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https://reachmd.com/programs/cme/schizophrenia-and-bipolar-disorder-improving-adherence-and-new-therapeutic-updates/14991/

Released: 03/22/2023
Valid until: 03/22/2024
Time needed to complete: 30 minutes

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Schizophrenia and Bipolar Disorder: Improving Adherence and New Therapeutic Updates

Announcer Intro:
Welcome to CME on ReachMD. This activity, entitled “Schizophrenia and Bipolar Disorder: Improving Adherence and New Therapeutic Updates”, was developed through the joint providership of the University of Cincinnati and CORE Medical Education, LLC. and is supported by an educational grant from Alkermes and Intra-Cellular Therapeutics, Inc.

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Dr. Russell:
Schizophrenia and Bipolar Disorder are difficult to treat and are associated with substantial morbidity and mortality, particularly when suboptimally managed. Medication adherence is a key component to successful treatment and optimal outcomes. There are significant barriers to adherence, and physicians and patients need to collaborate to overcome this challenge. The lack of consistent adherence to therapy is a significant issue. Newer therapies are, however, now available that not only provide efficacy but are better tolerated, positively impacting adherence. So what are the new tools and treatments taking our approach to the next level? Stay tuned. That's what's to come on today's program.

This is CME on ReachMD, and I'm Dr. John Russell. Joining me to discuss the latest in the management of Schizophrenia and Bipolar Disorder is Dr. Joseph F. Goldberg. Dr. Goldberg is Clinical Professor of Psychiatry at the Icahn School of Medicine at Mount Sinai in New York, New York.

Dr. Goldberg, welcome to the program.

Dr. Goldberg:
Thank you very much, Dr. Russell.

Dr. Russell:
Medication adherence is a significant problem across every type of medicine. But what are some of the specific challenges and strategies to improve medication adherence in our patients with Bipolar Disorder and Schizophrenia?

Dr. Goldberg:
Well, arguably poor adherence is the biggest predictor in relapse in serious mental illnesses. AA lot of people have a hard time remembering to take all their pills, especially if you're taking more than one medicine or more than one kind of medicine. So, experts would say that good adherence is if you're taking about 80%, of what's prescribed for you in psychiatry for serious mental illnesses, like Schizophrenia and Bipolar Disorder. And the goal is to try to figure out almost on a patient-by patient-basis, ‘What are your reasons that might make it hard to reach that, roughly 80%?’ complexity of a regimen and the number of medicines someone's taking tend to be fairly high on the list, followed by the side effect burden. We know from studies that there are certain factors that make some people more likely to miss that 80% adherence mark. Some of these are demographic features like younger age, lower education level male sex being without a partner or unmarried, ethnic, racial minorities patients with Alcohol or Substance Use Disorders or Comorbid Substance Use Disorders.

And then we get into things like lack of awareness about their illness or insight. So somewhere comes my question, 'What's your understanding of why you take these medicines? What are they there to do for you?' And here I'm not just asking the patients to recite for me, 'I take this for my Bipolar,' –but – if they have some connection to it, 'Well, when I take this medicine, I find that it makes me a lot less irritable, and I can sleep better through the night,' and '–'I'd like them to be able to claim some possessive language about what this medicine does for them. Because if they don't know, I guarantee you they're going to be nonadherent. Studies show lack of that awareness is itself a predictor, but also just logically want the patient to own the fact that they're doing something for themselves, And it also gives you a sense of their investment in the treatment.

some patients –may come to a point where they don't think medicines are necessary, or they're curious to see, ' what happens if I stop?'' ''And that's a very fair question to ask, especially'– if you've felt well for a while. If you find yourself having that question come up I have one request, which is you talk about it with me. ''So if you've building out a therapeutic alliance, and they know what you're interested in to try to keep them well, and they know that they can and should and hopefully will come to you with concerns about is the medicine really doing anything? Is there something else or something better? –

