are not based on science. And so they are doomed to fail.

Stephen Calabria: They're doomed to fail, uh, in part due to misdiagnosis?

Michal Elovitz: No, due to that, so when we talk about preterm birth, right? So this is a condition where women, when we talk about spontaneous preterm birth, in pregnancy deliver before term. They deliver before 37 weeks or 34 weeks. And that results in a very preterm baby that is at risk for a lot of neurological and other medical complications.

We know it's labor happening at an inbarant time. Right? But we don't know how term labor happens, so it's really hard to know how to stop pre-
term labor from happening. So we make a lot of guesses. The uterus contracts too much. The cervix opens before it should. And because we make guesses instead of biology, we do all these clinical trials.

[00:07:22] So for years we did clinical trials on stopping uterine contractility. They all failed. And now we're trying to do things about keeping the cervix from opening, but it's not based on the biology of this really interesting organ. So we're doing these clinical trials and routinely they fail.

[00:07:37] **Stephen Calabria:** When dealing with women as patients, how do you advise women to remain resilient in a system that heretofore has not seemed to prioritize their health?

[00:07:47] **Michal Elovitz:** Would it be awful if I said I don't think the burden of resilience should fall on women because people aren't attending to their care? In saying that, I consider myself a resilient woman. I consider a lot of my patients, my colleagues, my peers, my mentees to be resilient. But I think there's been this expectation that we need to be more resilient to compensate for the lack of science and research on women's health care.

[00:08:07] And it's an unfair and inequitable burden.

[00:08:11] **Stephen Calabria:** On the flip side of that resilience question, what counsel do you give to doctors and nurses to help shore up resilience within their patients?

[00:08:19] **Michal Elovitz:** Ah, be proactive. You know your health better than anyone else. I think our health care system has a lot of issues, right?

[00:08:26] And women in general are, you know, the term uterus, right? Hysteria, right? Right. So a lot of women, perfect example, we talked to you asking about chronic conditions, endometriosis, nonspecific symptoms that mirror other gynecologic, other gastrointestinal disorders. And women are routinely told that there's something else wrong or nothing wrong.

[00:08:48] And so the delay in diagnosis can be eight to ten years with women with endometriosis. And so part of that is to say, be an advocate for yourself, seek out other doctors. And I tell women in general, amplify those physicians who are able to really listen to women and to care for women. And I try to do the same.
Stephen Calabria: As far as you yourself are concerned, and the institution of Mount Sinai as a whole, you mentioned clinical trials, but other than clinical trials, what else is being done to move the ball forward and address some of these gaps in the research and our knowledge?

Michal Elovitz: So a tremendous amount, right? It gives me great hope and great pride.

So I was recruited here to be this Dean of Women's Health Research with the idea that Sinai is invested in moving this needle, right? So we won't have to rely on women being resilient. We are going to figure ways to improve and optimize their health. So in that role, we're helping to elevate and amplify and create new research across all institutes, all departments in all different areas of women's health.

And the second thing, Sinai has invested in me and this institute called Women's Biomedical Research Institute. The sole purpose of this institute is to reveal sex and female-specific biology. So, all of the things that we just talked about that we don't know why, that we actually can start saying, this is why.

And once we say why, we can start thinking about preventative therapeutics to limit those adverse outcomes and those burden on women.

So it's an excellent question. When we talk about gender health and equity, right, there is a tremendous amount that we must recognize about intersectionality, that race being of black race and being a female, you know, is really, unfortunately, is synergistic in in causing excess burden.

So we think some of the things that come to mind. So almost all the adverse outcomes that we talked about are increased among communities of color, but one of the ones that I think has been in the lay press, it's been on my mind for years and hopefully being in the lay press will elevate it is preeclampsia, maternal mortality.
We know the burden on black communities is so incredibly great. And I think it is beholden on me and all of us when we think about how we address the burden on black communities and women and black women is to think about how racism and all the downstream effect of racism alters outcomes, both from a health care delivery, but also the biology, right?

We know that race is a social, not a biological construct. So a lot of times we think about, well, race can't then affect biology. We're not saying that. What I think is missed is that racism, right? Neighborhood deprivation, air pollution, chronic stress from discrimination undoubtedly affects your biology, which impacts your health and disease.

And we must attend to that when we talk about female specific biology.

Stephen Calabria: Yes, of course. There was a massive clinical questionnaire sent to women in the past year or two by a university. You would know better more about this than I would, about effects on women's menstrual cycle and the COVID vaccine. What do we know now that we didn't know in the first phases of the pandemic.

