

# The Carlat Psychiatry Report

AN UNBIASED MONTHLY COVERING ALL THINGS PSYCHIATRIC

VOLUME 8, NUMBER 5

WWW.THECARLATREPORT.COM

MAY 2010

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## Suboxone: An Overview

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Dr. Sonkiss and Dr. Carlat have disclosed that they have no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

Opioid drugs represent one of the great triumphs of medicine, because they are extremely effective at relieving pain. Since the 1960s, multiple forms of synthetic opioids have been introduced, including such well-known drugs as hydrocodone (Vicodin) and oxycodone (Percocet, Oxycontin). Unfortunately, the array of opiate options has led to an exponential rise in the abuse of prescription opiates, and a corresponding explosion of deaths due to opiate overdose. (For a good review of these issues, see Lanier W and Kharasch E, *Mayo Clinic Proceedings* 2009;84(7): 572–575.) Equally unfortunate is that getting off of opiates is extremely difficult, and the best that many addicts can hope for is opioid maintenance, which is essentially trading one narcotic addiction for another.

For decades, methadone was the mainstay of opioid maintenance. Methadone has the advantage of being a very long acting oral opiate that can substitute well for street drugs such as IV heroin. And although methadone is effective for many patients, it poses problems. In

order to prevent diversion of methadone, the federal government requires patients to visit federally-licensed methadone clinics daily—in effect handcuffing patients to a methadone clinic lifestyle. Patients with full-time jobs or those who want to travel or live in rural areas have a very hard time participating in methadone maintenance programs.

In 2002, the FDA approved Suboxone (sublingual buprenorphine/naloxone) for the treatment of opioid dependence. Suboxone revolutionized opioid maintenance treatment because it is less abusable than methadone, and therefore can be prescribed by physicians from their offices. The main ingredient in Suboxone is buprenorphine, a semisynthetic opioid that has been available as an injectable narcotic (brand name Buprenex) since 1981. Buprenorphine is a partial opioid agonist, meaning that it occupies the opiate receptors but doesn't cause quite the same intensity of receptor activation (or "high") as full opiate agonists such as oxycodone or methadone. The other ingredient in Suboxone is naloxone, which is an opiate blocker best known for emergency treatment of opioid overdose. Suboxone is composed of buprenorphine and naloxone in a ratio of 4:1.

Why, you might ask, would you combine an opiate *antagonist* with an opiate *agonist*? This is a neat pharmacological trick to prevent Suboxone from being ground up and shot intravenously. When taken as directed (sublingually), the buprenorphine works, but naloxone is

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**Learning objectives for this issue:** 1. Describe the benefits and proper use of Suboxone for opioid maintenance treatment. 2. Explain the strengths and limitations of drug testing for your patients. 3. Outline the methods and questions used in motivational interviewing. 4. Understand the most current findings in the literature regarding psychiatric treatment. This CME/CE activity is intended for psychiatrists, psychiatric nurses, psychologists and other health care professionals with an interest in the diagnosis and treatment of psychiatric disorders.

poorly absorbed through the buccal mucosa and has only a minimal effect. However, when the tablets are crushed up and injected, naloxone comes alive, preventing the high and causing immediate withdrawal symptoms in patients addicted to opiates. Methadone, on the other hand, can be injected and will deliver a potent high, making it far more prone to abuse and diversion than Suboxone.

Although Suboxone has been shown to be superior to clonidine for opioid detoxification (Ziedonis DM et al., *Drug Alcohol Depend* 2009;99(1-3):28-36), its greatest strength lies in its FDA-approved use as an alternative to methadone for opioid maintenance therapy. A pivotal 52-week trial demonstrated Suboxone's superiority to placebo in maintaining opioid-negative urine tests (Fudala PJ et al., *N Engl J Med* 2003;349(10):949-958); two randomized trials demonstrated non-inferiority to methadone maintenance therapy at 17 weeks and six months (Kakko J et al., *Am J Psychiatry* 2007;164(5):797-803); and clinical studies have shown effectiveness in maintaining sobriety in "real world" primary care settings (Cunningham C et al., *Fam Med* 2008;40(7):500-506).

