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Kevin Gregory: Hello, and welcome to the HDInsights podcast. I'm Kevin Gregory, Director of Education, Communications and Outreach at the Huntington Study Group. Over the next 30 or 40 minutes, we're going to share some insights on Huntington's Disease Research from someone working to make a difference for those dealing with the effects of HD. Our goal with this podcast series is to introduce you to some of the amazing people behind the research. For this first episode of the HDInsights podcast, I had the pleasure of sitting down and talking with Dr. Daniel Claassen. Dr. Claassen is an associate professor of Neurology at Vanderbilt University. He's the director of the HDSA Center of Excellence Clinic at Vanderbilt University Medical Center. He's also the chief editor of our HD Insights publication.

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Kevin Gregory: In today's episode, I really sit down and we talked through to get to know Dr. Claassen a little bit more, the person behind the science, behind the research. I think you'll enjoy this episode and this interview with Dr. Daniel Claassen.

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Kevin Gregory: Dr. Claassen. We appreciate you joining us today on this very first episode of the HDInsights podcast. I just want to kind of dive right into it and talk a little bit about your early career. Tell us a little bit about what got you interested in neurology. Specifically, how did you end up in the Huntington's Disease field?

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Dr. Claassen: Yeah. Thanks, Kevin. I'm excited about this podcast. Hopefully, it'll have a good audience and be interesting to people. My own career, I actually started a career that was completely the opposite of neurology. I actually started as a music major. I was a viola player. Insert all the viola jokes you want to, but I started off as a music performance major, and played with symphonies around the Southeast United States. That was kind of my job. Then decided that I may want to do something different. Through a number of crazy, unusual experiences, I found myself in a research lab under mentorship of a professor who studied mitochondrial genetics and metabolism. So I was first introduced to neurology per se through that work where we were looking at patients that had neurologic manifestations related to mitochondrial genetic abnormalities.

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Dr. Claassen: Then decided to go either do a PhD or an MD. I applied to medical school and got in. Went to medical school and I really found that the best teachers that I had were neurologists. I really enjoyed the field. I thought that the patient population was fascinating. I think, in particular, the patients that had neurodegenerative conditions manifesting with motor and cognitive dysfunction that really grabbed

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[00:04:30] my interest. That's kind of how I started. I went through my training at Mayo Clinic in Rochester, Minnesota. I spent about four winters there. Really got great exposure to a wide variety of neurologic diseases that really cut my teeth with understanding the intersection of neuroscience and neurology. Then did my postdoctoral training at the University of Virginia. It was really there that I experienced Huntington's Disease Center of Excellence model of care.

Dr. Claassen: Worked with Lynn Harrison there and she really taught me a lot about the Huntington's Disease population, all the way from genetic counseling visits to late stage HD. And became really interested and passionate about Huntington's Disease through that experience. Then I was recruited to Vanderbilt, primarily to work with building a research lab and cognition and movement with a focus on neural imaging. While I was here, we started a Huntington's Disease clinic. It was my expectation that I may have about 50 patients or so in that Huntington's Disease clinic. But it turns out that sometimes you're wrong. Our clinic has grown substantially over the last about five or six years to where now we probably take care of about 400 patients and families in the Middle Tennessee and surrounding regions.

Dr. Claassen: Have gotten really involved with clinical research, investigator driven research. And I really enjoy the collaborations with basic science and other specialties that really makes my job interesting from a research perspective.

Kevin Gregory: Nice. Well, that's a pretty interesting career move and path. So I got to go back to what you started out with, with your musical career. Where are you with that now? Do you still play symphonies on occasion? How would you classify your musician status at the moment?

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Dr. Claassen: Well, I live in Nashville so every second person in Nashville is a musician. I have one patient that jokes with me. He says that you know you live in Nashville when the violist in your chamber music group is also a neurologist. Yes, I still play. I play mostly chamber music now. Don't play in any symphonies. But I play in a string quartet, piano quartet. Do some piano duets. I probably play on average about once or twice a month. Everyone that I play with has jobs and so we kind of try and find time in the evening when the kids go to bed and meet up at someone's house and play music. It's good. Once you start, you can't stop.

