Scott Redding: Welcome to the 3 Ps of Cancer Podcast, where we'll discuss prevention, preparedness and progress in cancer treatments and research. Brought to you by the University of Michigan Rogel Cancer Center. I'm Scott Redding.

Scott Redding: We're here with Dr. Dan Hayes, the Stuart B. Padnos Professor of Breast Cancer Research and the Clinical Director of the Breast Oncology Program at the Rogel Cancer Center. Dan has close to 40 years of oncology practice, as well as a member of many medical and oncological organizations. While his clinical and research focus is on breast cancer, his years of experience and participation in national organizations give him a deeper perspective on where cancer care has been, where it's at now, and what the future might look like.

Scott Redding: Welcome, Dan.

Dr. Dan Hayes: Hey, Scott.

Scott Redding: Let's start off with probably the most sought-after answer around cancer. When are we going to cure it?

Dr. Dan Hayes: I probably get that question once a month, especially when I was the President of ASCO, the American Society of Clinical Oncology. And my answer actually is that we already do. We cure a lot of cancers with a combination of surgery and radiation, and systemic therapies like chemotherapy and others, endocrine therapy. Now more recently, immunologic therapies. It's that the word cancer is not a single being. It's like when are we gonna cure diseases? Well, there a lot of different diseases. There a lot of different kinds of cancers, and we cure a lot of them. In fact we have gotten recent data that suggest, a very exciting, actually, data, that the odds of dying of cancer in this country have been dropping probably by as much as 25% over the last 30 years. And that's by a combination of screening and judicial application of both old therapies and new ones, and giving them in better ways. So we do cure a lot of cancers.

Dr. Dan Hayes: The real question is when are we gonna cure all cancers? When are we gonna cure enough cancers? And enough in my opinion is all. And that's the big issue, and there's a lot of research going on. A lot more research needs to be done. Reducing the odds of dying of cancer by a certain percentage, a quarter, is great, but it should be by 100%. So we need to work together as a society between the clinical researchers and the laboratory researchers and our patients, altogether be willing to support the cost it will take to do this. I'm shameless. We need the money to support this. This research is very expensive. So the NIH budget has been going up over the last three or four years. We're extraordinarily appreciative of that, that the government's been very generous. But that's after 10 years of flat funding.

Dr. Dan Hayes: So when you filter in inflation with that we actually lost about a quarter of the funding for the National Cancer Institute over the last decade until about three or four years ago. It's been going up about $2 billion a year to the NIH, and

within that, then money comes to all the institutes, including the National Cancer Institute. And that's where our major source funding is. That research is a great investment, and that's what's gonna lead us to cure more cancers.

Dr. Dan Hayes: So it's a long-winded answer to something I feel very passionately about. We're only gonna cure cancer by doing good research, not by accident or ... It doesn't happen magically.

Scott Redding: How do you respond to people that question whether the money that is raised, that goes towards cancer research, is actually making a difference? You hear stories that, "I give money to X organization for cancer research, but how do I know that that's actually making a difference?"

Dr. Dan Hayes: Let's separate two things. The one I just talked about, which is your tax dollars going in to support the National Institute of Health and the National Cancer Institute. That money is spent very responsibly with lots of oversight, and maybe even too much peer review, because it's so hard to get grants. Right now, for example, the odds of having your grant approved in the National Cancer Institute is one in 10. And I would ask anybody listening to this, would take a job where you had 10% chance of getting paid? Probably not. Now, our young people do get paid, but the point here is that those are the grants that keep them alive and academics doing research, and it's gotten to be very frustrating if you don't have a very good chance of getting funded.

Dr. Dan Hayes: So that leads to the second source of funds, which is philanthropy. And I agree with you. You have to be very careful, Scott. There are fly-by-night, and charlatans out there that start foundations that you can't trust, and they take the money and don't do good things with it. But there are a lot of groups out there that do great work, and there are ways to look up on the internet whether they are respected foundations and how much they spend on administration as opposed to giving out the grants, and who they give the grants to and how it's used. And so it's not that hard to figure that out, and the money you give, if you give it to a really legitimate organization, is used well. I mean, the American Cancer Society, for example, my own, ASCO, the American Society of Clinical Oncology, the American Association of Cancer Research. I could go on and on. There are a number of these that use the money to support really important and ground-breaking research.