Let me just add a few additional points around issues of medication adherence in Bipolar Disorder. So a couple of important studies, the NIMH Systematic Treatment Enhancement Program, or the STEP-BD study, one of the largest studies ever done in Bipolar Disorder, over 3,600 patients 48,000 visits. I was an investigator in that study. So, we identified nonadherence, as I said, not taking medications as prescribed on, more than 20% of visits, about a quarter of our patients met that definition. And when we looked at some of the factors in the STEP-BD that were associated with medication nonadherence mood symptoms, in particular depression symptoms, were significantly associated with poor adherence, Comorbid Psychiatric Disorders, particularly a Comorbid Anxiety Disorder Current Alcohol Use Disorder. Interestingly, history of rapid cycling in the past 4 years, that means four or more distinct episodes, separate episodes in the last year. All were statistically significant predictors of poor medication adherence in Bipolar Disorder.

Another study called the FACE-BD cohort, a European study, additionally looked at risk factors for poor adherence in Bipolar patients, found that here female gender was a predictor. There was no difference between Bipolar type I or type II No difference with age with respect to adherence. Illness duration was a correlate, so the longer you had been sick especially if you're a woman and having side effects and a lot of depression severity, but not mania severity interestingly. So side effects, depression severity, female, age, and longer duration of illness in that study was found to be predicted.

And lastly, looking at both Bipolar Disorder and Schizophrenia, some of the psychological dimensions that have been examined with respect to adherence include this concept that we might call locus of control. We all have a locus of control that could be internally based or externally based. Internally based locus of control, 'I need to be in charge, I have to be the one who decides what's going on,' as opposed to external locus of control, 'You decide for me, that may mean you, my doctor, or you, fate and destiny or something outside myself. It turns out people with a high internal locus of control, tended to fare more in the realm of poor adherence. And some speculation that high internal locus of control might also correlate with distrust of other people I can take a generalizable rule away other than to say, if a patient seems to express an importance about, 'I have to be in charge of how this goes, I don't want someone else telling me how to do this,' respect that very highly. It may be a very important contributor to ultimate poor adherence.

Dr. Russell:
So Dr. Goldberg, with all those things in mind, it sounds like adherence is very important, that you can often identify who's going to have trouble with it. But what type of interventions are used to improve medication adherence?

Dr. Goldberg:
So, high on this list would be behavioral interventions, and educational interventions.

In terms of behavioral interventions for poor adherence in both Bipolar Disorder and Schizophrenia, this will include things like motivational interviewing That would mean, helping the patient decide what's important to them, what do they want. So if the patient is telling you, 'I really don't like to take all these pills,' and you say, Tell me what are your goals in treatment? What is it you want to see accomplished?' So rather than gripe about the pills, let's talk about, I really don't want to be in the hospital, again. I really want to be able to go back to work' So if you and the patient can get to the point, through a motivational interviewing style of establishing, we agree, these are the things you want, then we can move on to say, 'To what extent do you find these medicines help you reach those goals? Where do they fall short? And what can we do to make that better?'

Some of the behavioral techniques like checklists and alarms, that would be helpful for patients on a medicine taken multiple times per day. Helpful, supportive family members can sometimes make it easier for a patient to remember things. Younger patients, if they have – living at home, if they get any assistance, say with meals or chores, you can almost fold medication-taking into the chores. And you're trying to instill some sense of autonomy, If a So in a very non-meddling, but, gently concerned way, getting the family involved in that fashion can be helpful.

Educational strategies there are website tools and materials that clinicians can help patients with.

Among the one takeaway I hope to have from this discussion is that patients need to understand why they're taking what they're taking so that they'll have a sense of accountability and ownership. And then there's combinations of behavioral and educational approaches.

