

THE ROADMAP TO LONGEVITY

#### Announcer

Welcome to the session. Please take your seat. The session is about to begin. Please welcome the panel on the roadmap to longevity, moderated by correspondent at NBC News, Gadi Schwartz.

2025 GLOBAL CONFERENCE

TOWARD A FLOURISHING FUTURE

#### Gadi Schwartz

I think this is going to be the most existential panel of all of Milken this year. Everybody here is most likely here because you either want to live on this earth longer, or you want to share more time with your family here on this earth. And so we're going to be diving into that. —Before we even start, I was at my brother's wedding this weekend—. My father is, I think, 69 going into his 70s. And I have two kids. One of them is three, one of them is one, — one's 28 pounds. The other one's like, definitely 35 pounds. And I remember watching my dad, and he was dancing the night away, and then he was just taking my kids and throwing them up in the air. And I had this thought. I said, like, okay, well, when Rio is is my age, I want to be a father, a grandfather, just like my dad is, you know, dancing with my kids and throwing them up. And then I did some quick math, and if Rio, my son, waits as long as I waited to have kids, I will be 84 years old trying to throw children up in the air with reckless abandon. So it's not just about longevity, it's about how to stay healthy and increase that health span. And so, hopefully, this panel, you all help me, in my 80s, be able to throw children around very recklessly at weddings.

This panel is incredible. We've got Dan Buettner: he is a National Geographic fellow; he's an explorer; you might recognize him from so many things; he's written "Secrets of the Blue Zones," which is probably— required reading for anybody that's come here; and he is the host of "Live to 100." So welcome, thanks so much for being with us. Laura Deming, founder-partner of the Longevity Fund, and the CEO of Cradle, and I can't wait to get into the work that you're doing at Cradle. It is like "Star Wars," Han Solo, getting frozen; It's so futuristic, we're going to be diving into that. Then we've got Dr. Richard Isaacson: he is the director of the Atria Precision Prevention Program; founder of the first real Alzheimer prevention program in the United States; incredible work that you're doing. Dr. Eric Verdin: president and CEO of the Buck Institute for Research on Aging, the pioneering biomedical research institute dedicated to all things aging and age-related disease. And then we've got Dr. Vonda Wright, a pioneering orthopedic sports surgeon and researcher; she is the author of "Unbreakable" and she is an advisor to so many of the world's most elite athletes. So this is a very fascinating panel. We've got an hour with all of you.—For all of us here that want to live as long as we possibly can, and I hate to you know, use the word hack, but when it comes to stretching our life out as much as possible, given everything that you've seen in science, everything that you've

seen in the people that you've met, give us the one thing that you do to make your life on this earth a little bit longer.

## Dan Buettner

Since you're talking about kids, I'll tell you one thing. Sardinia produces the highest concentration of centenarians in the world. And in 300 surveys of people who made it 100, the third-biggest predictor of making it to 100 in Sardinia was having daughters. The guys most likely to make it to 100 had five or more daughters.

## Gadi Schwartz

Five or more?

# Dan Buettner

Yes, we don't know if—daughters take better care of their fathers, or if it's because, if he can survive five adolescent girls, making it to 100 is no problem, but there's a longevity hack. But more to the point, I think of what we can do, you know, if you want to live to 100. If you want to eat to 100, you have to know what people ate as young children and middle-aged and newly retired. So, we actually did a meta- analysis of all five blue zones where people are living the longest—155 dietary studies done over the last 80 years—and when you average it out, people making it to 100 are eating about a 90 percent whole-food, plant-based diet. They do eat meat, but only about 20 pounds a year compared to the 220 pounds that the average American eats. It's mostly whole grains, greens, garden vegetables, tubers like sweet potatoes, nuts, and beans, and if you're eating a cup of beans a day, it's worth about four extra years of life expectancy. But the key is, how do you actually eat like that? And I'll tell you one way not to eat like that is to go out to eat. When we go out to eat, we eat about 300 extra calories every day, and those calories tend to be laden with sodium and ultra-processed foods and saturated fat. The key really, is this: Eating at home.

# Gadi Schwartz

-with your five daughters.

## Dan Buettner

With your five daughters. Ideally, they're cooking for you. And the number one reason people don't cook at home is because they perceive that they don't have enough time. And actually, if you are eating a whole-food, plant-based diet, and you're 50 years old, it's worth about six extra years of life expectancy. And if you average those six years back into sort of a daily average, it's worth about four extra hours a day. So we all have plenty of time to really cook at home, but the easiest way to do it is to get an Instant pot. I have nothing to do with the company,

Instant pot, but all of the diets of longevity are peasant food. They tend to be cooked in one pot, and if you have an Instant pot, it's easy to chop up the food in the morning, put it in, hit the button. At night, you have a meal formulated for longevity. You can make it maniacally delicious, and it's worth six extra years. So that's my hack.

## Gadi Schwartz

And Laura, how about you?

### Laura Deming

-I work in the field of longevity science, and it's really exciting. -There's so many different ways you can take different organisms, like a mouse, and change their genetics and make them live longer:-10 percent longer or even more. But I think what's been the most exciting in the field is the upcoming market availability, probably in the next year or so, of a drug for dogs to make them live longer. So you might have heard of this company, Loyall, for dogs. The drug's not approved finally yet, but it's likely that in the next year, we'll have the first-ever approved drug where the label on the bottle actually says for lifespan extension. And so soon, your dogs will be able to actually take a medical drug that does that. And that's so exciting for the field. We've never had that before, that kind of recognition that might be upcoming soon, in the next year. Again, not approved yet, but the drug is kind of nearing that stage of development, and so that's been really exciting. And the possibility of translating that kind of medical label of lifespan extension, FDA considering that for humans, is one of the things that I'm the most excited about for the next decade.

