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Psychiatry Practice Boosters

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EDITED BY JESSE KOSKEY, MD, MPH
ASSOCIATE EDITOR: ZACHARY DAVIS

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Psychiatry Practice Boosters, Fourth Edition

Edited by Jesse Koskey, MD, MPH
Associate Editor: Zachary Davis

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Acknowledgments

It was a privilege to edit this edition of *Practice Boosters*. And it was a task to consider which of the hundreds of research updates from the past three years of Carlat and its permutations (addictions, child, geriatric, and hospital) were the most interesting, practice-changing, and relevant. The final selections run the gamut from the FDA's newest psychiatric medication approvals to some disappointing (but informative) negative trials, crossing an array of subspecialties and practice settings. I hope that breadth, and the down-to-earth, concise overviews, combine to make for high-yield reading.

I am grateful to our fantastic team at Carlat Publishing, especially the invaluable assistance of Zachary Davis. This project also could not have happened without support from my wife Kee.

The original research updates adapted for this publication were authored by:

Chris Aiken, MD
Deepti Anbarasan, MD
Rehan Aziz, MD
Sonya Bakshi, MD
Paul Barkopoulos, MD
James Black, MD
Peter J. Farago, MD
Kamron Fariba, MD
Joshua Feder, MD
Kristen Gardner, PharmD
Heather Goff, MD
Christina Guest, MD
Victoria Hendrick, MD
Edmund Higgins, MD
James Jenkins, MD
Thomas Jordan, MD
Gregory Lande, MD
Anne Li, MD
Jesus Ligot, MD
Pavan Madan, MD
C. Jason Mallo, DO
Brian Miller, MD, PhD, MPH
Richard Moldawski, MD
David Moltz, MD
Randall Moore, MD
Susie Morris, MD
Benjamin Oldfield, MD
John O'Neal, MD
Michael Posternak, MD
John C. Raiss, MD
Sean Ransom, PhD
Nicholas Rosenlicht, MD
Talya Shahal, MD
Susan Siegfreid, MD
Batya Swift Yasgur, MA, LSW
Lara Tang, MD
Amy Ton, MD
Sanya Virani, MD
Dax Volle, MD
Mikveh Warshaw, NP

Introduction

Do you sometimes wish you were a pathologist? Or an oncologist? Imagine *seeing* what ails your patients on a cellular level—visualizing the pathophysiology of depression or psychosis. Or knowing *exactly* how a drug targets and ameliorates the processes that cause symptoms. Or being sure of which side effects patients will experience and how long treatment will take.

Clinical psychiatry can seem pretty primitive at times. That may be part of the appeal. Every patient and treatment course is unique because there is so much variety in the genes, environments, and brains of our patients. This requires us to consider both the stories our patients tell *and* the best evidence we have for a particular diagnosis. Sometimes this means relying on the knowledge base we've been using for years. Sometimes this means expanding that knowledge base, or rejecting it.

That's hard to do when you're working full time with patients, or teaching, or researching—not to mention "just" balancing work and life.

That's where we hope this book can be most helpful. *The Carlat Psychiatry Report* and the *Addiction Treatment, Child Psychiatry, Geriatric Psychiatry,* and *Hospital Psychiatry* reports are pithy, clinically focused psychiatric news digests. Research updates (RUs) are a staple of each issue: careful examinations of new studies with real-world implications. For this book, we collected the most relevant, impactful, and significant RUs from all five Carlat reports over the last few years. We weighed them from a clinical perspective and, when possible, updated them with the most recent data. We feel this collection is the best of the best of Carlat—a boiled-down extract of essential evidence to keep you up to date, engaged, and enjoying your practice as a psychiatrist, psychologist, psychiatric NP, PA, or other mental health professional.

For each RU, we give you a summary of the background, methods, findings, and significance. We address any quality-related or methodological limitations. And we end with the "Carlat take" and "Practice implications," giving you a quick takeaway of both the study and its relevance to practice.

For this edition of *Practice Boosters*, we've also revised our primer on scientific research to include more study designs while doing our best to stay as concise as possible.

We hope that you'll agree with our analyses and recommendations, whether or not they change your practice. That will always come down to your clinical judgment regarding the patient in front of you. But generally speaking, we suggest that if a clinical trial is very large and shows a marked advantage of a new treatment over placebo (or another first-line treatment), it should probably find its way into your toolbox. If a study is small, we recommend it if there aren't significant risks or many other options. If the study has practice-changing potential, but is small or otherwise problematic, we want you to know

A Novel Treatment for Methamphetamine Use Disorder

REVIEW OF: **Trivedi MH, Walker R, Ling W, et al. Bupropion and naltrexone in methamphetamine use disorder. *N Engl J Med.* 2021;384(2):140–153.**

STUDY TYPE: **Randomized, double-blind, placebo-controlled trial with sequential parallel comparison design**

Methamphetamine use disorder is increasingly a cause of overdose deaths in the U.S. Pharmacologic options to treat methamphetamine use disorder are scarce, but pilot studies suggest that bupropion and naltrexone may be effective, either alone or in combination, and this study tested them in combination.

