NAMI Ask The Expert
National Alliance on Mental Illness

NAMI Ask the Expert:
Bipolar Disorder: Advancements in Research & Treatment
Featuring Dr. Andrew Nierenberg
November 16, 2023

Dr. Ken Duckworth (00:00:00):

Hello, everybody and thanks for joining. We have well over 1,500 people to hear the good Dr. Andy Nierenberg, who is an international expert on bipolar disorder and has a remarkable portfolio of professional activities. He's written just under 600 papers and the last three or four are going to depend on when the journals come through and he's a full professor at the Harvard Medical School, but also a genuinely kind and thoughtful person. When I wrote NAMI's first book, You Are Not Alone, in the back of the book, I attempted to answer all the common questions that I get on webinars like this and at our convention. The most common question that I get in the bipolar space is, "Do I have to take these meds forever?" So, of course I asked Dr. Nierenberg if he'd be so kind to write an answer. He wrote a thoughtful, compassionate essay in one day and I had no idea that the whole book wasn't going to be that easy.

So Andy, I think this is your third or fourth visit with us. We're very grateful for your expertise and generously sharing your time. Now, with 1,700 people on this webinar, I'm going to do my best to organize your questions into categories that the good doctor can answer, but I won't get to everyone with... We're closing in on just under 2,000 people. Thank you again, Dr. Nierenberg, for all you do and for giving us your time today.

(00:01:29):

Here's NAMI's helpline. It's available from 10:00 AM to 10:00 PM, Monday through Friday. If you need help, you want to problem solve or make sense of the mental health so-called system, there are trained volunteers that are there to help you. We take over 75,000 calls, texts, and chats. This is not a suicide prevention lifeline, that of course is 988. Let's go to the next slide. So, here's the good Dr. Nierenberg, and he again, isn't giving specific advice, just as I won't get to every question, but really I would say he knows as much about bipolar disorder as any person in America and we consider him a great friend to NAMI because of his compassionate and approachable manner, and I think you'll see that in this presentation. We already have 11 questions, so I'll come back to the Q&A after a very nice talk by Dr. Andy Nierenberg. So please welcome Dr. Nierenberg, and thank you, Andy, for all of this.

Dr. Andrew Nierenberg (00:02:32):

Well, thanks, Ken, and thanks to NAMI for doing this. I hope that the audience is able to get something out of this and certainly ask questions. We'll try to answer as many as we can in the time that we have, but thank you very much for all spending your valuable time and I hope that I'm able to teach you something that you didn't know before. So, this talk will be on bipolar disorder advancements in research and treatment, and I will try to give an overview of what the state is now, and I'll give you a little bit of a preview of what we'll do. The first chapter of this, it's in three chapters, fast facts. Second chapter will be in interventions, and the third I'll outline some gaps and hope for the future.

Dr. Andrew Nierenberg (00:03:26):

The other thing that you'll notice in some of the backgrounds of the slides will be paintings by Van Gogh, who is thought to have had bipolar disorder and sadly died by his own hands, but it attests to the creativity and the brilliance of Van Gogh even though he had bipolar disorder and how he saw the world in such a marvelously different way than any of us.

So first, let's go through some of the fast facts, some things you might know, some things you may not know, but it's good to just get the basics done for this, and a couple of new things for you. First is that there are thought to be two major types of bipolar disorder. So, type one is those people who have full manic episodes and depression, type two with hypomanic episodes and depression, and I'll tell you a little bit about that in the next few slides. One of the things that makes it so complicated is that people with bipolar disorder have other problems frequently as shown here in terms of substance use, anxiety, personality, and for reasons that are not really clear, people with bipolar disorder are also more likely to have chronic physical conditions, and I'll show you a little bit more details about that in a moment.

In terms of its prevalence in the United States, about 2.1% of people will have bipolar I and bipolar II, and that's about 7 million people. That is a lot of people, and then what's really extraordinary at the bottom end of the estimate for people below the age of 20 is around 0.6%, close to half a million, and there's also a way to think about bipolar disorder in youth in a spectrum and that may be as high as 3.9%, which is almost 3 million. Now, the thing I'd like you also to realize, and many of you do, it's not just the person who has bipolar disorder, it's all the people who love them, know them, have relationships with them. And so, if you have a low estimate of how many connections people have of four, you have to multiply those numbers by four So, it's an enormous number of people. It costs the United States more than $200 billion in terms of direct care and in terms of lost productivity. So, it is not a rare disease. It is really a huge problem.

(00:06:32):

This is from a really important study that Kathleen Merikangas did from the National Institute of Mental Health and looked at the age of onset, and here you have three categories, bipolar I: mania, bipolar II: hypomania, and then subthreshold bipolar, which is not quite meeting the full criteria, but really what's remarkable about this that I tried to draw by hand in the squiggly red line there that you'll see is that if you look at the age of 20 and you go then over to the left, what it means is that more than 30% of people will have the onset of the disorder below the age of 20. And there's a lot of controversy about kids and other things. I'll talk about that also a little bit later, but what's clear is that there's a lot of people who will have their first episodes, first symptoms below the age of 20.

