A feasibility study for testing the effects of extended-release naltrexone (Vivitrol) on recidivism and other participant outcomes in drug court settings

IMPORTANCE

Millions of adults with substance use disorders and often co-occurring mental health disorders enter US jails and prisons each year.[1-3] With insufficient access to treatment and a tradition of criminalizing addiction, people with substance use disorders are more likely to be incarcerated than they are to receive the treatment they need.[1-5] However, there is a growing bipartisan awareness among US policy makers and leaders of behavioral health and criminal justice systems that the long trend of over-incarceration has been counterproductive and unsustainably costly.

Drug treatment courts comprise one of the most promising approaches to diverting offenders with substance use disorders away from the justice system, offering offenders with non-violent misdemeanor or felony convictions the opportunity to engage in community treatment while under court supervision in lieu of traditional adjudication. Drug treatment courts have broadly been conceptualized as a form of "therapeutic jurisprudence"[6] because they incorporate therapeutic principles into specialized courts to improve criminal justice and clinical outcomes. Meta-analyses and systematic reviews of drug court outcome studies have generally shown that these interventions significantly reduce re-arrest and incarceration.[7-13] Reductions in recidivism average 50% among participants compared to 38% among comparison groups receiving typical criminal sentencing. Still, there is room for significant improvement in drug court outcomes: approximately 40% of drug court participants drop out of treatment prematurely and only 50% graduate from the program.[14] Predictors of poor participant outcomes include inadequate length and intensity of treatment,[15] low treatment motivation,[16] and heroin use.[16]

One necessary step toward optimizing drug court outcomes is providing participants with access to the best, evidence-based treatments available for substance use disorders. Medication-assisted treatment (MAT)—medications for treating substance dependence paired with psychosocial treatment—demonstrates strong benefits in achieving abstinence and long-term recovery. But it is also a mode of treatment that has been vastly underutilized in justice-involved populations largely based on ideological objections to a more therapeutic approach and preferences for drug-free treatment; inadequate knowledge about the benefits of MAT; concerns about misuse and diversion; and lack of qualified medical staff to prescribe medications that are frequently unfamiliar to physicians.[17, 18] Many drug treatment courts have also traditionally banned the use of MAT among their clients, despite its demonstrated evidence base, FDA approval, and strong support from national public health leaders.[19] Signaling an important shift in collective thinking about addiction, and in a specific effort to improve MAT access and implementation, the Office of National Drug Control Policy instituted a new policy in April, 2015 requiring all federally-funded drug courts to allow eligible clients to use FDA-approved medications for the treatment of substance use disorders. Furthermore, federal funding guidelines encourage drug courts to use up to 20 percent of their federal grant dollars to fund MAT for clients.

Very little is known, however, about the extent to which MAT can help optimize drug court participants' outcomes by reducing recidivism, improving health outcomes, and potentially yielding significant cost savings to the treatment and criminal justice systems. A 2010 pilot *observational* study of extended-release naltrexone (XR-NTX, Vivitrol) for alcohol-dependent clients in three Michigan and Missouri drug courts demonstrated very promising results, in which the Vivitrol group had 57% fewer missed court sessions, a 35% reduction in ratio of positive drug and alcohol tests to total tests, and substantial reduction in new arrests (8% with new arrests in Vivitrol group vs. 26% in standard care group).[20]

Vivitrol, one of the newest medications for treating both opioid and alcohol dependence, has strong promise for use by justice-involved adults with substance use disorders. The once-monthly injection formulation (as compared to the daily tablet form) can dramatically improve treatment adherence;[21] reduce cravings and block euphoric effects of opioids, allowing the individual to focus on other fundamental aspects of their recovery; and because Vivitrol has no narcotic properties, there are no concerns about misuse or diversion of this medication. Also, unlike methadone and buprenorphine (two other types of MAT), Vivitrol requires no special prescriber licensure, which can otherwise create a barrier to access in localities with few qualified providers. A 2016 multi-site randomized controlled trial (RCT) of Vivitrol for criminal offenders demonstrated very promising results in a broader population of justice-involved adults, with the

Vivitrol arm having significantly lower likelihood of, and time to relapse as compared to the control group.[22] The study did not detect lower rates of incarceration, though those recidivism data were collected by participant self-report only and so were potentially unreliable. The new Vivitrol RCT studied a general population of offenders living in the community, who were currently or recently under community correctional supervision (e.g., probation or parole) or had been released from jail in the past 12 months. While this is a highly relevant study population, its participants were not necessarily engaged in community treatment, nor were they under any type of court leverage to do so; the important differences in context preclude generalizing the findings to the drug court setting.