Dr. Dan Hayes: Furthermore there are sone less well-known but private philanthropic organizations, or people who just wanna give money to an institution. Where that money actually can be used on really innovative shooting [inaudible 00:06:08] kind of experiments. So for example, if I wanna get a grant funded through the federal government I almost have to have the research done before I put in the grant, because the pure review is so strict and the people look at it and say, "Well, I'm not sure it can be done," and blah-blah-blah-blah-dah. All of which is okay. That means we're really funding first-rate out of that. But it means you can't really take a chance. You can't put a grant in that says, "I think cutting people's arms off is gonna cure cancer." I'm making a joke. We're not

gonna cut people's arms off. But really innovative shots in the dark to see if there's something there.

Dr. Dan Hayes: So we have people who give philanthropy to the University of Michigan to support, in my case it's the breast cancer program, and I tell them lots of times I use that to support young people or people who aren't in the field who I think have a pretty good idea that may never pan out, but if somebody doesn't put money into it we'll never know that. And you don't know a seed will grow unless you plant it. My favorite story, just two weeks ago I had one of my young people in my office with what I think is a really good idea. She turned in a grant and I understand they funded three people, and she was fourth. At least that's what we've heard. And, "How am I gonna do this? How am I gonna do this? Woe is me." That evening I went to a fundraising celebration of some people in the local area who have given us well over 60 or $70,000 over the last few years, and I told them, "This is the kind of money that I can say to a woman like that, 'I still want you to turn in the next grant. I still want you to go back in and keep working on the peer-reviewed grants, but this is gonna keep you alive until you do it.'"

Dr. Dan Hayes: And that's a great use of that money. So that even if it's not a successful project, it's a successful person. And it's those people who will do successful projects down the road. I'm enormously devoted to making sure that we have young people who come in the field and stay in the field, 'cause they're who are gonna make a difference now in the next 10 years.

Scott Redding: So you had mentioned that mortality rates for cancers have decreased over the last 23 or so years. Does that mean that cancer is moving more to be a chronic disease?

Dr. Dan Hayes: Let me once again jump again. Cancer is not cancer. Some cancers are. Some are not. For example, testicular cancer, which in 1970 had a 90% mortality rate if you had metastatic testicular cancer. By 1980 it had a 10% mortality rate. And in fact, if you have metastatic testicular cancer and you get the chemotherapy that cures people now, and then it all goes away, if it hasn't come back within two years you're probably cured. So that's not a chronic disease. That's big bang, and we treat those guys right to brink of death almost. 'Cause we're not trying to make them feel better. We're trying to cure them. And we know we can do that. But there are other cancers that have been notoriously difficult to treat frankly, that are becoming increasingly more like chronic diseases now.

Dr. Dan Hayes: There have been people who have taken offense to saying it's gotta be like hypertension or diabetes. I agree. It's not like hypertension or diabetes. It's more profoundly frightening and impact on your life. But nonetheless, for example, I do breast cancer work. When patients develop a recurrent breast cancer outside of their breast, again, a metastasis, I tell them it's bad news and good news. And the bad news is, I think, the worst news I can tell a patient, which is we're probably not gonna cure this, try we might. And we keep trying and we keep doing more research. We keep trying to do things where I don't

have to say that to a patient anymore. If that's the case, what's the good news? Well, the good news is it's metastatic breast cancer, and by that I mean we have armamentarium of treatments that 30, 35 years ago when I started in this field I couldn't of even imagined.

Dr. Dan Hayes: And We converted in many ways into a chronic disease. Instead of having a life span expected of a couple of years from the time I have that talk with patients, it's now much longer than that. And for some aspects of breast cancer, really long. And so it doesn't mean we've cured it, but I tell patients my goal of therapy in that case, outside of a clinical trial where we're trying to change the discussion, is to keep people feeling as good as they can for as long as they can, and that means picking therapy most likely to work with the fewest side effects. And we're pretty good at that. And we've been good at that in breast cancer for a number of years. But we've got so many new things now. The new anti-estrogen therapies. All the new therapies against HER2, another molecule that cancers make. And now we even have therapies besides chemotherapy that work against cancers that don't make estrogen receptor or HER2, so-called triple negative cancers.

Dr. Dan Hayes: The same thing is happening in lung cancer. My successor in ASCO, Dr. Bruce Johnson from Harvard, is a lung cancer doctor. When you're the ASCO President you give a presidential address. I happened to give mine on all the things that our society can do for people. But he gave his on lung cancer, and he made the point that we've done exactly what you just asked. We've taken metastatic lung cancer and, not as well as we'd like, and we're not curing people right and left, but in many respects we've turned it into, in many parts of lung cancer, into chronic diseases, where either taking some pills or the new immunotherapies can help people get to feeling better without a lot of side effects and live pretty normal lives. And I have to tell you, I never thought I would say that about metastatic lung cancer in my career. So that's been great.