Before I said that people with bipolar disorder frequently will have other disorders. The data that I'm showing you here are called odds ratios. You can interpret it as if an odds ratio is one, that would be the same as compared to people who don't have bipolar disorder. If it's two, they're twice as likely to have it, and so you can see that people with bipolar disorder, twice as likely to have substance use, anxiety, PTSD, and five times likely to have a personality disorder. Now, I've been in the field for many decades. I don't really understand what a personality disorder is anymore.

Dr. Andrew Nierenberg (00:08:28):

I think it's more of problems with social cognition and problems with understanding how to have relationships. So, I don't like calling it a personality disorder. I worry that's like blaming somebody, but it's not meant that at all, but some people will have more difficulties in managing, establishing, continuing relationships, and that's something that I think psychotherapy can help a lot with. Now, just looking at cardiovascular conditions that go along with bipolar disorder, more than two times likely with bipolar I, same with bipolar II, and even more than major depressive disorder. You might ask why. Why would it be such a problem? And it's probably a mixture of lifestyle, medications that cause weight gain, and increased blood pressure, and abnormal fats, lipids that people can have, but it also may be that there's a genetic overlap between bipolar disorder and cardiovascular disorders.

What's the course of bipolar disorder? Well, it's squiggly and complex. In a recent paper that my colleagues and I published on a broad review of bipolar disorder in the Journal of the American Medical Association, we had this graphic put in there. And if you look at it, the bipolar I, that's with mania, with manic episodes, that's in orange, and people go from depression to mania, to feeling okay, to having rapid cycling. Technically, the rapid cycling is at least four distinct episodes in a year, and then what's really remarkable, and many people don't understand this, if you look all the way on the right, you can have episodes with mixed features. What that means is that people can experience both depression and mania at the same time, so you can actually mix it together if they're not mutually exclusive. With bipolar II, they can still get quite depressed, but they don't reach the level of mania.

(00:11:08):

It's hypomania, which is less severe or less disruptive, a shorter duration as compared to mania. And people with bipolar II can also have mixed episodes and mixed features, along with a lot of anxiety that can co-occur with this at the same time. If you look at the percentage of weeks that people spend with mood symptoms, if you look on average over a year, and this is really from data from looking at people close to 13 years, people with bipolar I can spend a third of their time with depressive symptoms or depressive episodes, much shorter amount of time in mania, and half the time they could spend without any problems, the technical term is just asymptomatic, without symptoms, and bipolar II is not a lesser form of bipolar disorder. It's different, and people with bipolar II can spend half of their time with depressive symptoms or depressive episodes and much, much less time with hypomania.

But the biggest burden really is depression, and about of all the time that people spend ill, they can spend 75% of the time ill in depression, and it's one of the more challenging experiences that people can have and it's also challenging to treat, but I'll talk about treatments in the next chapter. One other thing I just wanted to mention is that there's a lot of advances in understanding the genetic architecture. Now, what do by genetic architecture?

Dr. Andrew Nierenberg (00:13:20):

One of the things that we have learned in the field is that the genetics are complicated. It's not just one gene and that's going to cause it, but it's multiple genes that can contribute in very complex combinations to the risk of bipolar disorder, but every year we get a better and better map of this. Now, all of this alphabet soup that you see here are these different genes that have been implicated in bipolar disorder, and there's a lot of interest in the top one, which is AKAP11 and along with some of the other ones. But as we learn more and more, I think we'll learn more about the biology, about the risk factors, and this can lead to newer medications with better efficacy and smaller side effects. So, there's great hope in terms of drug development as we understand the genetics better. So that's chapter one, just a little bit of an overview for you and a little bit of just some basics about it.

So, now let's move to what the interventions are, and I have to say overall there are a lot more treatments now than there were 40 years ago, and the treatments really can help a lot, but as I tell you about these individual treatments, what is really remarkable is that the median number of medications that people take is three, and that's because no one medication for most people is good enough. And some people can take more, some people can take less than three, but three is the usual number of medications that people can take. By and large, studies haven't looked at three medications together, sometimes they'll look at two, but nevertheless, I think that when you work with the person who's prescribing for you, it's really important to let them know what is working and what is not working.

(00:15:56):

It's also important to, I think, measure how you're doing. There are a whole bunch of apps out there and there are thousands of them that can help you track, but if you track carefully and systematically, it can help you and your treater share measurements together, and if you share the measurements, you both know what's going on and that can lead to shared decision-making, which I think is really optimal. So, I just want you to keep this in mind as we go through some of the interventions.