The authors designed this double-blind, randomized, placebo-controlled study in two phases. First, patients were randomized to treatment or placebo for six weeks, with three times as many assigned to placebo. In the second stage, patients who responded to placebo were removed, and the remaining placebo subjects were re-randomized to either more placebo or active treatment for another six weeks, this time with equal numbers in the placebo and treatment arms. The point of this design was to dampen the placebo response in the second phase of the study.

The subjects were adults with moderate to severe methamphetamine use disorder who wanted to quit or reduce use, recruited through advertisements and direct referrals. On average, they had used methamphetamine on 27 of the previous 30 days. The active combo treatment was extended-release (ER) naltrexone 380 mg intramuscular every three weeks (a relatively high dose) and ER bupropion 450 mg daily.

There were 403 participants in stage one, and 225 who did not respond to placebo were re-randomized to stage two. Overall retention was good (77.4%). The primary outcome was response, defined as one out of four urine tests negative for methamphetamine in the last two weeks of stage one or stage two.

RESULTS:

Naltrexone-bupropion was significantly more effective than placebo. The weighted average response was 13.6% for the active group and 2.5% for placebo ($p<0.001$), and the number needed to treat (NNT) was 9. Adverse events, such as nausea, vomiting, and constipation, were evenly divided between active and placebo conditions.

Stigmatizing Smoking: An Effective Deterrent?

REVIEW OF: **Cortland CI, Shapiro JR, Guzman IY, Ray LA. The ironic effects of stigmatizing smoking: Combining stereotype threat theory with behavioral pharmacology. *Addiction*. 2019;114(10):1842–1848.**

STUDY TYPE: **Randomized controlled trial**

Tobacco use is the single most preventable cause of death, disease, and disability in the United States. The American government spends $50 million each year on tobacco cessation efforts, including many public service campaigns that attempt to shame or stigmatize smoking as an undesirable behavior. This study investigates how the social stereotype threat—creating concern that one will be judged unfavorably by others—may impact one's ability to resist the next cigarette.

In this randomized controlled trial, 77 non-treatment-seeking, otherwise-healthy adult smokers were recruited from the community and randomized to either receive a stereotype threat or a control message after 12 hours of abstinence. Specifically, the stereotype threat group was told that the investigators were interested in "whether non-smokers are superior across all positive traits or only certain types [such as] willpower, laziness, weakness and responsibility," bringing to participants' minds the negative stereotypes of people who smoke. Both the intervention group and the control group were given a lighter, an ashtray, some of their favorite cigarettes, and a small monetary reward for delaying smoking during hour-long observation periods.

RESULTS:

The investigators found no significant difference in time-to-smoke data between groups. However, when they controlled for baseline latency-to-smoke, they found that the stereotype threat was associated with lesser latency-to-smoke (hazard ratio 0.50; 95% CI [0.30, 0.85]). The researchers concluded that the stereotype threat actually functioned as a "smoking-promoting message."

Major limitations of the study included generalizability to the real world, including observing the participants for one hour and the simplicity of the stereotype threat, which may not replicate the complex nature of stereotypes in specific communities and in society. Another major limitation was that the control group did not receive a non-stigmatizing, smoking-related cue.

CARLAT TAKE:

While it doesn't readily approximate the complex nature of stereotypes or stigma, this study

New Canadian Guidelines for Eating Disorders in Children

REVIEW OF: **Couturier J, Isserlin L, Norris M, et al. Canadian practice guidelines for the treatment of children and adolescents with eating disorders. *J Eat Disord*. 2020;8:4.**

STUDY TYPE: **Systematic review**

In 2020, a 24-member team of Canadian psychiatrists, parents, and patient representatives published new practice guidelines for eating disorders. Their systematic review screened thousands of abstracts to find several dozen articles, prioritizing randomized controlled trials. They assessed psychotherapies, including family-based therapy, cognitive behavioral therapy (CBT), and dialectical behavior therapy; medications (primarily atypical antipsychotics and SSRIs); and treatment sites.

Of the studies reviewed, many suffered from significant potential bias, and many showed no significant effect of treatment. There were some interesting positive studies; one compared CBT with psychodynamic therapy for 81 girls with anorexia nervosa. The two treatments were comparable, each yielding remission rates of about 33% after an average of 37 weeks of treatment.