Dr. Dan Hayes: And we're making progress like that in many of the disease, not as fast as we ought to. But there are a lot of people with metastatic disease who are living pretty decent lives on therapy with some side effects, but still getting along. What would be even better is if we could prevent their getting metastatic disease in the first place. What could be even better is keeping them from getting cancer in the first place. But in the absence of that we'll keep making progress in the way we are now.

Scott Redding: So you just shared a story about your success over at ASCO and talking about lung cancer, and how it's progressed in those treatments from where it was to where it is now. How have you in your career seen cancer treatments progress, as well as even some of the new ones we hear about, like immunotherapy?

Dr. Dan Hayes: So that raises one of my favorite jokes, which is when I'm asked this question I often say I wish I was 30 years old again, because there's so much excitement in our field. There are a lot of other reasons I wish I was 30 years old again. I can't run anymore. But having said that, there's so much excitement, and I think the

new young doctors coming into the field are doing so because of this. In the old days the stand-by treatment for most cancers was chemotherapy. I actually trained with the people who first started giving chemotherapy. Some of my mentors were the first guys who put one and one together and got two and saw cures. Very exciting. But chemotherapy is tough to take.

Dr. Dan Hayes: Breast cancer has for a long time, and prostate cancer too, used what we call hormone therapy, which is anti-estrogen or anti-testosterone therapy, and that's a little easier to take usually. So that's been good. And that set the stage, I think, for what we now call targeted therapy. And targeted therapy, unlike chemotherapy, which is kinda dumb therapy. You give it to people and hope it works. Targeted therapy is you understand the biology of the cancer and you give stuff that attacks what's making that cancer behave poorly. So for example, with the anti-estrogen therapy in breast cancer we know that about 80% of breast cancers make the estrogen receptor. I tell patients that's like the gas tank in the car. The nucleus is like the engine and estrogen's like the gas. And we have ways to screw that up. We can keep people from making estrogen. We can blow up the oil well, if you will, or we can prevent the refinery from working and things like that. I tell them Tamoxifen is like putting water in the gas tank. It gets in there and screws it up.

Dr. Dan Hayes: And HER2. So for example it wasn't discovered until 1983 or four. By '87 we knew it was a bad thing to have in cancers. By the early '90s we had an antibody that's now called Herceptin. Trastuzumab is the generic name. We now have six or seven different active therapies against HER2. We have patients who, I think, 20 years ago would have been dead within a year or two who look like they may be cured by using these drugs. We now have moved Herceptin up early in the [inaudible 00:15:31] setting and reduced mortality substantially in patients who have that.

Dr. Dan Hayes: Lung cancer? It used to be the only treatment for metastatic lung cancer was combination chemotherapy. Now somewhere between a third or more of patients we can find genetic abnormalities for which there are drugs that attack that genetic abnormality, and are quite effective with very few side effects.

Dr. Dan Hayes: So this is called targeted therapy. And in fact now there are big trials going on in this country, sponsored by our tax dollars, in which patients have a biopsy done and have their cancer sequenced. It's called next-gen sequencing. There are various implications of how to do that. But anyway, and then to see whether or not, regardless of where their cancer started, whether it's breast or lung or colon, if they have the abnormality maybe that drug would work no matter what. We're finding that's not true, actually, that the context in which it started is still important. If it's breast cancer it's still different than colon cancer, even if it has the same mutation. But nonetheless it's still broadened our ability to treat patients, and all of us have seen patients where we would never have imagined they would respond to drug X, we did next-gen sequencing, we found mutation number one, which drug X hits, and put them together and had really nice responses. So this is a very exciting area.

Dr. Dan Hayes: The second is the immunotherapy breakthroughs. So people have been wanting our immune system to go after our own cells for well over 100 years. Dates back to the, really, 1870s, 1880s. But evolution has not wanted that to happen for millions of years, and the reason we can all sit here and be healthy is because our immune system is designed to go after invading organisms, and we have other systems inside of us to keep us from getting cancer. And there's a firewall between that, and that's good. It's why we don't all have lupus and rheumatoid arthritis. And so most immunotherapy research up until about 10 or 15 years ago was kinda beating our head against the wall. And about 10 or 15 years ago some really smart people figured out how to break through that firewall. I tell patients it's like, if you're a Harry Potter fan, our own cells, and therefore our cancer cells, which are our own cells, have cloaks of invisibility, and we figured out how to ... We didn't. Somebody smarter than me figured out how to break through it.