So, the first one I want to talk about is lithium. Lithium is actually a metal, it's a shiny metal, but when it's combined with something like chloride or carbonate, it's like sodium chloride or sodium carbonate. It's an ion. It is the simplest medication in all of medicine. And despite it being an element, besides it being an ion, we still don't know exactly how it works. We know some of the things that it does, but John Cade in 1948 in the outback of Australia found that this was helpful for patients. It didn't come to the United States until about 1972, and that was in part because in the 1930s they used lithium chloride instead of sodium chloride as a salt substitute for people who had hypertension, but people would salt their steaks and then they would kind of take too much lithium and people thought it was toxic. What John Cade and other people found is that the blood level has to be within a range so that it can be effective, but not toxic.

Dr. Andrew Nierenberg (00:17:54):

One of the remarkable things about lithium is that it decreases all causes of mortality, so decreases all cause mortality, and what's really interesting to me, and I'm really intrigued by it, it looks like it might have some anti-aging effects, and you may or may not know that Perrier water has it, and there are communities that have some lithium in their water. So this lithium as the prototypical, as the gold standard mood stabilizer, it works better acutely for mania than depression, but it also helps people keep well over time. If people take it for decades, there is a small risk of kidney problems with it, and that's what people worry about the most. So it's not perfect, but we've had many decades of use and understand it in terms of its actual use. And in many of the guidelines, it is thought it is the drug for maintenance treatment for keeping people well, decreasing the probability of having another episode.

There are a lot of ant-manic agents besides lithium, and I won't go through with these in any detail, but the thing to know is that there've been a lot of studies of these. There are two categories of the mood stabilizers. One category are the things like lithium, there are the anti-convulsants like carbamazepine. There's another anti-convulsant, which is called lamotrigine, and the other one is valproate, so lithium, valproate, carbamazepine, lamotrigine are considered to be mood stabilizers. As I said earlier, lithium is better for mania than depression. Lamotrigine is better for depression than mania. So, a lot of people will combine the lithium and the lamotrigine. The other drugs were first developed as antipsychotics, and these antipsychotics also are strong anti-manic drugs, and that's why many people end up taking those because they can treat acutely and they can prevent the mania. And I'll show you that there's a subset of some of the drugs originally developed as antipsychotics, but they also work as antidepressants.

(00:20:55):

So, that's the anti-manic part. If you look in the categories, antipsychotics and so forth, and you look at the response rates, they all hover around 50%. What that means is that the probability of getting better with any one of these drugs or one of these categories is around 50%. We don't know who's going to respond to what, so it's very empirical. People do the best they can with guessing what may work and what you might be able to tolerate. Now, if 50% respond, that means 50% won't respond, and then if somebody doesn't respond to the first med, then somebody will try another med either within the same category or in a different category to see what works. The real point is that you have to continue to persist because you don't know exactly what's going to work. So if several things don't work, the next one actually might work. You just don't know.

If you look at the treatments that are available for bipolar depression, there are fewer of them, but at least it's much, much more than there were 20 years ago. Of all of these, these are also the drugs that were originally proposed and developed for psychosis, they're antipsychotics, and the only one that actually includes something that really is and was developed as an antidepressant is fluoxetine, also known as Prozac. The combination of olanzapine and fluoxetine or Zyprexa and Prozac, is the only treatment that includes an antidepressant, and I'll talk about the antidepressants in a moment. All of these have different side effects. Again, it's a matter of tolerating it or not. Now, I did mention earlier that lamotrigine is a mood stabilizer, better for prevention of depression than mania. And remember, lithium is better for mania than depression, so people combine it. Now, lamotrigine is not approved for acute bipolar depression, but people prescribe it anyway, and it's a complicated story of what the evidence is or is not, but a lot of people actually like it because it has very few side effects.

Dr. Andrew Nierenberg (00:23:41):

It has one rare side effect, which is a very serious skin rash that can be really bad and cause all sorts of problems, but you can minimize that side effect by starting really low and going up really slow, but the main thing... Remember, I told you that Zyprexa, Prozac... Prozac's the only antidepressant that's been approved, no other antidepressant, none have been approved for bipolar depression, and there's a remarkable lack of data that shows that they work or that they don't work, and many people will get it anyway, and I'll talk about that a little bit later.

The other thing that's really important is that they're evidence-based psychotherapies and the psychotherapies are as important as the medications. They can really help a lot, and there are these different ones that have been studied carefully. I'm not going to go through each one of these. It's really good to see if in your area there is somebody who actually knows how to do one of these things, particularly the first four have been specifically developed for bipolar disorder and for depression. The unified protocol for emotional regulation is really interesting because it's a kind of blend of several different things. The dialectical behavioral therapy has been studied less in bipolar disorder, but it's been found to be particularly helpful for people who struggle with suicidal thoughts and behaviors.

