

Charles Ryan:

Hello, everybody. Good evening, good afternoon, good morning depending on where you are and it's great to see you all again on this webinar. This is our second Prostate Cancer Foundation webinar on the issues most important to prostate cancer patients. And I am Chuck Ryan, I'm the CEO and President of the Prostate Cancer Foundation, and our next guest, Dr. Cooperberg. Dr. Matt Cooperberg is somebody I've known for over 20 years now because we were colleagues together at the University of California San Francisco.

Matt is a urologist who's a specialist in prostate cancer. He practices at the UCSF Helen Diller Family Comprehensive Cancer Center, and he's also the chief of urology at the San Francisco VA Medical Center. Matt is a true global thought leader on many aspects of decision making with regards to localized prostate cancer, in particular regarding early detection, diagnosis and management of early stage prostate cancer, as well as the integration of biological testing and genomics into this process. Matt has written over 400 research articles and published. He's written nine book chapters and lectured nationally and internationally on this topic. And before all that started, he was a PCF Young Investigator, so we again are going to claim credit for you as well. Matt, it's great to see you. Thank you for joining us and we're going to talk about a really interesting topic, I think one that doesn't probably get the attention that it deserves and that's treatment regret. Tell us what treatment regret is and what do you mean when you use that term.

Matthew Cooperberg:

Yeah, it's a pleasure. First of all, thanks for the invitation. It is great to be here. I am going to show a couple slides just to orient our discussion. It is a perfect dovetail topic from what you're discussing with Alicia because in many respects, treatment regret is the other side of the coin from shared decision making because most often treatment regret results from a patient feeling like his expectations did not meet the outcomes which ultimately transpired. And it is that disconnect, which does tend to drive regret. And again, just a couple minutes, I think we're increasingly clear on how prostate cancer should be treated and it's all about disease risk. I'm not going to get too much into the details of what is meant by risk, but the typical risk factors are things like the Gleason score, the PSA, the stage, the number of cores involved with diagnosis.

And these allow us to determine the risk that a given prostate cancer will ultimately progress. And when we say progress, what that typically means is the likelihood that it will ever spread or threaten life. And of course most of them don't, which is why the top line here for patients with lower risk disease, active surveillance has really been more and more consistently endorsed as the preferred management strategy for men with low risk disease. Basically at this point, all Gleason six, three plus three, or grade group one prostate cancer is eligible for active surveillance. There are exceptions, but it is never an emergency and almost all men in this category can start with surveillance. Slightly higher risk tumors are now increasingly eligible for focal therapy with HIFU or cryotherapy or other energy sources. Moving on to the solidly intermediate risk group, these are men that typically are treated with surgery or radiation to the whole gland.

Higher risk still, we're often talking about combining treatments. These cancers often require surgery plus radiation or some combination of radiation and systemic therapy. And finally, the ones that are really aggressive or already metastatic at time of diagnosis will typically be managed first with systemic therapy, with hormonal therapy or other treatments. And of course the issue is that all of these treatments can cause side effects and a lot of the discussion is really about surgery versus radiation therapy or surgery versus radiation versus active surveillance. And for all the fact that there's controversies pretty much everywhere in prostate cancer, I would say there's not much controversy left

about the quality of life impact of surgery versus radiation therapy. There have been some really, really good long term cohort studies over the past 20 years. We ran some of these at UCSF, I've been a part of some of the others and it is pretty clear at this point the surgery causes more urinary incontinence, which is leakage.

Radiation tends to cause more urinary irritation symptoms. That's having to go to the bathroom all the time to urinate or have a bowel movement or both. Radiation does tend to cause more bowel symptoms. Both surgery and radiation can affect sexual function. Surgery will tend to cause an immediate drop in erections that then recover over time. Radiation therapy will cause more of a delayed drop in sexual function and that delta, the difference between them gets less and less as the years go by. And a man who's treated with radiation together with hormonal therapy will face the additional effects of the hormonal therapy as well. And again, there's not much controversial on this slide and I can't say that very often about any slide that I put up about prostate cancer. The question is how well counts of men are going in and how well they understand what the implications of this treatment decision are likely to be.

And there's actually a rich literature on this. We study absolutely everything there is to study about prostate cancer including decision regret and this is one of the more recent ones. There's dozens of papers on this topic in the last five years. This is one of the more recent that came out this year. This looked at men mostly treated in lower volume practices that were identified the patients, the men were identified through the SEER registry run by the National Cancer Institute. We supplemented these with men from the capture registry, which was the registry we ran out of UCSF for a number of years. And they asked the question, who regrets treatment five years after treatment, radiation or active surveillance? And this is what we call a forest plot and what you're looking at here for each of the risk factors on the left here, the boxes show whether there is more or less regret.