#### Gadi Schwartz

But what do you do to make your life longer?

#### Laura Deming

Well that's the thing. I work in approved therapeutics. That's all I can speak to and for me personally, it's actually just increasing present-moment awareness through meditation. that probably increases—

## Gadi Schwartz

Meditation?

#### Laura Deming

Yeah, I think if you perceive time more slowly than effectively, you might decide to have more time. That's the only thing I can speak to medically, personally.

# Gadi Schwartz

Wow. And Doctor?

# **Richard Isaacson**

So, if you're looking for a hack so that you can live forever, I've also got a bridge to sell you. So the word hack is something that kind of rubs me and grinds my gears a little bit because-I think if we're trying to think about longevity, and the three legs of the stool that I think about are: longevity, how long you live; health span, which is like the quality of life you have based on your medical conditions; and then brain span, which is the quality of life you have based on your cognitive health, the meaningfulness that you have as we age-if you're looking for one hack to solve all of that, it ain't gonna happen. So to me, it's I'm going to give you my hack, which is knowing your numbers. I'm a little maniacal, so I wouldn't maybe recommend this. But whether it's one wearable here, one wearable here, getting blood draws every three to six months at a minimum, everyone needs to know your numbers. What is your blood pressure? Easy, right? Go to a pharmacy. What is your blood sugar, your fasting blood sugar? Continuous glucose monitors or CGMS are now available over the counter. What is your cholesterol? What is your apolipoprotein B (ApoB)? Ever heard of it? Learn about it. It's a \$7 blood test. What is your fasting blood sugar, fasting insulin levels, what is your- these are the types of-what is your nutrition markers? Are you eating enough fish? Well, check your blood for omega-3 fatty acids. What are your genetics? What are some lowhanging fruit that you can do to know about your genes so you can win the tug of war against your genes, change your behaviors, and make your genes work better for you. You asked for one hack, but to me, it's knowledge, and knowledge is power. I think the other thing, you know, as the brain guy, I should not forget about the emerging field of blood-based biomarkers for Alzheimer's disease. What we're working on is, you've heard about the cholesterol test, where people in their 20s, 30s, 40s, 50s, 60s, 70s, 80s and beyond can go to their doctor and get a cholesterol test: HDL, LDL, triglycerides. You've heard those terms? Well, the cholesterol test for the brain is coming soon, and we're working on it. And I think I see the patterns. We're in the black and white television phase. We're not in color yet, and we're not in the high def, 4k, 8k, whatever it is. But the cholesterol test for the brain is coming. Promise not to over promise. There are blood tests out there now that are kind of cool, but not yet amazingly amazing. But something is coming, and knowing your numbers in terms of the brain markers is going to be one of the most powerful things that all of us can do to live better as we age.

# Gadi Schwartz

And Dr. Verdin. I know hack is something that journalists use, and for the scientists that are here on the stage, there's going to be an adversary relationship between the journalist who's just like, "Tell me how to live longer," and you guys being like, "No, no, there's science here." And yet, we're kind of living in this age where you've got hype and you've got science that has been—doing the hard work for decades and decades and decades. So I am going to stick it to it. Doctor, give us your one or two strategies that you're using to live longer.

## Eric Verdin

Before I do this, I'd like to go back to the assumption that actually underlined your question, which is that, Is there something that you can actually do about your aging? And it turns out that many people have a very — fatalistic view of their own aging. But the science actually tells us that most of your aging—the way you're going to be aging, how old you're going to be living—whether you're going to be sick— is depending on your lifestyle. As a matter of fact, it's about 93 percent of your health-span and lifespan [that] are determined by lifestyle factors. And I think when I first saw that data, I thought this was incredibly empowering, because it means it is on you, unless you have a first-degree relative who is a centenarian. For most of us, it's going to be determined by the choices that you make every day. Now, when I think in terms of hack, there are five variables that are determining lifespan, and you all know them, because this is what our mothers and grandmothers told us. This is nutrition, it's sleep, it's physical activity, it's stress mitigation, and it is human connection, which, by the way, is the most important and is the least studied. Now, so when I think about these in terms of what my hack is to, really, I think about each of these as a bank account in which I'm investing. And every day, I try to do something that addresses each of these issues: either some form of exercise; either one really healthy meal; trying to sleep, go to bed on time. So there's a lot that you can do. The beauty is, each of these bank accounts are stackable.

I hear from a lot of people, well, I'm exercising a lot, therefore I can eat anything I want. That's not true. So if you eat well, it will stack on top of sleeping well, and it will stack on top of moving enough. So again, you know, if the key question is, what are you supposed to do for each of these bank accounts? How do you optimize each of these lifestyle factors? This is one area where the field is actually moving very aggressively, because we now have biomarkers of aging that allow us to determine which lifestyle interventions actually are most efficient. If you hear me saying "physical activity," what does it mean? Does it mean jogging? Does it mean lifting weights? Does it mean balancing, yoga? And so right now, we are in the process of studying all of these in lifestyle intervention, and trying to determine what is the best combination, not only for nutrition, but also for physical activity, stress mitigation, human connection.

## Gadi Schwartz

And yet—sorry to push you a little bit more—but for all of you who have not been able to shake his hand yet, on the stage here, he's got the most firm handshake. So I've got to put you on the spot. What are you doing? Let's put the longevity aside. What are you doing to keep healthy?

## **Eric Verdin**

That's interesting. I'm actually happy to hear that because grip strength is one of the strongest predictors of life expectancy. I do an hour of physical activity every day, and for me, it's part of lifestyle. It's a religion, and it just makes me feel, you know, I'm 68 years old. I feel better today than I have my whole entire life. Your story resonated with me because I just became a grandfather.