(00:25:36):

The last psychosocial, psychotherapy type of thing, which I really like is listen to your mother, and I'm actually not kidding. When I say listen to your mother, what is that there are things you can do that you heard from your mother that will help stabilize people over time. And what do I mean by that? It makes sense, it's not going to be a surprise to any of you, but your mother told you not to do some things and your mother told you to do some things. Your mother said, "Look, don't smoke. It's really bad for you. It's bad for your health. Don't smoke," and smoking can actually, believe it or not, there's data that smoking can be an independent risk factor for suicidal thoughts and behavior, complicated reasons, but don't smoke. Your mother told you, "Don't do drugs, just don't do that. It's really not good for you."

And everybody's smoking marijuana these days, how much it helps, how much it hurts, it's a risk factor for actually developing hallucinations and delusions. So, it's not as benign as you might think, but your mother told you and said, "Look, don't do drugs." The other thing your mother told you is, "If you're going to drink, don't drink a lot, and really do it modestly if you're going to do it at all," and those are three things not to do. Now, your mother also told you to go outside and play with your friends and it's good to go outside, it's good to get exercise, and it's good to have connections. Your mother also told you to get a good night's sleep, and that's really for people with bipolar disorder. And the last thing your mother told you, which I think is really interesting, "Brush your teeth, really take good care of your teeth."

(00:27:44):

And it turns out there's a dental-mental connection and that gum disease is an independent risk factor for Alzheimer's and may actually cause brain inflammation. My colleagues and I are about to plan a study to look at that, but if there's one thing that you get from listening to me today, brush your teeth, take good care of your teeth, floss your teeth, clean them, go to a dentist, make sure they're okay. All right, so listen to your mother, really important. Then, there's this whole area of neurotherapeutics, ranging from electroconvulsive therapy, all to transcranial direct stimulation. These are really interesting ways of providing energy to the brain and to, in a sense, help change the circuitry of the brain. Now, the circuitry of the brain is really complicated and they're complicated networks, but look, ECT was found in the 1930s. It's still around because it works.

Dr. Andrew Nierenberg (00:29:00):

It does cause temporary memory problems. There's a minority of people who say that it affects their memory terribly, but most people really can help, and it can be enormously helpful for people who are suffering, believe it or not, not only bipolar depression, but also mania. It can work for that too. Repetitive transcranial magnetic stimulation, which is given as a magnet that's put against your head and the magnet gets turned on and off really fast, it also can work, but it is not approved for bipolar depression unfortunately, and I hope that changes soon.

And then there are the more invasive sort of things of vagus nerve stimulation. You actually have to implant a stimulator and deep brain stimulation for people who just haven't responded to anything else, and there's a whole really interesting field of a very mild current transcranial direct stimulation that's going on. And the last thing I'll mention that's not here, there's also a way to use light and not through your eyes, but there's a spectrum of light called near-infrared and people are studying near-infrared light that can actually just go right through your head. Your head can be invisible to that. So, these are other options for people, and I think really interesting.

(00:30:33):

Now, if you've never heard of this, this is the other thing that I would want you to take away from hearing me today or when it's archived, is this is a great resource for people. So, this is the family and patient guide to the Canadian guidelines, the CANMAT group, Canadian Anxiety and Mood Disorders, I think that's what it's called, CANMAT, and the ISBD is the International Society for Bipolar Disorders. And they got together and put this guide together and you can get it for free online, and I think it's really great because that will help you or your loved ones be able to ask whoever's trying to help you, "Hey, look, you're giving me this, this says this, can you help me understand this?" Or, "Did you know that this is available?" Because there are CANMAT guidelines for the clinicians that they can actually use, which is the best compilation of evidence and data that I'm aware of. It's really pretty good. So again, there's only two things I want you to take away, brush your teeth, you should also floss, and here's the patient and family guide for the guidelines for bipolar disorder.

That was chapter two, now we go to chapter three. In chapter three, I'm going to talk a little bit about the gaps that we have because we never know enough and we don't know everything at all, and some hope for making things better, and again, the purpose of this is to be able to give you a sense of where we can do better, what we need to do, and how to get things better. So, the first thing is there's a puzzling trend, and this is a study that Greg Rhee and a couple of us put together just a couple of years ago, and all I want you to do is look at the green line. The green line is the percentage of people treated with lithium between 1997 and '98 and 2015 and 2016. Now in '97-'98, about 30%-plus of people who had bipolar disorder were taking lithium.

(00:33:20):

And what's happened over the years is that's been decreased down to about 15%. And at the same time, what has risen are the antipsychotics and the second generation antipsychotics. So, lithium went down and antipsychotics went up. And if you remember what I said earlier, is that every guideline says, "Look, lithium is the gold standard. People should at least have a chance to get it," and it's something to at least, again, talk about with your treater if you have bipolar disorder or your loved one does, why wasn't lithium at least tried at some point? And that's I think just a quality of care type of thing. Now again, some people can reject it and say, "I don't want to take it or I don't want to think about the risks that are available with it," but again, something to consider. So again, first thing is there's been a decrease in lithium.

