Interviewer: Can you elaborate on the presentation of bipolar disorder in older adults and the factors influencing its episodes?   
Dr. Beyer: As we examine bipolar disorder across the lifespan, we observe that depressive episodes increase in frequency with age, in contrast to mania or hypomania. Consequently, the most common presentation of a patient with bipolar disorder to their physician is one of depression. The likelihood of switching back to manic episodes is influenced by the patient's prior exposure to antidepressants. Specifically, patients with significant exposure to antidepressants, particularly without the use of a mood stabilizer, exhibit heightened sensitivity to rapid cycling and switching later in their condition.  
  
Interviewer: What are the treatment options for bipolar depression in geriatric patients, particularly regarding lithium and lamotrigine?   
Dr. Beyer: Lithium is the gold standard for treating bipolar disorder. However, data on lithium's effectiveness in bipolar depression is limited. We have substantial data for geriatric patients with mania, where lithium proves to be a highly effective treatment, even more so than valproate. Yet, information on its use in bipolar depression among geriatric patients is scarce. In examining lamotrigine registration trials, we found that lamotrigine, when used as maintenance treatment, was compared with lithium and placebo for preventing relapse of depression or mania. Both lithium and lamotrigine significantly improved patient outcomes, reducing the recurrence of illness. Notably, lamotrigine appeared more effective in preventing recurrence of depression, while lithium was better at preventing recurrence of mania. This suggests that although lithium has been used as an augmentation strategy for unipolar depression and is the primary treatment for bipolar disorder, it may be more effective for manic symptoms than depressive symptoms, supported by data indicating its effectiveness in both.  
  
Interviewer: What are the current treatment options for bipolar depression in geriatric patients?   
Dr. Beyer: The options for treating bipolar depression have significantly expanded over the past two decades. Twenty years ago, treatment options were limited to ECT, an antidepressant plus lithium, or lithium alone. Even ten years ago, only three medications had FDA approval for treating depression. However, as of 2022, we now have five FDA-approved medications for bipolar depression, along with increased experience in using other medications for this condition.   
  
A challenge arises because these medications have primarily been approved for adults, with research predominantly conducted on younger adults. When focusing on the geriatric population, we often rely on data from registration trials to determine the efficacy of treatments for older adults. Fortunately, data from two or three trials indicate that older adults respond comparably to younger adults. Thus, we have five different medications available for use.   
  
However, older adults with bipolar disorder often have a history of trying multiple medications, which may limit our options. My primary consideration is whether patients have previously responded to a specific medication. If they have, I prefer to continue that medication. Many patients arrive already on medications, and if they experience recurrent depressive episodes while maintaining some stability, I may keep that medication as a baseline and seek additional treatments to support them. Conversely, some patients come in without any medications, which provides more flexibility in choosing initial treatments.   
  
From an evidence-based perspective, quetiapine and lurasidone show the best data for geriatric patients with bipolar depression. This is supported by clinical trials that included older adults, specifically those over 60 and 65. In one study, we analyzed 142 patients over 55 to assess their response to lurasidone, and another trial included 72 patients over 55 for quetiapine. The findings revealed that older adults responded as well as younger adults. Therefore, quetiapine and lurasidone are often the best evidence-based options for initial monotherapy in geriatric patients with depression.  
  
Interviewer: Can you elaborate on the role of second-generation antipsychotics in the treatment of bipolar disorder?   
Dr. Beyer: Data from the early 2000s indicated a potential role for second-generation antipsychotics in treating bipolar disorder, particularly the combination therapy of olanzapine and fluoxetine. Research showed that nearly all second-generation antidepressants effectively treat mania. However, few studies explored their efficacy in bipolar depression, leading to some controversy regarding their response rates. Among the antipsychotics, olanzapine and fluoxetine, quetiapine, lurasidone, cariprazine, and lumateperone have received FDA approval for bipolar depression. While we lack robust data for quetiapine and lurasidone, the combination of olanzapine and fluoxetine has limited data due to a small initial study group. Notably, individuals over 55 responded well to this combination, which appears effective for significant depressive symptoms in bipolar patients, particularly in geriatric populations. The future of new medications remains uncertain, as we await information on their use in older adults, specifically regarding cariprazine and lumateperone, and I anticipate their integration into our treatment options.  
  