The thing that's probably worth, emphasizing is the therapeutic alliance and its impact on medication adherence. So, patients themselves will say that they themselves tend to be more likely to stay with the medicine and take it as prescribed when they perceive that their provider is conveying a sense of empathy and collaboration, and accessibility. Those three things are characteristics patients talk about. Providers, for their part will often say that having regular contact with patients and regularly reviewing how the patient's doing tends to be the aspect of the therapeutic alliance that can foster adherence. And this is also where measurement-based care can be helpful, if I can say to a patient, 'we're tracking your depression. And on this measurement scale, it's 46% better. I'm giving you some tangible basis from which you yourself will probably have some buy-in and maybe I'll appeal to your internal locus of control, so that you're likely to say on your own, 'wow, I think I'm going to stay with this, it seems to be helpful.'

Dr. Russell:
So Dr. Goldberg, so many of our patients take so many medicines. So, what is known about combination pharmacotherapy in Bipolar Disorder and Schizophrenia?

Dr. Goldberg:
Yeah, it's a really important topic. Because a lot of patients with these conditions end up taking more than one medicine. And so that means we have to think about drug interactions and cumulative side effect burdens and cost and feasibility. And yet, in clinical trials, typically, there is a study of one drug versus placebo, or maybe two drugs versus placebo. In Bipolar Disorder our group published a paper a couple of years ago showing about a third of Bipolar patients across 49 studies that we looked at, about a third were taking more than three psychotropic medicines. in reality the factors that seem to go into extensive combination therapies are not always of what the medicines are or their mechanisms, it's more about the severity of the patient. And we end up throwing a lot of medicines around often because of more extensive depressive illness burden psychosis history of multiple suicide attempts, more psychiatric comorbidities. And these are some of the key clinical features that stood out in our review, that really painted the picture of this is somebody who's going to wind up with poor adherence.

People on polypharmacy also end up taking subtherapeutic doses. Sometimes a low dose of something may offset the side effects of something else that might need a higher dose. For instance, lithium with its narrow therapeutic index, if the patient's having side effects at a high dose, maybe I can lower the dose and augment it with a low dose of something else. But more often than not, we found, well it may go the other way; it may be that to use low doses, ends up leading to more extensive polypharmacy. And it may be the case that you're just buying unnecessarily expensive side effects and never really getting your bang for your buck out of the first drug because you didn't really get it to a therapeutic dose.

Taking multiple medicines may or may not lead to a greater side effect burden. In part, it depends on what you're taking. I Imagine if you're on five or six psychotropic drugs, and you're having dry mouth. And your healthcare provider says, 'Now, you think the dry mouth is coming from drug number six?'. So, it just makes it murkier. And I think it almost undermines the credibility of what we're doing.

Whereas if we can say, 'This particular medicine, I want to be very cautious about because of its side effects.' So, we're going to change only one thing at a time, and make the patient almost a deputy monitor of their own experience. That is, 'If we're going to change this dose, let's see how you do, and if a higher dose isn't working let's reduce it or you may even get rid of it.'. It's another way of helping the patient anticipate side effects in a proactive way, with a good internal locus of control. 'My doctor told me if this isn't helpful to me, and I don't think it's helpful to me, we're going to get rid of it and try something else.

One interesting study that looked at co-prescription of antipsychotics. This study, actually suggested that the greater number of multiple antipsychotics being used was a predictor of nonadherence or poor adherence over the course of a treatment trial. Age was also a covariant in that equation, but, when you think about what you're combining there's an interesting controversial literature on the value or efficacy or lack of efficacy of combining two or more atypical anti-psychotics. There's some data using certain agents to counteract a side effect like high prolactin levels. But people that are taking three or more atypical antipsychotics, it starts to get difficult to justify a higher and higher level. And that study found that there was just a high risk of nonadherence as the number of antipsychotic medicines goes up.

Dr. Russell
So Let's talk about the various tools you use in patient management now. So how do you address impaired insight in the context of shared decision-making?