Compared with methadone, Suboxone's most obvious advantage is that it allows office-based maintenance treatment of opioid dependence. The difference in quality of life between patients on Suboxone versus methadone maintenance can be tremendous. Suboxone is also safer than methadone, since as a partial agonist, it is less likely to cause respiratory depression in overdose—although it can still cause significant sedation and respiratory depression when combined with benzodiazepines or other CNS depressants. Since Suboxone is still under patent, it is expensive, but because fewer office visits are needed, the overall cost of treatment is comparable to that of methadone maintenance (Doran CM, *Expert Rev Pharmacoeconomics Outcomes Res* 2005;5(5):583-591).

Although Suboxone theoretically is less abusable than other opiates, diversion and abuse of the drug have become extremely common. Because of this, the

DEA tightly regulates its use. Physicians must complete an eight-hour CME course in order to obtain a special DEA number (known as a DATA 2000 waiver) before they can prescribe Suboxone. Even with the waiver, the DEA limits the number of patients on your Suboxone "panel" to a maximum of 30 during your first year of prescribing, and a maximum of 100 patients thereafter. (See the SAMSHA website at <http://bit.ly/73fMfd> for more information.)

So let's assume you've attained your DATA 2000 waiver and are ready to prescribe Suboxone. Here's how it's typically done. The first phase of treatment is called the "induction." Before a patient

receives the first dose, he must be in opiate withdrawal. Why? Because if the patient has opiates in his system, Suboxone will bump the opiates off the binding sites and will precipitate a withdrawal—not a great way to foster the doctor-patient alliance! As a rough rule of thumb, Oxycontin users should have taken their last dose no less than 24 hours before Suboxone to insure adequate withdrawal, and heroin users, about 12 hours. But to accurately assess the degree of withdrawal, you should use the Clinical Opiate Withdrawal Scale (COWS), which is available for free online at <http://bit.ly/d0E9Ur>. The scale will walk you through an assessment of the typical signs of opiate withdrawal, such as sweating, chills, yawning, muscle aches, nausea and vomiting.

drawal, you start by giving a 2 or 4 mg dose, then have the patient wait in the waiting room for an hour, and then reassess. If the withdrawal symptoms have disappeared, you have a good starting dose. If the symptoms have improved somewhat, you should give another 2 to 4 mg. And if the symptoms have worsened...well, then you've pretty much blown it because this means the patient was not in enough withdrawal at the beginning of the process. After you've estimated an adequate dose, you should see a patient daily for two or three days, then less often once you feel comfortable that he or she has been properly induced. Eventually, visit frequency is titrated down to monthly for most patients. A typical final target dose of Suboxone is in the range of 12 to 16 mg per day.

During each visit, the first thing to ask is: "Have you used?" because relapse to opiate abuse is common, as is abuse of other substances such as amphetamines, cocaine and benzodiazepines. Assess for signs of withdrawal at each visit, asking particularly about waking night sweats (which some patients may not realize is a symptoms of withdrawal), and about craving, which is often the "last stand" of the withdrawal syndrome and puts patients at high risk of relapse. If withdrawal symptoms occur, this generally means that the dose of Suboxone should be nudged higher.

Therapy during Suboxone visits should focus on identification and avoidance of triggers for drug use, support for efforts to get a job, and general encouragement to create as much structure in the patient's life as possible. As you might imagine, many Suboxone patients have substantial psychiatric comorbidity, especially anxiety and mood disorders. While this could make treatment very complicated, most patients see a different psychiatrist for issues outside the realm of the addiction. "Farming out" treatment of comorbidities allows you to keep focused on the addiction while ensuring that patients still receive adequate treatment for other issues.