And one here is basically odds of one, meaning right down the middle, no more, no less than average. And the boxes that are more to the right, these are men who have more regret, off to the left would be less regret. And just to bottom line this, there are not a lot of drivers here. So age was not a big one. Men who have lower sexual function going into treatment tend to have less regret, perhaps not surprisingly. The text of the paper noted that men who had surgery had slightly more regret than those who had radiation. But this is a really trivial difference between the two. What really stands out here are these two all the way at the bottom here. So first of all, there's a third from the bottom. This is men who developed new health problems due to prostate cancer treatment at the six month mark after treatment.

But this wasn't nearly as strong of a driver. This is we call a logarithmic scale here. So these guys were about 50% more likely to have regret than the average men. But what really stands out men for whom the perception of treatment did not match their outcomes, these men were five times as likely to have regret or more five years after treatment. So this box here was perception of treatment effectiveness compared to expectations. And this one here is perception of treatment adverse effects. So side effects compared to expectations. So who regrets their treatment decision? It's men who are not where they are five years later, they're not where they expect it to be. And in a way regrets sort of rolls together all of the non-cancer associated things that can happen after prostate cancer treatment. And it's all about the mismatch between expectations and outcomes.

A man who is told you were going to leak for six months after surgery and is leaking six months after surgery typically is more or less with that because he made the decision with open eyes as opposed to the man who was told the robot will definitely not cause any incontinence or saw the billboard for the proton center and was convinced that he had absolutely no risk of side effects and has side effects. That man is going to be much less happy even if he has the exact same functional status. Again, a man who's

leaking at six months and expected it may be perfectly okay with that as opposed to a man who expected to be dry and is leaking the same amount at six months. So this is the biggest thing is the mismatch between expectation and outcomes. And the other thing I would say is that we don't always manage the side effects all that well.

So we see all the time in clinic and my colleagues in reconstructive urology see even more frequently, men who have been through surgery or radiation have pretty substantial side effects, incontinence, bad urinary irritation symptoms, bleeding after radiation, things that we can manage and they've just been suffering in silence or complaining to neighbors but not loudly enough to their medical team to get the attention that they need because these side effects are quite often fixable. So obviously the best way to manage regret is to prevent it. And I would say the most important points here before we get into discussion is to really understand where your cancer is in the spectrum of risk. We are doing better and better at not overtreating low risk disease, but there's still a huge degree of variation from practice to practice, even from urologist to urologist.

This may be a shocking statistic, but the likelihood of getting active surveillance for a low risk prostate cancer, one that is extremely unlikely to cause any symptoms or loss of life, ranges depending on whose door you knock on from 0% to a hundred percent. Now this is not unique to prostate cancer, it's not unique to active surveillance, it's not unique to urology. We call this a small area variations problem in healthcare and we see it everywhere. We have the courage to pick up the rock and see what's under it. It's a big problem. And the only way to deal with it, there were a lot of questions in the Q and A already about second opinions, get second opinions. Get a second opinion at an academic center or center of excellence. It's easy to do on Zoom now. Prostate cancer is rarely a time pressured situation.

It's not a ticking time bomb. You've got plenty of time at diagnosis in almost all cases to collect opinions and make sure you're doing the right thing and make sure you have realistic expectations about local outcomes. The surgeon or radiation oncologist you're talking to should not be quoting outcomes from the published literature. They should know their own outcomes. What are their rates of cure of urinary side effects, of bowel side effects? And I would also really stress especially from men with aggressive high risk prostate cancers. Just because the cancer comes back and the PSA rises does not mean that the treatment failed or that the treatment had no purpose or no value.

It is often the case especially as we are now treating much higher risk cancers with surgery and radiation than we would have five or 10 years ago, the cancer may come back, the PSA may recur, but we have some sense, and we're still trying to figure out whether this is true, we have a sense that we are pushing back the cancer often by years and we're setting back the clock by years so that whereas the PSA may rise, we're probably avoiding the onset of needing permanent hormonal therapy and onset of symptomatic metastatic disease often by years. And finally, like I said, don't suffer in silence with the side effects of treatment. So I'll stop there.

Charles Ryan:

Great. So excellent overview. And I think to summarize, it's communicate before the procedure, communicate after the procedure, right? How to [inaudible 00:11:24] their regret, because if you know going in what you're expected to achieve, you are not going to be likely regretting it. I think that you've touched on this, but it seems to me that most regret comes from overtreatment and side effects of treatment. Is that fair?

