

**Article:**

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**Guests:** Dr. Robert Califf is Vice Chancellor for Health Data Science and Professor of Cardiology in the Duke University School of Medicine and a former Commissioner of Food and Drugs at the USFDA. Dr. Haider Warraich is a physician, writer, and clinical researcher with the Division of Cardiology at Duke.

Bob Barrett: This is a podcast from *Clinical Chemistry*, sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I am Bob Barrett.

In almost all high-income countries, the U.S. included, women live longer than men. As we enter a new era in which biomedical data are increasingly ubiquitous, current and future research may help us understand the fundamental issues that drive differences in longevity and other health outcomes between men and women. Our ability to measure the entire spectrum of information about the human biological, environmental, and behavioral condition will become both routine and relatively inexpensive from genes to genomics. From clinical data to the electronic health record in insurance claims. From digital information about behavior and social interaction to geospatial referencing.

The January 2019 issue of *Clinical Chemistry* is devoted to topics of men's health and in that issue, an article examined differences in health outcomes between men and women and underlying biological, behavioral, and societal factors. We are pleased to have both authors of that article as our guests in this podcast.

Dr. Robert Califf is Vice Chancellor for Health Data Science and Director of Duke Forge, the Center for Actionable Health Data Science at Duke Health and Professor of Cardiology in the Duke University School of Medicine. From 2016-17, he served as Commissioner for Food and Drugs at the U.S. Food and Drug Administration.

Dr. Haider Warraich is a physician, writer and clinical researcher with the Division of Cardiology, Department of Medicine, Duke University School of Medicine in Durham, North Carolina. And we will start with you, Dr. Warraich. What explains the difference in mortality between men and women, is it biology or behavior or just something else?

Dr. Warraich: I think for a long time it was perhaps believed, especially over the first half of the century, that biology might explain

the differences in lifespan between men and women, but I think one of the things that we are seeing increasingly as we can widen the lens and start to think of other factors that affect human health, that it's probably a combination of not only biology but also behavior and societal factors.

Certainly, if you look at trends in the United States, trends that have led to relative widening of the gap in mortality between men and women, I think it is our belief that at this point at least, the reason for that is more behavior rather than biology.

Dr. Califf: I would just add that behavior has some base in biology and some base in -- obviously in culture and socialization and the way it happens, but I think it's almost irrefutable now that men take more risk earlier in life in ways that are detrimental to longevity than women do.

Bob Barrett: Does this mean if a man has made it past 65, are they about equal after that?

Dr. Califf: The difference is they do even out once people get older but there's so many differences earlier. I think almost everyone now has a relative who has been in the nursing home, and if you look at the nursing population, it's vastly majority women because of the men are dead by that time.

Dr. Warraich: If you look at centenarians and super centenarians, people who are even older than a hundred, the ratio between men and women becomes even more stark just to add to Dr. Califf's great point.

Bob Barrett: So how can modern digital technology help bridge the gap, if it all?

Dr. Califf: So, I would say some of this could be helped by digital technology if it gave, sort of, promoted better health habits and less unnecessary risk-taking and one could argue that actually digital technologies have been reinforcing risky health behaviors up until now because of the way advertising works and the way certain things are glamorized that men tend to be attracted by, extreme skiing being one example I think about with my two sons. But you can imagine that the same kind of technology since it reaches almost everyone could be used to inform people better about risk and what it means to their future. This is a difficult topic though. It's very hard to reinforce what's called executive function, which is the function of being able to not do something now because it will lead to benefits in the distant future.

Dr. Warraich: I mean, I couldn't agree with Dr. Califf more and I think this is really an important time in which people that we as

physicians, public health experts, need to sit down with experts and with people in the Silicon Valley to really start thinking about A) identifying what are the broad implications or impacts that digital technology, the internet, social media are having on human health, and then maybe start to come together and find ways of mitigating some of these -- some of its ill effects, but also thinking about how can we sort of take the next step and use the tools that we have, the connectivity that we have, to really be able to find synergy because as Dr. Califf has mentioned, so far, I think as a society, as a species really, we're just grappling with understanding just how much human life has changed over such a short period time and what the impacts of that are. We're just beginning to, I think, scratch the surface.

Bob Barrett: We're hearing of course recently that men are living shorter lives today because of an increase of deaths from opioids, that is a general question but what can you think could be done to stem this epidemic?

Dr. Califf: Well, you've really—that' a huge topic with many, many facets and many sort of culprits in the system who have been involved. But I do think there is this underlying theme of what's been called diseases of despair and it's addiction, overdose, suicide are the main components of this, and one interesting part of the suicide issue is that the proliferation of guns which tends to be dominant in men, leads to an increase in what's been termed successful suicide, that is if you're trying to commit suicide by other methods, it's actually hard to do it and people end up not completing the suicide but if you use a gun, it happens and the dominant form of suicide in men is with the use of guns. On the opioids, I think that is men and women actually. Less of a divide there but men tend to be more extreme in their use of drugs and I think that does lead to some difference. Haider, I don't know if you have a view on that.

Dr. Warraich: I mean, I think that you're right. I mean, I think that the opioid epidemic is a symptom of so many different things, trends have been going on. There's a lot of economic disparities. There's a big rural/urban divide that's starting to open up in health and finances. There is this weakening of the social fabric that connects people together in communities and certainly, I think I'd be remiss not to say that the health system had at least if not a causative part, a small part in promoting the use of opioids without perhaps being able to forecast or foresee what this might turn into.