### Suboxone Resources

- Suboxone Talk Zone (<http://suboxone talk zone.com>) is a blog written by Jeffrey T Junig MD, PhD, a physician and recovering opiate addict. He sells an e-book on his blog called *User's Guide to Suboxone*, which is a helpful handbook for both patients and prescribers.
- A standard Agreement for Treatment with Sublingual Buprenorphine/ Naloxone (Suboxone®) is available at [www.thecarlatreport.com](http://www.thecarlatreport.com). You are free to download and use this document in your own practice.

receives the first dose, he must be in opiate withdrawal. Why? Because if the patient has opiates in his system, Suboxone will bump the opiates off the binding sites and will precipitate a withdrawal—not a great way to foster the doctor-patient alliance! As a rough rule of thumb, Oxycontin users should have taken their last dose no less than 24 hours before Suboxone to insure adequate withdrawal, and heroin users, about 12 hours. But to accurately assess the degree of withdrawal, you should use the Clinical Opiate Withdrawal Scale (COWS), which is available for free online at <http://bit.ly/d0E9Ur>. The scale will walk you through an assessment of the typical signs of opiate withdrawal, such as sweating, chills, yawning, muscle aches, nausea and vomiting.

Once your patient is clearly in with-

Because of the risk of diversion, working with Suboxone patients requires firm ground rules, and the dictum “I trust you, but I don’t trust your addiction” applies. Let patients know that there are no refills on their prescriptions, and if they miss an appointment, they will have to wait for another opening before they can get a new script. Most

clinics require attendance at 12 step meetings, and require enrollment in a random urine drug testing program. Some states have a searchable database of all patients who have filled prescriptions for controlled substances, and looking up each patient every two or three months is a required safeguard to help detect doctor shopping.

With all the hoops to jump through, you might find the idea of prescribing Suboxone daunting, but it can be fulfilling to work with this clientele, and for some practitioners it has become a lucrative practice model.



## A Primer on Drug Testing

Daniel Carlat, MD  
Associate Clinical Professor  
Tufts University School of Medicine

Dr. Carlat has disclosed that he has no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

If you are a typical psychiatrist practicing in a setting other than a substance abuse clinic, chances are good that you rarely order drug testing on most of your patients. But should you be doing this more? Possibly. Here are some reasons why you might want to order drug testing:

1. To monitor the sobriety of patients who are acknowledged drug/alcohol addicts or abusers, and who want to get clean.
2. To determine whether a patient who has acknowledged abuse of one substance (such as alcohol) is also secretly abusing other substances. In one study of 248 treatment-seeking alcoholics, two-thirds (68%) reported using illicit drugs in the past 90 days: 33% powder cocaine; 29% crack cocaine; 15% heroin, and 24% cannabis (Staines GL et al., *J Addict Dis* 2001;20(4):53–69).
3. Finally, to determine whether an apparent primary psychiatric disorder is actually caused, or worsened, by drug use. Many patients with mood, anxiety, and psychotic disorders are abusing drugs, whether you know it or not. The estimated lifetime prevalence of drug or alcohol abuse in depression is 16% to 27%, in bipolar disorder 43% to 56%, and in schizophrenia 20% to 65%, depending on the study methodology

used (see Bradizza C et al., *Clinical Psychology Review* 2006;26(2):162–178). The lifetime prevalence of drug abuse in the general population is around eight percent (Compton WM et al., *Arch Gen Psychiatry* 2007;64(5):566–576), and alcohol abuse is around 18 percent (Hasin DS et al., *Arch Gen Psychiatry* 2007;64(7):830–842).

Most substance abuse clinics have a standard procedure for doing random urine toxicology screens, often including semi-supervised urination to prevent patients from substituting someone else’s clean urine for their own. But assuming that you work in a private practice with a middle class clientele, your approach to drug testing will likely be different. When should you consider asking a patient to get tested? Examples would include: Patients who are not improving despite aggressive treatment; patients to whom you are prescribing frequently abused substances, such as stimulants or benzodiazepines; patients who are being treated with opioids by another physician; any patient with an acknowledged history of substance abuse, even if remote.

