BRIAN PALMER: Hi. My name is Brian Palmer. I'm a psychiatrist here at Mayo Clinic. Today, we'd like to discuss bipolar and borderline, the interface between these two disorders, and ways of distinguishing them diagnostically. We'll begin with an overview of borderline. We'll look at diagnosis, co-occurrence, and differentiation from bipolar. And then we'll look at the course and outcome of these two complex, but often related, disorders.

So first of all, considering personality disorders, borderline is a Cluster B personality disorder. It is characterized by five of the nine criteria listed on the screen. I've grouped these in four areas.

First is an inner personal hypersensitivity-- abandonment fears, unstable relationships, and emptiness. In reaction to the interpersonal context, the other symptoms emerge-- affective and emotion dysregulations, instability of affect without elation, inappropriate, intense anger. And the next area of behavioral dyscontrol, we separate out the self-harm and suicidal behaviors from impulsivity and other areas-- sex, driving, binging, and finally, a disturbed inner sense of self-- discontinuity of self over time, an unstable or distorted self-image, and transient depersonalization or derealization under stress.

John Gunderson who's a psychiatrist and professor at Harvard Medical School groups the criteria in this way. And this slide emphasizes the context in which symptoms emerge. At the top, we see that when the patient with borderline feels held or connected, they can be idealizing, dependent, rejection-sensitive. Inevitably, there is a stress to their interpersonal life, the context here. And then the patient feels threatened. It's in this threatened state-- threatened with aloneness, that we see the devaluative, self-injurious, angry, anxious, and help-seeking behaviors that most psychiatrists recognize as consistent with borderline.

In reaction to these behaviors, either the other person withdraws, pulls away, in which case, the patient is alone. This is on the right side of the slide. Or on the left side of the slide, the other person increases their support. If there's more support, the patient returns to feeling held and can again feel idealizing independent. If this state of aloneness does emerge, this is when we see the disassociated, paranoid, impulsive, and help-rejecting phenomena that are also characterized in the diagnostic criteria. And finally, when this state is met with further withdrawal, patients often become quite desperate. And borderline patients are at real risk of killing themselves when they conclude that they are not lovable.

Borderline is common in the population. 15% to 20% of clinical samples in psychiatric practice and approximately 5.9% in the general population. I included a question mark there, because that actually comes from the largest door-to-door study, the National Epidemiologic Survey on Alcohol and Related Conditions, but it hasn't been seen to be quite as high in other samples. It's more female in clinical samples, although the gender breakdown actually changes in community samples. And the disorder tends to be more balanced among men and women.

And it's highly heritable. It was questioned whether the heritability was a result of independent inheritance of each of those four phenotypes that I described earlier, the four groupings of the diagnostic criteria. It turns out, however, that a single latent factor most likely accounts for the co-occurrence of all four of those parts. And that's been true across two twin studies and one family study in recent years.

This is often very under-diagnosed and misdiagnosed. For example, 40% of patients who have borderline but do not have bipolar, have been previously inaccurately diagnosed with bipolar. We certainly have seen that in clinical practice here. Comorbid depression does not affect the accuracy of borderline assessments. So borderline can be accurately diagnosed in the midst of a major depressive episode by taking an accurate history and focusing on symptoms.

Now here's where it starts to get interesting is with the overlap with bipolar. As we consider bipolar, especially bipolar II, we think of an illness that is characterized by periods of sleep-deprived energy enhancement, hypomanic periods and depressive periods. But those of us in practice are well aware that there's high levels of comorbidity comorbidity with other disorders, suicide attempts, an unstable course, frequent recurrences, incomplete and/or episode recovery, and mixed states with irritability and agitation. These factors make the diagnostic distinguishing from borderline quite challenging, even for experienced clinicians.

In an effort to sort out the difference between borderline and bipolar, clinicians may turn to the mood disorder questionnaire, which is a useful 13-item questionnaire with sensitivity and specificity for bipolar. Unfortunately, a positive MDQ gives equal likelihood of bipolar and borderline diagnoses. So it's essential that clinicians think critically about the implications of a positive finding.

Complicating matters is that these diagnoses can co-occur. And they frequently do. In the Collaborative Longitudinal Personality Disorder Study, a large multicenter study with 196 borderline patients, 19.4% had bipolar at the time of study entry.