Dr. Dan Hayes: That led to two scientists who discovered that winning the Nobel Prize this last Fall, the Fall of 2018. Absolutely deservedly so. Wonderful prize for these guys. And not only did they find out how to break the firewall, they found drugs that could do that, and also combined with drugs we already use ... Probably the first big hit that made me realize there was something going on is we saw data that 20% of patients who had metastatic melanoma, which was always probably the toughest thing for us to treat. Those patients didn't do well and passed away in a hurry. 20% of those patients may be cured with immunotherapies. They are so-called checkpoint inhibitors.

Dr. Dan Hayes: Non-small cell lung cancer, again, what I was talking about with precision medicine, notoriously difficult to treat. Chemotherapy was the only option. I don't think those patients are being cured now, but they're being turned into people with chronic diseases, if you will, with the use of immunotherapy. And so and so forth. And we're getting more drugs. We're finding more things that cause the cloak of invisibility, so we can break through those as well. We're combining them. That's extending the therapy into diseases that didn't traditionally be immunoresponsive diseases. It's a very exciting field. I wish I was 30 years old again, 'cause it's really exciting to see it move so fast.

Dr. Dan Hayes: Here's the downside. Just saw a publication in the last six months that 1% of all patients who get these drugs die from the therapy. They're dying. On the other hand, many patients that get them have no side effects. And so we're trying to figure out why some people get horrible side effects and other people do great, and everybody in between. That's a whole other area of very active research. And I'm really excited about that field. In fact I'm excited about both of those field, because they build on things we already suspected, but now we know how to do it. We've got better tools in the toolbox to get to these things.

Dr. Dan Hayes: So what's next? I don't know. I suspect it'll be something I haven't thought of, like I'm sure it is. And that's why we need to keep young people in the field, 'cause they need to keep thinking about how to make things better.

Scott Redding: Can you tell us a little bit how you've seen changes in both care and treatment for cancer patients?

Dr. Dan Hayes: It's really been a remarkable run for me. I graduated from medical school in 1979, and I finished my oncology fellowship in 1985. So I've either been in this 35 or 40 years, depending on when you wanna start the clock. And during that time it's just been amazing progress to me. Let's stick with breast cancer, 'cause that's what I know the most. In 1979 there was little or no evidence that screening was a good thing to do. Adjuvant chemotherapy and adjuvant endocrine therapy, being anti-estrogen therapy, were under trials, but nobody really showing that giving stuff early better than late. The surgery was horrific. The surgeons were doing radical mastectomies with the feeling that that probably wasn't enough, so they needed to put radiation on top of that. And people had the surgery right down to their ribs, and then got big swollen arms from the radiation. We didn't have any anti-nausea medications in those days. So if we did give chemotherapy we just put them in the hospital and gave them barbiturates, because there just wasn't any anti-nausea medication. Those really didn't work. They didn't keep you from throwing up. They just kept them from remembering how awful it was so they'd still come back and take some more. It was pretty, I don't wanna say barbaric, but pretty primitive.

Dr. Dan Hayes: Nowadays, in breast cancer I'll start out by saying we've seen the odds of dying of breast cancer in this country drop by somewhere between a third and a half. And what I don't mean there is case fatality rate. In other words, if I diagnosed a bunch of things that we call cancer, but were never actually gonna hurt people, and the same number of people die, then we'll still have a lower case fatality rate. This is true. 100,000 women walking down the street, never have breast cancer. What do they die from in the next year, and the odds of it being breast cancer have dropped by almost a half, not quite. And why is that? It's because we've got nine trials showing that screening is better than no screening and reduces the odds of dying. Not by as much as we'd like. Maybe by about a fifth. But still worth doing. It's because we have proven that giving adjuvant, and by adjuvant I mean early, systemic therapy, and by systemic therapy I mean chemotherapy and anti-estrogen therapy, and now anti-HER2 therapy, reduces the odds of dying considerable. And it's because we have convinced most women that it's not as awful as they think and they need to come see us. None of these things works if we never see the patient.