Broaching the topic of drug testing can be uncomfortable for both you and your patient. You can introduce it by saying something like: “You might have heard that there is an epidemic of drug abuse in the U.S., and doctors are being encouraged to test most of their patients, especially those who are not getting better on standard treatment. How would you feel about getting tested?” Generally speaking, most patients will agree to it. Those who are particularly resistant are likely to be those who know they won’t test “well.” Hopefully, the whole conver-

sation will encourage patients to be forthcoming about any hidden drug use, which would be the best possible outcome.

Assuming your patient agrees, how do you go about getting the test done? Some psychiatrists have testing kits in their offices, but most might feel uncomfortable handing a patient a urine cup and asking him or her to go into the office bathroom and return with a sample. A more genteel approach is to ask the patient to go to the lab sometime within the next six hours. You can write out an order for a urine tox screen on your prescription pad and ask that the results be faxed to your office. The lab report will include the time that the sample was delivered, allowing you to verify that your patient complied with the six hour time limit.

What about the patient who tests positive but swears the test is wrong? There’s no question that false positive results, also known as cross reactivity, are common, especially with urine drug screens. False positives reported in the literature include amphetamine with diphenhydramine (Benadryl), chlorpromazine (Thorazine) (Adhami S, *Psych Bulletin* 2005;29:276), trazodone (Desyrel) (Roberge RJ et al., *J Clin Toxicol* 2001;39(2):181–182), bupropion (Wellbutrin) (Weintraub D et al., *Depress Anxiety* 2000;12(1):53–54) and many others. THC can come up as a false positive with the proton pump inhibitor pantoprazole (Protonix) (Srinivas B et al., *Curr Psych* 2006;5(8)), and LSD can cross-react with sertraline (Zoloft), chlorpromazine, and paroxetine (Paxil)

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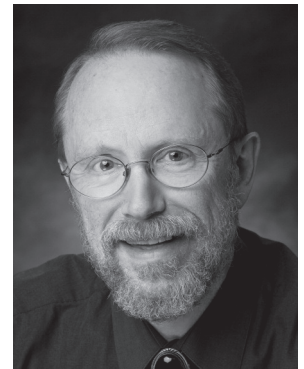
Q & A  
With  
the Expert

*This Month's Expert*

Motivational Interviewing  
William Miller, PhD

*Emeritus Distinguished Professor of Psychology and Psychiatry  
University of New Mexico*

Dr. Miller has disclosed that he receives royalties for books published by Guilford Press and that he is a senior advisor to The Change Companies. Dr. Carlat has found that there is no evidence of commercial bias in this educational activity.



**TCPR:** Hello Dr. Miller. You have developed a method of working with people with substance abuse called motivational interviewing. Please tell us what it's all about.

**Dr. Miller:** Motivational interviewing is really a way of talking to people that calls forth their own motivations for change. Instead of telling them that they need to change, it's a way of encouraging them to want to change.

**TCPR:** I'd say the goal of most therapists and psychiatrists is to help people with substance abuse problems change. So how is this different from the usual way we work with addicts?

**Dr. Miller:** Most of us got into this field to help people, but it doesn't come naturally to let people help themselves. My research partner Steve Rollnick and I have written about the "righting reflex." That is, the desire to set things right and put people on the right path. Essentially this is telling them what to do. The problem with it is that a lot of people are ambivalent about their addictions. So when you take up one side of an argument—saying, "You have to change," they instinctively take up the other side of the argument—"No I don't."

**TCPR:** So an example of the usual way of talking to an addict would be if a patient who is an alcoholic comes into the office, saying to him: "Look John, you have a real problem. You are killing yourself. You need to stop this and I am going to help you stop it. You need to go to AA meetings," et cetera?

**Dr. Miller:** Right. You're doing this with the best of intentions. You are trying to set this person on the right path. But what happens is that you activate within that person the opposite argument. If you behave in a way that causes a person to argue against the change, they can actually talk themselves out of it.