Dr. Goldberg:
I'm glad you asked about impaired insight. It's one of these critical points when we're talking about an ailment that interferes with reality testing and the ability to know what is accurate and what is not objectively reality. That very phenomenon can interfere with the awareness of illness, the need for treatment. I will sometimes forecast that for patients. I will say to them, especially when they are well, 'You should know one of the things about your ailment is that it can sometimes rob you of the ability to know whether the things that you're experiencing and perceiving are accurate. And that includes the need for treatment itself. So that if there comes a time in the future,' - you can refer back to it. It's just a very helpful way of enhancing the therapeutic alliance. 'You know, there may come a time in your future, where you're going to say, 'I don't think I need treatment anymore, or I don't trust you,' and that may be part of the illness. And as much as I very, much want us to be collaborators in the decision-making I need you to be able to collaborate I need you to be able to assess the information that I have so that doesn't feel like it's a one-sided endeavor. Let's take the scenario where someone, has poor insight, and they don't think they need treatment, you may fall back on motivational interviewing, where you're not trying to clobber the patient over the head saying, 'Look, you're manic and you don't realize it. And so, you got to take this pill,' that's not going to go very far at all.

And once you recognize that poor insight is there's no need to keep bringing it up again and again, other than if you're trying to test improvement down the road.

So, go after what they're looking for, you're looking to see if they can express a preference. So, 'Here are some treatments that I think are very appropriate for you. You know, maybe you can help us together think through you, the patient, and me, the doctor, of these thoughts you might have.'' And you kind of winnow through your list as best you can, because you're the one presenting the reasonable alternatives. And then you're trying to get the patient to involve themselves however they can, so that they have some ownership in the project. That's the spirit of shared decision-making, rather than just informing a patient of what's going to happen.

For patients for whom decision-making capacity or insight is not grossly impaired, we're going to use decision support tools. There's all kinds of web-based tools that can be used and paper materials that can be downloaded to help patients think through what are your priorities and then go through these together. So my priorities may be, 'I don't want any weight gain.' Or 'I want fast onset,' or 'I want a drug that's just once a day,' So you're again, tallying the patient's priorities. And then you go through them from the reasonable list of options that you as the healthcare provider know, and hopefully you can come to some fruitful collaborative determination of what's best for the patient.

Dr. Russell:
So Dr. Goldberg, these medicines are not always the easiest to take. So what's new in that therapeutic landscape for things like weight gain or tardive dyskinesia?

Dr. Goldberg:
Yeah, so these are two of among the more vexing problems that prescribers of psychotropic drugs have dealt with for an awfully long time. Again, it buys credibility, and it's just honest to forecast for patients. Look, everything can have side effects.

And so, for the patient who comes in from the get-go and says, 'I want no side effects,' we have to ally with them emotionally and say, 'I hear you can't blame you. If there was a perfect medicine with no side effects, I'd give it to you, but there isn't. So, let's make sure we understand what the appropriate medicines are for addressing the symptoms you've told me you want help with.

So weight gain's a frustration, in part because people with Bipolar Disorder and Schizophrenia are inherently at higher risk for being overweight or having obesity as well as excess cardiovascular disease and mortality.

So the best way to manage weight gain when it's a high risk with the drug is to prevent it, rather than try to reverse it. We do have a new molecule which is the pairing of olanzapine with the Kappa receptor partial agonist mu opioid receptor antagonist, samidorphan. So that's an opioid product that appears to have some modulating effect around appetite and satiety and weight gain. And indeed, the proprietary pairing of olanzapine with samidorphan has been shown to diminish the degree to which weight gain might occur.

So for example, in one of the initial studies in Schizophrenia that went on for 3 months over the course of that time, patients who were given olanzapine alone on average gained 3.8 kilos, that's about 9-10 pounds. Whereas those who are given the combination of olanzapine plus samidorphan gained a little bit under 2 kilos, 4.5-5 pounds. So about a 50% reduction So it's an important step and important tool, especially because in the case of olanzapine some clinicians might suggest that this is among the more high potency molecules that we have to offer patients. And, many clinicians will just avoid this medicine because of the fear and expectation of weight gain. So it's nice to have a potential proactive tool to diminish the weight gain and anybody who's concerned about weight gain would benefit from being on this compound in order to be able to take olanzapine.