Kevin Gregory: Yeah, very nice. Well, and that's not the only thing you play as well. Your Twitter bio refers to yourself as a frustrated golfer. I've got to ask, frustrated by how you play or?

Dr. Claassen: Yeah. If you want to learn humility, it's to take up the sport of golf. But yeah, I do enjoy playing golf. I actually have two boys. They are ages 11 and eight and they both play a lot of golf. The 11-year-old just beat me last week, which is a problem. But yeah, we play here in Nashville we play golf. It's a great outlet. It's something that you always have to work on. It's a great sport for patients.

Kevin Gregory: Absolutely. All right. Well, so you talked a little bit about some of the folks that you've served in a mentorship capacity under. If it's one of them or if it's somebody else, who do you most consider your mentors, as far as the person that's really driven you to get to where you are now and the person that you've become professionally?
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Dr. Claassen: Yeah. I think mentorship changes over time and may be different in certain parts of your career. I mean, as a medical student, I certainly appreciated the mentorship of my then chair, David Haas, who is a stroke neurologist, who really encouraged me to pursue a career in clinical research and applications of clinical research to understanding patient problems. He was very instrumental in encouraging me to do that, and teaching me about things like K Awards and career development awards and give me opportunities to get exposure to learning about the pathway to independence.
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Dr. Claassen: And then when I was at Mayo, there's a number of people that really helped me a lot. Keith Josephs is a neurologist who really specializes in this intersection of motor and cognitive investigations of neuro-degeneration and neuroimaging. He was super helpful and helped me in getting my career started. Then in Virginia, Lynn Harrison and Fred Wooden were amazingly helpful in giving me time and patient encounters to develop questions and I developed really good collaborations with a neuropsychologist named Scott Wiley and other folks in University of Virginia. Then when I came to Vanderbilt, different folks in neuropsychologist named David Zald and a neuroimaging specialist, Bob Kessler, became very good mentors to me in terms of helping me start my lab, start getting the early career development awards and progressing towards independence.
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Dr. Claassen: And I think the big thing from a Huntington's perspective, we are on an HDInsights phone call, was really appreciating the mentorship of the HSG community. So when we started our HD clinic, um, we, we didn't really know what we were doing, sometimes we still don't know what we're doing. But one of the things we did early is we had people like Martha Nance, Mary Edmondson actually come to Vanderbilt and sit with us, and talk to our support group. Talk to me personally about what do we need to do to get a clinic up and running? What do we need to have? And that was really helpful from a Huntington's point of view. And I've actually found that one of the great things about the HSG is that, when you're part of the HSG you have instant access to a peer support and even mentorship for getting your work started and going. And so I actually still benefit from a lot of mentorship from the HSG in regards to these kinds of issues.
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Kevin Gregory: It sounds like you've put a really strong emphasis on that, that part of your career development. Mentors have obviously been a big component of what you've done. I'm assuming, and it sounds like from the work that you've been doing, you've kind of taken on that same role now too. So you try and provide that level of mentorship to other people. What are some of the takeaways or the things that you focus on in

[00:12:30] your role to be a mentor to the next generation that's coming up through the ranks?

Dr. Claassen: Yeah, I don't think you ask to become a mentor it just kind of happens. And I've certainly had the opportunity to work with really great junior investigators, and try and help them along the path. I think from my perspective the top three things that I can do for junior investigators is, one, provide opportunities. So if they want to ask a question or they want to pursue an investigation on a certain topic is give them the opportunities to do that, whether it's make their clinics focused on the patients that they want to enroll, get them access to data, get them access to research funds to get preliminary data, and be available for them to talk about some of the challenges with getting research started. I think.

Dr. Claassen: So that's really the main one. And secondly, I think is being available for them. And so I try and for my junior faculty members have at least a once a week meeting for at least a half an hour it doesn't have to be a long time. And we may talk about science, we may talk about challenges that they're having, maybe talk about timelines, for me to go over paper rejections, hard paper resubmissions or grant revisions. And so make yourself available. And I think the third big one is realize that you have to be flexible. And so not every mentor or mentee relationship is going to look the same. There are different issues for different people on different stages of their academic journey. And so I think I've learned that you just have to be really flexible to know that there's not a one size fits all template.