**TCPR:** How did you come up with motivational interviewing?

**Dr. Miller:** I sort of came about it organically while I was working with a group of young psychologists in an alcohol clinic in Norway. During role-plays, they kept asking me why I would ask a question this way, or why I reflected this instead of that. So I wrote down some decision rules that I seemed to be using and sent the discussion paper around to some of my colleagues. It was published in the British journal *Behavioural Psychotherapy* as a clinical piece, and I thought that was the last I'd hear about it. Instead, it took off like a rocket, and out of sheer embarrassment, I had to begin doing research.

**TCPR:** And that research proved that it worked?

**Dr. Miller:** Well, there are a number of meta-analyses out there now and the results are pretty strong. The effect size is in the small to medium range on average, but highly significant (Lundahl B et al., *J Clin Psychology* 2009;65(11):1232-1245). There are also quite a few trials in the type of setting some of your readers work in—psychiatric settings with patients with dual diagnoses of a major mental disorder and substance abuse. These trials, too, are showing the same nice effects that we see in other populations (Burke B et al., *J Consulting and Clin Psychology* 2003;71(5):843-861; Rubak S et al., *British Journal of Gen Practice* 2005;55:305-312).

**TCPR:** While I know it takes a long time to master motivational interviewing, can you give us some tips to apply it to our practice now?

**Dr. Miller:** There are three elements to the underlying spirit of motivational interviewing. The first is *collaboration*—the doctor/therapist and the patient are working together. The second is *evocation*—calling forth patients' own motivation to change, rather than installing motivation in them. And the third is respect for patients' *autonomy*—which means truly knowing that they get to make the choices about their own lives. Without this mindset, you're not likely to be successful with this method.

**TCPR:** Let's take my hypothetical patient, John. I'm thinking that since he is coming to see me, he wants to get over his drinking problem. How might I use motivational interviewing to help him?

**Dr. Miller:** What you should be doing is arranging a conversation in a way that causes *him* to make the arguments for change. Think about it like this: there is a continuum of clinical styles. At one end is directing, or telling a patient precisely what to do, which is sometimes very appropriate in medicine. At the other end is listening, which is a classic supportive client-centered approach. Somewhere in the middle is motivational interviewing—a style Dr. Rollnick and I call "guiding." I need to initiate a conversation that will get *John*, and not me, to argue for quitting drinking—why he should do it, how to go about it, why it is important.

**TCPR:** How do I get that kind of conversation going?

**Dr. Miller:** Most simply, you ask open questions, the answers to which are what we call "change-talk." Change-talk is anything a patient

says that's moving him in the direction of change. There are five questions that can get a person on the path to change. The first four fall into what we call the preparatory category, and the last one is action-oriented and indicates the commitment phase of this process toward change.

**TCPR: What are the questions?**

**Dr. Miller:** You can remember the first four with the acronym DARN; for desire, ability, reason and need. The last question is all about committing to the change. The **first question** is, "Why would you *want* to make this change?" Everybody wants something. Maybe they want to lose weight, get healthy, live to see their grandchildren. The **second question** is, "How could you do it in order to succeed?" The person needs to perceive that he or she can actually make the change. The **third question** is, "What are the three best reasons to change?" This is different from the desire question in that it's asking for concrete reasons. For example, "My doctor said I am going to get liver cirrhosis if I don't stop drinking." The **fourth question** relates to need: "On a scale from 0 to 10, where 0 is not at all important and 10 is most important, how important is it for you to make this change?" When they give you the number, you then ask, "Why are you at that number and not 0?" It's helpful to give back to the person a short summary of what they've said about their motivations for change. And then there's a **fifth question**, which is the action one, "So what do you think you'll do?" A psycholinguist who works with us found that commitment language is the best predictor of behavior change.

**TCPR: Now what happens when you go through this whole process and you determine that your patient is not motivated to make significant change?**

**Dr. Miller:** That's the autonomy piece of it. That has to be okay. That doesn't mean that you don't have any advice for that person or that you can't voice your concern. You can say, "I am rooting for you to make this change because it will have a huge impact on your life, but it is really up to you." You can leave the door open and continue to elicit change-talk. Often the change is happening under the surface even if you don't really see it.