## Gadi Schwartz

And your handshake resonated with me! I was like, with these hands, I could throw anybody

### **Eric Verdin**

And catch them.

# Gadi Schwartz

And catch them. Yeah. And Dr. Vonda, what do you do to stay young?

### Vonda Wright

Well, you know, my lens is coming to you as a practicing orthopedic surgeon, right? So, in the musculoskeletal lens, and although muscle is everywhere, and I actually we were talking, I come from a satellite cell muscle stem-cell lab. What I think people do not remember, and I'm going to get really granular, the thing I want you to do is to remember your bone health. Because if you are one in two women, it's either me or you who is going to break a bone in your lifespan, or [if] you're one of the 2 million men in this country, that is one of the quickest ways to draw a complete halt to your longevity. So as an orthopedic surgeon and longevity person, my role is to increase your bio-resilience, right? Not necessarily add years, but the resiliency down to a cellular level. And the way I want you to remember to do that is with your bones. And bone health starts with our children, because we reach peak bone mass at 30, and I find many 22-year-old people in my office, because I measure everybody's bone density—who come to me with very bad bones, and that has to do with the way that we're building bone, right? So if you want the one thing at your age, my age, we teach our children to bash their bones. They need to be out there jumping. They need to be eating. We gotta get the thing out of their hands where they're sitting around. And for us, if you do not already have a skipping, jumping, hopping, pounding practice in your one hour a day, please do that, because bones respond by Wolf's law and they love to be bashed.

#### Gadi Schwartz

Wow! What a spectrum of advice. Thank you guys so much. Amazing.

[Inaudible]

### Gadi Schwartz

As soon as I get home I'm like, sorry, kids, I learned a lot today. Let's do some bashing. Now, Laura, I do want to start with you when it comes to what we're looking at over the next 10 to 15 years. In terms of cutting research, I know you've been investing in some of the most cutting edge tech startups in this particular space, and then Cradle is just mind blowing, what you guys are working on. So, as we try to figure out what is signal and what is noise, what are the things that you look for? What are the things that we can just kind of put a pause on for maybe decades later? And what are the things that are right now on our horizon?

### Laura Deming

Yeah, so it's a really extraordinary time in the field. For context, I've been working in longevity labs since I was 12 years old, actually, and started my first one when I was 17 or 18. So it's like my whole life at like 20 years has been like, in this field, like, just really, really wanting these, you know, drugs, to be available and for the science to go forward.

### Gadi Schwartz

Wait, sorry, at 12 years old dude? We all were like hold on, let's do some math here. What inspired you to start thinking about longevity at 12?

## Laura Deming

Well when I was a kid, I was like this is just the worst, this is the biggest disease. It's like, if you put, you know, it's like, what's the thing that we all want? We all want to, just like, have as many moments of healthy, awesome life as possible. So that was just like the label of the thing that I wanted to solve for. But yeah, so, I mean, the thing that's been incredible is just the shift, and there's like, multiple stages. So from about, I'd say, 2011 to maybe 2018, 2019 or so, it was just like, grind. Like I'd walk into a room to talk about investing in longevity. It's like, what's longevity? It's crazy to work on aging. The thing that's frustrating is, in the field of longevity, there's just all these studies, like study after study, where you can take mice just genetically manipulate them in very simple ways and have them live longer, and we just know that lifespan is a malleable parameter. Again, the thing that I would watch out for is, if anyone's telling you, like, an extra 50 years, an extra 100 years today, total bullshit, like, there's nothing that will increase your lifespan by that much today. And like, longevity is something that we can affect deterministically, just not very much right now. Now, the thing that's exciting for the next decade, and it's just so fulfilling of being in the field since you're a kid and seeing it like grow is that we're actually starting to take the science that you know, so many people like Eric and others have pioneered and translating into a drug that the FDA is looking at, where the FDA is actually seriously thinking about, what does it mean to approve a drug for a longevity indication? And again, I'm first starting with the CVM division and thinking about this product for dogs, but just like all this momentum of trying to figure out how we define longevity biomarkers and clinical trials that are measurable, and so we'll plausibly have drugs on market for people in the coming decades that can increase that parameter. Again, if anyone's telling you 100 years, currently, not at all in the realm of feasibility, but deterministically, where a drug actually increases that parameter. Now, the thing that's the craziest in the field, and just such a weird time to now shift into, is that everything is now changing, like by default, without any external stuff. We kind of thought, all right, the next couple of decades are about the first approved longevity drugs. Once those get on market for just

some amount of increase, you know, you have, like, 50 plus years to get, like, larger increases. But with all the just technical advances that are happening, timelines are super insane for how fast things might accelerate. And like, honestly, no one in the field has any fucking idea, like, what? Sorry, sorry. But just like, it's really, like, this crazy, like, time where we can't tell you, like, what the timelines are for longer increases. We don't know that they're deterministically going to happen soon, but it's very uncertain. The thing, though, that I'm the most excited about, personally, is cryopreservation. So it's a kind of totally different angle to the problem, that took me a decade to fully understand. But there's this idea, if you've ever seen "Interstellar," medical hibernation, like if you get in a spaceship, again, a totally different lens, but just one that I'm so excited about right now. And let's say, in the movie Interstellar, you want to go to like, the farthest regions of space, but you go in a hibernation capsule, and it's fascinating that you know, it's like I, and some people that I, you know, love, know people who were within years or months of missing a life-saving drug that could have prevented their cancer from metastasizing, or that could have given them years of remission, or even like a chance of full survival. And if we just could pause biological time for people who had terminal illness like that, would actually just bridge the gap to future technologies.