Michal Elovitz: So we know COVID is bad. So that we know COVID-19 is a bad virus. We should try not to keep getting it. The COVID vaccine, right? We know that the nanoparticle, the LNP, the way the vaccine was made was novel to our population. We know that certain lipid nanoparticles have been used in non pregnant and pregnant individuals.

We have a lot more data on that about safety. I, with some of my colleagues at Mass General Hospital, Dr. Edlow, have stood up some of the studies to actually look at the COVID vaccine in pregnant individuals, and there are others have stood up, as you mentioned, the study looking at the menstrual cycle and the COVID vaccine. And I think, I think it's great that we have that data. I would offer that we should have had that data way before we had the pandemic.

The idea that pregnant women and any reproductive age women that, even the chance that you might get pregnant excludes you from so many clinical trials. Instead of protecting women from clinical trials, we need to embrace and encourage them and make it feasible and safer than be part of clinical trials.

So, if anything, COVID 19 stood up just even more gender health inequities in that we discourage or don't even allow women to be part of so
many of these clinical trials. And therefore, when we are hit with an acute event, we don't know how to best care for them. And so we've done them a disservice.

[00:13:25] Stephen Calabria: Related to that, why is the impact on women's health often considered later, like an afterthought with regard to clinical trials and clinical research generally?

[00:13:37] Michal Elovitz: I'm going to say it again, misogyny and patriarchy, because women are not the focus. Um, there have not even, and it's, you know, so if you look at leadership, right, there is some evolution in more women becoming leaders, but there's still not enough. And it's not enough just to say there needs to be a female leadership. There needs to be female and males in leadership. Who care about gender equitable care and science.

[00:14:00] Stephen Calabria: So many women enduring a number of different symptoms ultimately opt for hormone replacement therapy. It's a controversial issue, but could you walk us through - what is hormone replacement therapy? Is it safe? And perhaps when and how could one start?

[00:14:16] Michal Elovitz: That is a loaded question that would require about, I don't know, 20,000 hours of discussion.

[00:14:20] Stephen Calabria: Right. And a whole other podcast.

[00:14:21] Michal Elovitz: The whole other podcast. But, you know. Simply, right, hormone replacement therapy is based on the principle that as women enter menopause, your naturally-occurring estrogen progesterone decline.

[00:14:31] And so all of the good things that we benefit from hormones, right, are lost. So we know as you enter menopause, a lot of the risk, like for cardiovascular disease, gets accelerated. So the question becomes how much do hormones, these sex-specific steroids, impact vascular function, cardiac function, bone health, cognitive function, all of it.

[00:14:53] Consistent with the message that women are not centered, a lot of the initial studies looking at hormone replacement therapy, in my opinion, were very flawed. They did not use what we, in a very generic way, would call natural hormones, so my biggest problem is with the progesterone hormone that was used.
[00:15:09] In a lot of the original studies, something was used that was called Majoxyprogesterone acetate, or this very big progesterone, big meaning powerful in its biological effect, because it doesn't just affect its typical receptor, the progesterone receptor, it affects the glucocorticoid receptor, which is a steroid receptor.

[00:15:25] And I don't need to tell you about how over steroid use has negative effects. So these studies that use that type of progesterone, are very confounded in my mind in interpreting the clinical outcomes because the biology again, we're back to biology, of how that hormone worked is very different from how we do hormone replacement therapy.

[00:15:44] Now we're going to be honest, how we should have ever done it.

[00:15:46] **Stephen Calabria:** This whole conversation is kind of rooted in resilience among patients, among yourself, among practitioners. Another important aspect of resilience we talk about is resilient role models. You yourself have been outspoken about the importance of mentorships and sponsorships in medicine.

[00:16:04] **Why do you think mentorship is so important, particularly in research, and what makes a good mentor in this field?**

[00:16:11] **Michal Elovitz:** So now we have another podcast that we're going to do about mentorship?

[00:16:13] **Stephen Calabria:** Yeah, right. We're, we're throwing out podcasts here.

[00:16:15] **Michal Elovitz:** So I actually just, we'll see if it, when it comes out, just wrote an article about mentorship for, um, one of the scientific journals.

[00:16:21] And let me just first say that in general, female scientists and physicians have a decent amount of mentors. They really lack from sponsorship. So what male physicians and male scientists do very well for their male mentees, is sponsor them for awards, for talks, for appointments, for leadership roles. In general, that doesn't happen as much for females.

[00:16:44] Mentorship and sponsorship, in the way that academia in this world is set up, mentorship and sponsorship are crucial for advancement. I think one of the key things to me, for someone who didn't really have any great mentors, for mentorship, aside from sponsorship, for mentorship is to really work with
your mentee to figure out what they want and then figure out the path to help them get that.