**TCPR: Are there any particular books or training methods you can recommend that can help psychiatrists to learn more about this technique?**

**Dr. Miller:** "Motivational Interviewing in Healthcare," by Steve Rollnick et al., is written specifically for doctors, nurses, PAs, and others whose contact is brief. I would say find a good motivational interviewer in your area and have him or her coach you. You will need to record your sessions, so they can hear exactly what is going on and pick up on opportunities that you may miss. Using just written notes to coach on this method is like teaching someone the piano without hearing them play.

**TCPR: Thank you Dr. Miller.**

**Five Questions for Effective Motivational Interviewing**

1. Why would you want to make this change? (desire)
2. How could you do it in order to succeed? (ability)
3. What are the three best reasons to make this change? (reason)
4. On a scale from 0 to 10, where 0 is not at all important and 10 is most important, how important is it for you to make this change? Why that number and not 0? (need)
5. So what do you think you'll do? (commitment)

## Drug Testing: A Primer

*Continued from Page 3*

(Acosta-Armas AJ, *Psychiatric Bulletin* 2003;27:17-19).

Any chemistry lab will be able to give you a cross-reactivity booklet with a dismayingly long list of very common drugs that can cause false positives. For example, both coffee and ibuprofen are often listed as cross-reacting with the ampheta-

mine test. Generally, if there is a positive result, labs will confirm it by sending it out to a different lab for gas chromatography, which is more precise, though not always perfectly accurate.

The table below lists a variety of drug testing options. Most are capable of testing for the usual panel of drugs,

including amphetamines, barbiturates, benzodiazepines, cocaine, methadone and other opiates, LSD, PCP, and THC.

(Acknowledgments to Susan Hochstedler, RN, of Addison Gilbert Hospital in Gloucester, Mass., and Karen Toscano, Core Lab Supervisor at Anna Jaques Hospital in Newburyport, Mass., for providing some helpful information for this article)

### Available Drug Tests

| Test                            | Detection Time Frame     | Notes   |
|---------------------------------|--------------------------|---|
| Urine                           | 6-24 hours               | Test can be faked; false positives due to cross-reactivity; false negatives due to dilution |
| Blood                           | 6-12 hours               | It hurts!   |
| Hair                            | 7 days to several months | Expensive, but good for discovering use in more distant past                                |
| Saliva                          | 24 hours                 | Up and coming   |
| Breathalyzer (for alcohol only) | A few hours              | Often used by patient's family to assess driving safety                                     |

Research Updates  
IN PSYCHIATRY

Section Editor, Glen Spielmans, PhD

Glen Spielmans, PhD has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this article.

SOCIAL ANXIETY

**CBT Plus MAOI More Effective for Social Anxiety than Either Alone**

SSRIs are the mainstay of medication treatment for social anxiety disorder (SAD), while cognitive behavior therapy (CBT) is at least as effective. Oddly, combined SSRI and CBT treatment has not clearly outperformed each treatment alone in controlled trials. But a new study implies that MAOIs combined with CBT may be particularly effective.

In this study, 128 patients with SAD were randomized to one of four conditions: combined cognitive behavior group therapy (CBGT) and the MAOI phenelzine (Nardil), phenelzine alone, CBGT alone, or placebo. CBGT was given in weekly 2.5-hour sessions to groups of four to six patients for 24 weeks. Phenelzine was started at a dose of 15 mg/day and was gradually increased to a potential maximum dose of 90 mg/day, with the final average dose ending up at about 65 mg/day. Patients didn't take any other psychotropic medications, except chloral hydrate or zolpidem (Ambien) as needed for sleep.

Patients were assessed at six, 12 and 24 weeks with well-known anxiety rating scales. After 24 weeks, the greatest improvement in Clinical Global Improvement (CGI) response rates was seen in the combined treatment group—78.1% response rate (25 of 32 participants). Combined treatment was statistically superior to the phenelzine only group (48.6% response rate), the CBGT group (52.9%), and the placebo group (33.3%) (Blanco C et al., *Arch Gen Psychiatry* 2010;67(3):286–295).