## Gadi Schwartz

Just to clarify, so, recently someone lost someone to dementia, or they died when they had dementia in the family. Are you saying that, you know, if somebody has dementia down the road, with obviously all the approvals, they can basically pause, freeze themselves, and then just wait until you all figure it out and then be reanimated?

## Laura Deming

Yes. I'll try to quickly compress the full explanation of caveats to make room for the other panelists, because I don't want to promised too much, but dementia is probably the hardest disease, probably the last disease that you apply this for. But imagine you're like a patient with stage four, let's say, pancreatic cancer, and you don't really have any other options. And you know there might be therapy coming in the coming decades, but there's no other way. Medical hibernation is really one where it's like, "how can we help those patients who have no other options?" To be clear, this is nowhere near scientifically completely validated. There are many questions that [inaudible] take this. And the reality is, in cryobiology, many scientists are working towards, cryopreserving whole human organs in the very near term to help transplant patients. And so this question of, "Can we scale that to a whole human?" And so that's what I'm working on right now. And I just find it so exciting to find a problem that's so beautifully - it's like, again, much technical speculation and scientific risk to be [inaudible], but you know, with IVF or embryo freezing, we freeze human embryos fully for decades, and then we warm them decades later. And you know, this question, "can we scale that to a whole human?" that's what I'm excited about.

### Gadi Schwartz

The journalist in me wants to ask you about timelines, but I believe your quote was "no fucking idea," right? Yeah, right? Something along those lines?

### Laura Deming

[inaudible] Apologies. I'm a bit more optimistic [inaudible]

### Gadi Schwartz

But in terms of in terms of how much is changing, and in terms of how much uncertainty there is with the timelines, Dr. Verdin, I do want to ask you, the understanding of biology and aging and telomeres and all that, has that changed? Or are we still on a pretty solid foundation here?

#### **Eric Verdin**

It changed. Some of you might wonder, why the hype these days about longevity? It seems that I cannot open a magazine without seeing an article. The clinics are opening everywhere. So what we're seeing is the normal cycle where there was a revolution in our understanding of the aging process. Back in the mid '90s, 1995, Cynthia Kenyan actually was one of the pioneers of this. And when Laura mentions that she started research at age 12, she chose the right lab because she was in Cynthia's lab and others, Tom Johnson, Gary Riff, consider a whole group of amazing discoveries. And I think what these discoveries were was that you could make a single point mutation in an organism, change one letter in the genetic code, so little worm has a 3 billion base pair, 3 billion letters, you change one letter, and you double the life expectancy of that worm. You add another modification, and you increase its lifespan 10-fold. So these were discoveries about mid-'90s. First, no one believed it. Then it was reproduced in other animal species, which showed fruit flies, eventually moved into mice, and slowly, you know, 15 to 20 years later. So when you identify these mutations, it tells you that aging is a tractable problem. If you can find a mutation, that means you can probably find a drug that will target the same enzyme, the same protein, and have the same effect. And so today, that's where we are in animal models: we can routinely double the life expectancy of many species. Little less, it gets a little harder as we move up the evolutionary tree. So you can do 10-fold in C. elegans, a little worm, you can do probably three- or four-fold in the fruit flies, when you get into the mice, it's one-and-a-half-fold. And in humans, the question is, we don't know, but clearly, there's the whole idea that aging is a malleable variable, and we've identified the dials so we can tweak it: either make it faster or make it slower. Now, when we get into humans, there's a whole new barrier, which is these drugs that we anticipate will increase lifespan and health span have to be incredibly safe, because these are potentially drugs that you would give to someone who's at risk for accelerated aging initially, but in the future, could be everyone. And by the way, we might already have some of these drugs around. There are, I would say a number of drugs that some of you might be taking, like Glucophage or Metformin or Rapamycin or Ozempic, and all of these new GLP-1 agonists might be anti-aging drugs, they certainly behave like this in many respects. So we're right at that transition where there's an enormous amount of excitement where the field is moving from animal models to humans. And you know one thing, the last thing that I want to make clear, is that at this point, there are no supplements and - no matter what Instagram says - no supplements, no medicines that are known or documented, to safely increase human lifespan. And so, this is my argument for actually optimizing your lifestyle, because if you do so, hopefully, within the next five years, I predict we will have at least one approved drug in humans for aging. There are at least five Phase III clinical trials ongoing right now that are targeting the aging process. If you look at the rate at which these trials succeed, one can reasonably predict one of those will come. There's Loyall, as we've heard, going to document this in animal models. But there's a-l just wrote, with a number of colleagues, a review looking at the

whole space of these drugs and there's going to be an avalanche of these drugs and interventions coming in the next few years. So I think the bottom line is, do everything you can to stay as healthy using what we know works, and it's not a minimal effect. The last point I want to make is, if you are—the evidence points to the fact that if you were to optimize everything in terms of lifestyle factors, there's 15 to 20 years of extra healthy life. So most of us could expect to live to 90-95 in good health today, based on what we know. And that's already pretty amazing, if you consider the fact that we're living to 65 on average in good health and 75 on average as a population. So to me, this is the exciting thing. Do everything you can to optimize your current lifespan, and some amazing things are coming in the next 10 to 15 to 20 years.

#### Gadi Schwartz

And having your body last that long is one thing, having your mind last that long is a whole other. Dr. Isaacson, I wanted to ask you, I mean, an extra 10-15, possibly 20 years and cognition, like, if you can't beat your kids at Wordle, what's the point? Right? So what is your research? What's your research showing us in terms of, how do we keep our mind sharp?