Dr. Claassen: Sometimes people's goals change during their career. I mean, I'm certainly an example of that where if you'd asked me 20 years ago when I wanted to do it, probably didn't have much to do neurology, but more to do with playing music for a living. So I think people can change and that's good. And you kind of have to just embrace that and help people kind of figure out how to do that. So mentoring is hard work because it does require time and it's not always rewarded. But I think it's actually probably one of the most personally, enjoyable parts of my job is seeing other people succeed and seeing people become valuable members to the community of patients that you're treating, the larger regional and national community of scientific discovery, and see people progress towards independence is just a really great opportunity.

Kevin Gregory: Again, we're talking with Dr. Daniel Claassen. Your research has focused a lot on the behavioral aspects of HD, like impulsivity, self-regulation, action control. Can you tell the audience some of the things that you've learned along the way in your work in that area?

Dr. Claassen: Yeah, so I would say, my main entry into clinical research was on the topic of self regulation of behavior. And so one of the things that really interested me was in Parkinson's disease, when you give patients certain medications like dopamine agonists, you can see a marked change in a person's interest, they've become compulsively interested in gambling, shopping, sex, eating, hobbies. And it was just personally really fascinating to me how a medication could really change

[00:17:00] someone's behavior. So I think early on in my career, trying to figure out ways to investigate that I really benefited from working with cognitive neuroscience scientists who were coming up with ways to assess action, control reward-based behavior, risk taking behaviors, and impulsivity. And so I started looking at that in Parkinson's and using medication designed studies where you'd take patients off their medicines and giving them medicines and seeing how it changes some of these neuroscience based measures.

[00:17:30] Dr. Claassen: And then after that I said, well how does this look in the brain? Where is this localized? Can I understand some of the biology? And so that led me to explore neuro imaging methods that can assess these kind of biologic substrates to these behavioral changes. And of course with Huntington's disease, it turns out that a lot of patients also have problems with impulsivity. And we've noticed that in our clinic, especially in younger folks, who will engage in high risk behaviors, who perhaps will engage in addictive behaviors, it's not infrequent that we will first meet our patient because they've been arrested or they've had some kind of run in one with the law. Or there has been some issue at school.

[00:18:30] Dr. Claassen: And so that's really taking techniques that have been developed in other populations and applying them to Huntington's disease is currently one of the ways that we're trying to do this. So we look at reward-based behaviors, risk-taking, motor impulsivity, action control, and then the biologic substrates to that to understand how we can identify and hopefully treat patients who have these changes. And so that's kind of how, in terms of Huntington's, I've been able to kind of take principles from other disorders or at least principles that were explored in other disorders and look at it in a Huntington's disease population.

[00:19:00] Kevin Gregory: And how have you seen HD care evolve in your time running the clinic at Vanderbilt? And extension of that what do you see as the most important changes that are kind of on the horizon that the field has to be ready for?

[00:19:30] Dr. Claassen: So in our experience, when I started, we were seeing a lot of patients that were motor manifestations that maybe even more advanced patients where we would spend a lot of time going over how to control some of the motor symptoms they're having, the [inaudible 00:19:45] the Dystonia, the gait instability. And I would say that one of the biggest changes for us was really taking care of the family as a whole. I think that's really one of the biggest changes in the last four years that's become really evident to us. So one of the things that we emphasize in our clinic now is really family based care. And that patient is certainly part of that family, but then there's a caregiver who may be having a lot of emotional or cognitive or financial challenges that may impede the care that they're providing to their loved one.

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Dr. Claassen: So how do we look for after that caregiver. And then in the children, I think is a big one. So how do we take care of kids who are watching a parent have manifest symptoms of Huntington's disease with the knowledge that they have a 50% chance of having that same gene? How do we help them cope? How do we understand the stress that they're under? How do we provide constructive avenues for them to deal with those issues and be productive in school and yet still at the same time have all the stress of a chronic disease and the potential that they may or may not have of this gene? So I think ultimately our team has gotten bigger since when we started, and it's gotten bigger because we really want to take care of the whole family.