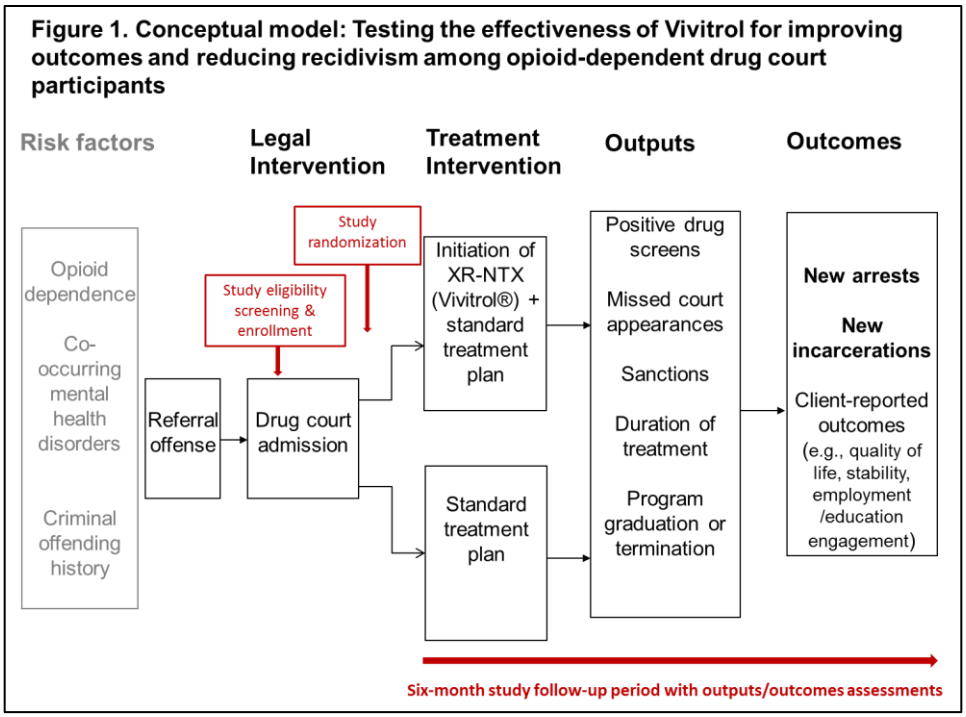
Vivitrol has especially strong prospects for people who are under legal leverage and court-mandated treatment. Most will have detoxified, which is necessary for starting Vivitrol treatment and otherwise *very* unlikely among actively-using opioid-dependent individuals in the community; and this highly effective treatment comes at a time when more typical reluctance to fully engage in treatment is often outweighed by the individual's desire to succeed in drug court and stay out of jail. The drug court setting offers a unique window of opportunity for a vulnerable population that is otherwise difficult to reach and engage in treatment, connecting clients to evidence-based treatment at a time when they have the advantages of structure, supervision, and accountability, as well as the support of a multi-disciplinary team that aims to help move them into recovery and out of the CJ system.

A RCT of Vivitrol in drug courts—the criminal justice context that, by design, actively partners with the treatment system—would add rigorous evidence about the extent to which it can improve drug court outcomes by reducing relapse and recidivism, and thereby improving public safety. In preparation for a Vivitrol-drug court RCT, its feasibility must first be assessed to ensure that such a trial would be workable in this complex criminal court setting, including as it coordinates with the community treatment system. Feasibility testing will include both addressing special concerns around conducting research with this vulnerable, court-involved population, and also assessing study eligibility, interest, and retention to insure the next-stage RCT is sufficiently powered for generating conclusive results.

Building the evidence base for MAT in drug courts could have important, actionable policy implications. The drug court setting includes a criminal justice-treatment infrastructure that could support active implementation of Vivitrol given its well-defined collaboration with the treatment system and that it is connecting many clients to treatment for a first time. This feature of drug courts is distinct from other types of community corrections, which may sometimes link individuals under their supervision to treatment, but not as a primary objective. Also, most drug court clients currently have very little access to MAT despite its promise for optimizing program outcomes, especially in states that have not expanded Medicaid, where the large majority of clients are uninsured and out-of-pocket medication costs are prohibitive. Rigorous evidence demonstrating whether MAT helps reduce relapse and recidivism among drug court clients would directly inform policy decisions by both drug treatment courts and public behavioral health systems about allocating resources to fund MAT for their uninsured clients. Finally, building the conclusive evidence base for the effects of Vivitrol on recidivism and other important outcomes for drug court clients would inform drug courts' policy-making around MAT, in particular among courts that use local funds only and continue to have MAT bans in place.

