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Editor-in-Chief

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Patient Education

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Feature Article. CBD oil may reduce anxiety, but at a dose that carries a high price and a high risk of drug interactions.

Research Update on page 5. Steroid-induced manic symptoms are common, affecting 1 in 30 in the general population, particularly at doses above 40 mg prednisone.

Research Update on page 6. Lithium = esketamine = aripiprazole in a meta-analysis of treatment-resistant depression, but IV ketamine has a bigger effect.

CBD for Anxiety: An Update

Steven Hamilton, PhD, MD. The Permanente Medical Group, Department of Psychiatry, Kaiser Permanente San Francisco Medical Center.

Dr. Hamilton has no financial relationships with companies related to this material.

Sarah, a 28-year-old teacher, has struggled with generalized anxiety disorder (GAD) for years. She has tried selective serotonin reuptake inhibitors and psychotherapy with moderate benefit but dislikes the sexual side effects of the medications. A friend recommends cannabidiol (CBD) oil, which Sarah finds appealing, but she wonders whether CBD reduces anxiety.

What is CBD?

CBD is a non-intoxicating cannabinoid from the cannabis plant. It is distinct from tetrahydrocannabinol (THC), which can induce psychotic symptoms and cognitive impairment (Hindley G et al, *Lancet Psychiatry* 2020;7:344–353; Lo LA et al, *Neuropsychopharmacology* 2024;49:1425–1436). In contrast, CBD may reduce psychotic symptoms in schizophrenia and has neuroprotective effects. It is sedating, and has positive small trials in anxiety and insomnia (McGuire P et al, *Am J Psychiatry* 2018;175:225–231; Landucci E et al, *Int J Mol Sci* 2021;22:9773).

CBD has more than 65 molecular targets. Its anxiolytic effects are likely due to serotonin 5-HT1A agonism and calcium channel inhibition. CBD is anti-inflammatory and acts on various receptors involved in pain. It has a weak affinity for cannabinoid receptors (CB1 and CB2), where it inhibits some of THC's effects.

CBD is available by prescription (Epidiolex, which is FDA approved for a rare form of seizures) and over the

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Q&A With the Expert

Complex Communications
Dana Dieringer, MD

Assistant Professor, UW Medicine, Department of Psychiatry and Behavioral Sciences, Seattle, WA.

Dr. Dieringer has no financial relationships with companies related to this material.

TCPR: What is the best way to talk about difficult topics with patients?

Dr. Dieringer: Patients want direct communication from their doctors, as do their family and supports. They want more information. They want to exert their autonomy and engage in collaborative decision making. This isn't easy in high-acuity settings—like inpatient—or when we are rushed during brief medication visits.

TCPR: Should we tell patients their diagnosis?

Dr. Dieringer: Yes. We live in a world where patients have access to their notes, so they already have a direct view. Furthermore, the evidence suggests that sharing diagnostic information with patients is helpful. It's about transparency. Studies tell us that most patients and their families want to learn about their diagnosis (Maybery D et al, *BMC Health Serv Res* 2021;21(1):1073).

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CBD for Anxiety: An Update
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counter. However, quality control is inconsistent, with one study finding that nearly *half* of CBD products sold online contained inaccurate amounts, and 20% contained THC (Bonn-Miller MO et al, *JAMA* 2017;318:1708–1709). Clinical trials have utilized CBD as an oral solution; however, many patients prefer to vape CBD.

Recent evidence for CBD in anxiety

A phase 3 RCT in India tested a CBD oral solution (300–600 mg daily) vs placebo for efficacy and safety over 15 weeks in 178 medication-free adults with mild to moderate nonspecific anxiety (Gundugurti PR et al, *Asian J Psychiatry* 2024;97:104073). The CBD in this study was unique in two ways. It was synthetic and free of impurities such as THC (even prescription CBD contains up to 0.15% THC, according to the US patent). It was also nanodispersible, which means the active drug is encapsulated in a vesicle. Nanodispersible drugs cross the blood-brain barrier more efficiently and have greater bioavailability and longer half-lives than their natural equivalents.