## **Richard Isaacson**

Yeah. So what I would say is, when I went to medical school, there were no treatments for Alzheimer's disease. The words Alzheimer's and prevention couldn't be used in the same sentence. And if you're here, and if you hear that, you know you're upset because your family member has-I have four family members with Alzheimer's, and some of them did live reasonably healthy lives. Forty-five percent of dementia cases - conservative estimate - may be preventable if that person does everything right. Okay, so [what] I want to say is, in full transparency, probably about half of cases of dementia may be preventable, but there's other people that could do everything right and still get dementia. So I just want to start with that. That being said, there are so many things we can do. We published a paper in 2019 that showed that, on average, when we give people, on average, 21 different things from a universe of many more based on emerging principles of precision medicine (and I'll define what I mean in a minute), different people need different things. So if you have this gene, you're going to need maybe this sort of cocktail. If you're a woman, women and men have different brains. Wait a minute. Wow! I never learned that in medical school either. Women's brains. Women's brain health, the critical window of opportunity for women is the perimenopause transition, and we don't think about perimenopause as a brain disease. Some doctors don't even think about perimenopause as a disease, and that's terrible. We were taught the wrong things. We have to pay attention to women during the perimenopause transition, because 25 percent of women have a gene that increases risk, and hormone replacement therapy can maybe take that woman off the road to Alzheimer's disease. So the concept here is precision medicine, whether you give a person a targeted plan based on whether they're male or female, based on their individual lifestyle factors, high blood pressure, high cholesterol, blood sugar, whether we look at other genetic factors, there are so many things we can do. The challenge is that each person needs a little bit of a different path. We have software that's trying to make this easier. We've learned and we've published on what works and what can we do. We showed that in 18 months at the Alzheimer's Prevention Clinic in 18 months, we were able, projection- wise, to delay the likelihood of developing-18 months, by four to eight years-depending on how aggressive or comprehensive that person took that plan. If we can live better, brainhealthier lifestyles for five years, 10 years, 12 years, 15 years or more, we can really move that needle. So it's not a panacea. We don't have magic pills, magic potions. I agree with you. There's not something on Instagram that you

can take to fix everything, but it's the biological principle of synergy. One plus one equals three. Exercise is the No. 1 thing anyone today can do to loosen up that amyloid, the toxic protein in the brain. What type of exercise? It's not just go and exercise, personalized exercise plans, doing a DEXA. A DEXA scan if you haven't heard of it, D, E, X, A, it doesn't just look at bone density, while that's really important, it looks at body fat, where the body fat is, and it looks at muscle mass. And as the belly size gets larger, the memory center in the brain gets smaller. And different types of exercise and activity can reduce body fat. Strength training — absolutely critical. If you're doing all the exercise in the world, but you're burning the candle at both ends, and you're not sleeping: well, that's a problem too. So again, things have to be done together. The other thing I'm really excited about are some of these emerging drugs. Can't take a magic drug and prevent Alzheimer's, but GLP-1s, for example, GLP-1s, the Ozempics, the Zepbounds, the Mounjaros, all these things, these drugs, have been around for decades, for 20 years. Dan and I have the same primary care doctor in Florida, and he's been talking about these drugs for 20 years. They're not new, they're just being deployed differently. And in the right person, at the right dose, and for the right duration of time, if we can deploy these in a precision medicine, personalized-based way, that's when we can kind of win the battle.

## Gadi Schwartz

Fascinating. Going back to something you brought up right at the beginning, the differences between male and female aging, and exercise seems like the big common denominator. But Vonda, I want to ask you, your book is about this. It deals a lot with how women age, right? So are there big differences between men and women as they advance in age?

## Vonda Wright

You know, I think when we think about aging and the and the hallmarks of aging, the papers which have expanded from 6, 12, 13 biological hallmarks of aging, you know, I think it is, and I don't believe anybody in this room would do this, but the general public believes that men and women biologically are pretty much the same. But I can tell you, even at a stem cell level, when we were looking at muscle- derived stem cells, if I stimulated cells from a male mouse versus a female mouse, they made completely different tissues. Well, right? And so the way that translates into aging, and the way I want you to think about this, whether you're a venture capitalist or whether you're clinicians or curious minds, is that men do lose their anabolic steroids, their testosterone, although it's kind of in a linear fashion, and it declines. But like this, women have a midlife cataclysmic event that begins in their—as early as 35, sometimes earlier surgically. But the belief that estrogen, testosterone, progesterone, for women, are only sex hormones, is seeing none of the picture. Estrogen is an anabolic hormone. There are alpha and beta receptors for estrogen on every tissue, brain. I don't have to name the tissues, brain, everything. So, even a curious mind will say, well, if one of the stimulants for every tissue type is now gone, what is that going to do? So, women do not age like this. Women age, and then they age like this. And unless we step in front of it, the suffering gap, there's a health gap, there's a health span gap: 64 to 81, 79, depending. Australian women are living to 85. Those years are not healthy years; Those are suffering years. And so we're behind in venture capital. There is a 200 percent increase in investment in companies that look at women's health over 40, and it still represents 2 percent of all venture capital dollars. There is a 1 percent-1 percent of all research dollars go to research for women after 40. One percent of all health research. And so I just feel like the more awareness, the more understanding that at a very cellular level,

men are from Mars and women are from Venus, as the book goes, the better we'll be able to serve the 51 percent. The five sisters are the majority.

### Gadi Schwartz

The five sisters, yeah, and they're the key to longevity too. Dan, I want to bring you in because so much of what we've been talking about, it's individual we're also talking about, you know, advances in western medicine, and yet, so much of what you've studied is longevity through design and design of kind of like an ancient wisdom almost. What have you found in your Blue Zones that tell you what the roadmap might look like, using both the things that we've learned accidentally and the things that we're learning today?