Dr. Andrew Nierenberg (00:34:24):

That's a gap. Second thing, remember I told you antidepressants, there's no real evidence that they work, except with the combination of olanzapine, fluoxetine, Zyprexa, Prozac, and all I want you to do is look at the top line. 97'-'98, about 45% of people were taking any antidepressant, and by 2015, 2016, it rose up beyond 60%. There's a lot of use of the antipsychotic. People assume that it's kind of like the olanzapine-fluoxetine combination and you can combine an antipsychotic and an antidepressant, but it's just not clear if in fact that's true. We're about to hopefully embark on a study funded by the Patient-Centered Outcomes Research Institute called SMART-BD, and one of the things we're going to be doing is see how an antipsychotic and antidepressant works compared to some of the other medications that are approved for bipolar depression.

The other thing is, remember I told you bipolar II, you have hypomania and depressions, but it's actually remarkable that it hasn't been studied that much, and the big leaders in the field of bipolar II, Holly Swartz from Pittsburgh and Trisha Suppes from Stanford, they're really at the forefront of this, and there are big gaps. I think we have to know more about it. Some people think that antidepressants work better in bipolar II than bipolar I, and do you really need a mood stabilizer over time, yes or no? But it's certainly something that we need to study more.

(00:36:23):

I also mentioned earlier that a lot of people, 30% of people with bipolar disorder can have the onset below the age of 20. The whole area of young people below the age of 20, below the age of 12 who develop bipolar disorder early on, there's a whole controversy about what to do, and there's even controversy about the diagnosis in youth, and it's just really unclear what the best short-term treatment and long-term treatment is.

And one of the problems is the other disorders that people can have when they're very young, especially ADHD, and how do you distinguish ADHD from bipolar disorder, and how do you make sense when ADHD is included with bipolar disorder? And then how do you treat it? Because if you treat the ADHD, you might make the bipolar disorder worse. So again, it's a really, really big gap in terms of what needs to be done. I also told you earlier there's a whole problem with cardiovascular disease and other medical diseases, and our system is a little broken, let's say, and that the medical care is here and the psychiatric care is there, and too many times it's not put together, and I think we need a better system to take care of this.

(00:37:56):

There's one other problem, and that if you think about the whole system of care, it's usually people are on their own. You see a clinician and that's it. The clinician sees you, you see the clinician, and there's no sort of team of people that really has input, oversight, guidance of what's going on. My colleagues in the Dauten Family Center for Bipolar Treatment Innovation led by Louisa Sylvia and Roberta Tovey put together a team-based treatment where every week they review the progress of everybody, they are able to have a discussion about what the problems are and what needs to be done. Does medication need to be changed or not? But it's a constant review of the quality, and I think that's the sort of thing that we really need a lot more of. Now, one way that my colleagues and I are trying to address the problems of the system is to build something called a learning health network.

Dr. Andrew Nierenberg (00:39:16):

And this is based out of a model that's been highly successful that comes from Cincinnati Children's Hospital and they've built 15 of these. And to put it in a nutshell, it's a radical collaboration between patients, families, clinicians, researchers, data analysts, administrators, insurance companies, maybe even pharma companies that are focused on the single purpose to get better outcomes and to use sophisticated ways to organize, work together, collaborate, and get the data to do quality improvement in some of these system problems that happen, and also to discover what's going on. One of the beauties of it is that you can have multiple healthcare systems meet, collaborate, communicate, and then what you can have is people, institutions, information technology, and a lot of getting together to be able to get improved outcomes. My colleagues and I wrote about this earlier this year in the Journal of Bipolar Disorders, and I think it's a great hope to drive the field forward to be able to look at variation in outcomes.

If one healthcare system is using a lot more lithium, for example, and it turns out the outcomes are a lot better, people are feeling better, there's a higher proportion of people who are doing well, there are less visits to the emergency room, so forth, the system will learn from that. And the places that aren't using lithium so frequently will learn from the places that are using lithium, deploy it, and then use quality improvement cycles like, "Is it working? Did we do it? Did we do it right?" And again, the whole system can bring that together.

(00:41:17):

We're really blessed and lucky that we have some philanthropy to start this, and just last week we had 18 healthcare systems willing to come together to be part of this new adventure and this new journey, and we're in the middle of a planning design phase and we should be able to really launch no later than next September. So, that gives me great hope to move things forward, and it's also a platform for people to participate in research for anyone to lead initiatives, including patients and their families, and the other part of this is we're doing this for kids, adolescents, adults, and it also brings together people to crowdsource solutions in ways that have never been done before, so I'm really, really excited about this.

I hope in the time that we've had together in going through chapter one, reviewing some of the fast facts of just the basics about some of the interventions that are available, maybe some newer ones, some gaps in that, and maybe some ways to improve that, and there's always hope that we can drive the field forward, understand what's going on, get a better system of care and do more discoveries. With that, I will end and then turn it, I believe, over to Ken.