Anxiety disorders were diagnosed based on ICD-11 criteria and assessed for severity using the Depression, Anxiety and Stress Scale (DASS-21) questionnaire. The authors did not report the nature of participants' anxiety disorders, but the study notably excluded those with panic disorder, OCD, and PTSD. In any case, CBD led to a reduction in anxiety with a medium to large effect size. Key findings included:

- 73% reduction in GAD-7 scores (baseline score 11.8, endpoint score 3.1)
- Significant improvement in secondary outcomes: Hamilton Anxiety Rating Scale (HAM-A), sleep quality, and depressive symptoms
- No serious adverse events

The trial used a placebo run-in, wherein subjects received a placebo for the first week and those who responded were removed from the trial. This design helps reduce the placebo effect in both arms of the trial but also reduces the generalizability of the findings.

Before this trial, the evidence for CBD in anxiety was mixed, with some suggestion that a medium dose of CBD (300 mg) is anxiolytic while lower (150 mg) and higher (600 mg) doses are not (Fliegel DK and Lichenstein SD, *Psychiatry Res Commun* 2022;2:100074; Lichenstein SD, *Curr Addict Rep* 2022;9:473–485).

Other benefits

CBD improved cannabis use disorder in a phase 2 randomized trial at 400–800 mg but not at 200 mg/day (Freeman TP et al, *Lancet Psychiatry* 2020;7(10):865–874). Other medications with this potential include gabapentin (300 mg QAM, 300 mg Qnoon, 600 mg QHS), naltrexone (50 mg/day), and N-acetylcysteine (1200 mg BID), but patients often find it more acceptable to transition to CBD.

CBD also reduces psychotic symptoms, both in cannabis users and in clinical populations with Parkinson's disease and schizophrenia. In a pair of small double-blind RCTs, CBD 800–1000 mg/day reduced psychosis in schizophrenia both as monotherapy and as augmentation to an antipsychotic (Garel N et al, *J Psychiatry Neurosci* 2021;46(1):E164–E165).

Safety, side effects, and drug interactions

CBD is generally well tolerated, with side effects that include:

- Common: Fatigue, sedation, diarrhea, somnolence, reduced appetite
- Rare but serious: Elevated liver enzymes, pneumonia (Stout SM and Cimino NM, *Drug Metab Rev* 2014;46:86–95).

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CBD: Quick Facts	
FDA Indications	Seizures due to Lennox-Gastaut syndrome, Dravet syndrome, or tuberous sclerosis complex.
Other Uses	Possible benefits in anxiety (300 mg/day), psychosis (800–1000 mg/day), and cannabis use disorder (400–800 mg/day).
Side Effects	• Common: Fatigue, sedation, diarrhea, somnolence, decreased appetite. • Rare but serious: Elevated transaminases, pneumonia.
Interactions	CBD is metabolized primarily through CYP2C19 and CYP3A4. At doses ≥ 300 mg, it is a strong inhibitor of CYP2D6, 2C9, 3A4, 2C19, 1A2, 2B6, 3A, 2E1, and 2C8; and UGT1A9, 2B4, and 2B712 (see the table "Potentially Serious Drug Interactions With CBD" on page 3).
Contraindications	Severe hepatic impairment; pregnancy and lactation.
Cost	$125–$600/month for 300 mg/day.

CBD for Anxiety: An Update

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Patients often prefer to vape CBD rather than ingest the oil, but vaping carries additional risks to the lungs. On the other hand, for those who are switching from cannabis, vaped CBD is much safer than smoked cannabis.

CBD inhibits the enzymes encoded by the CYP2C19 and 3A4 genes, which affects the metabolism of medications like citalopram and escitalopram and potentially raises their levels (Anderson LL et al, *J Clin Psychopharmacol* 2021;41:525–533). (See the table "CBD: Quick Facts" on page 2.)

Cost

CBD is expensive, costing $125–$600 per month for an effective dose. ConsumerLab, which tests products for purity, identified only a handful of brands that were THC-free: cbdMD, Garden of Life, Green Roads Relax, and MedTerra. Among these, cbdMD Broad Spectrum Gummies are the most affordable, though still expensive ($125/month for a 300 mg/day dose).

CARLAT VERDICT New data support CBD as a rapid-acting anxiolytic, but the effective dose is cost-prohibitive.