Dr. Dan Hayes: But for example, now we went from radical mastectomy to modified radical mastectomy, to what we call breast-preserving therapy, so that 50% or more of patients who have a new breast cancer don't even need to have a mastectomy. They have a lumpectomy and radiation, and that's as or more effective than having a mastectomy. That's terrific. And we now have terrific anti-nausea medications. We don't put anybody in the hospital to give them chemotherapy anymore. In fact the only people we put in the hospital are the ones that we have failed. And almost all of our treatment is in the outpatient setting. And while occasionally somebody gets sick. I never say never. It's pretty unusual. Most patients don't get sick. Most patients don't get, and by most I mean 99%,

don't get infections. Used to hear in the old days you get chemotherapy you're gonna have an infection. Almost not true anymore. And people work through while they're getting the chemotherapy and stuff. It's really been remarkable.

Dr. Dan Hayes: And then even if their cancer does come back, unfortunately if does, the treatments we have, we talked earlier about converting this into a chronic disease. And it's really fun to be an oncologist because you get to know the patients and you've seen all the things that have happened, and all the advantages. I mean, we really owe a lot to our forefathers who had the courage to do the crazy things they did, and to challenge dogma and not just accept the fact that we can't do anything. And I have enormous respect for these guys. Some of them trained me. And what they did and how they did it. And also I have to say for the American population, the American populace has been willing to put in the tax dollars to support our research, been willing to support our foundations to do the research and get along and participate in the trials.

Dr. Dan Hayes: Takes an enormous amount of courage and also extra work for a patient to be in a clinical trial. It's tough for them just getting regular therapy. And I always tell patients, "We'll do whatever you wanna do, and I rarely hit people below the belt, but I'd like you to be in this trial for two reasons. It might be better for you, but we don't know that. That's why it's a trial. It's at least standard of care." And moreover almost every word I've told that patient before I get to that point has come out because one of them before them have been in clinical trials. And what they will do, whether the study is positive or negative, will help the next group of patients. And people say, "Yes, I agree. I'll buy into that." Which is, I think, just really terrific. I mean, it's why we've been able to get the things done we have. Wish we could do better. Wish we could move faster.

Dr. Dan Hayes: I'll tell you a cute story, and then I'll shut up. So the cute story is that in patients who have estrogen receptor positive breast cancer we have seen the odds of their cancer coming back get lower and lower and lower through the years. So we ran a trial in which we have something called a 21 gene recurrence score, that if it's low it tells us that patient doesn't need chemotherapy, and if it's high she does. And we have an intermediate score, and we didn't know what to do. So we ran a great big trial, a nationwide trial. The results of that have now been published. But anyways, this is three or four years ago.

Dr. Dan Hayes: And one of my patients had an intermediate score. And I said, "I don't know the right answer here, because we're doing a trial where half those women get chemotherapy and half don't, and if I knew the answer we wouldn't be doing that trial." And she said, "Dr. Hayes, I need to know when are the results of that trial gonna be out?" And without thinking I said, "Well, the problem is you're all doing so well we can't get an answer as fast as we thought we could." Well, as soon as I said that I said, "Wait a minute. That's not a problem. The good news is you're all doing so well it's taking longer for us to see the results of our trials because our estimates were made on how people were doing in the 1980s and '90s, and the people in the 2000s are doing better than they used to because of

all this research and all these benefits." So it's a good problem to have, that we're really helping people get along better, live better and live longer.

Scott Redding: We hear more and more, and I don't know if it's the advent of social media or what, but we hear more and more about people having cancer and talking about cancer. Are the incidence rates, we talked about mortality going down, but are incidence rates going up?

Dr. Dan Hayes: I hear this quite a bit. "It seems like everybody in my neighborhood has breast ... Everybody in my bridge club has cancer." And actually there are two, three reasons for this happening. One of those is we talk about cancer. When I was a kid it was embarrassing to have cancer. And I grew up in a good god-fearing Methodist family, and at dinner table we weren't allowed to talk about women who were pregnant, because that has certain implications, and we never talked about women who had cancer, or anybody who had cancer. Well, a select group of celebrities went public 30 or 40 years ago and changed that. Betty Ford, of course, is one of our famous ones from Michigan. And you probably remember Katie Couric had a colonoscopy on camera, 'cause her husband died of colon cancer. Ronald Reagan had colon cancer, and as President of the United States admitted he had colon cancer. And that changed a lot of things. And so all of those were good in terms of just bringing cancer out of the closet. But what that meant was you probably knew other people who had cancer before that. You just never talked about it or you didn't know what they had. They died of consumption or old age, so to speak.

Dr. Dan Hayes: The second thing that's happened is that-

Scott Redding: Actually, if I can interrupt. It's funny you say that 'cause when my dad was diagnosed with cancer he was asked anyone in your family have cancer, and he said, "Oh no." And I said, "What about grandpa?" 'Cause he actually had that oat-cell lung cancer. And he said, "Oh, he died of a heart attack." He died of cancer. So that's [crosstalk 00:29:09].