RESULTS:

After synthesizing the studies, the researchers arrived at two main recommendations. First, family-based treatment is clearly effective for both anorexia nervosa and bulimia nervosa. Second, less restrictive treatment environments (eg, family-based or day treatments) are more effective than lengthy hospitalizations. The following five modalities were also recommended, but with less confidence: multifamily therapy, CBT, adolescent-focused psychotherapy, yoga, and olanzapine or aripiprazole with anorexia nervosa "if monitored carefully."

CARLAT TAKE:

Eating disorders in children and adolescents are not easily treated pharmacologically, which makes them harder to study and complicates the establishment of definite treatment algorithms even after a concerted approach by a multidisciplinary team. However, less-restrictive treatments, and family-based treatments, are preferable.

PRACTICE IMPLICATIONS:

This exhaustive review favors evidence-based psychotherapies, particularly family-based treatments, in the least restrictive environments for children and adolescents suffering from eating

Anticholinergic-Associated Cognitive Impairment in Schizophrenia

REVIEW OF: Joshi YB, Thomas ML, Braff DL, et al. Anticholinergic medication burden-associated cognitive impairment in schizophrenia. *Am J Psychiatry*. 2021;178(9):838–847.

STUDY TYPE: Cross-sectional study

Schizophrenia is associated with impaired cognition. Medications with anticholinergic properties can worsen this problem, including antipsychotics, benztropine, and antidepressants, and may confer an increased risk of dementia. What we don't know is the size of this impact on cognition, which this study investigated.

Researchers examined the magnitude and types of medications with anticholinergic properties. They assessed both global cognition and cognitive subdomains in 1,120 adult outpatients under age 65 with schizophrenia or schizoaffective disorder and enrolled in the larger Consortium on the Genetics of Schizophrenia-2 study. Most were young (mean 24 years); 69% of subjects were male, 43% were White, and 40% were Black. Researchers assessed psychopathology, anticholinergic burden (using the Anticholinergic Cognitive Burden [ACB] scale), and cognition (using the Penn Computerized Neurocognitive Battery). The ACB is a validated expert rating scale that assigns dose-independent, categorical ratings to medications based on anticholinergic properties (1=low/minimal, 2=moderate, and 3=strong/definite).

Most of the total anticholinergic burden was attributable to antipsychotics, followed by "traditional" anticholinergics (eg, benztropine, diphenhydramine, hydroxyzine, and trihexyphenidyl), antidepressants, mood stabilizers, and benzodiazepines (see also "Anticholinergic Properties of Selected Psychotropics" table). Most patients (90%) were taking a second-generation antipsychotic, 18% were taking two antipsychotics, and 20% were taking benztropine or a similar medication.

RESULTS:

Greater anticholinergic burden was associated with significantly worse cognition scores after controlling for potential confounding factors, including dose and number of antipsychotics, psychotic symptom severity, illness duration, number of hospitalizations, and smoking. The global cognition of patients with high or very high anticholinergic burden was approximately 0.5 standard deviations below patients with no anticholinergic burden—meaning a moderate difference.

Limitations of this study included the cross-sectional design, which precludes causal inferences, and the exclusion of patients with significant medical conditions (leading to a likely underestimation of the

CARLAT TAKE:

Anticholinergic medications may impair cognition in schizophrenia.

PRACTICE IMPLICATIONS:

Consider antipsychotics with a lower anticholinergic burden, particularly for patients who are elderly, have cognitive problems, or are taking other anticholinergic medications.

TABLE: Anticholinergic Properties of Selected Psychotropics

Class	ACB Score		
	Strong/Definite	Moderate	Low/Minimal
Second-generation antipsychotics	Clozapine Olanzapine Quetiapine		Aripiprazole Asenapine Iloperidone Lurasidone Paliperidone Risperidone Ziprasidone
First-generation antipsychotics	Chlorpromazine Fluphenazine Perphenazine Thioridazine Trifluoperazine	Loxapine Prochlorperazine Thiothixene	Haloperidol
Mood stabilizers		Carbamazepine Oxcarbazepine	Valproic acid
Antidepressants	Amitriptyline Clomipramine Doxepin Nortriptyline Paroxetine		Bupropion Citalopram Duloxetine Escitalopram Fluoxetine Fluvoxamine Mirtazapine Nefazodone Sertraline Trazodone Venlafaxine

Quetiapine in Bipolar With OCD

REVIEW OF: Sahraian A, Ghahremanpouri B, Mowla A. Is quetiapine effective for obsessive and compulsive symptoms in patients with bipolar disorder? A randomized, double-blind, placebo-controlled clinical trial. *CNS Spectr*. 2022;27(5):634–638.