Potentially Serious Drug Interactions With CBD

Medication	Clinical Relevance of Higher Levels*
Second-generation antidepressants	• Higher levels (2- to 3-fold) • QT prolongation (especially with citalopram) • Dysphoria on trazodone (from mCPP metabolite) • Not affected: Desvenlafaxine
Tricyclic antidepressants	Arrhythmias, death
MAOI antidepressants	Only selegiline (Emsam) is affected (risk of hypotension)
Antipsychotics	• Akathisia, dystonia, extrapyramidal symptoms, QT prolongation • Not affected: Paliperidone
Clozapine	Hypotension, myocarditis, arrhythmias, seizures
Carbamazepine	Seizures, mental status change
Lamotrigine	Stevens-Johnson syndrome (when initiating lamotrigine)
ADHD medications	• Stimulants, modafinils: Hypertension, arrhythmias • Atomoxetine, viloxazine: QT prolongation • Clonidine, guanfacine: Hypotension, bradycardia, fatigue
Benzodiazepines and hypnotics	• Sedation, falls, respiratory depression • Benzodiazepines metabolized by the UGT system are likely affected (lorazepam, oxazepam, and temazepam)
Fentanyl	Respiratory depression, death
Methadone	QT prolongation
Flibanserin	Syncope
VMAT2 inhibitors (deutetrabenazine, valbenazine)	QT prolongation
Other	Caution with levothyroxine, warfarin, immunosuppressants (for organ transplant), and chemotherapy agents

**These interactions are dose-dependent and apply to CBD ≥ 300 mg, where it is likely to raise levels of other medications 2- to 3-fold.*

Expert Interview

Continued from page 1

TCPR: But many clinicians withhold diagnoses.

Dr. Dieringer: There is this notion that knowledge is harmful and requires us to protect our patients. This belief can lead providers to avoid conversations about diagnosis. To worsen the situation, psychiatrists receive very little training in complex communication around diagnosis and prognosis (Outram S et al, *Acad Psychiatry* 2015;39(2):174–180). Withholding a diagnosis is very paternalistic, and the evidence doesn't line up with that. Instead, outcomes improve when we welcome patients and their families into that space and talk openly about diagnosis, prognosis, and treatment options (Wolf D et al, *J Nurs Care Qual* 2008;23(4):316–321).

TCPR: What if your diagnosis causes conflict with the patient?

Dr. Dieringer: I find there is less conflict when we come at the diagnosis from a place of transparency. They may say, "Bipolar disorder? Are you sure? Don't you think you're overreaching? Don't I need a blood test?" I'll respond, "I can only imagine how overwhelming this must all be. Let's take it a step at a time together—I want to answer all your questions." I'll allow a lot of silence so they can process the information.

TCPR: Do you ever change your diagnosis if they disagree?

Dr. Dieringer: Not if I think it's accurate, but diagnostic formulation is a work in progress, so it's important to have a dialogue with the patient, particularly when diagnoses are stigma-laden. I'll say, "You have the right to know this, and we may not agree on it, but I do want you to at least know my perspective and what's in your chart." I want the patient to be able to ask questions and share their perspective. Being open to disagreement and discussing diagnoses with patients is a stance that can build rapport and trust.

TCPR: How do you take that stance?

Dr. Dieringer: Let's say my patient is experiencing schizophrenia and they have a rigid belief that their neighbors are trying to poison them. We may explore how this belief isn't serving them in the long run. Sometimes they may *Continued on page 4*

Expert Interview
Continued from page 3

not want to do this exploratory work, or they may disagree that the belief is unhelpful. However, I do my best to be honest and compassionate. It's okay to disagree sometimes.

TCPR: It's almost like you're saying, "I value my truth, and I value yours as well."

Dr. Dieringer: Exactly. I want to understand their perspective. It's not that I'm more objective or right. It's about how each of us sees it, and respecting the other's perspective. I also try to use person-centered terms and stay away from words like "delusional" or "paranoid." And I acknowledge that the DSM is a tool that has its own limitations and evolves over time.

TCPR: What if the ICD code in the chart is "schizophrenia"?

Dr. Dieringer: I'll start by asking permission: "Would it be okay if I tell you how I see things, and what I'm worried about in terms of a diagnosis?" If they agree, I'll ask, "To make sure we are starting from the same place, what have doctors told you about the voices before? What is your understanding of them?" Asking the patient what they have heard or currently understand helps you tailor the next step, which is delivery of the diagnosis. "I'm worried that you may be experiencing something called schizophrenia." I slow down at this point, as it is a loaded word, and say, "Would it be okay if I tell you what I mean by that?'

TCPR: It's interesting that you jump right into the medical term "schizophrenia" instead of softening it with words like "rigid thinking."