Matthew Cooperberg:

Yeah, I think it's more the side effects than the overtreatment. The example that I gave, the two men, one of whom expected to be leaking and one of them who didn't expect to be leaking. Obviously it's a

worse case for both those men if they were overtreated, no matter how perfectly achieved urinary incontinence, if the guy didn't need the surgery, that was a bad treatment. But the fact of the matter is even if men need the surgery or need the radiation and they go in and have side effects that they did not expect to have, that's going to drive unhappiness.

Charles Ryan:

So what are you finding as the recourse that patients take after they have a treatment regret? Is it just something where they're living with it? Or if you're a patient out there and you have a regret of treatment, who do you go to for support for this and how do you deal with that?

Matthew Cooperberg:

That's a great question and I think everybody finds their own path here for better or worse, I think men that have access to good support networks, either local support with family and friends or community organizations can lean on them. Although they're not likely to get much relief necessarily aside from psychological support. And support groups, there was a question in the Q and A about support groups, it is always a great idea to find a good support group. And I know PCF has some terrific lists of support organizations around the country. This is always a good idea. And this is one of the things that's easier and easier in the Zoom era. A lot of these groups meet by Zoom now, so you don't have to drive hours necessarily. It's good to hear the experience of other men that have been through the same treatments, maybe suffering the same side effects and know is your experience atypical or not.

So some men just suffer in silence. There is a lot of resilience and I think a lot of men feel like, well, it's best to just grin and bear it. And I'll sometimes meet men who were treated 20 years ago and have been dealing with leakage that we could easily have fixed, or not easily, but we could have fixed. And they just say, "Well, this is how life is now." And they're just living with it. And that's okay as long as it's really true. But it's not uncommon that we will say, "I'm happy to have you talk to one of my colleagues about a relatively straightforward procedure to fix this." And the guy says, "No, I'm fine." And the wife in the back is saying, "Come on, don't you want to have this conversation?" And it's always at least worth the conversation. I would say you absolutely want to at least hear what the options are to deal with the side effects.

Charles Ryan:

Yeah. I think in a situation like this, how men make decisions when they're diagnosed with prostate cancer, probably mimics how they make decisions about other things in life, whether it's buying a house or buying a car or business decisions that they might make. And I think that the other way to look at that is that there are some people who really have always struggled with big decisions and are going to struggle with almost any decision they make. And last month, we had Andy Roth from Memorial Sloan Kettering, a psychiatrist who deals with prostate cancer patients. We just had a great chat with Alicia Morgans about shared decision making. And I guess what I'm getting at is what should we as a field be doing better to try to avoid these things? And I know the answers communicate, but dive into that a little bit more.

Matthew Cooperberg:

It's easy to say communicate, it's actually not that easy to implement. I did listen in on the conversation with Alicia, and a lot of the comments were totally salient to my practice too. But what you're describing is yet another thing that we actually study in prostate cancer, which is decision making preferences. And people legitimately vary on this. There are men that come in with a stack of internet research and as the

urologist or the diagnosing clinician or oncologist, I'm really just there to help him validate what he's already decided and he knows his path.

And at the other extreme, there's people who really just want to be told what to do. And I think, like you said, we resist that in contemporary practice because it seems like in older paternalistic practice. But there are men that really get stuck. And really the most common question that I think I get at the end of a 40 minute new diagnosis conversation is, "So what would you do?" And like everything else, we've studied that. Right now, this is not a UCSF study, but there is research that we can go on for an hour and a half with the conversation and all the guy walks away with is the answer to that question.

So when I answer it, it's with explicitly a few tablespoons of salt. So I think it is one of the things that is really in the domain of art of medicine is trying to get a sense with the new patient encounter through that, establishing that relationship where this person is in that spectrum. Is it somebody that really is going to need some guidance or somebody that really just needs validation? And most people, of course are somewhere in between.

Charles Ryan:

Yeah. I want to ask Alicia that question of how do you respond when somebody says, "What would you do?" And I get asked that question and I always say, "Well, I'm not you. I don't have the same life experience as you. I don't have the same body as you. I don't have the same expectations and fears and concerns as you, so your decision is uniquely yours. My decision is uniquely mine and it's not that simple."

Matthew Cooperberg:

It's not that simple.

Charles Ryan:

I actually, to the patients out there, I would discourage asking that question because I don't know that's productive, I guess. You may disagree.