Dr. Ken Duckworth (00:42:50):

Back to me. Thank you, Dr. Nierenberg, that was comprehensive and compelling. Super work you're doing, and one of the first questions is, how do I participate in this research? So, I want to start with that because you're one of our national leaders in researching these questions.

Dr. Andrew Nierenberg (00:43:09):

So, there are a couple of places to look at research going on, particularly clinicaltrials.gov. If you go on clinicaltrials.gov, and you can search for bipolar disorder, and you can search for active studies, and you can see in your area what's the clinical research that's going on and the opportunities for clinical research and to be a participant, a collaborator in research. That's the place to find that. As we build the learning health network and we hope it spreads, we'll spread the word about how people can participate and be part of that.

Dr. Ken Duckworth (00:43:56):

All right, we'll have you back and you can help people figure out how to get connected. So let me just say to everybody, we've gotten hundreds of questions, we have 2,300 people on this webinar, so I'll just do my best. We had about eight people ask variations on the question that I asked you to write for NAMI's book, do I have to take these meds forever? And people's stories are different, "I'm on clozapine, which has been helpful, but it's not easy to take. I'm starting to worry about my kidneys after 15 years on lithium. I haven't had an episode in a decade. Do I really have to take these meds forever?" It keeps coming up, so I wanted to come to that, and I loved your answer for NAMI's first book. So, I want to take that up because it keeps coming up and it's the most common question that I am asked on this entire topic, so thank you.

Dr. Andrew Nierenberg (00:44:48):

So Ken, forever is a long time and I would never say that somebody has to take something forever, but I would say they always have to reevaluate the benefits and the risks. And for some people, they might have one episode and then not necessarily have another episode again. You don't know what that is. One mistake I made when I was training was that somebody was stable for a decade and I said, "Oh, maybe you don't need the medication anymore," and stopped the medication. That person got sick pretty quickly. So, I think it's always understanding the benefits, the risks, the side effects, the risks of anything that's long-term, and to always renegotiate that, always collaborate, always have shared decision making with your clinician in order to constantly monitor what is helping and what is not. T.

Here are people who try to see how they do without meds, and I've had plenty of people who said, "Look, I really don't want to take the meds anymore," for whatever reason, and we talk about the benefits and the risks and if they want to come off of the medication, that's certainly their choice and I go, "Look, how's it working for you? Let's meet periodically and make sure that it's not coming back," but it really has to be a collaboration and shared decision making.

Dr. Ken Duckworth (00:46:23):

Thank you, Andy. Only one person asked this question, but I want to make sure we discuss it. This is a question about continuing bipolar medicines during pregnancy, and of course Dr. Marlene Freeman answered that question in NAMI's first book, but I recommend people to look at the MGH Center for Women's Mental Health where they are doing big studies of these exact questions. Andy, I don't know if you want to comment on that. Only one person asked it, but I thought if a person was pregnant listening to this webinar right now, it might be important to send them in the right direction.

Dr. Andrew Nierenberg (00:46:58):

I would definitely defer to my colleagues and the experts in it. The main thing here too is to look at the benefits and the risks of continued medication and being well versus the risk of coming off of medication and risking not being well. And again, that's an important decision that you should make informed by people who really are well versed in this, and I do defer to my colleagues at [inaudible 00:47:31] Hospital.

Dr. Ken Duckworth (00:47:32):

So, it's the MGH Center for Women's Mental Health, and they have literally studied this question, and if you look at the book, You Are Not Alone, NAMI's first book, Marlene Freeman answers this exact question, it's at your local library if you don't want to buy it, and she reviews the literature on this question in some detail in a very compassionate way. I hope to have her on one of our Ask the Experts down the road. Dr. Nierenberg, we're going to shift gears. "How do I support somebody with bipolar disorder? I'm in a relationship with them..." And this is a multi-part question because I have a dozen questions on this, "When they're acutely ill or how do I support them in an ongoing way?" And more provocatively, "How do I discern an episode from difficult behavior?" So I know that's a lot, but we're going to take it away from the medication question, back into the relationships, which of course are critical for life and actually doing well in many aspects of recovery.

Dr. Andrew Nierenberg (00:48:35):

So, I think the most important thing is to be there and to be as supportive as possible, educate yourself about bipolar disorder, I think that can help. There's a lot of support groups through NAMI and through the Depression and Bipolar Support Alliance, so you should know that you're not alone. And I think that helping somebody get through the episodes by just being supportive is probably the most helpful thing. What is clearly not helpful is to react angrily, to turn up the temperature of any sort of conflict, that really doesn't help much at all. The other thing that could certainly help is family focus therapy, and if that's not available, you can do family therapy and encourage people to be involved with their treatment and to also make sure that they're engaged in their treatment. The other thing I particularly do is I always like to meet with family members. It's not a secret of what's going on, and I see the family members as part of the team, and if you can be part of the team also, I think that can help.