### Dan Buettner

Well, it lines up perfectly with what Eric was saying, what Richard was saying, Mark Hyman's in the audience here, it's the same things. He sort of preaches the five characteristics. But I spent a lot of time thinking about, how do you actually get people to do the right things for long enough to make a difference? And, you know, I put behavior modification kind of in the same bucket as the Easter Bunny and Santa Claus. You know, there's a lot of hope behind them, but they rarely deliver. And if you look at the recidivism curves of diets, you know they have about a three month half-life, and exercise programs have about a four-month half-life, and they sort of run out of gas in a year or two. They don't work very well. People in Blue Zones, they don't try to live a long time. They don't get on diets or exercise programs or look for longevity hacks or run down to Central America for stem-cell treatment. They just live their lives. And the big insight here is that they live in environments that govern their unconscious behaviors, not their conscious behavior. So they're eating the right foods and getting that physical activity and being socially connected and living on purpose, not as an act of conscious will or discipline or presence of mind, but because that's our environment. So you know, my daytime job is not nearly as exciting as Laura's or Eric's over at the Buck Institute, but I get paid by insurance companies for lowering the disease load of entire cities, and the insight to do that is not trying to change a million people's behavior, but change their environment so they're nudged. And one of the best sort of design hacks there is, and this is gonna sound unbelievably boring, but it works. It's walkability. There's something called the complete streets of policy package that essentially tells city council that every time you design a new street, and most of our city streets are designed once every seven years, and it can be designed for cars. If you invite cars, wide lanes and high speed-limits, you're going to get cars, you're going to get traffic, you're going to get pollution, and you're not going to get very much walkability. Or you can design those streets for human beings, bike lanes, and wide sidewalks and trees. The difference is vast. So if you live in a city like Atlanta or Houston or Phoenix, which is sprawling suburbs, the average person in these cities gets about 4,000 steps a day without thinking about it, you know, just sort of walking around their house or whatever. But if you live in a walkable city like Boulder, Colorado, Santa Barbara, or New York City, you're getting about 10,000 steps a day without thinking about it. Well, what does that mean for our life expectancy? For every incremental 1,000 steps we take, it lowers all-cause mortality by about 12 percent, so your chances of dying by about 12-drops by about 12 percent. So, for the person living in Boulder, Colorado or New York, over the person living in Phoenix or Houston, that's about 5,000 extra steps a day. For a 40 year old, getting those 5,000 extra steps a day without thinking about it, it's worth about 45 percent lower rates of all-cause mortality, which translates to about four or five years of extra life expectancy. Eric and I agree on everything. I do believe the Buck Institute or Laura's lab is going to produce that thing that you know is like penicillin, which gives us a huge leap in

life expectancy. But until then, I think we have to shift our focus away from the folly of thinking we're going to get 350 Americans to change their behavior, to designing their environment so we're setting them up for success.

# Gadi Schwartz

I mean, your work has been incredible, and I can't think of a single person on Earth that's met as many people in their hundreds, as you have, and I'm hoping, I don't know, maybe you can give us a peek behind the curtain. What does, what does life past 100 right now today, look like in some of the best cases?

# Dan Buettner

Well, Vonda brought up a really good point. You know, for women—in America, for every one male centenarian, there's five female centenarians, but the male centenarian has about a 50 percent chance of reaching age 100 and being in really good shape. For the female, it's only about 20 percent of them make it to 100 in good shape. But there are a few encouraging things. You should aim for 100 by the way. So Eric's right, the life expectancy, right now, sort of maximum average life expectancy, if you do everything right, is probably 95 or 96 for females, 91, 92 for males. But since 1840, life expectancy has been going up two and a half years per decade. So if you're –50, and looking around—I can see you guys are a lot younger than that—but you can expect, you know: 50 now, if you can make to 90, you should get about 10 bonus years. So most people sitting in this audience, if you're doing everything right, you can aim for 100 and the good news about making it to 100 when it comes to happiness, age is on a U-shaped curve. We tend to start out pretty happy in our 20s and optimistic, between the ages of 45 and 55 there's a trough that tends to be the least happy years of our lives, but if you retain your health, happiness continues to rise. In the cohort that are the happiest are people over 100, so you might not be able to run a marathon or throw your baby up at 100, but you'll have a smile on your face.

# Gadi Schwartz

Wow. In keeping it, you know, on this wide angle lens here, Eric, I'd love to ask you, what role do you think the public sector has in taking some of these designs and implementing them, and taking some of the cutting edge research and implementing that in a way that is kind of democratized for everybody that can't afford a, you know, particular protocol, I guess.