Dr. Dieringer: You can do it both ways and, again, assessing the patient's understanding helps you decide where to start. We have a tendency in medicine to start with easier terms or long summaries, like listing the symptoms the patient came in with. I find it helpful to be more direct, starting with the "headline" and then unpacking it. Now, I'm not jumping into this after meeting them for 15 minutes. I want to make sure I've gathered a full history, done my homework, and hopefully gained some trust so they know I care. Then I check in with them. "To make sure I'm being clear, could you tell me what you're taking away from our conversation so far?" or "I imagine this is a lot of new information. I want to make room for your thoughts or reactions so far."

TCPR: How do you unpack it?

Dr. Dieringer: I focus on what the diagnosis means to them. What can they expect down the road? What is their perspective? What do the symptoms mean in their culture? I have to tread lightly when discussing psychosis as these kinds of symptoms carry so much meaning within different family or cultural systems. I want them to know that their spiritual faith is important. I want them to trust that I will share my medical opinion and what is in the chart. I'll connect the diagnosis to their experience, such as by saying, "Schizophrenia looks different for everyone. You have this intense concern that someone's poisoning your food, and I'm worried this belief is making it hard for you to know who to trust. I'm worried it isn't protecting you in the long run and may be getting in your way."

"It's not that I'm more objective or right. It's about how each of us sees it, and respecting the other's perspective."

Dana Dieringer, MD

TCPR: What if they press you about whether you think the delusions are true?

Dr. Dieringer: I do my best to redirect and focus on how those beliefs are affecting their functioning. "Let's think about what you want to do and how can we you help get there." Using a cognitive behavioral therapy framework can be really helpful. For example, sometimes hypervigilance just eats up all their time, but sometimes it is helpful to them, like if they are experiencing homelessness.

TCPR: How do you explain borderline personality disorder?

Dr. Dieringer: The criteria often resonate more than the stigma-laden term. Before I use the diagnostic term, I'll discuss each criterion and explore how it fits or doesn't fit with their life or experience. Once you understand which criteria resonate with them, it's easier to explain the diagnosis in a way they understand.

TCPR: How do you engage patients in treatment decisions?

Dr. Dieringer: First, I'll say off the bat that medications should never be the only available tool. That's true for any psychiatric disorder. When we discuss meds, I want to hear their honest experience—positive or negative. So if they say aripiprazole gave them terrible akathisia, I'm not going to discount their experience with "but," as in "but we can treat that with propranolol." Instead, I'm going to reflect that back and ask for more: "Any other problems with aripiprazole?"

TCPR: Talking about propranolol can give hope, but it also shuts down the conversation.

Dr. Dieringer: Yes, because you're the doctor. You're the authority. The patient may be sharing the side effect to relay a feeling or an "emotion cue." They are expressing frustration, dissatisfaction with care, and I need to pay attention to that before jumping into a problem-solving mode. So I'll validate: "That sounds miserable. Tell me more."

TCPR: What are other examples of emotion cues?

Dr. Dieringer: In a family meeting, when I introduce the possibility of schizophrenia, the parent might jump in with, "What if it's just that they're smoking too much pot?" Usually, the parent is not looking for a medical lecture on substance-induced psychosis in that moment. Instead, it's an emotion cue that a schizophrenia diagnosis is hard to accept. So I'll respond to the emotional undertone behind the question: "I can imagine how hard this is to hear right now."

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Expert Interview
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TCPR: Do you find that introducing nonpharmaceutical approaches enhances the trust with meds?
Dr. Dieringer: Yes. If they're not interested in taking medications, they probably have good reasons that I need to understand. Maybe they've had side effects or traumatic experiences in the mental health care system.
TCPR: What are ways to phrase things that empower the patient?
Dr. Dieringer: Asking permission. For example, I'll ask, "Would this be an okay time for us to talk about treatment?" I'll give them space to share. I might say, "Before I start spouting ideas, I want to hear what you think is best." If I know what they are interested in first, I can craft better options for treatment. Then, I'll offer two or three treatment options and give some context so the patient understands each one.
TCPR: How do you talk about long-acting injectables?
Dr. Dieringer: That depends on the patient. I may say, "I'd like to go out on a limb a little bit with you. There are medications that we can give to you once a month through an injection form. Have you heard about this?" Then I'll ask what they've heard and gauge their reaction. I'll use a similar approach with clozapine and lithium, seeking their permission every step of the way. If they reject it, that's okay. We may just plant a seed and come back to it later.
TCPR: How do you elicit feedback from the patient?
Dr. Dieringer: When I find myself rattling on a lot, I'll slow down and say, "Hey, I'm giving you a lot of information. Can I check in on how this is sounding so far? What are you taking away? What are you worried about?"
TCPR: What are warning signs that the discussion is going the wrong way?
Dr. Dieringer: Having the same conversation over and over is a sign that the communication isn't working. At that point, I'll step back and look at what the barriers to communication might be. Maybe there are cognitive barriers or I'm not picking up on emotion cues. Then I'll address that: "I feel like we've been having this conversation a lot. What are your thoughts on why we keep revisiting this?"
TCPR: What if anger erupts?
Dr. Dieringer: Hopefully, I can anticipate and plan ahead. For example, if we're going to have a family meeting to talk about something the patient and I often disagree on, I'll say, "There have been times when we see things differently. What should we do if things get intense?" We might plan to take a break, but empowering them ahead of time can help defuse the conflict.
TCPR: Thank you for your time, Dr. Dieringer.