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Dr. Claassen: So it's not uncommon for new patient visits to have seven or eight people in the room, where we have the patient, but then we have some times the uncles and the cousins and the children. And so we have to learn as a team how to deal with all the challenges that that brings. I think one of the biggest challenge is in genetic counseling. If you disclose genetic counseling results to a patient when there are kids in the room, and the kids are just learning about their risk for HD, when that disclosure happens, that may not be the best way to do it. So thinking about ways to engage genetic counselors, social workers, neurologists, child neurologists, and that whole family based care. I think that's been the biggest difference. It does make it challenging from a clinical management standpoint because you have a lot of different team members, sometimes in similar space.

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Dr. Claassen: It's really hard in the infrastructure of a hospital system to tell an administrator that you really are not interested in just creating neurology return visits. But we've got to come up with other ways to get non neurology care in a certain area. I think that's a shared challenge across multiple institutions, especially academic institutions, which tend to often be very inflexible in how to deal with these kind of changing healthcare dynamics. But I think going in the future, I really foresee HD care to not be necessarily neurologic centric. I think it's going to be a team based care where there are going to be different ways that you engage that team depending on the life cycle of HD in your experience. So if you're a child, you're going to engage a team very differently than if you're a young adult who's thinking about having children, versus a person who's motor manifest with early career versus someone who may be wheelchair bound and is looking at assisted living or nursing home facilities.

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Dr. Claassen: And so I think the future of HD is really looking at HD as a treatment of a disease, treatment of families, instead of these kind of singular kind of specialty based care.

Kevin Gregory: Are there areas in that, that team-based concept that you see particular shortfalls in, whether it's the amount of people getting into that area? We can always use more neurologists, more specialists, more everything. But is there one particular area of concern to you at this point where if you had the opportunity to encourage somebody to follow this path, which one would it be?

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Dr. Claassen: Yeah, my perception is that one of the biggest impediments is the way we're currently reimbursed in the United States for care. We're reimbursed from a procedural or visit based encounter. And so I think, we really need to think as a community, is that really the best way to deliver care to Huntington's disease? And there are certainly different examples of how you can get away from that kind of per visit, per ENM code, per procedure reimbursement. And in that context I really see a lot of need for people that are interested in neurodevelopment, whether it be counselors, pediatric neurologist, psychologists, really understanding the ideas of how does living with HD or living with a parent with HD, how does that affect the development of a child's or young adults intellect, emotional responses, psychiatric symptoms and developing expertise in how to assess that, how to address it clinically?

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Dr. Claassen: I think there's a huge opening and opportunity for that kind of new specialty to come up. And certainly, if indeed some of these novel experimental therapies, if they come to the clinic that's certainly going to change the care model, where now we're going to have, for instance if antisense oligomers work, we're going to be now giving intrathecal delivery at multiple centers across regions. How to integrate those care. How do we assess efficacy? So I think there's an opportunity for even physical therapists, occupational therapists, speech pathologists to become critical members of that team. And I think there's some need for that subspecialty expertise in that field as well.

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Narrator: We'll return to the interview on the HDInsights podcast in a moment. We hope that you're enjoying this episode. As a nonprofit organization, the Huntington Study Group relies on the generous support from the community and listeners like you, to continue bringing you in depth content on HD, like this podcast series. If you like what you're hearing and are interested in supporting HD insights through a grant or donation, please contact us through our email address info@hsglimited.org or by calling toll free at 1-800 487-7671. We greatly appreciate your support. And now back to our episode.

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Kevin Gregory: I want to shift gears now and talk a little bit with you about HDInsight. So HDInsights is a semi-annual publication that the Huntington Study Group has put out for a few years now, and it's really the kind of where this idea for a podcast was born out of, the detailed content that came out of that publication. So you're currently serving as the chief editor for HDInsights. Tell the audience a little bit about your interest in the publication or publications in general, and specifically how you got involved into this role?

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Dr. Claassen: Yeah, so I used to read HDInsights. It would come to me as a web click, and I'd click it and I'd read interviews with different people in the HD field. So one day I got a phone call from Ray Dorsey. And in his way, he basically said, "Hey, I want you to think about becoming editor of HDInsights." And it's really hard to say no to Ray, so I said, "Okay sure, but can I change it?" He said, "Absolutely, absolutely. Change it whenever you want." So from my perspective I saw a need for HDInsights to

address a wide kind of audience of healthcare providers as well as potentially interested patients, to look at thematic concepts that we're dealing with, contemporary issues in Huntington's disease.