STUDY DESIGN

In preparation for a large-scale RCT of Vivitrol effectiveness in drug courts, our team proposes a feasibility study in the Wake County, North Carolina drug court, where an estimated 50% of clients are opioid dependent.[22] The two primary aims of the feasibility study will be to (1) pilot-test the delivery of Vivitrol treatment for 10-20 interested and eligible clients of the Wake County drug court; and (2) in parallel with the pilot administration of Vivitrol, study a range of feasibility issues for scaling this research to a RCT that would examine court processes, treatment delivery, and relevant clinical and justice outcomes, in a study design that provides more definitive results and also addresses IRB-related concerns in working with this particularly vulnerable, court-involved population.



Aim 1. Pilot Vivitrol study. The pilot delivery of Vivitrol in the Wake County drug court will be carried out with 20-40 eligible drug court clients who would be willing and eligible to take Vivitrol as part of their existing drug court treatment plan, and willing to be selected to approximately 10-20 Vivitrol slots by a lottery process. Eligibility criteria will include being aged 18 or older, opioid dependent but detoxified, having no medical contraindications for Vivitrol, not pregnant or breastfeeding, and graduation from drug court not expected within the upcoming 6 months, to allow at least 6 months to follow study participants. **Figure 1** depicts the conceptual pathway through drug court treatment – with and without Vivitrol – and the related intermediate and ultimate outcomes of interest, as well as the structure of the proposed study around that pathway through treatment for participating court clients. Study participant court outputs and outcomes will be measured at varying intervals throughout a 12-month follow-up period (**Table 1**). Referral conviction type will be recorded, and new arrests (by type) and new incarcerations will be the primary outcomes of interest. New incarcerations are recorded and categorized by Fellowship Health Resources, the treatment provider for the drug court, as serious (e.g., new criminal offenses) and non-serious (e.g., technical violations of probation like curfew).

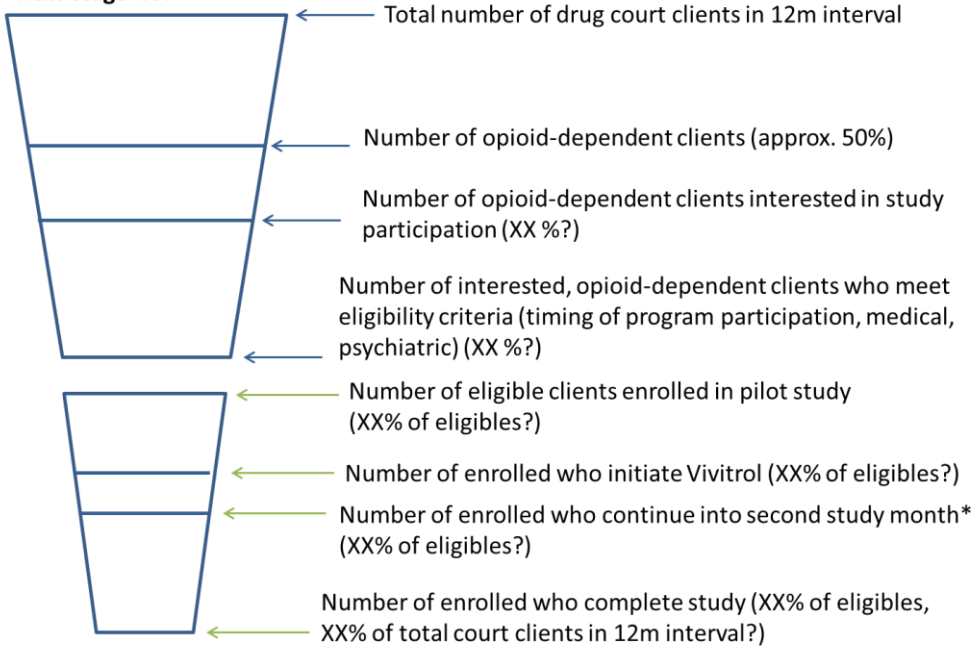
Table 1. Pilot Vivitrol study	**Schedule of assessments**				
Study measures	**BL**	**3m**	**6m**	**9m**	**12m**
Client characteristics[a]	x				
# of missed court appointments	x				x
# of positive drug screens	x				x
# of sanctions imposed	x				x
# of new arrests (e.g., violent, non-violent, drug, felony, misdemeanor)	x				x
# of new incarcerations	x				x
Duration of treatment		x	x	x	x
Client-reported outcomes[b]	x		x		