**TCPR's Take:** While the results were statistically significant, there were fairly high drop out rates in the various treatment arms, and the total number of participants was rather small. But the results are suggestive and imply that combining MAOI treatment with group cognitive therapy is an effective—if rarely feasible—option.

BIPOLAR DEPRESSION

**Seroquel For Bipolar Depression: The BOLDest and Best?**

In 2005 and 2006, two trials showed a substantial advantage for quetiapine (Seroquel) over placebo for bipolar depression. Based on these trials, which were known by the acronym BOLDER I and II, quetiapine received an FDA indication for the condition.

AstraZeneca recently published an additional two trials, which compared the drug to lithium and paroxetine (Paxil) in the treatment of bipolar depression. The monikers this time: EMBOLDEN I, which compared quetiapine 300 mg (n=265 patients), 600 mg (n=268), lithium 600 to 1,800 mg (n=136), or placebo (n=133); and EMBOLDEN II, which compared quetiapine 300 mg (n=229), 600 mg (n=232), paroxetine 20 mg (n=118), or placebo (n=121). Both trials were eight weeks, randomized and double-blind. They used the Montgomery-Asberg Depression Rating Scale as their primary outcome measure, along with several secondary measures.

In the two trials, both quetiapine doses (300 mg and 600 mg) were superior to placebo on the MADRS and most other secondary measures, whereas lithium was no better than placebo on any measure, and paroxetine was only better than placebo on one outcome (anxiety). Across the two studies, patients on quetiapine gained about three to four more pounds than patients on placebo. Patients on paroxetine *lost*, on average, less than one pound relative to patients on placebo.

Dropout due to serious events was slightly higher (but not statistically significant) on quetiapine relative to lithium, but higher on paroxetine than quetiapine. Paroxetine had a higher rate of mania during treatment (9%) than either 300 mg (2%) or 600 mg (4%) of quetiapine, though these rates were not significantly different. Sleepiness, sedation, and dry mouth were the most common side

effects on quetiapine (McElroy SL et al., *J Clin Psychiatry* 2010;71:163–174; Young AH et al., *J Clin Psychiatry* 2010;71:150–162).

**TCPR's Take:** These studies solidify quetiapine's position as the medication with the largest evidence base for bipolar depression. However, we can't resist pointing out some methodological issues. About 35% of patients on lithium did not achieve the targeted serum level of 0.6 to 1.2 mEq/L, which could have disadvantaged lithium. The side effect profiles of the medications in this study are fairly distinct, so it is possible that the raters could distinguish which patients were taking which medications, thus compromising the double-blind. Finally, rating scale differences in favor of quetiapine over lithium and paroxetine were small and generally not statistically significant. Nonetheless, quetiapine clearly appears effective in bipolar depression, with its main disadvantage being its side effects of sedation and weight gain.

PSYCHOSIS

**Accurate Prediction of Psychosis? Maybe**

The early detection of schizophrenia is a hot topic in psychiatry. If we could detect schizophrenia during the "prodromal" phase, before overtly psychotic symptoms became problematic, perhaps early intervention could prevent or delay the onset of full-blown schizophrenia. But most efforts to date have been disappointing, with high rates of false positives, people who were predicted to develop a psychotic disorder but did not actually become psychotic. For example, in one recent study only 35% of people predicted to develop psychosis actually became psychotic over a 2.5 year follow-up (Canon TD et al., *Arch Gen Psychiatry* 2008;65:28–37).

But a freshly published study may provide cause for optimism. Researchers included 245 participants, who were

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## CME Post-Test

To earn CME or CE credit, you must read the articles and log on to [www.TheCarlatReport.com](http://www.TheCarlatReport.com) to take the post-test. Please see the study guide listed below to prepare for this month's post-test. Learning objectives are noted on page 1. You must answer at least four questions correctly to earn credit. You will be given two attempts to pass the test. Tests must be taken by April 30, 2011.