Over the longer haul, over 24 weeks, it's been shown in patients on olanzapine would then go on to gain 6% of their body weight. But if

samidorphan is added, they'll gain about 4%. So again, there's a statistically and clinically meaningful difference between the combination of samidorphan with olanzapine as compared to olanzapine alone.

So among the newer second generation antipsychotics that are emerging lumateperone has come along and 23 pages actually has a favorable side effect profile with regards to metabolics and weight gain both in Bipolar Depression where lumateperone received its FDA approval in December of 2021. And in Schizophrenia, where the indication came sooner. So studies have shown that over the course of 6-week trials with lumateperone for a major depressive episode, in Bipolar Disorder the average weight change is about 0.11 kilograms. That's pretty good over the course of a 6-week period, not different from placebo. Lipid factors such as cholesterol, LDL and HDL and triglycerides also minimal change from baseline. And blood sugars actually did not go up in the course of the short-term trial. One of the things that can cause weight gain is insulin resistance that some of these drugs can cause, and that was not seen, with lumateperone. So again, all else being equal, here's a newer treatment option that might bypass some of those concerns.

Now another strategy arguably one of the most exciting new things to come along is this class of drugs called GLP-1 agonists. So glucagon-like peptide is a hormone that enhances the activity of insulin. If an atypical antipsychotic causes insulin resistance, it interferes with insulin doing its job, it prevents insulin from getting sugar into your organs, it stays in your bloodstream, goes to your liver, you make fatty acids, you make cholesterol, then you get lipid formation, and so on. Whereas if you could enhance the activity of insulin, you'll burn sugar more efficiently.

But GLP-1 agonists all of which are currently FDA approved, specifically for the management of diabetes and one in particular, a variation of the drug semaglutide, is FDA approved for just obesity or overweight, that means a body mass index over 27 with at least one obesity-related medical condition, like say hypertension or hyperlipidemia. These drugs have been shown to have profound effects on weight loss. They've been used off label in a few studies thus far. One study looked at the GLP-1 agonist, liraglutide, over 16 weeks in patients who became obese and prediabetic while taking clozapine or olanzapine. On average, they lost a little over 5 kilograms, which was substantial and about a 4-centimeter reduction in waist circumference, as well as improvement in metabolic parameters, like LDL cholesterol goes down.

So there's some exciting research coming along with this class of new agents to try to reduce weight. Some of these compounds in just people with obesity have shown upwards of a 20-22% reduction in body weight from inception over the course of about a year.

And the other side effect we were touching on before was tardive dyskinesia. So, among atypical antipsychotics extrapyramidal side effects can happen. That includes Parkinsonism, it includes akathisia, dystonias, and also tardive dyskinesia. It's a type of extrapyramidal symptom.

And up until a few years ago, we really had no treatment for tardive dyskinesia. The perception was that when atypical antipsychotics came along, there was a lower chance of seeing TD, , as compared to the earlier first-generation antipsychotics, So studies vary now it'll say atypical antipsychotics may have a maybe a 3 to 5% annualized risk. And it's higher still with first generation drugs.

But the breakthrough has been this class of medicines called vesicular monoamine transporter type 2 inhibitors, let's just call those VMAT2 inhibitors for short. What's VMAT2? So, it's a chaperone protein in the cytosol, on the presynaptic side of a neuron that escorts dopamine catecholamines through the endoplasmic reticulum to be exocytosed out into the synapse. . So put more simply, it's a way to reduce the presynaptic outflow of dopamine and overcome what we think is the supersensitivity to dopamine that causes tardive dyskinesia.

