## Title
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## Authors
Shoptaw, Steven
Trivedi, Madhukar
Potter, Jennifer S

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# If there were an effective pharmacotherapy for cocaine use disorder, what would it do?

**Steven Shoptaw, PhD**,
Department of Family Medicine, University of California, Los Angeles, Los Angeles, CA USA

**Madhukar Trivedi, MD**,
Department of Psychiatry, University of Texas Southwestern, Dallas, TX, USA

**Jennifer S. Potter, PhD**
Department of Psychiatry, University of Texas Health Science Center, San Antonio, TX, USA

## Abstract

While thirty years of research into an effective cocaine pharmacotherapy has yielded no treatments, knowledge gained doing this work underscores the importance of rigorous clinical design, of attention to medication adherence and of defining endpoints. The field needs a high-risk/high-reward strategy to engineer new compounds that help people to use less cocaine and to preserve gains made during treatment, particularly during lapse/relapse.

### Keywords

cocaine; pharmacotherapy; research

In their outstanding comprehensive review, “Pharmacotherapeutic strategies for treating cocaine use disorder – what do we have to offer?,” (1) Brandt and colleagues organize 30 years of clinical trials to develop a medication treatment for cocaine use disorder. The piece is almost a chapter – not quite a systematic review and yet more than a thought piece. Most valued in this piece is the “been there, done that” wisdom that shines throughout. I will teach from this paper as it is the fairest, most comprehensive discussion of pharmacotherapy development for cocaine use disorder to date. Yet, their main question, “…what do we have to offer?” is left largely unanswered.

Their question is critical for the field -- especially as we develop new scientists considering a career in cocaine pharmacotherapy research. We have rigorous clinical trial designs and statistical methods, recognize the importance of medication adherence and selection of primary endpoints, but we remain in the starting blocks when it comes to identifying candidate medications for trials despite years of work and investment. Periodic reports from funders optimistically describe current and potential candidates for cocaine use disorder (2–6). An ambitious evidence-based approach, NIDA’s Cocaine Rapid Evaluation Screening

Corresponding Author: Steve Shoptaw PhD – sshoptaw@mednet.ucla.edu.
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Trials, fielded seven randomized controlled trials of 18 medications using parallel design, multiple arms, a common placebo condition and identical outcomes to develop data to guide selection of candidates for full-scale testing (7). Three candidates emerged; none produced an effective medication.

While reviews and pilot studies for identifying medications have yielded disappointing results, there is little in the way of innovation to address this problem. Despite staggering morbidity and mortality, people with cocaine use disorder have no political or economic power to motivate big pharma investments in medication development similar to conditions such as cancer, Alzheimer's, and diabetes. No fleet of medicinal chemists, stands at the ready to feed new compounds rationally derived to treat key aspects of cocaine use disorder, such as reversing overdose, initiating abstinence, preventing lapse or relapse. This failure to lobby the full weight of the drug development infrastructure within our disposal should serve as a call to action to us all.

Nascent efforts in the field carry potential for success. One notable example involves medication development for cocaine overdose, a monoclonal antibody that sequesters cocaine in circulating blood (8). An effective overdose medication would have significant health impact, an effect that perhaps could be boosted when co-administered with an opioid reversal agent in emergency settings and overdose of opioids and cocaine.

Still, the next fleet of addiction scientists should (and do) demand new cocaine medications be developed that have clear, rational purpose and that people will use. For example, development of an engineered small molecule that could sequester cocaine in blood – is similar to the antibody approach, but better. Such a medication would work well in emergency settings, but would also carry potential for long-acting formulation. A long-acting agent would extend cocaine reversal into the daily lives of patients to mitigate periods of lapse or relapse. Patients would no longer have to start at "day one" in their treatments following lapse/relapse to cocaine. The approach would allow patients to resume treatment following lapse, preserving gains in psychological, employment and social functioning. This treatment strategy would be a game-changer, would transform the behavioral support, and would finally provide a treatment option that patients could choose based on a more positive treatment experience.

Without this type of prospective, energetic approach, we are left with repurposing existing medications. Thirty years of outcomes using this strategy suggest only modest success. Brandt et al, (1) highlights the call for a high-risk/high-reward strategy to engineer new compounds. To this end, we require mechanisms and partnerships for addiction scientists and medicinal chemists to meet and to consider building new molecules to help people not only to use less cocaine, but also to use treatment to build their lives with function – socially, psychologically, and productively.

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## REFERENCES


1. Brandt L, Chao T, Comer SD, Levin FR. Pharmacotherapeutic strategies for treating cocaine use disorder-what do we have to offer? Addiction. 2020.
2. Johnson DN, Vocci FJ. Medications development at the National Institute on Drug Abuse: focus on cocaine. NIDA research monograph. 1993;135:57–70. [PubMed: 8289904]
3. Vocci FJ, Acri J, Elkashef A. Medication development for addictive disorders: the state of the science. The American journal of psychiatry. 2005;162(8):1432–40. [PubMed: 16055764]
4. Montoya ID, Vocci F. Novel medications to treat addictive disorders. Current psychiatry reports. 2008;10(5):392–8. [PubMed: 18803912]
5. Vocci FJ, Elkashef A. Pharmacotherapy and other treatments for cocaine abuse and dependence. Current opinion in psychiatry. 2005;18(3):265–70. [PubMed: 16639150]
6. Skolnick P, White D, Acri JB Synopsis of Expert Opinions and Conclusions. CNS & Neurological Disorders - Drug Targets. 2015;14(6):773–6. [PubMed: 26073938]
7. Kampman KM, Leiderman D, Holmes T, LoCastro J, Bloch DA, Reid MS, et al. Cocaine Rapid Efficacy Screening Trials (CREST): lessons learned. Addiction. 2005;100 Suppl 1:102–10. [PubMed: 15730354]
8. Wetzel HN, Zhang T, Norman AB. A mathematical model of a recombinant humanized anti-cocaine monoclonal antibody's effects on cocaine pharmacokinetics in mice. Life Sci. 2017;184:81–6. [PubMed: 28694087]