Matthew Cooperberg:

No, I agree. But it is the most common question. I say something very similar to what you said. And if I'm pushed, I'll answer it. And usually we'll have some bias. I mean, it's rare that my opinion is truly 50/50 for a given question. It'll usually be 60/40 and then I'll couch it in those terms if I am going to answer the question. I think we also sometimes kid ourselves about our objectivity. I mean, I can present the same information lots of different ways and subtly shift a decision. I can tell somebody they're 99% likely to live or 1% likely to die. That's the same statistical information, but I'm subtly shifting the first guy towards surveillance and the second guy toward treatment.

We can go one further than that. I could read you the same scripted paragraph and say, "Mr. Jones, you have a low risk prostate cancer, you're going to be fine. If this progresses in the future, we'll treat it. Don't worry about it. Surgery will be an option down the road." Or I can say, "Mr. Jones, you've got a low risk prostate cancer, you'll probably be fine. In the future, I think we can do radiation therapy." I mean we could read the same paragraph with different inflection and be subtly directing what that decision is going to look like. People do that for all kinds of well-intentioned or less well-intentioned reasons in clinical medicine.

Charles Ryan:

The biggest problem with doctors is that they tend to be human. The biggest advantage or the most important quality of doctors is that they tend to be human. I'll put that one in my memoir. But this I think gets to the point of, again, a shared decision making point as well, which is we had IBM Watson, we had this idea that we are just going to... All that mattered was the data. And what we found was that the data didn't really set us free in the way that we hoped it would because we have to interpret the data through the lens of our humanity. And that's a challenge on both the decision making and the regret side. What do you do when patients come to you and you didn't treat them, but they are voicing regret and upset with their doctor and they're saying, "Did I get the right treatment? Should I have done differently?" Do you get faced with that a lot?

Matthew Cooperberg:

Yep. I wouldn't say all that frequently, but we definitely do see it. And generally speaking, we try to face forward and make sure that whatever's going on, whether it is a recurrent cancer or side effects that have been undermanaged, we're putting resources in front of the patient to try to get them back on track and try to deal with the situations as best we can. I mean that's not an uncommon situation. It is uncommon that somebody's really pushing for an opinion about, "Did Dr. Smith screw up?" And twice in my career have I said, "Yeah, that was pretty bad," when it's egregious. Because the fact is it's easy to Monday morning quarterback these decisions, especially in prostate cancer because there are so many shades of gray with all these decisions. And quite frankly, often what I would've told you today might be different from what I would've told you in 2018 when you made this decision.

Science marches on, knowledge marches on, and knowledge diffuses. So I think today, even though we've been doing active surveillance at UCSF for 20 years now, I think it is different for a community urologist to still offer aggressive radiation or surgery for the little three plus three micro spec than it would've been even four or five years ago and less defensible in community practice. So you really have to think about where the patient's journey has taken them through all this. And like I said, we try to face forward. And again, a lot of the regret happens in terms of, well, things are not going well. If you were overtreated but had a good recovery, well you might grumble a little bit and say, "Well, I didn't need to go through all this, but basically life is okay, let's just move on." It's usually folks that have ongoing problems and we can often fix the problems.

Charles Ryan:

But I mean, as you point out, recurrence isn't the major source of regret.

Matthew Cooperberg:

Yeah, it's not. That's right.

Charles Ryan:

It's recurrence is probably a biological construct that is out of our control and happens despite our best efforts as physicians and the best efforts of patients and the right decisions being made all along. And so that's one of the bigger challenges. How do you think this notion of treatment regret has been received by the urology community? By that I mean in the academic world, is this something that I could go into any urology practice or any academic center and talk about treatment regret and people are going to know what I'm talking about?

Matthew Cooperberg:

I would say everybody is conceptually familiar with it. There is a reasonably robust literature about it in prostate cancer. I think everyone viscerally understands it. I don't think it's something that is approaching clinical practice the way we routinely now as part of clinical care, not research, we routinely collect patient reported surveys on urinary function, sexual function, anxiety, things like this. We do not have a regret question in a standard clinical tool yet. And I'm not aware of anyone else that does yet either. Maybe it's the kind of thing that we should think about, because the fact is the medicine center is doing this. All these satisfaction Press Ganey surveys that are going on out there, they're all about communication actually. Not so much about how satisfied are you with your outcome, but we are heading that way. I mean, satisfaction is a pretty imperfect proxy for quality of care. But it's something that-

Charles Ryan:

I want you to reset. You said it's pretty imperfect.

Matthew Cooperberg:

Imperfect, imperfect. Yeah.

Charles Ryan:

Yeah. I think of a patient satisfaction survey as not the same thing as expressing no regret.

Matthew Cooperberg:

Not at all. Not at all.