As a subscriber to *TCPR*, you already have a username and password to log on [www.TheCarlatReport.com](http://www.TheCarlatReport.com). To obtain your username and password, please email [CME@thecarlatreport.com](mailto:CME@thecarlatreport.com) or call 978-499-0583.

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*Below are the questions for this month's CME post-test. This page is intended as a study guide. Please complete the test online at [www.TheCarlatReport.com](http://www.TheCarlatReport.com). Note: Learning objectives are listed on page 1.*

1. Which type of drug test detects usage in the most distant past (L.O. #2)?
  - a. Urine
  - b. Saliva
  - c. Hair
  - d. Blood
  
2. When Suboxone is taken improperly (crushed up and injected rather than dissolved under the tongue), users can get high in the same way they can when injecting methadone (L.O. #1).
  - a. True
  - b. False
  
3. A typical final target dose of Suboxone is in the range of (L.O. #1):
  - a. 2 to 4 mg QD
  - b. 4 to 8 mg QD
  - c. 8 to 12 mg QD
  - d. 12 to 16 mg QD
  
4. Motivational interviewing is a way of talking to people that calls forth their own motivations for change.
  - a. True
  - b. False
  
5. In the Blanco study, the response rate among participants who received both CBGT and MAOI was which of the following (L.O. #4)?
  - a. 78.1%
  - b. 52.9%
  - c. 48.6%
  - d. 33.3%

**PLEASE NOTE: WE CAN AWARD CME CREDIT ONLY TO PAID SUBSCRIBERS**

|                |           |                            |
|----------------|-----------|----------------------------|
| First Name     | Last Name | Degree (MD, PhD, NP, etc.) |
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E-mail (REQUIRED FOR CME CERTIFICATES)

**Your evaluation of this CME/CE activity (i.e., this issue) will help guide future planning. Please respond to the following questions:**

1. Did the content of this activity meet the stated learning objectives? L.O.#1:  Yes  No L.O.#2:  Yes  No L.O.#3:  Yes  No L.O.#4:  Yes  No
  2. On a scale of 1 to 5, with 5 being the highest, how do you rank the overall quality of this educational activity?  5  4  3  2  1
  3. As a result of meeting the learning objectives of this educational activity, will you be changing your practice performance in a manner that improves your patient care? Please explain.  Yes  No
- 
4. Did you perceive any evidence of bias for or against any commercial products? Please explain.  Yes  No
- 
5. How long did it take you to complete this CME/CE activity? \_\_\_ hour(s) \_\_\_ minutes
6. **Important for our planning:** Please state one or two topics that you would like to see addressed in future issues.
-



# Research Updates IN PSYCHIATRY

Continued from Page 6

referred by various mental health providers or self-referred due to concerns regarding warning signs of psychosis, such as declining functioning, poor concentration, and suspiciousness. Participants were assessed with two types of ratings used in prior research: 1. ultra-high-risk criteria (UHR) and 2. cognitive disturbances (COGDIS). Follow-up occurred at nine and 18 months.

Of participants who scored positive on both UHR and COGDIS, only 24% developed psychosis at follow-up, providing an atrocious false positive rate of 76%. However, using a complex statistical model that combined features of both UHR and COGDIS, 83% of those predicted to become psychotic did so, and 87% of those predicted not to become psychotic were not psychotic at follow-up. The predictive model included positive symptoms, bizarre thinking, sleep disturbances, schizotypal disorder, functioning in the past year, and years of education (Ruhrmann S et al., *Arch Gen Psychiatry* 2010;67:241-251).

**TCPR's Take:** This seems like a major improvement in accuracy, but there is one major caveat: The predictive model was generated retrospectively to best fit the data; it was not generated before the study began. To produce reliably credible results, the same predictive model would need to be used on a different set of participants and generate similarly strong predictive accuracy. For more discussion of early detection of psychosis, please see the December 2009 *TCPR*.

May 2010

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*This Month's Focus:*  
Substance Abuse

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