Dr. Ken Duckworth (00:50:01):

One of the things I've seen in my practice is the safety in having somebody say, "I think we might be running into symptoms." It takes a lot of trust and love for the person to say, "You only play the spinners when you're beginning a manic episode," and I'm not kidding, it's this classic example. The same music or the same behavior or the same word or sentences, paragraphs can be an early indicator, and the safety in that relationship to not interpret as blame or judgment, but rather to say, "Okay, we're walking this journey together." So, I've been very impressed by how the safety and love in a relationship can also catch things early, but I loved all your points as well.

(00:50:52):

So MDDA, Manic Depressive and Depressive Association, NAMI support groups, these are all things happening all across the country that are free that you can DBSA, the Depression of Bipolar Support Alliance, these are all places that you can find help. Okay, another question, let's talk about the question, is getting help earlier making a difference at the biological level? So, there's a lot of questions related to kind of the developmental phase of onset, but one way to approach it is, how about this idea that getting earlier intervention makes a difference in your course? Has that been shown based on your research?

Dr. Andrew Nierenberg (00:51:39):

It's complicated. The reason it's complicated is that when it occurs early, it can interfere with development and it makes things a little more difficult to figure out how to help somebody in the long run, but certainly I believe, and there's not a lot of data, that the earlier the intervention, the better that someone can learn to cope with it, to live with it, to take treatment over time, and there's a big gap between the time that people have their first symptoms and then get their first diagnosis, which can be eight to 10 years. So, I think a better systematic way to get a diagnosis earlier and to get appropriate treatment is really important.

Dr. Ken Duckworth (00:52:35):

Are you going to trademark things your mother told you?

Dr. Andrew Nierenberg (00:52:39):

No, my mother told me those things, so it's not trademark.

Dr. Ken Duckworth (00:52:45):

Because really, that's NAMI music to our ears. NAMI was founded by mothers, by the way. That's music to our ears, but let's develop one of them, which is sleep. Many people consider sleep kind of the harbinger of an onset of an issue, and if you have good sleep, your chance of a recurrence is lower. How do you think about that one aspect of what your mother told you?

Dr. Andrew Nierenberg (00:53:09):

So I think there are several things, one is that it's good to have a regular sleep schedule and to try to go to sleep at the same time. It turns out that if you wake up around the same time, you'll go to sleep around the same time, so try to wake up the same time regardless if it's during the week or on the weekend, and keeping that regular schedule can really help a lot. It clearly does not help to stay up really, really, really late and then not get enough sleep, and that can provoke mania. The other thing is to avoid the things that can interfere with sleep. For some people, they can drink caffeine and they sleep fine, or other people, if they have one small cup in the morning, they can't sleep at night, so you have to watch your caffeine intake at the same time. Oh, that's something else your mother told you, "Don't drink too much caffeine."

Dr. Ken Duckworth (00:54:03):

I'm telling you [inaudible 00:54:04]-

Dr. Andrew Nierenberg (00:54:05):

So, you have to watch that also.

Dr. Ken Duckworth (00:54:05):

You should absolutely trademark that. Back to that slide where you showed the episodes, some people ask, do most people convert to rapid cycling? I don't think it was clear from that slide. I think the answer is no, but I just wanted to ask you about that slide because that question came in.

Dr. Andrew Nierenberg (00:54:28):

No, not everybody will have rapid cycling. There are some people who never have it. There are other people where at one [inaudible 00:54:37] of their journey with it, they might have it, but not ever again, so it can be highly variable. By the way, for some people, antidepressants can cause that, and one of the things that many savvy clinicians will do is assess the current medications, and if somebody is rapid cycling, they'll say, "I think it's possible that the antidepressants may be causing this, and you may want to think of stopping it."

Dr. Ken Duckworth (00:55:06):

So, you mentioned second generation antipsychotics. Of course, the tragic flaw of them is they tend to cause weight gain, metabolic syndrome, increased cholesterol, and people don't like those symptoms very much, and of course, education not blaming people. Do you have any take on metformin or the new medications that are out for weight loss, and is there a research on that yet? Both for metformin, which is used in the stages of diabetes that are relatively controllable, or for the new weight loss compounds, for people who've gained weight with bipolar disorder who've taken a compound that just has this as a fight effect and it has an FDA black box warning associated with it?

Dr. Andrew Nierenberg (00:55:55):

So, Melissa DelBello in Cincinnati actually led a very large study of metformin for youth with bipolar disorder and found that it really helps, and I think although it hasn't been studied directly, the spread of the newer medications, the GLP-1 agonists, the glucagon-like peptide agonists, Wegovy, Mounjaro, all of those seem to be working remarkably well. And I know that there's a group in Denmark that has been studying that and to see specifically, does it help with weight gain that has occurred as a result of medications. So, we don't have the definitive answer, but it's certainly spread through clinical practice.

Dr. Ken Duckworth (00:56:42):

There's no known contraindication. If you have bipolar disorder, and you're taking a second generation antipsychotic, you've gained 25 pounds as a direct result of the side effect. There's no contraindication that you're aware of to one of these new compounds?