## **Eric Verdin**

First, I want to applaud Dan for his work, because I think it's based on an important recognition that it should be easy, it should not be an effort. But the fact of the matter is that we live in an environment which is not conducive to proper health. So the question is, how can we change that environment? I also believe there's another dimension, which is the whole aspect of education, especially starting with our kids in school and really, lifestyle factors that are, you know, leading to health are not complicated. And, you know, I'm horrified, frankly, sometimes by hearing the discrepancy between what we know is actually healthy behavior and what is not. Look at the standard American breakfast, orange juice and a muffin. By longevity standards, it's a complete aberration. I have not had a drop of any orange juice or any fruit juice for the last 15 years, and neither should any of you, frankly. So you know. And this is, I can guarantee you, if you survey 100 Americans, probably about five will know about this. Now there's something happening. So there's clearly a gap between the knowledge of what is a healthy behavior and what actually is lived in. And some of it is, frankly, is driven by economic circumstances. So you know, one of the strongest predictor of your life expectancy is your zip code and how long you're going-you think you're going to be living. So I think there are a number of policy decisions that need to be made. You know, we're looking at what's happening in Washington with some degree of trepidation, in terms of there's some talks about increasing the health of all Americans, that is actually really encouraging. On the other hand, there's slashing of all federal budgets for research, including in aging. That is—at risk of destroying the NIH, which, by the way, is what got us to where we are today. So if you have a chance, please write to your congressmen. The NIH needs to be supported. It is – I did not say this for applause, but—you know for every dollar that is invested by the NIH yields \$2 of net economic output. I think I defy any politicians to find any other government investment that yields the same thing. Ninety-eight percent of the drugs that were approved in the last five years by the FDA originated in an NIH grant. So we are essentially—at risk of killing, you know, the Mother Goose, what yielded, you know, this incredible increase in life expectancy of two years every decade for the last 150 years. So that's an incredible achievement, and we are, frankly, at risk of destroying this because-basic research is the foundation that yields everything, including the research on aging. Where we are talking about longevity today is based on discoveries that were made with NIH money back in the 1990s. So, one last word is: I think there is something really interesting that's happening right now. What we are seeing is the fact that longevity, or health, is becoming something that young people are interested in. It's becoming cool. There's nothing that could be more important, we're in California, that we are, in some way, one of the hotbeds of this whole movement of health being cool. And I think this is something to be celebrated, because it really means that people are starting to really assume the responsibility for their own health. Now, along with this, we need a complete reform of the medical system that we call health care. It's actually not health care. It's sick care. A medical system that is based on actually keeping people healthy, and instead of salvaging whatever is left when they are, you know, 65 or 70. So there's a lot of movement in every one of these areas. I think one of the things for me that is really the most important is the idea that the longevity field be viewed as Longevity for All, and not sort of medicine by the wealthy, for the wealthy, which it has a little bit of that connotation right now, but I think I'm confident that, given the intention of many of the people in the field, that I know that we will improve human health. And so I, I'm, you know, quite optimistic about what there is for us, all of us, as a nation, in the future.

## Gadi Schwartz

I'm so glad you mentioned the NIH. I would argue that NIH got us to where we are today, and all the breakthroughs that we see on the horizon are thanks to the public sector investing in this. Laura, —I hate to ask you the hardest question of the day here, but given the current climate, do you think that the private sector—have you seen enough in the private sector to carry that mantle forward if we do see reductions, mass reductions, in a lot of the research that has gotten us to this point?

## Laura Deming

Not really, or like, that's like, such a complicated like...

# Gadi Schwartz

I know, I'm sorry.

# Laura Deming

I think honestly, what's the most missing is, just like, people with a lot of agency starting longevity companies or doing longevity projects. So, like, the funding could increase but the mistake—when I was first entered the field, I started a venture capital fund because everyone told me that funding was the problem, and I think it is, but on it, like, I think the biggest thing is just, there's so much to do, and it's really hard and very complex, and we just see more people, and that's, yeah, that's, that's what I feel the most strongly about.

# Gadi Schwartz

Do you see the private sector, do you see investment, you know, picking up some? it's not even picking up slack, you need the public sector and the private sector working in tandem to tackle something like this. Do you see that happening in the next five to 10 years?

## Laura Deming

I don't. It's like the next five to 10 years like I'm just really confused about. But one thing that I will say that's been very interesting is this rise of what's called FROs or focused research organizations. So this is a concept that Adam Marblestone and Sam Rodriguez at MIT came up with where you kind of say, there's, look, there's some projects that are not like, not the Manhattan Project scale, but kind of similar, like they, you can't really do them in a single lab, necessarily. They kind of require \$50 million plus in funding. They might require, like teams of 10 to 20 people from different disciplines. We have to pay salaries that are competitive with industry. And for those kinds of projects, what if we could just get people to kind of fund them as though they were a company? But they're not actually a company, they're sole nonprofit. And it's hard to explain, but just someone proposing this idea resulted in this massive increase of projects that are doing incredibly ambitious things and have actually gotten this amount of funding, and it's kind of like someone proposed that we should do this, like, for example, this company, this nonprofit called E11, which is trying to do kind of whole brain connective mapping, you know, in a very ambitious way, got the thing of \$50 million plus. Like, is actually going after it. You know, I think even companies like Cradle, where, you know, we have, we're not, we're a company, not a nonprofit, but we're kind of in a similar vein. We're just like, let's just go do this. Like, you know, it's a hard science project. We could do it in a lab. Like, let's just go do it in a company and just ask for the funding and just try and get it started. And so there's, there's something happening right now where you're seeing more of these kind of mid-size, they're not billion dollar projects, they're not like couple million, but they're like, 15 to 100 million [dollar] projects. People are just like, let's just go do this, like, and just see if we can make it happen. And that's been really exciting too.

### Gadi Schwartz

Yeah, it's a very exciting time. Vonda, I want to ask you, you know, one of the things that has brought all of us to this conversation is the hype versus science of it all, right? And as we go forward, oftentimes the most sensational headline, the biggest promise, is the thing that gets the attention. And these days, attention and money have this very symbiotic relationship. But you've been communicating the science on so much of this for quite some time. How do you see the future of like, you know, I hate to say it, like some people that are like, hey, I've got the fountain of youth, which is a tale as old as time, versus the people that are doing the work and the projects that are actually needing the funding?

## Vonda Wright

So I have thoughts on this, on both sides of the aisle, if you will, that as research scientists, often we work in our labs for decades. You know, one project in our lab could take 5, 10 years, and we get to the outcome, and we publish it in a journal, and it's behind a firewall, meaning, for those of you who are not in research, you've got to pay \$5,000 for the journal to make it accessible to everyone. I had a paper recently that we just paid the money because it was that important to me for people to know about the musculoskeletal syndrome of menopause. That paper, not because it's God's gift to papers, but it has been downloaded 338,000 times. The average brilliant paper from the top journals are downloaded 10,000 times, and 50 percent of all work is not read by anybody except the authors. So if we want the best science to get out there, we need to make that accessible. On the other side, I think that curious people, or maybe charlatans, are preying on the hope of people who just want to feel better. You know, I take—in my career of taking care of at least 100,000 people, and the common thread that people come to me with is "I'm in pain and I want to feel better," and so without educators, real scientists, being able to communicate in a way that the public understands, or feeding journalists in a way that can be disseminated, who's going to step in? People with the megaphones. And I think there's a purpose to public education, but I prefer to call what I do publicly education. It's the same thing I did at the University of Pittsburgh, just to a different audience versus influencer. I think there's a difference.