So, there are two VMAT2 inhibitors. They're both variations on an old drug, tetrabenazine. It's got a lot of side effects, can make you depressed, got to take it a bunch of times a day it may have some cardiac concerns. So the two workarounds with these new drugs, the first one called valbenazine, the second called deutetrabenazine is as follows.

Valbenazine is tetrabenazine with a valine amino acid group stuck to it to make it a pro drug. And then it's broken down into several products that are essentially isomers of tetrabenazine. And one in particular is the one that seems to have therapeutic benefit when it comes to tardive dyskinesia. So Valbenazine has been shown with a once-a-day dosing schedule 40 milligrams a day for a week, then 80 milligrams a day thereafter to produce anywhere from a 24 to 40% improvement over the course of an acute trial of treatment over several weeks, with a number needed to treat of about 7 to 4. Anything under 10, we consider to be a clinically meaningful, nice, low number of people you have to treat before you'll get one additional beneficial case.

Deutetrabenazine is deuterated tetrabenazine. So instead of hydrogen molecules, or atoms that are attached to the tetrabenazine molecule, heavy hydrogen deuterium. But heavy hydrogen actually prolongs the duration of action of the drug, so you don't have to take it as often as tetrabenazine. And seems to help with some of the other pharmacodynamic properties that make it feasible to take. So it's a twice-a-day drug, begins at 6 milligrams twice a day and then increases weekly to a maximum of 24 milligrams twice a day, similar efficacy of about twice as great an improvement rate as with placebo in the short-term 12-week trials in patients with primarily

Schizophrenia or Schizoaffective Disorder who have tardive dyskinesia over the course of 12 weeks, and an NNT of about 7, which is kind of a nice, nice, low number.

Dr. Russell:
So how can clinicians best address common comorbidities and their effect on treatment adherence in bipolar disorder and Schizophrenia in particular?

Dr. Goldberg:
Comorbid Psychiatric or substance use disorders are common in serious mental illnesses. Sizeable proportions of patients with both Bipolar illness and Schizophrenia have comorbidities.

In the case of Schizophrenia, for example, Comorbid Substance Use Disorders were found in a little over 40%. In one very large meta-analysis that encompassed over 165,000 patients' illicit substances tended to lead the list, cannabis at 26%, then alcohol at 24%. In the case of Bipolar Disorder, Substance Use Disorders have a high prevalence, 58% lifetime prevalence of any Alcohol Use Disorder, close to 40% prevalence of any Drug Use Disorder Comorbidity And then we have to remember all the other psychiatric comorbidities besides Substance Use Disorders. So next to Substance Use Disorders, Anxiety Disorders, over half of people with bipolar disorder. So, something like 64% of people with Bipolar Disorder in the NESARC study, this 40,000 Plus patient database, 64% had a Comorbid Personality Disorder.

So people with Bipolar Disorder usually have two or three or more Psychiatric or Substance Use conditions. It's challenging for diagnostics, it's challenging for therapeutics, because you're treating more than one ailment. Which means there may be medicines involved, or substances the patient brings into the picture that's going to affect drug-drug interactions and outcomes. So speaking of the impact of comorbid psychiatric and substance use on treatment, efficacy, and adherence, , I tell my patients, I want them to be informed consumers. If you are a heavy consumer of alcohol, , you need some basic awareness that alcohol is going to make your liver metabolize medicines that I give you faster. If you like cannabis, it's going to inhibit certain enzymes that will break down certain drugs that I might give you. If you are an aficionado of cannabis, you have to be aware that apathy and amotivation and cognitive impairment are often measurably evident, especially with chronic cannabis use. So you have to know what you're doing to your brain. I'm here to help you make healthcare decisions. I am here to point things out so that we can collaboratively help you make the best decisions you can.'

So let's talk about the patient where we have a clear diagnosis, say a Bipolar Disorder, and Comorbid Alcohol Use Disorder.