Dr. Dan Hayes: So that's the point. There's no shame in having cancer. It's a shame you have cancer, but there's no shame in having cancer.

Dr. Dan Hayes: The second is that we are an aging population, and things that used to kill us before we got old enough to have cancer, and cancer is on the most part a disease of old age, have decreased substantially too. That's another good problem we have. Coronary artery disease has dropped substantially. Do you know anybody that's had tuberculosis?

Scott Redding: No.

Dr. Dan Hayes: Near my hometown there was a tuberculosis sanitarium, and it was full when I was little. It's gone. It's not even a building now. And that's kinda the point. You probably never met anybody with polio. I have. Those things, they're all gone,

and that's great. But what that means is our population's getting older, and cancer doesn't occur in very many kids. Certainly the pediatric cancer occurs but it's awfully rare. Part of that is, again, evolution. Is that our species exists because we reproduce. So if we got cancer before we reproduce and die we're not gonna reproduce, so we're not around. So there are a whole bunch of biological, genetic issues that keep us from getting cancer when we're young. As we get older those begin to break down.

Dr. Dan Hayes: And the third then are environmental exposures. And although a lot of those have actually gone away because of many of the environmental concerns that we've had back in the '70s, and the Clean Water Act and the Clean Air Act and all that kind of stuff. And the smoking has dropped. Something like 70 or 80% of adults smoked in the 1950s. That's down to about 20%. Should be zero, but it's down to about 20%. But those things also kick off cancers.

Dr. Dan Hayes: And so I think those three things together make it sound like there's more cancer than there used to be. The final thing is screening. The screening's good. So you think that what's he gonna say about screening? Well, it's because we're finding cancers that we didn't used to find. Now we're finding some cancers that we would've known about anyway, 'cause they would've occurred later, and those are the ones we hope we do find early and treat before they become really lethal cancers. But we also know with screening we're finding a lot of things we call cancer, but probably would have never become clinically-evident cancers in a patient's lifetime. So that patient is labeled as having had a cancer, but probably would never have had cancer. And so probably that's not a fair label, but that increases the incidence as well.

Dr. Dan Hayes: And it's hard, I think, for the average layperson to distinguish that kind of cancer from the cancer that is gonna kill somebody. So for example, in breast cancer, if a patient has ductal carcinoma in situ, frankly speaking that's really a pre-malignancy. It's called cancer, but it's not really a cancer. And a lot of us had wished we could change that, but we aren't able to. So that patient's told she has cancer, and she goes to work or whatever she does, and tells her friends, "I have cancer." And they say, "Oh, you have cancer. That's awful." And I wish people didn't have this. I'm not downplaying the impact, but it's a condition that's a precursor for cancer, increases the risk for real cancer, but it's called cancer. So now you think your friend has cancer. So that increases what you hear about it.

Dr. Dan Hayes: So I think the three things. One is we talk more about it. Two is the aging population. And three is screening and more visibility of cancer, and so therefore it's more apparent and we think it's gone up.

Dr. Dan Hayes: There are some cancers that have truly increased in incidence for reasons we don't fully understand. But there are others that have dropped, again, for reasons we don't understand in this country, and that's why god gave us epidemiologists, to figure all of this out.

Scott Redding: Well, Dan, I really appreciate the time today. As we wrap up, where do you see cancer going in the next five to 10 years?

Dr. Dan Hayes: My crystal ball is getting cloudy. Certainly in the short run I think I know where we're going. I think the precision medicine story is gonna get hammered down better and better. It's kinda been the wild west the last five years, and people are beginning to understand when to use it, where to use it and how. What we need there is better training. Well, in the 12 months of 2018 there were 60 drugs approved for cancer by the FDA. There is no human being who could keep track of 60 new drugs. So if you're an average oncologist in a community setting taking care of all kinds of cancers I don't know how you could possibly keep up with this. So we need to help people learn how to learn. We need to help people learn information, and I think that's gonna be a big push forward.

Dr. Dan Hayes: The other is this precision medicine thing. There are 15,000 genes in the human genome. Each of them has thousands of base pairs. Do the math. We're talking about billions of pieces of information. And you were trained how to listen ... You weren't. I was trained how to listen to hearts and lungs and diagnose heart failure. I wasn't trained to do bioinformatics and next-gen sequencing and stuff. And neither is almost any other clinical oncologist. We need to help them learn how to use this stuff. Help them learn how to apply it. Really help them learn how to learn it. And I don't mean they have to have it in their head anymore. The first line, the younger generation knows that they can learn by Googling things. My generation felt we had to memorize everything and spit it back out.