Interviewer: What are the considerations for managing medications in older adults with comorbidities?   
Dr. Beyer: In older adults, it’s common for patients to be on five to ten medications. Therefore, adding medications to this vulnerable population must be approached with caution, which is why we advocate for monotherapy when possible. Most older adults we treat have four to five significant medical comorbidities, such as hypertension, coronary vascular disease, diabetes, and kidney disease, which is prevalent and often strains the kidneys.   
  
Considering these common medical comorbidities, certain medications may pose challenges. For instance, with lithium patients, we must recognize that kidney and thyroid diseases, which are more frequent in older adults, may limit its use, necessitating careful consideration.   
  
Additionally, we must acknowledge that older adults often have metabolic issues, particularly with second-generation antipsychotic medications. If patients are obese or have cardiovascular disease or type II diabetes, I am particularly concerned about the metabolic side effects associated with medications like quetiapine or olanzapine.  
  
Interviewer: How do you approach monitoring practices for older adults compared to younger adults, particularly in the context of comorbidities?   
Dr. Beyer: Monitoring practices are determined less by age and more by presentation and medical frailty. For a healthy older adult, I typically do not make significant changes in monitoring practices, except in cases of cardiovascular disease history. For instance, if I consider lithium for such patients, I would check an EKG, which I might not do for a younger, healthier adult. Generally, I ensure appropriate monitoring as recommended by the American Diabetic Association or the APA for psychiatric medications, unless there are significant health concerns. For patients with kidney strain, particularly when using lithium, I monitor creatinine and kidney function more frequently than I would for younger adults, as these conditions can change rapidly.  
  
Interviewer: What is the role of antidepressants in treating bipolar depression, and what are the associated risks?   
Dr. Beyer: We have data on antidepressant use in bipolar depression, with fluoxetine approved only in conjunction with olanzapine. The understanding of antidepressants' role in bipolar depression is mixed, primarily due to limited evidence regarding their efficacy. The number needed to treat for positive outcomes is high, raising the question of whether antidepressants are genuinely helpful in this context. Despite this, antidepressants remain the most frequently prescribed medications for bipolar depression in clinical practice.   
  
It's crucial to clarify our goals for using antidepressants, consider the available data, and assess the patient's history with these medications to determine their response. There are several reasons to avoid antidepressants in bipolar depression, particularly given the minimal efficacy data. One significant concern is the potential for harm, especially in patients with mixed features or rapid cycling bipolar disorder. Additionally, treating a patient with an antidepressant without a mood stabilizer can also lead to adverse outcomes.   
  
While antidepressants may have a role in bipolar depression, they should not be considered first, second, or even tertiary treatment options. Their use should be carefully evaluated based on the individual's history and the understanding that they can cause harm, alongside the recognition that their efficacy is limited.  
  
Interviewer: Can you elaborate on the recent developments in medications for bipolar disorder?   
Dr. Beyer: Over the past three years, we have progressed from two FDA-approved medications for bipolar depression to five. We anticipate that brexpiprazole will submit data regarding its role in bipolar depression within the next year. Additionally, studies are currently exploring ketamine's potential in treating bipolar depression. Ketamine is already indicated for treatment-resistant depression and severe depressive episodes with suicidal ideation. We are eager to see how ketamine may serve as an effective intervention for bipolar depression.  
  
Interviewer: Can you elaborate on the effectiveness of lithium and valproate in treating bipolar disorder, particularly in older adults, and discuss the role of lamotrigine in this context?   
Dr. Beyer: I’ve been pleased to be part of a research study published in The American Journal of Psychiatry, led by Dr. Robert Young, examining the effectiveness of lithium and valproate in older adults with bipolar disorder. Our studies demonstrate that both lithium and valproate are effective treatments for bipolar mania, with lithium showing slightly greater efficacy, although it may be less tolerated than valproate. This is significant for our older population.   
  
Additionally, we have a range of other treatments available for bipolar mania, reflecting a shift towards ensuring comprehensive protection for patients. One medication that warrants attention is lamotrigine. While antidepressants are the most commonly prescribed medications for bipolar depression, lamotrigine has emerged as the fastest-growing class of medication in this area over the past 10-15 years. It may help prevent relapses in depression and address underlying depressive symptoms. Although lamotrigine lacks FDA approval specifically for bipolar depression, it is approved for bipolar maintenance and may be beneficial for some patients, particularly in combination therapies.  
  
Thank you for your time, Dr. Beyer.