Over the first two years of the study, and additional 8.2% were seen to have bipolar. Similarly, the McLean Study of Adult Development is another large NIH-funded study under principal investigator Mary Zanarini. In this study, 9.5% had baseline bipolar. And 5.7% developed new bipolar over the first six years of the study. Some caution is indicated, because with the Collaborative Longitudinal Personality Disorder Study, the co-occurrence of major depression, substance abuse, and PTSD were all more than twice the bipolar co-occurrence. And most of these diagnoses of bipolar were made retrospectively.

Turning to the mood disorder literature, if we look at samples of remitted bipolar and unipolar depressed patients, one study examined borderline traits in these populations. And this did not meet full borderline personality disorder criteria, but five borderline trait items were seen in 30% of remitted depressed patients and 46% of remitted bipolar II patients. The authors did a logistic regression to try to analyze which factors were most associated with bipolar II, and concluded that the grouping of symptoms they labeled that are affective instability, specifically, mood, relationship problems, identity disturbance, emptiness, and anger. Those five features were most associated with bipolar II. But impulsivity and paranoia were somewhat less associated.

And other authors that have looked at this also conclude that the affective instability is different between these two disorders. Bipolar II more likely to see depression, elation, and shifts between depression and elation, whereas borderline is more likely to present with anger, anxiety, mood reactivity, irritability, aggressiveness, and impulsivity. The key feature in distinguishing between these two disorders is context.

Thinking interpersonally for borderline can really help the clinician understand the difference. Abandonment intolerance and self-injury in reaction to the interpersonal context are key discriminating features for borderline. Irritability and anger with activation of the attachment system rather than with strangers-- these are the features that should make you think borderline. For bipolar, thinking about periods of sleep-deprived energy enhancement, as well as periods of elation or cycling mood disorder related to other life stressors can be critical.

In the last four slides, we will look at the relationship between the course and outcome of borderline personality disorder and bipolar disorder. If we look at the borderline personality disorder longitudinal course, we see that I've plotted on this slide two different studies that looked at the long-term outcome. In the orange bar, this is data from the Collaborative Longitudinal Personality Disorder Study.

At the time of study entry, time zero, you can see that the average patient in the study met 6.7 of the nine criteria for borderline. By year one, it was 4.2, down to 3.8, on down, that by the end of year 10, at follow-up, the average patient only about 1.7 of these nine criteria. This was confirmed in a second study, the McLean Study of Adult Development, which showed that in year two, 34.5% of the patients in that study no longer met criteria. Up to 50% by year four, all the way up to 82%, 81.7% by the end of 10 years. So the natural history of borderline personality disorder is one of improvement.

Now, a third of those patients, by the end of 10 years, had full time-jobs and stable marriages. But 2/3 did not. Obviously, this is a significant mental illness that affects people's life trajectory.

So if we think of how borderline interfaces with unipolar depression, one of the best studies comes from a reanalysis of the NESARC data. This was the 40,000 door-to-door interview study that I mentioned earlier. And Andy Skodol and his colleagues found that 15% of patients in that study had persistent depression between the initial interview and the reinterview three years later. 7.3% had a recurrence of the depression.

The question was, why did that depression persist over three years? And they controlled for all Axis I and II disorders-- age of onset, prior episodes, family history, treatment, illness duration, anything they could think of to control for, and determined that borderline was the most robust predictor of persistence, such that 57% of those persistent cases would not have persisted in the follow-up period in the absence of borderline. So we can conclude that unipolar depression remains treatment-resistant until borderline improves. Borderline has a highly negative effect on unipolar depression.

What about bipolar and borderline? A reanalysis in the CLPS data suggest that there is actually no impact of bipolar I or II on the borderline course, in terms of remission, functioning, or treatment utilization. This is the same thing they found with unipolar depression. Depression and bipolar don't tend to impact borderline very much. And new onset bipolar was not a borderline evolution.

However, unlike the depression findings, with bipolar, we find that the course of borderline is generally independent of borderline, with only modest evidence that improvement in borderline improves the bipolar course. This was a small in. But bipolar I seemed to improve more than bipolar II once the borderline symptoms had achieved remission.

So the take-home points from this brief discussion are that co-occurrence between borderline and bipolar is common. Borderline is often undiagnosed and misdiagnosed, and that the interpersonal features, the context, really help distinguish and discriminate diagnostically between these two disorders. Major depression tends to remain treatment-resistant until borderline improves, and that borderline has a much more modest impact on bipolar course. But bipolar has no impact on borderline course.

Thank you for the opportunity to present this material. I hope it's been helpful.