Dr. Dan Hayes: We laugh. My generation, it's called pimping. We'd be on rounds and the senior doctor would say, "What's the differential diagnosis of blue sclera?" And we'd go, "I just read that somewhere." You'll list off a bunch of stuff, and if you got it right you felt proud, and if you got it wrong you were totally ashamed. I can't do that anymore, 'cause I say, "What's the differential diagnosis of blue sclera?" Within 10 second their iPhones are out and they come back and read it back to me, which is actually great. So it's just too much to memorize. So I think that's another area where the field's gonna go, is helping us help the oncologists help our patients. And there's a lot to that, and ASCO is very interested in that. I actually think the curriculum's gonna have to change in how we teach of fellows.

Dr. Dan Hayes: The second thing is the immunotherapy, and I think this is really booming business. Again, we talked a little bit about finding new checkpoint inhibitors besides the two systems we already know about, and those are starting to already being reported. New drugs against the ones we know about. New drugs against the new ones. Better ways to avoid or treat the toxicities. Putting them together so that they're more effective than any one together. Putting them with already standard therapies, like chemotherapy and breast cancer endocrine therapy and HER2 therapy. All those things are huge opportunities, and I'm really excited about that. So I think that's where the field's gonna go.

Dr. Dan Hayes: The third thing, I think, is related to the local therapies. Kind of remarkable with breast cancer. I talked about going from radical to modified radical to breast preserving therapy. For example, in the old days the surgeons would take out 70 or 80 lymph nodes. Now they take out one or two. And maybe they don't even need to do that. And again, this is true almost across all of cancers. Can we do less surgery and get the same amount? This is called de-escalation. We're also asking those questions about I do, systemic therapy, what the radiation oncologists do. All of these areas are areas of de-escalation, and perhaps even going into really novel ways of doing this stuff without ever cutting anybody and that sort of thing. So I think that's another area where the field's going.

Dr. Dan Hayes: I think the final area the field's going is in economics, and there are two really important issues there. One is the cost of drugs. And all the great drugs in the world doesn't do any good if people can't afford to take them, and we've got to do something about the cost of drugs. It's very complex. It's much more complex than just saying, "Oh, you greedy pharmaceutical companies, drop your prices." We don't wanna kill the goose that's laying golden eggs. 60 new drugs in cancer in the last 12 months. They're not all blockbusters, but that's a lot of new drugs. And that didn't happen by accident. It happened because of hard work and lots of money going into it. I'm a not a shill for the drug companies, but we wanna be sure that kind of progress continues and moves forward.

Dr. Dan Hayes: On the other hand, the drug prices are just astronomical. I mean, it's not just in oncology, but many of the oncology drugs are just too expensive to give people. And we even have a term for that now, financial toxicity, where a patient's not taking drugs, not because it's making their hair fall out or throwing up or whatever. It's because they can't afford it. Well, that's heartbreaking.

Dr. Dan Hayes: The second part of this economic issue then is how we pay for healthcare in this country. And the Affordable Care Act in my own opinion was a real step forward. It covered a lot of people who used to just walk in and get free care, which meant they waited until they were too sick to really be helped, and then we would have to write it off as a hospital. Many of those people got covered. I'm proud of the fact that even within a Republican administration the State of Michigan accepted the ACA and went for it with Medicare and that sort of thing. So that's great.

Dr. Dan Hayes: It's still, though, a work in progress. It's been almost 10 years since the ACA was passed. It's not perfect. It has some huge flaws in it. It probably overreached in many respects, but I think that we can't continue to pretend that medicine is a free market business. It's not like you want a new car so you decide how much you can afford and whether you want a blue car or red car or big car or a little car or a tractor. That's your choice and the salesman tries to sell you the most expensive one. But you know what you want and what you can afford and what the value is. In medicine, your salesman, you pretty much believe them wholeheartedly, because it's your doctor. And on top of that there aren't that many choices and you pretty much gotta take what you're offered, and somebody else is paying the bills for you.