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Dr. Claassen: And so while the periodical was previously basically transcribed interviews, I really thought it could be fun to have kind of a thematic periodical with perspectives around that theme from different people that may touch HD in different ways. So for instance, I feel like there's a great wealth of experience and expertise from clinical coordinators, who see a lot of HD patients. And I'd love to hear what they thought about a certain topic or social workers or clinicians who have been doing HD for 50 years, or young starting out positions. And so the initial goal of HDInsights was to pivot from just kind of a, here's an interview and it comes from the great kind of summaries of science to really kind of more thematic perspectives around a topic.

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Dr. Claassen: And so the first issue we did was on this issue of irritability in HD. And we really took the caregiver perspective, the coordinator perspective. We looked at a trial that looked at irritability in Huntington, sponsored by the [inaudible 00:30:10]. And we had interviews with Walter Coriship and colleagues from a company that was working with that trial. And then recently we took on the issue of antisense oligomers, which could probably be four issues and maybe there'll be another one on it. But really looking at what is a clinician's perspective? We've got a great article from Mark Gutman on that one, to some of his personal experience. And Mark's a profoundly experienced HD person, but he had to change his practice to look at how does he as a neurologist become an expert in intrathecal drug delivery?

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Dr. Claassen:

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And he talks in his article about this and from a brand new social work intern, her first experience in HD social work in where the topic of came up and how did that topic go over? How did she interpret that? And we have a number of other great articles in this theme. So that's how I got involved in HDInsights. And I think, personally, we've gotten so much great feedback from this approach that I'm really hopeful that this will kind of grow and just develop even better. I think the next edition we're going to have is really going to be focused on kids. And so we're going to do a similar approach where we look at experts who take care of kids with HD or kids that are affected by HD. And then other kind of perspectives around that.

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Dr. Claassen:

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So it's been a completely different experience for me, because it's not scientific writing. You're not writing for a journal in a kind of a structured manner. You're really having to think creatively and thematically and really try and pick up as many perspectives as you can to have a product that looks pleasing to the eye, that could be read by a wide variety of specialties and people. So it's been a complete joy to do and I hope it keeps getting better.

Kevin Gregory:

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Were there any surprises when you got into this, taking over a publication like that for the first time or something that you go back to Ray Dorsey now and say, hey,

you didn't tell me about this or something that you didn't anticipate that you've kind of learned along the way?

Dr. Claassen: There's a lot of things. One is you have to pay for things. You have to advertise HDInsights. And we've gotten really great sponsorships. I can't thank the companies enough for investing their money in supporting HD insights. We've had just really great interactions with different companies on sponsoring this periodical. I think getting people to write is always hard. I kind of figured that would be hard. But sending 17 reminders, hey, by the way, I need your publication submission last week, that's a challenge. And I think just thinking creatively about how something looks on paper. I think that was something I wasn't expecting, but that ended up being a lot of fun and working with our design artist on a concept. So that's been fun.

Kevin Gregory: What's your vision for HDInsights over the next two to three years? How do you see it evolving? Where in your mind does this periodical fit into the overall landscape as a source of knowledge for the HD community?

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Dr. Claassen: Yeah, I mean, I think there's a whole bunch of different avenues of information streams right now for HD. I mean, there's HD Buzz, which is just amazing and really taking kind of scientific concepts to a vernacular that everyone can understand. So certainly really need to keep that resource going. The Internet. We used to have so many patients that come to our clinic, learn about HD on the internet and there's different kind of chat forums and things like that. So there's a lot of different ways that people can get information about HD. And personally where I see HDInsights going is that I feel like it's going to be a periodical that is going to be interesting to clinicians and healthcare providers. They're going to read it because they're just going to have fun reading it. They're going to get perspectives from different people. It's going to cause them to think about different issues. It's going to keep them up to date with contemporary issues regarding clinical trials.

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Dr. Claassen: We're finding out that a lot of patients actually enjoy reading, at least all patients caregivers. So it may be something that sits in the waiting room of a clinic, or it's easily accessible via clicking from the community. We've mostly focused on US related author but there could be potential that it becomes a little bit more international, which is always great. I think HD is just an international community. And so really learning how to engage and get perspective and insights from our European colleagues will be a lot of fun as we go forward.