Research Updates IN PSYCHIATRY

MANIA

Mania and Corticosteroids: Beyond Bipolar Disorder

Sy Clark, MD. Dr. Clark has no financial relationships with companies related to this material.

REVIEW OF: De Bock M and Sienaert P, *World J Biol Psychiatry* 2024;25(3):161–174

STUDY TYPE: Systematic review and meta-analysis

Sussing out steroid-induced mania and hypomania can be tricky—as can treating them. How prevalent are they? Who is at risk? And how do we best manage steroid-induced manic and hypomanic symptoms? De Bock and Sienaert performed a systematic review and meta-analysis, and summarized their answers.

They found 10 prospective studies, 3 retrospective studies, 31 case reports, and 3 case series published through early 2023. The total population of 1,256 adults was about 60% female, with an average age of 44. All but one study mentioned prednisone, prednisolone, or methylprednisolone; other included steroids were cortisone, hydrocortisone, dexamethasone, and fluocortolone.

A weighted average of the population studies yielded an incidence rate of 3.25% for steroid-induced hypomania or mania, which were the most common psychiatric side effects of steroids. Steroid doses above 40 mg/day were most likely to cause (hypo)mania, but even doses as low as 2.5 mg/day were implicated. These symptoms mostly occurred within the first days to two weeks after starting steroids. Route of administration, psychiatric history, and sex were not found to be risk factors, but long-term steroid treatment, young or advanced age, and a family history of bipolar disorder or psychosis were. Physiological risk factors included hypoalbuminemia and higher serum levels of corticosteroids.

The first treatment for steroid-induced hypomania or mania is reducing the steroid dose to less than 40 mg/day of prednisone equivalents, and gradually stopping the dose entirely, if possible. If this is not feasible, or if symptoms persist, recent studies recommend using atypical antipsychotics as first-line therapies. Evidence favors olanzapine and risperidone and suggests that lithium can be used both as treatment and prophylaxis.

CARLAT TAKE
It's not ethical to study steroid-induced side effects via RCTs, so this admittedly heterogeneic evidence is the best we have. Collectively, it suggests we should be vigilant for symptoms in both younger and older patients who are taking higher doses of steroids for longer periods of time. Consult with steroid prescribers to collectively balance their risks and benefits, and if reducing or stopping them isn't possible or doesn't work, consider brief treatment with an antipsychotic or lithium.

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Research Updates
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DEPRESSION

Lithium as Effective as IV Ketamine Augmentation in Treatment-Resistant Depression

Alex Evans, PharmD, MBA. Dr. Evans has no financial relationships with companies related to this material.

REVIEW OF: Terao I et al, *J Affect Disord* 2024;346:49–56

STUDY TYPE: Network meta-analysis

There are many augmenting agents for treatment-resistant depression (TRD). Which works best? Without many head-to-head studies to draw from, these researchers employed a meta-analysis to compare common medications.

They included 21 placebo-controlled trials of the most-studied augmentation agents in TRD: lithium, intravenous (IV) ketamine, intranasal esketamine, and aripiprazole. One study of lithium vs aripiprazole was also included (in which they had similar efficacy). All trials used standard measures of depression as primary outcomes, but they were heterogeneous in other ways. Study sizes ranged from around 10 to almost 400. They defined TRD as a failure of one antidepressant (AD), except those studies involving IV ketamine, where TRD was defined as the failure of two ADs. IV ketamine studies were also more likely to be shorter—some only one week. The lithium studies tended to be older and involved augmenting tricyclic antidepressants. Patients in the esketamine studies tended to have higher baseline levels of depression.