Dr. Dan Hayes: So it's screwy right now. That's the only word I can think of, and it's grown up the way it has. I'm not a wide-eyed socialist, but on the other hand I do think we need to resolve a lot of these issues, so that patients who have cancer can get the kinds treatments and the progress that we've been talking about today. Pills do no good in the bottle. They only help you inside you, and so we need to figure out how to get there. There's actually a really great map. You know those voting heat maps by county, where it's blue and red? So there are maps like that now for cancer mortality, and what's frightening about them is that in some states there'll be one county that's light yellow, surrounded by counties that are bright red. Now that's either epidemiology, the people in the yellow county didn't smoke much and the people in the red counties did, so lung cancer is killing people. I don't believe that. I think it's access to care, and that the people in the yellow are probably in an urban area that is lots of people with jobs and had heath insurance, and the reds were probably more rural areas where they didn't have access to care, or the doctors weren't there to take of them. Well, we need to fix that. That's just ridiculous.

Dr. Dan Hayes: So ASCO is working hard to do that, and during my presidency we spent of time worrying about these issues. And I know this is more than you asked for, but I think this is one area where the field has to go so that we can get these treatments to people no matter where they are. I hope people come to Ann Arbor and get treatment at Michigan Medicine, 'cause we do a great job. But not everybody in Michigan can get to Ann Arbor for their therapy. We need to be sure that the people outside of Ann Arbor get access to high-quality oncology care, the same way they would as if they could drive in and park at Ann Arbor. So these are the challenges.

Scott Redding: So those key areas actually then would be the access to care through trying to help fix financial toxicity, getting more access to other treatments such as immunotherapy and having precision medicine as a treatment option. Then also I would say when we talk about the large quantity of drugs that were created in the last year, that all goes back to even clinical trials and having access to some of those pieces to that.

Dr. Dan Hayes: We're coming around to clinical trials no matter what you ask me. It's the only way we make progress. I'll just say the one other issue, frankly, is accessibility in terms of workforce. So it's pretty clear there aren't enough doctors in this country, and one reason why is we've eliminated the number of med schools and the number of doctors who are educated. It's also pretty clear there aren't enough oncologists, when you get to my own thing. And the question is how do we do that and how do we keep not just their training while they're training, I talked about that earlier, but once they're already trained. So there's a whole effort to get, for example, people who might not be doctors and medical oncologists, but would still be able to provide good care with oversight. There's practitioners, physician assistants. ASCO thinks this is all a great idea, and I do too. And we've been using nurse practitioners and PA internally for years, but I think they can help in areas, in the counties that don't have an oncologist, but

maybe it's a itinerant oncologist who's there on Monday, and the nurse practitioner's there on Tuesday, Wednesday, Thursday, Friday, whatever.

Dr. Dan Hayes: The second is to provide guidelines and pathways. And this is controversial, 'cause there are doctors who feel that they shouldn't have someone else telling them how to practice, 'cause they know how to practice 'cause they're doctors. When I hear that I always say, "When you were a doctor as an intern, did you not have anybody tell you how to practice?" "Well, yeah. The resident told me how," or, "My attending told me how." I said, "Okay, so how's that different now?" If somebody knows more about a topic than I do, and tells me how to apply that topic to take better care of my patients, that's not offensive to me. That's how I learned as an intern. That's how I learn now. And so what we need to do is get those guidelines out. Get those pathways out, so that doctors who are in practice who are faced with a multitude of different cancers, again, 50 new drugs in the last year, 60 new drugs in the last year, all this next-gen sequencing, all these new things, have access to a way that there is a level of treatment that is relatively standard across the country. Now, there's still always gonna be doctors who have better judgment than other doctors. There's still always gonna be doctors who are a little bit ahead of the curve. I'm not a fool.

Dr. Dan Hayes: But I think we can raise the bar so every patient has at least access to what we would consider be a minimal standard by pathways and guidelines, and paying doctors for adhering to those pathways and guidelines. Or finding out why they're not, and if they're not, change the pathways and guidelines if they're not good. And I'll say it again. I'm very proud of ASCO, as you can tell. But ASO's working hard on this, and so are people at Michigan Medicine. There's a lot going on working closely with some of the insurance companies in the state. I really am optimistic about our ability to do this. The doctors, and I'm pointing the finger at myself, have to get over it and accept this, and make it happen. Instead of grumbling, work with it. Make it happen. Make it your success. And we're all for that.

Scott Redding: Well great. Dan, I really appreciate the time today. Great information and keep up the good work.

Dr. Dan Hayes: My pleasure. It's been great to talk to you. Thanks for the opportunity.

Scott Redding: Thank you for listening, and tell us what you think of this podcast by rating and reviewing us. If you have suggestions for additional topics you can send them to cancercenter@med.umich.edu, or message us on Twitter @umrogelcancer. You can continue to explore the 3 Ps of Cancer by visiting rogelcancercenter.org.