## Gadi Schwartz

And Richard, are you optimistic that that can be done, given our current environment?

#### **Richard Isaacson**

It's been a tough couple of weeks. I mean, you're asking me. I mean, I've never struck out before. We had a letter of intent that we submitted for a grant. I mean, this is, like, everyone thinks their research is great, and I get all that, and that's cool. This is, this is cool stuff. I mean, cholesterol test for the brain, like, fund that, like that needs to be funded. We struck out, like, two NIH grants not scored. We whiffed on a letter of intent, like letter—we didn't even get past the letter of intent stage on another grant. I'm not sure what's going to happen to be honest with you. I think the next three to four years—I asked a mentor of mine what the heck to do, and he's like, you've got to pivot. You've got to do something different and whether it's public or private or company or nonprofit, like we got it all, like we've got to figure out how to do it. I'm not not optimistic, but I'm not scared, but I'm thinking. My gears are grinding. I'm trying to figure out, like, how are we going to fund this? Because what we've done in the last 20 years? That ain't happening again for the next couple of years. I don't believe so. We can call all the senators and congressmen we want. I just don't think things are going to change in the next couple of years. Not a political statement, just trying to be realistic. We've just got to do something different. And to me, it's got to be public and private philanthropy, venture philanthropy and forward. Like what you said is it. You need \$10, \$12, \$15, \$20, \$50 million to do the types of things. That's not a seed round, that's not a \$2 million here, that's not an angel oh help me out. This is— these are big projects and and that's the way to be successful. I don'tknow how to capitalize that.

### Gadi Schwartz

Eric, do you have thoughts on this?

### **Eric Verdin**

I could not agree more. One of the interesting factors is this time when all of this funding is threatened is a time where biology is showing the greatest potential ever. And I think, if you think as to, you know, to look back at the 20th century, in the 1920s you had a group of scientists actually setting up the setting for a revolution in physics. You know, 20th century, a century of physics with Einstein and Planck and all of this. And it incubated for 20-30, years and then it started. In the 50s you had the first transistor, and it went to the chip, and eventually it led to us having every one of us a supercomputer in our lab, and to be connected to the whole world, to the whole knowledge. And thinking back, you know, when I was in high school, -I saw the first HP calculator, which was absolutely mind-boggling at the time. The idea that you could punch two times three and it would show six was mind boggling. And this is where we are. So the 21st century is going to be the century of biology. If you think about, you know, the decoding of DNA in 1950s, we had this 50-year lag. And I can promise you that the next 50 to 100 years in biology are going to be nothing short of amazing. And it is incredibly paradoxical and frankly, sad for me, because we are jeopardizing a whole generation of new young scientists. I see them in my life run a lab and an institute, 25 young people coming from all over the world with the same dream and the same aspiration to change the world, to change health, that I had when I came to this country in 1982 with a suitcase and a diploma, and I really worry about us, you know, killing the spirit. And frankly, many of them have asked me, "What am I supposed to do for the future?" So there's more than our immediate funding that's at stake. It's the whole enterprise. The US is a clear leader in the whole world in terms of biomedical research. And I think we are at the risk of relinquishing this. I'm from Europe, so I still have a lot of attachment there. And I just saw that they just issued a \$500 million, 500 you know, \$100 billion dollar offer for refugee scientists from America. I never thought in my, in my dream that we would see this, but the brain drain has already started. I can tell you, many of the young people were in their 30s or 40s. I've seen the writing on the wall there's-this is not the place to continue my career. So you know, despite all of the optimism that I still harbor in terms of what we're going to be doing, it's hard not to be a realist, as Richard just said, about what's going to happen in next two to four years and the damage that's going to be done. So we've just run out of time. I'm going to give you the last question, because I really do want to ask it real fast. Give us - this is a 2-, 3-, 4- year perspective. What about the 100 year perspective? What about the centuries perspective? Are you optimistic on, you know, society pushing the lifespan forward, as we've seen over the last few decades. - The average lifespan is now in the 70s. Do you think that we're going to continue to do that? Whatever the winds are?

# Dan Buettner

Not in America. Things have flattened off in America. But this project I'm doing right now is, we found the five areas in the world with the highest health-adjusted life expectancy, and in every case you know, they're investing. We found one in Scandinavia, and Southeast Asia, another one in the Mediterranean area, but these places are living an extra 12 years in full health over Americans because they have set up their society so people—they're not looking for the silver bullet. It's silver buckshot. It's nudges and defaults at the population levels that nudges people to move more, to eat better, more whole food, plant-based, to connect more. And in most cases there probably the biggest thing is educating women of childbearing age. That's probably the single most powerful policy we could implement to raise life expectancy. Why? Because children—because educated women produce fewer children who are—get better health. They get better educated, they grow up to be more productive. They make better voting decisions, and it creates an upward spiral, which will do more to put up upward pressure on life expectancy than just about anything.

## Gadi Schwartz

Fountain of Youth: turn to women, just like we've been talking about this entire time. Five daughters. With that, we've got to wrap it up. Thank you—so very much for coming. I think the panelists are going to stick around to answer some questions. Thank you .

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