[a] E.g., Substance use disorder diagnosis, mental health diagnoses, demographics, CJ history

[b] E.g., Level of functioning, stability, quality of life, employment/ education engagement

Aim 2. Assess RCT feasibility. The study team will work with community and court partners to assess a range of feasibility issues for scaling this to a multi-site RCT of Vivitrol effectiveness in drug courts. Without pilot data it would be difficult to mount such an effectiveness trial because of the number of unknown parameters in this unique setting. Key areas for generating pilot data include: 1) assessing the impact of any potential protocol modifications that might be required by the human subjects approval process; 2) assessing the flow of eligible patients in one or more courts to inform operationalizing a protocol with inclusion/exclusion criteria; 3) assessing the variability in number of eligible clients across drug courts; 4) estimating dropouts and post-randomization exclusions in this population; 5) selecting specific criminal justice and clinical outcome measures sensitive to change; and 6) estimating effect sizes for the primary and secondary outcomes of interest (criminal justice recidivism and clinical remission) in this specific population. **Figure 2** illustrates the various filters unique to the drug court setting that must be estimated to sufficiently power a large-scale RCT. Sufficient data do not currently exist to make stable estimates of statistical power and required sample size, the number of study sites needed, and the modification of human subjects protocols required to study such a vulnerable population. For these reasons, we propose a pilot study to assess these factors in preparation for a more definitive trial.

Figure 2. Vivitrol-Drug Court Feasibility Model: Estimating number needed to enroll for next-stage RCT



* Attrition in Vivitrol arm could be above average at the outset of Study Month 2, when participants are scheduled for a second injection.

Step 1 of the feasibility assessment will involve monitoring and characterizing the flow of all drug court clients through the program, gauging the extent of their substance use, interest and clinical appropriateness for Vivitrol, and insurance status (if uninsured, Vivitrol is effectively inaccessible due to prohibitively high out-of-pocket cost). These assessments will be made by *reviewing de-identified court and treatment records* over the past 24 months for all drug court clients (N=200; approximately 90 clients in program at any given time), and a set of *brief client interviews* about treatment experience, including interest and experience with Vivitrol or other types of MAT. It will be important to estimate study participant attrition for the RCT due to program drop-outs, re-incarcerations, or other factors throughout the steps of these selection processes.

Step 2 of the feasibility assessment will involve identifying training, supervision, and monitoring needs for the RCT, in part by tracking the range of tasks performed and coordinated in the pilot-study participants' utilization of Vivitrol, and assessing the extent to which it adheres to the evidence-based model for Vivitrol provision. Fellowship Health Resources already provides Vivitrol for some of its agency clients, and so training for them will be minimal at most. For judges and other court-involved actors, education about MAT and Vivitrol, in particular, will be important. Step 2 assessments will be made via *court observation* and *qualitative interviews with court-involved actors* (judges, court administrator, probation officers, county prosecutors, public defenders, treatment providers).

Step 3 will involve developing the full-scale RCT protocol with community partners, including identifying appropriate inclusion/exclusion criteria, personnel needs for data collection and record reviews, and reaching agreement on appropriate court and treatment access by study personnel. Fellowship staff and the study team will collaborate on joint development of the RCT protocol. We will also build consensus on clinical and functional measures and labs for the RCT, and the data collection schedule. *Qualitative interviews* and *group meetings with the study team and community partners* will be primary modes of assessment and planning for the development of the RCT protocol.

Step 4 will involve developing the IRB protocol for a full-scale RCT. We will identify and address special concerns in conducting research with this vulnerable, court-involved population, including ensuring there are no elements of coercion (real or perceived) for drug court clients introduced by participating in the feasibility study or future RCT while under court-mandated treatment, recognizing that the drug court itself, while voluntary, in its own right can be perceived as coercive. Potential barriers will be identified and addressed via *group meetings and interviews with study team and community partners*. We will also discuss *a set of case vignettes* with our community partners to explore potential scenarios that could pose a challenge to randomization in this context and a potential threat to the validity of a full-scale RCT. It will be critical to evaluate with all stakeholders the promise and feasibility of the next-stage RCT, drawing from successful precedents of other types of RCTs conducted in drug court settings and new MAT RCTs in other justice-involved populations.[13,14,22,24] We will aim to minimize general concerns that arise in randomizing an evidence-

based practice, especially to justice-involved individuals. Duke School of Medicine IRB, Wake County review board, and Fellowship Health Resources review board will be consulted for review and oversight of research on human subjects.