And so what was particularly interesting was the impact of divalproex compared to treatment as usual, on the use of alcohol in this actively drinking population. Patients who were given divalproex had a lower proportion of drinking days fewer drinks per heavy drinking day lower proportion of heavy drinking days, and fewer drinks per day overall. So, if I'm looking to make inroads on a Bipolar Disorder patient's Alcohol Use Disorder, I might favor divalproex, at least based on, one particular study that suggests it may have a direct beneficial effect in reducing alcohol use.

So now Comorbid Anxiety Disorders Depending on the source, one looks at 40 to 50 or so percent or more of people with bipolar disorder may have an Anxiety Disorder, Generalized Anxiety Disorder could be 20%. Social Anxiety could be 20%, panic disorder could be 20%. We don't have perfect treatments for that clinical scenario, in part, because there really haven't been dedicated studies looking at how should I treat Generalized Anxiety Disorder in a patient with Bipolar Disorder?

But let me say a few things about what we do know from pharmacology literature.

Quetiapine, lurasidone, cariprazine, olanzapine, fluoxetine combination all had been studied in Bipolar Depression, and found to reduce anxiety symptoms in the context of treating Bipolar Depression.

Divalproex also has been shown to reduce anxiety symptoms in the context of treating Bipolar Depression. There's a little bit of data with lamotrigine, single-blind studies suggesting it also can improve anxiety symptoms. And here's the interesting part, clinicians often say, 'Well, should I use an SSRI for anxiety and Bipolar?' And the answer is, who knows? There's no prospective studies of using any SSRI, specifically targeting an Anxiety Disorder in someone who has Bipolar illness. The closest to an exception is there was a teeny dataset looking at paroxetine in the treatment of acute Bipolar Depression, where it failed to treat the depression, but the paroxetine did seem to improve the anxiety symptoms in these Bipolar depressed patients.

And then we have some experimental concepts to gabapentinoids, such as gabapentin or pregabalin. Some of the practice guidelines advocate their potential value to be considered, but we don't really have empirical trials to help there.

Dr. Russell:
So Dr. Goldberg, we've certainly covered a lot of ground today. If you had to give our audience some takeaway points on all the material

you've covered, what would be the important points you think our audience should remember?

Dr. Goldberg:
So I think it's fair to acknowledge medication adherence is a significant challenge in Schizophrenia and Bipolar Disorder. It can interfere with effective treatment. We can have patients we label as treatment resistant, who are really pseudo treatment resistant, that are poorly adherent. And so, it becomes hard to just say, 'Well, let's try more and more new medicines,' when in fact, the problem is not that the medicines don't work, it's that the medicines aren't getting taken properly. And so that's going to jeopardize clinical outcomes.

So nonadherence is affected by Pill burden, the number of medicines that you're taking comorbid conditions potential insight into the illness medication side effects, attitudes and beliefs about medication, do I still need it or not?' We surely need a lot more studies to address strategies to help in these areas to reduce pill count burden, to manage side effects. We're starting to get some of these trials and ways to provide drug delivery systems that are most acceptable to patients in ways that can improve their tolerability and simplicity and adherence.

Newer atypical antipsychotics showing us an improved clinical profile when it comes to cardiovascular and metabolic risk. I gave the example of lumateperone, and we hope to see more in the months and years ahead.

And, lastly, this notion of a collaboration between clinician and patient in devising treatment plans that can point out what the obstacles are to adherence for a given patient,' And how can the clinician and the patient, be real teammates and collaborators in the process of trying to make them better and achieve the best outcomes.

Dr. Russell:
Thanks so much for summarizing all that for us, Dr. Goldberg. And as that brings us to the end of today's program, I want to thank you for helping us to better understand the latest updates in the management of Schizophrenia and Bipolar Disorder. Dr. Goldberg, it was a true pleasure speaking with you today.

Dr. Goldberg:
Dr. Russell, thank you so much for having me. And it was a great pleasure for me to have the chance to talk with you here.

Announcer:
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