STUDY TYPE: Randomized controlled trial

SSRIs are first-line medications for OCD, but they may pose risks of mania and rapid cycling when patients also have bipolar disorder. These two conditions overlap more often than we'd expect by chance, but only one controlled trial has looked at how to treat OCD in bipolar disorder (it was positive and involved topiramate). This eight-week study tested quetiapine for obsessive-compulsive symptoms in patients with stable bipolar disorder.

The patients were adults with bipolar I disorder who were not in an active mood episode but who had active symptoms of OCD. All were on lithium and clonazepam and no other psychotropics. Although the authors did not make a formal diagnosis of OCD, the participants scored in the moderate to severe range (≥17) on the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS).

A total of 47 patients entered the study after other psychiatric, substance use, and medical diseases were excluded. A total of 40 individuals completed the trial, of which half received placebo and half quetiapine. Doses were increased until the patient either became symptom-free or couldn't tolerate more. Patients completed standard clinician-rated scales for OCD (Y-BOCS, the primary outcome), mania (Young Mania Rating Scale [YMRS]), and depression (Hamilton Depression Rating Scale [HAMD]) at weeks zero, four, and eight.

RESULTS:

On average, Y-BOCS scores fell by 9.1 in the quetiapine group and 0.3 in the placebo group. Half of the quetiapine group had a significant response (>34% decrease in Y-BOCS), compared with 5% of the placebo group. The average dose of quetiapine was 325 mg, although the dose range wasn't reported. All patients remained euthymic during the eight-week trial, based on YMRS and HAMD scores.

Of the 47 participants who entered the study, seven dropped out, none for reasons associated with quetiapine. Those who took quetiapine were 2.3 times more likely to report side effects, particularly drowsiness, increased appetite, constipation, and orthostasis.

CARLAT TAKE:

Quetiapine is difficult to tolerate, but it may be worth trying when OCD is causing significant impairment in patients with bipolar disorder. It made a meaningful difference in this study

PSYCHIATRY PRACTICE BOOSTERS, FOURTH EDITION

Insights from research to enhance your clinical work

As a clinician, you need to keep up on the latest developments in psychiatry. But you can't possibly read every potentially relevant research study published each year. At Carlat Publishing, we try to make your life easier by sifting through the contents of the major psychiatric journals for you. The studies that meet our criteria—tackling interesting topics and yielding actionable recommendations for your practice—have made it into our new edition of *Psychiatry Practice Boosters*.

This fourth edition teaches you the key points of 63 of the most clinically relevant studies in psychiatry from the last three years. This book includes a quick course in how to understand research design and statistics—so that you can be a more informed reader of the medical literature.

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- Starting Buprenorphine: Is Timing Everything?
- Does Mirtazapine Treat Agitation in Dementia?
- Lithium Exposure In Utero: How Bad Is It Really?
- Do Structural Brain Abnormalities Predict Cognitive Impairment With Electroconvulsive Therapy?
- Antidepressants for Suicidal Ideation in Depressed Patients?
- Psilocybin: The New Holy Grail for the Rapid Relief of Major Depression?

EDITORIAL TEAM

Psychiatry Practice Boosters, Fourth Edition is edited by Jesse Koskey, MD, MPH, and associate editor Zachary Davis, and continues in the tradition of the first edition by adapting the research updates published in the Carlat family of newsletters (*The Carlat Psychiatry Report, The Carlat Child Psychiatry Report, The Carlat Addiction Treatment Report, The Carlat Hospital Psychiatry Report*, and *The Carlat Geriatric Psychiatry Report*). This edition's research update authors include: Chris Aiken, MD; Deepti Anbarasan, MD; Rehan Aziz, MD; Sonya Bakshi, MD; Paul Barkopoulos, MD; James Black, MD; Peter J. Farago, MD; Kamron Fariba, MD; Joshua Feder, MD; Kristen Gardner, PharmD; Heather Goff, MD; Christina Guest, MD; Victoria Hendrick, MD; Edmund Higgins, MD; James Jenkins, MD; Thomas Jordan, MD; Gregory Lande, MD; Anne Li, MD; Jesus Ligot, MD; Pavan Madan, MD; C. Jason Mallo, DO; Brian Miller, MD, PhD, MPH; Richard Moldawski, MD; David Moltz, MD; Randall Moore, MD; Susie Morris, MD; Benjamin Oldfield, MD; John O'Neal, MD; Michael Posternak, MD; John C. Raiss, MD; Sean Ransom, PhD; Nicholas Rosenlicht, MD; Talya Shahal, MD; Susan Siegfreid, MD; Batya Swift Yasgur, MA, LSW; Lara Tang, MD; Amy Ton, MD; Sanya Virani, MD; Dax Volle, MD; and Mikveh Warshaw, NP.

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Contact us at:
info@thecarlatreport.com
866-348-9279

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