Unsurprisingly, all medications were more effective than placebo. Response rates were greater for augmentation with IV ketamine than for all other medications except lithium, where ketamine trended toward superiority but did not separate. The odds ratio for response with IV ketamine was 3.20 vs intranasal esketamine (1.43–7.16) and 2.90 vs aripiprazole (1.33–6.27). There was no significant difference in response rate between augmentation with esketamine, aripiprazole, or lithium. Both intranasal ketamine and aripiprazole had significantly more dropouts due to side effects than placebo. Noting the limitations inherent in their analysis, the authors rated the evidence comparing IV ketamine to other medications as low certainty.

CARLAT TAKE

TRD covers a wide variety of patients, and that's a problem for this study. Network meta-analyses assume that patients and placebo responses are comparable across trials. This study hints at results that we'd like to see elucidated in future research.

ADDICTION

Do Benzodiazepines and z-Hypnotics Lead to Long-Term or High-Dose Use?

Jeremy Mills, DNP, PMHNP-BC. Dr. Mills has no financial relationships with companies related to this material.

REVIEW OF: Rosenqvist TW et al, *Am J Psychiatry* 2024;181(3):246–254

STUDY TYPE: Retrospective cohort

Many of us are reluctant to prescribe benzodiazepines and z-hypnotics (BZRAs) because we worry about misuse, tolerance, and dependence. We all know patients who have started a "short-term" benzo only to end up taking it for years and at higher doses. But how common is this? This study provides a comprehensive look at how often patients end up on BZRAs long term and who is most at risk.

Researchers examined prescribing patterns for the entire adult population of Denmark from 2000 to 2020. They looked at three primary outcomes in this study. Two were related to "long-term use," defined as use for one year or seven years. The third outcome was "dose escalation above recommended levels," defined as 3 years of ongoing use with prescriptions reaching above 40 mg of diazepam equivalents for those under 65, or 20 mg for those 65 and over.

Among nearly 1 million adults ages 20–80, about 650,000 started benzodiazepines, and 600,000 started z-hypnotics. At 1 year, 22.9% of benzodiazepines and 17.8% of z-hypnotics were continued. Numbers fell at the 7-year mark to only 5.5% and 4%, respectively. Notably, 40% of patients filled only one BZRA prescription. A psychiatric diagnosis modestly increased long-term use risk for anxiolytic BZRAs, with substance use disorders being the greatest risk factor. Only 3,545 patients (representing 7% of those who continued BZRAs for 3 years or more) escalated their doses above recommended levels.

CARLAT TAKE

This large study spanning nearly a million people over 20 years is fairly reassuring: The majority of patients prescribed BRZAs do not end up using them long term, and only a small fraction escalate their doses to unsafe levels. While the study was observational and limited to a Danish population, it gives us confidence that most patients can manage well with relatively short courses and lower doses. That said, we should remain vigilant, especially with patients who have substance use disorders.

PSYCHOPHARMACOLOGY

Should We Prescribe Maintenance Antipsychotics for Patients With Psychotic Depression in Remission?

Viktoriya Golovatscka, MSN, PMHNP-BC, FNP-BC. Dr. Golovatscka has no financial relationships with companies related to this material.

REVIEW OF: Al-Wandi A et al, *Acta Psychiatr Scand* 2024;149(1):6–17

STUDY TYPE: Retrospective cohort

It's been clear for some time now that the best acute treatment for patients with major depressive disorder with psychotic features is a combination of antidepressants and antipsychotics. American Psychiatric Association guidelines recommend continuing antipsychotics during the maintenance phase, when the goal is to prevent relapse after initial treatment success. But the evidence for this approach is limited. This study explores whether continuing antipsychotics alongside antidepressants provides any additional benefit in preventing hospital readmissions or suicides during the