Charles Ryan:

Yeah. Satisfaction starts at mildly positive and moves up, but regret is a big deal. You regret having your cancer treated. And when people are first diagnosed with this, they can't imagine that that's something that happens.

Matthew Cooperberg:

I would say it's also driven. I mean, there is also the aspect where it's driven by marketing and there was a Q and A about HIFU and protons and things and say, "Why did I get my surgery? Why did you get my prostate out when I could have just had HIFU?" And a lot of the novel treatments, a lot of their development is really, really driven heavily by marketing and by anecdote rather than by data. And this is very hard.

Prostate cancer being so common, everybody has a neighbor, neighbor or a relative or a friend that's been through this. And a lot of the conversations are, "Bill got IMRT and had a terrible time," or, "Bill got surgery and had a terrible time," or, "Bill got protons and did just fine. Why can't I get protons?" And if there is a good thing about prostate cancer being so common, it's that we have tons and tons of really good data on these questions. And that is sometimes one of the more challenging parts of the conversation is trying to reorient away from the anecdotes and back toward what we know, because we know a great deal about what these treatments do and don't do.

Charles Ryan:

And this is advice to patients now like the guy sitting next to you in the waiting room or the guy you're talking to who's your best friend in your support group, the treatment that worked great for him or

poorly for him obviously may not apply to you because that's the challenge and that's the task of the physician is personalizing the treatment to you. And I think that this again is another topic that dovetails with the shared decision making, which is we physicians try to not let anecdotes drive our recommendations, but sometimes they do, I think. But that's a shared bias that both patients and physicians will have, which is anecdotes can weigh very heavily on our biases and our decision making.

Matthew Cooperberg:

I would say that's one minor caveat about support groups too, is that this is a massive gender generalization here, but most men treated for prostate cancer whose cancer is cured and have minimal side effects are not the ones in the support groups. They just want to never think about this again and move on with life. And that is a huge generalization, but it does tend to be true. The folks that are in support groups and are there to give support rather than seeking support are often the ones that have had a more complex journey. So that's just something to bear in mind too, in terms of trying to assess what is a typical or expected course.

Charles Ryan:

Right. Well, those are a couple of the issues that we here at the PCF are trying to help address with these webinars and these conversations that we have, which are pretty open back and forth about these various topics. And I'll take a moment to put a plug in about the launch of Cancer Patient Voices. That's [cancerpatientvoices.com](http://cancerpatientvoices.com) that will be launching probably next month. And one of the goals with that is to have patients talking about their journeys and to normalize I think some of the aspects of the journeys that happen. It's not all about anecdotes, it's going to be about seeing others who look and sound and talk like you talking about things that you're thinking or fearing that you're going to go through as well. So it is a big part of the patient support part of what the Prostate Cancer Foundation is trying to do. Final moments here, your advice to patients who are experiencing regret. You've made some points that I think are really good ones, but leave us on a high note, if you will. What do we do?

Matthew Cooperberg:

Help is out there. Get more opinions, find people. If there's a silver lining to the whole COVID pandemic, it's that Zoom is here to stay. Our practice at the cancer center at UCSF, we are still 70 to 80% virtual and it will be pretty much forever. People love not driving three hours and paying 30 bucks for parking. It is easier than ever to get access to high quality care, at least to start a conversation and see whether there are interventions that you want to think about because we can fix not all problems, but most problems. And there is help out there.

Charles Ryan:

Yeah, that's a really important point to leave us with. And I agree with everything you said, although I think your estimate of \$30 for parking might be a little low. I might be wrong.

Matthew Cooperberg:

It's subsidized for patients.

Charles Ryan:

Okay. All right. Well, thank you Dr. Matt Cooperberg. You've been a wonderful colleague for many, many years and I always learn something when I talk to you and I hope that the patients listening have had an opportunity to learn from you. And they should also, by the way, check you out on [urotoday.com](http://urotoday.com)



where you've absolutely recorded and written and given your thoughts on a variety of topics, many of them related to this and probably some of the data on the work that you've done around active surveillance and other things. And you and I have had many conversations on UroToday.

So we look forward to seeing you all. Thank you once again, and thank you everybody on the team at PCF for helping us to get this launched. And we want to put a final share here, visit us, look up for updates at [pcf.org](http://pcf.org) and we will have a November webinar. We're working around that. So we'll be sending out an announcement and a sign up for that shortly. And we are now planning the whole next year of webinars, so we're really enjoying doing these and getting good feedback. So please send us your feedback and let us know how we're doing. Great to see you all and take care and enjoy the rest of your day.

Matthew Cooperberg:

It was a pleasure. Thanks.

Charles Ryan:

Bye-bye.