[00:17:07] I think we get very, we get blinders on in academia that our mentees should follow a specific path. And for a lot of individuals, that path may not be their path to success and to joy. And so when we talk about resilience, I think we have to be very careful that we are not creating mini me's. Or we're not creating people that we think will only be held up by the existing structures because there are so many more paths and possibilities than we realize.

[00:17:32] **Stephen Calabria:** But what is, what would you determine to be the reason as to why it happens so much more for men than for women?

[00:17:41] **Michal Elovitz:** You want me to keep saying it?

[00:17:43] **Stephen Calabria:** Just, okay, alright, we can move on to the...

[00:17:45] **Michal Elovitz:** And part of it, it's not... And part of it, right, not, not everyone is... You know, there's internalized misogyny. There's the system.

[00:17:51] So it's not just each person thinking, Oh, I'm not going to, I'm not going to do this for women. Our structures, our processes are set up to elevate men more than women. It's a long in bed process. And unless you are a disruptor, unless you specifically think, "Huh, are my recommendation letters for men and women the same?", am I going to take that internal lens both as a male and a female and say, am I writing equitable letters where I'm writing that she's sweet and great to work with?

[00:18:17] She's pleasant to work with. Or she's argumentative or she's difficult, because they're demanding what they get. There's all this gender language that ends up in this academic process that not in the, and that's like the most simplest layer about how to avoid that. And, That trickles all the way through.

[00:18:32] **Stephen Calabria:** And that is not present nearly as much in males as opposed to females.

[00:18:37] **Michal Elovitz:** Oh, absolutely not. I mean, there's papers written about this, looking at it. And, you know, there's all these actual articles now saying how to check your letter, again, very low example here, letter of recommendation to see if it has gendered language.
And I can tell you when I sat as a fellowship director and would see all these fellowship candidates. Absolutely true. Once you pay attention to it, it's there all the time. But you have to want to pay attention to it and be willing to make changes.

Stephen Calabria: What's an example?

Michal Elovitz: Just what I said. I'm, in one of my own recommendation letters, I found a recommendation letter. Ask me why I have it, I don't know. I guess someone gave it to me. You're not really supposed to have them. It said I was a pretty girl from the South, but I was also smart. Actually, it said I was a pretty blonde girl from the South, but I was also smart. Now, you know, you can argue that was, I shouldn't give my age away, but I will, over 30 years ago.

But, there's, maybe it's not as overt, but you know, nice, gets along well, there's, there's all, there's a lot of language that is very gendered that we don't even realize until someone points it out.

Stephen Calabria: That has more to do with the person's personality or perceived personality traits than their medical acuity, their expertise.

Michal Elovitz: Sure, but it's also, you know, where you're kind of doomed if you, doing you're doomed if you don't, right? I am, I'm a go getter. I, I am labeled more often as aggressive. I'm confident that a male counterpart in my field would be seen as they get what they want, they are success, but I'm a little aggressive, right?

And so that gendered language and attitudes kind of filter all the way up. And down.

Stephen Calabria: We've also spoken on this show at length about the importance of realistic optimism when it comes to resilience, seeing things as they are. What advancements can we realistically expect over the next decade or two if current research continues apace?

Michal Elovitz: Ha. So, if we are successful, I think, and I want to be a little bit cautious, but have realistic optimism. I think the expanding world of immune therapeutics will ultimately play a role in several reproductive disorders, such as endometriosis and gynecological cancers, more so than it's doing now.
I think the idea of immunobiology driving adverse pregnancy and reproductive outcomes, such as preeclampsia and fertility and pre term birth, will be pretty big. I think as we reveal this biology, and I think that's, it requires more investment than just what we're doing here. That's, that's amazing and great way to accelerate, but we need more people to do this.

I think as you reveal biology with all the expanding therapeutics, there's such great hope for women's health. We just have to invest. Someone the other day asked me, well, you know, can you prove to me it will make a difference?

And my answer is COVID-19. In 12 to 18 months, we understood what receptors this virus was adhering to, what cells express it. We repurposed drugs, we developed new drugs. If we could do that in a year and a half, why can't we do that for women's health?

Stephen Calabria: What's the answer to that?

Michal Elovitz: Investment. Of scientists, of money, of infrastructure, of resources and people.

Stephen Calabria: None of which is paid as much to women's health as it is to, these other areas that are prioritized.

Michal Elovitz: Let me give you an example. So a lot of what I do in pregnancy health and what I'm now doing in reproductive non pregnancy health gets funded by the National Institutes of Health.

I just told you I, so my research is in reproductive, pregnancy, preeclampsia, pre-tumor, endometriosis, GYN cancers, all of this, right? The majority of that research gets funded by one institute at NIH. That institute is NICHD. Child Health and Development. Did you hear female or woman in that title?