Dr. Claassen: So I think, right now it's two times per year. It may go them more. I think the other part that's interesting to me is how we can engage education days. So at Vanderbilt we do in education day once a year and we had about 150 people show up. But if there is a way that HDInsights could start providing patient based information for those education days that are done by members of the HSG or other groups, I think that'd be one area that we see as potential growth. And I think also potential

growth for dialogue and commentary, other perspectives of HD that we don't typically think about. I think there's a lot of opportunities for that.

Kevin Gregory: Well, you've done a fantastic job, the look and feel of the publication has evolved tremendously. And like you said, the thematic concept of each issue, one story kind of building on the other or filling in the gaps that maybe the feature story didn't cover from a different person's perspective. So I really applaud you and commend you for the work that you've done on that. And also we appreciate your time on this podcast, but before you go, I just want to wrap it up with something maybe a little on the lighter side, a little on the personal side for you. We talked about golf and your love of golf. So I wanted to close and just get your thoughts on a few very quick hitting questions. Rapid fire here from you.

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Dr. Claassen: Okay.

Kevin Gregory: All right. So first of all, favorite golfer of all time?

Dr. Claassen: Phil Mickelson.

Kevin Gregory: Is that because you're a lefty as well?

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Dr. Claassen: Yeah, I just love watching him play. I think he's just a lot of fun to watch on the golf course. Yeah.

Kevin Gregory: All right. Favorite course you've played?

Dr. Claassen: Favorite course I've played? I just did a vacation in Colorado, and I played a mountain course, a cordillera, which was amazing. The views were just magnificent. You hit a tee and you look it over and you see these snow capped mountains in the distance. It was just phenomenal.

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Kevin Gregory: All right. Bucket list course that you haven't played yet, but want to?

Dr. Claassen: Easy. Augusta National.

Kevin Gregory: I figured. How about, as far as tournaments, the most memorable tournament you've gone to as a spectator?

Dr. Claassen: I went to the Augusta National for the masters and I saw another lefthanded golfer Bubba Watson win was just an amazing, and the play off with an amazing, he was in the rough and he did this hook onto the green on the 10th green. It was pretty amazing watching that happen.

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Kevin Gregory: That's wild. All right, so you've been to the masters, so I figured that might've been the answer to this next question, but it can't be, so bucket list tournament that you

haven't gone to that you would like to get to?

Dr. Claassen: The British Open is the next one I want to go to, especially if it goes up to St. Andrews, that'd be a lot of fun.

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Kevin Gregory: Absolutely. And then finally, last question. Any holes in one in your playing career?

Dr. Claassen: No, but my son just got one about a month ago and it really ticked me off because now he's gotten two and I have zero.

Kevin Gregory: So he just beat you and he has a hole in one, it's got to be rough living with him at this point?

Dr. Claassen: Yeah. Yeah. He rubs it in every day.

Kevin Gregory: All right. Well, Dr Claassen, again, appreciate your time on the HDInsights podcast. We'll continue to look forward to some great episodes on this, but also the upcoming articles for the fall edition of the periodical. Thank you so much for joining us.

Dr. Claassen: Excellent Kevin, and I think we're going to have a great podcast schedule in the future and let's hope it's better than mine.

Kevin Gregory: All right, we'll try and hold you to that.

Dr. Claassen: All right. Talk soon.

Kevin Gregory: All right, thanks.

Dr. Claassen: Thanks.

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Kevin Gregory: And that concludes our initial HDInsights podcast series. Again, my thanks go out to Dr. Daniel Claassen from Vanderbilt University, for taking the time to talk about not only his background, his experience, but to really introduce you to the HDInsights experience. And that is our semi-annual publication from the Huntington Study Group, as well as the launch of this brand new podcast series. We really hope that this podcast series gives you insight into the people behind the research taking place in Huntington's disease. And we hope you'll join us for continued episodes. Please subscribe to the podcast series, rate, review, provide your feedback, suggest other potential topics or people that you'd like to hear us interview, and we'll try and get that set up. But in the meantime, again, my name is Kevin Gregory, on behalf of the Huntington Study Group and HDInsights. Thank you for joining us.

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Narrator: We hope you enjoyed this edition of the HDInsights podcast. Remember to

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