I mean, there was a time when -- especially when I had started training that you know, pain was considered as a fifth vital sign along with heart rate, blood pressure, temperature, et cetera, and now a lot of medical societies like the MA, like the VA, et cetera have now realized that

perhaps that was not the best approach. So, I mean this is going to be -- to solve this both for men and for women, I think on the opioid epidemic, we all need to come together and figure out ways that cut across some of these silos to really be able to overcome it.

Bob Barrett: Well, let's talk about cardiovascular disease because that was traditionally seen as a disease of men, you know the harried executive with a cigar in one hand and clutching his chest with the other. But recent studies have shown that women have caught up when it comes to cardiovascular disease. How is this disease the same and different between men and women?

Dr. Califf: Well, I'd say women have caught up, that's sort of a yes and no thing. In terms of lifetime risk, women have definitely caught up but there is a difference in the incidence of cardiovascular disease, particularly the premenopausal phase in women is still significantly lower risk than men. The good and bad news here is that these effects are mostly mediated by risk factors that we understand, you know, blood pressure, lipid levels, smoking behavior, lack of exercise, obesity, and diabetes with high glucose levels being bad. You know, the mediators of these problems are pretty well understood, and the place where women catch up particularly in older age, that's a scenario where we still have a lot to learn about the interaction of aging and these risk factors.

Dr. Warraich: I think that's a great question and there has been a lot of debate about whether women in fact have different symptoms from men when it comes to -- when they experience heart disease. There are some data to suggest that a lot of women have so called atypical symptoms and not the classic symptoms of heart disease, that may lead to potential misdiagnosis but other studies show that that may not be the case. I think studies and surveys suggest that despite the knowledge that diseases like heart disease remain the number one killer of women as it is with men, there is just not enough recognition that it is a disease that affects both sexes at the same rate. So even though men especially early on in their lives have a higher incidence of heart disease, there is some data that we have cited that shows that when women do in fact have heart disease early on, their outcomes are in fact worse and now it's hard to know why that happens.

Some of it is because there is a delayed recognition both on the part of the patient that you know, a lot of -- there's a lot of qualitative data that suggest that you know, lot of women who had had heart attacks didn't really attribute their symptoms to that. And a lot of physicians sometimes can be, you know, less suspicious or less rigorous in trying to

diagnose heart disease in women because the incidence is lower so I do think that this is something that disparity does need to be addressed further with more research.

Dr. Califf: Well, yeah, I just want to emphasize that in a discussion about men, while it's definitely the case that we need to understand the differences that women face and we need to raise awareness about heart disease in women, I think this might a tendency to believe that we've got the problem solved as it relates to men when in fact that's not what the data shows. And so, it's not as if we know exactly what to do with men and are making tremendous strides, in fact death rates from cardiovascular disease have leveled off in our society in the U.S. in the last several years and it's a very alarming trend. The stroke rates are actually going up. We need to understand women better but we also need to focus some attention on men since they're dying at earlier ages from heart disease.

Bob Barrett: Okay, well since we are discussing men in this special issue of *Clinical Chemistry*, let's end with this one, the term toxic masculinity. It's a phrase that's often misunderstood. What are your views on the use of this term, toxic masculinity, Dr. Califf?

Dr. Califf: Oh, I'll let Haider take that one. He's an expert in that area.

Dr. Warraich: You know, I think that from time to time there is a certain term that becomes fashionable. But I do think that there is a ring of truth to this term. I think one of the things that as we've talked about already is that men, because of both biological differences but also behavioral differences and differences that occur because of how boys are raised, do end up more aggressive and violent and that's something that we've seen throughout history. And a lot of times that has been used by people, that has been used by autocrats and dictators and generals to conquer other nations and to fulfill their own goals but at the same time I think what's being missed is that a lot of these behaviors, the sort of classic, sort of masculine behavior or the sort of masculine form of, you know, I'm going to take care of myself, I don't need help, et cetera, et cetera, is now coming back to hurt men. We know that men are less likely to seek help, we know that they are less likely to visit a doctor, they're less likely to talk about things like depression and anxiety.

So, you know, I think a lot of people when they talk about this term, they think about the effect that the traditional or sort of the stereotypical masculinity has on other people, but I think what we're trying to show and I think what the data supports is at this is also equally dangerous to men themselves, and that this is being born-out by this increase in the number of men dying prematurely of what are

preventable reasons. So, I do think that there is some ring of truth to this term but we want to turn it around, we want to use this in a positive way to sort of focus on how can we help men take better care, not only of other people around them, but also of themselves.

Dr. Califf:

Yeah, just to reemphasize one part of this that Haider, I thought, gave a great explanation of thinking about it, the self-reliance thing, which is very much reinforced in men whereas on average, women tend to be more involved socially and emotionally in the issues, you know, a very high proportion of decisions, health decisions, about men are made by the woman in the family. And it's good that women help out and want to be involved but if men could seek help more actively and take better care of themselves, it would surely result in better outcomes and how to deal with that culturally, it's probably not a biological thing. Haider has pointed out nicely in the writing that in some cultures, men do take better care of themselves and it's something that we should strive for.

Bob Barrett:

That was Dr. Robert Califf, Vice Chancellor for Health Data Science and Professor of Cardiology in the Duke University School of Medicine and a former Commissioner of Food and Drugs at the USFDA. He was joined by his colleague, Dr. Haider Warraich, a physician, writer, and clinical researcher with the Division of Cardiology, also at Duke. They have been our guests in this podcast covering differences in health outcomes between men and women. Their article on that topic appears in the January 2019 issue of *Clinical Chemistry*, a special issue devoted to the area of men's health. I'm Bob Barrett. Thanks for listening.