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CME Post-Test

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1. Which brain receptor is most responsible for the anxiolytic effect associated with cannabidiol (CBD)?
   - [ ] a. Dopamine D2 receptor
   - [ ] b. NMDA receptor
   - [ ] c. Serotonin 5-HT1A receptor
   - [ ] d. Cannabinoid CB1 receptor
2. What does the evidence suggest about sharing psychiatric diagnoses with patients?
   - [ ] a. It often leads to increased confusion and distress
   - [ ] b. It is discouraged due to concerns about stigma
   - [ ] c. It improves outcomes when discussed through the lens of the medical model
   - [ ] d. It improves outcomes and aligns with patient and family preferences
3. According to De Bock and Sienaert's meta-analysis, what is the most common psychiatric side effect of corticosteroids?
   - [ ] a. Hypomania or mania
   - [ ] b. Depression
   - [ ] c. Anxiety
   - [ ] d. Psychosis
4. In the recent phase 3 RCT of synthetic CBD for anxiety, what was a unique feature of the preparation compared to standard CBD products?
   - [ ] a. It contained trace amounts of tetrahydrocannabinol (THC) for synergistic benefit
   - [ ] b. It was derived from whole-plant extracts
   - [ ] c. It was nanodispersible and THC-free, enhancing bioavailability
   - [ ] d. It required co-administration with food for absorption
5. According to Dr. Dieringer, how can clinicians foster rapport and trust when patients disagree with their diagnosis?
   - [ ] a. Avoid using medical terminology that may cause alarm
   - [ ] b. Refrain from sharing diagnoses that may be contested
   - [ ] c. Use passive language and euphemisms to soften the diagnosis
   - [ ] d. Create space for disagreement and emphasize mutual respect

Research Updates

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maintenance phase of treatment for psychotic unipolar depression.

In this retrospective cohort study, Al-Wandi and colleagues used Swedish national registers to track 4,391 patients with a diagnosis of psychotic unipolar depression. These patients were followed for 2 years after discharge from inpatient care between 2007 and 2016. They were divided into 2 groups: 2,972 patients received both antidepressants and antipsychotics, while 1,419 were treated with antidepressants alone. The primary outcome measured was the rate of hospital readmissions due to any psychiatric disorder, suicide attempts, or completed suicides.

Contrary to expectations, the study found that patients on antidepressant monotherapy had a lower risk of hospital readmission or suicide than those receiving the combination of antidepressants and antipsychotics. Specifically, 36.6% of the monotherapy group experienced these outcomes, compared to 42.3% in the combination therapy group. This difference was statistically significant, with a hazard ratio (HR) of 0.86 (95% confidence interval [CI]: 0.77–0.95), meaning that the risk of adverse outcomes was 14% lower for those on monotherapy compared to combination therapy. Mirtazapine was the most commonly prescribed antidepressant, at about 42% for both groups, and olanzapine was the most commonly prescribed antipsychotic, at about 50% in the combination group. Interestingly, a mood stabilizer, lithium, was the only medication associated with significant benefits, with an HR of 0.63 (95% CI: 0.48–0.82) for all subjects, indicating a 37% reduction in risk.

CARLAT TAKE

This study was observational. Perhaps patients who were more ill received multiple medications. That said, the results suggest that the routine use of antipsychotics in the maintenance phase for psychotic depression might not be as helpful as we thought. After remission from psychotic depression, consider antidepressant monotherapy, which might be more effective and avoids the potential for metabolic syndrome or tardive dyskinesia associated with antipsychotics.

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Note From the Editor-in-Chief

An App for Tardive Dyskinesia

Second-generation antipsychotics have cut the risk of tardive dyskinesia (TD) in half—from 7% to 3% per year—but it is still a problem. After a decade on an antipsychotic, 20%–30% will develop TD, and the rates are even higher after age 50 (Correll CU and Schenk EM, *Curr Opin Psychiatr* 2008;21(2):151–156). The early signs are mild and may be dismissed as nervous habits (indeed, anxiety does worsen tardive movements). Unfortunately, most cases are not detected until they cause problems, at which point they are harder to reverse.

A new app hopes to change that. Released this summer, TDScreen lets patients check for tardive movements. The screen takes five minutes and uses artificial intelligence (AI) to analyze videos taken above the waist. It may miss movements of the feet, legs, and trunk, but it otherwise performs very well. Compared to psychiatrists who were trained in the Abnormal Involuntary Movement Scale (AIMS), the app performed better. The overall accuracy improved as the AI model was trained, ranging from 85% to 98% (based on area under the curve) (Sterns AA et al, *J Clin Psychiatry* 2025;86(3):25m15792).

TDScreen is free at https://tdscreen.ai. The developer, Videra Health, hopes the app will attract physicians to their platform, where they offer more premium AI healthcare tools at a cost.

—Chris Aiken, MD

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