Dr. Andrew Nierenberg (00:56:58):

There is no contraindication. There's some interesting research that's being done on the effect of these medications on the brain that seem to be quite positive.

Dr. Ken Duckworth (00:57:11):

Great, so it's hopeful. It's a hopeful area. Well, we'll be following that research and we'll try to answer that question. We also had a question about the use of technology. Is there an app or a technology strategy that people can monitor to help them do pattern recognition, identify trouble ahead? Do you have a way that you use it? I know you have people fill out data points when they're in your waiting room. I'm guessing that's on an iPad, and then you integrate that into your record. Do people do this on their own if they don't have Dr. Andy Nierenberg?

Dr. Andrew Nierenberg (00:57:49):

There are a lot of really good apps, and I think it might be the APA and it might be another group that has tried to rate the apps in terms of evidence, usefulness, and so forth, and there are a whole bunch of them. There's not one particular one I would recommend at the moment. I don't think there's really a gold standard, but any one that you use and that you find useful, that helps you see the patterns over time, I think that's incredibly useful. I think the future will also use the data from the cell phones themselves and some of the apps try to do that. We're not quite there yet in terms of what really works or doesn't work, but in terms of a systematic way to record it, a lot of apps out there,

Dr. Ken Duckworth (00:58:41):

When you go to the APA's website, they'll ask you to pay attention to how companies handle your data and privacy. As you know, there've been a few instances where people are entering data and then it gets resold to third parties without your consent. I don't want to cast a dark cloud on it because I do think these kind of monitoring strategies sound like your experience matches mine, which for some people they could work because pattern recognition is a very big part of bipolar disorder.

Dr. Andrew Nierenberg (00:59:11):

Definitely.

Dr. Ken Duckworth (00:59:12):

All right, my last question is going to be on the conversation about hope. If you're diagnosed with bipolar disorder, should you have hope for your life? And how do you think about it? You've treated thousands of people with bipolar disorder, people don't receive this news with gratitude on most occasions, although some people have found that it explains some of their behavior. How do you think about providing hope for people who live with a condition that we still need to learn more about, and of course is responsible for a lot of creativity, innovation, and genius in our society? How do you think about that?

Dr. Andrew Nierenberg (00:59:52):

I think about it as there are a lot of complex, chronic disorders, diseases of mankind, of people kind, and we can learn to live with them, we can manage them. And particularly with bipolar disorder, there are some optimal ways to maximize the probability that people will thrive, and I think ultimately that's the goal. And if that's the shared goal between the person who has bipolar disorder and all of the people are trying to help them, I think persisting with treatment, many, many people can achieve that, and you want to be able to get the support to be able to manage some of the symptoms that may persist or not, but always persist and try to see if you can get the treatment that helps you reach your goals.

Dr. Ken Duckworth (01:00:54):

Well, that's a beautiful answer, Dr. Nierenberg. Thank you for everything you do. We still have 2,000 people on this webinar after an hour of your teaching, so let's go to the next slide, please. As we thank Dr. Nierenberg, I want to remind you NAMI does have an ongoing series, Mary Ellen Copeland, who invented the Wellness Recovery Action Plan, she is a superstar in the world of recovery, she'll be joining us in two weeks, and people with bipolar disorder actually benefit from creating a Wellness Recovery Action Plan. It's basically a self-determined way to understand what helps you and what might trigger you, and I'll let her explain it in much more detail. On Thursday, December 14th, we have suicide prevention inside of pretrial detention, and this is part of growing the continuum of care around the 988 suicide prevention lifeline and NAMI's ongoing efforts to help people create a crisis care system that is much more comprehensive and gets people clinicians, as opposed to a police response for mental health crises.

(01:02:10):

Let's go to the next slide, please. Dr. Andy Nierenberg is one of our stars in NAMI's first book, You Are Not Alone. In this book, I interviewed real people who use their names, many of whom have bipolar disorder. All the royalties go to NAMI, it's a straight-up love gift, and NAMI owns the copyright. And if you're interested in this, we have a promotion. If you're a NAMI affiliate, you can buy one and will be eligible for 45 free copies as part of our 45th anniversary.

(01:02:45):

And beginning in a couple of days, we're going to have a buy one, give one special where you can give it to a hospital, clinic, or somebody you care about, and the wisdom of people like Dr. Nierenberg are in this book, but also people who've lived with these illnesses and share what they have learned. Let's go to the next slide, please. You're not alone, and this is an informational series, we can't give medical advice, but obviously we try to attract the brightest people in America. We like donations, and I'll just make it that simple. Next slide, please. So, I want to say, Dr. Nierenberg, we so appreciate who you are, what you have devoted your life to, and how willing you are to teach us all, so thank you.

Dr. Andrew Nierenberg (01:03:33):

Thank you, Ken and thanks for the opportunity.

Dr. Ken Duckworth (01:03:36):

All right, have a great evening everyone.