So gynecological disorders, GYN health, obstetrical disorders, all fall under NICHD. NICHD gets 8 percent of the total NIH budget. So it's 8 percent of the total budget. And then pregnancy and reproductive health gets a little piece of that 8%. And that should tell you everything you need to know about how women's health is funded.

Stephen Calabria: We recently had on this show the founder of a non profit run by and for widows. Could you talk a little bit about the value of
networks of women, friends, and family members, as sources of guidance, as well as empathetic support for women who are confronting and coping with medical challenges, medical challenges that are specific to women.

Michal Elovitz: In my humble view of the power of a collective of women, I think about BRCA and breast cancer. So the idea that BRCA and how much of this is, and I will admit how much of this is reality and how much is my vision or my view of it. To me, the reason more research was done about BRCA and breast cancer was because of a group of women who kept getting breast cancer at too young of an age, started making a stink.

How much of that really pushed dollars or research or not? I'm going to stick with my vision. Because I think it really moved the needle. And I think the same way the discussions of maternal mortality right now, I'm hoping to move the needle. So in my lens, in my view, the collective power of women advocating for themselves and each other is huge.

Right? So I think that's the one biggest thing. That we have, we have a voice. Women are the ones who decide most healthcare decisions, for our families and for ourselves, so I think women are so much more powerful in the ability to change the narrative about where the investment is in medicine and science, and that the more we speak out and the more we come together, the more we're going to advance it.

I will also say there is power in the collective sharing of experiences, right? I think for too long people, whether it's a menstrual disorder or menopause or an adverse pregnancy outcome or even a pregnancy loss. People live in their little silos, and it becomes the same way we're not supposed to talk about periods.

Well, if you don't talk about periods, you don't know that when you're bleeding through five pads in an hour, that's not normal. If you don't talk about miscarriage or having a fetal death, heaven forbid, you think it only happens to you. Menopause, if you're having trouble remembering because you're 55 and having hormonal fluctuation and hot flashes, you don't know what is normal, what is shared, what should have help.

And so this shared kind of collective experience is, to me, really powerful in actually empowering women to ask for help and to get the care that they need.
Stephen Calabria: Let's stick with that and go a little further with that. What are some medical complications specific to women that aren't well known? Or as well known as they should be?

Michal Elovitz: So I think the idea, right, I have a talk lined up about the problem of periods. And it's kind of tongue in cheek because periods are because, so this really amazing thing happens with the uterus. The lining regenerates itself every month, which, if you think about it from a regenerative medicine standpoint, is friggin' fascinating.

If you think about it from a clinical standpoint, that lining sheds and you have a period, which everyone says, quote, is normal, and I'm putting my quotes up. But what is missed about this is, ask ten women, and I guarantee you somewhere between six to eight of them have had significant complications, meaning lost work, lost school days, really bad pain that most people would not consider that Advil would take care of.

And we don't really attend to this, right? It's, I mean, I look at my own experience. I missed a number of days of schools. I thought that was quote, just normal, right? I don't think that's normal for people to have to miss one to two days of school or work every month and just think, sure, let's go with that.

Stephen Calabria: Never happened to me.

Michal Elovitz: Exactly.

Stephen Calabria: Broadening it out to the wider community. What can the general public basically do to help accelerate the process and mitigate the effects of these diseases or medical complications that specifically target women?

Michal Elovitz: They have to be advocates. There are some people, not people I'm fans of, that like to say there's a line between politics and medicine.

There is not a line. There is absolutely not a line. Advocating for research, advocating for reproductive rights, advocating for women's health, everyone has to do. And who we hire and who we put in office determines both funding and patient autonomy and female autonomy. And those things are as meshed together as possible.
Stephen Calabria: Wrapping up. Where may listeners find out more about your work and the work of the Women's Biomedical Research Institute?

Michal Elovitz: So they can look at our website, you can Google women's biomedical research, you can google me and, and Sinai and you'll find out all about the research that we're doing.

Stephen Calabria: That's it for my questions. Was there anything else you wanted to say?

Michal Elovitz: Stay strong, be optimistic, be an advocate, and I hope next time we have a conversation that I have new science to discuss.

Stephen Calabria: As do I. Dr. Michal Elovitz, thank you so much for being on Road to Resilience.

Michal Elovitz: Thank you.

Stephen Calabria: Michal Elovitz, MD, is the Dean of Women's Health Research at the Icahn School of Medicine at Mount Sinai and the Director of the Women's Biomedical Research Institute, which performs state of the art research across women's entire lifespan.

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