Step 5 will include developing research partnerships with other North Carolina drug courts that support the use of MAT, with an objective of engaging 3-5 courts as RCT study sites. Potential court partners for the RCT that have been identified by Wake County drug court administrator Nicole Singletary include Brunswick County (which recently received a large federal grant to implement MAT), Guilford, Mecklenburg, and Orange Counties. As part of building potential site partnerships and assessing court-specific client flow and eligibility for the RCT, we will conduct court observations at each of the courts noted above to understand the extent to which variations in local opioid addiction, and related programming resources and referrals will influence client eligibility for the RCT. Requested study budget: $339,516; study duration 2.5 years (30 months). (Please see accompanying budget and justification for details.)

STUDY TEAM

Our study team includes a multi-disciplinary group of research and clinical experts to carry out the feasibility study and the next-stage RCT. Our team's expertise includes MAT services, policy, and clinical research, over 20 years of research on court-mandated treatment, MAT provision and clinical services, and extensive experience conducting RCTs. **Allison Robertson, PhD, MPH** (Principal Investigator) is Assistant Professor of Psychiatry and Behavioral Sciences at Duke University. Dr. Robertson conducts mental health and substance abuse services research, with a focus on policies, programs, and services that address criminal justice involvement in this population. She currently has a NIMH-funded career development award (NIMH K0100544) to study the effectiveness and implementation barriers of MAT among justice-involved adults with co-occurring mental health and substance use disorders, and a NIDA-funded study (R03-DA033435) of court-based jail diversion programs. She was also PI on a study funded by the Robert Wood Johnson Foundation of court-based jail diversion, in that case examining the effects of short jail stays before being diverted to community treatment on program participants' outcomes. **Marvin Swartz, MD**, is a Duke psychiatrist, Professor and Head of the Psychiatry Department's Social and Community Psychiatry division, renowned mental health services researcher, and Co-PI of the NIMH-landmark Clinical Antipsychotic Trials of Intervention Effectiveness study. **Jeffrey Swanson, PhD**, is Professor of Psychiatry at Duke, and renowned expert in mental health law research. He and Dr. Swartz have led multiple studies of court-ordered treatment for adults with severe mental illness, including a large-scale RCT in North Carolina. Drs. Swartz and Swanson were members of the decade-long MacArthur Foundation Research Network on Mandated Community Treatment that studied the use of such mandates. Drs. Swartz, Swanson, and Robertson collaborated on a New York State- and MacArthur Foundation-funded longitudinal, statewide evaluation of its court-ordered outpatient commitment program, examining program outcomes over eight years. Those study results were widely publicized and have had a direct influence on NY State policymaking on court-mandated treatment. Drs. Swartz, Swanson, and Robertson also conducted a study of the costs of criminal justice involvement among the full adult population of public behavioral health clients in Connecticut, in which they monetized a broad range of treatment service utilization and criminal justice involvement. Drs. Swartz's and Swanson's extensive expertise in conducting RCTs and rich experience studying individuals who are mandated to treatment in a court setting will be a major contribution.

Paolo Mannelli, MD, Associate Medical Director of Duke Addictions Program and Substance Abuse Consult Liaison Program, is an addiction psychiatrist with clinical and research expertise in MAT, including Vivitrol, and extensive experience conducting RCTs. Dr. Mannelli has conducted multiple clinical trials of MAT, including a new study of combined use of buprenorphine and Vivitrol. Dr. Mannelli will monitor clinical aspects of the study, including for participants taking Vivitrol. **Paul Nagy, MS, LPC, LCAS, CCAS** is Assistant Professor in Psychiatry, Training and Consultation Director of Duke Addictions Program, a community substance abuse treatment practitioner and consultant, and an expert in MAT policy and provision. Mr. Nagy will oversee the study team's work with Fellowship Health Resources in its provision of substance abuse treatment services to drug court clients and advise on related protocol development for the RCT. He will also play a central role in developing study site partnerships with drug courts and treatment agencies for the next-stage RCT. **Michele Easter, PhD**, a Senior Research Associate in Duke Psychiatry will serve as project manager, coordinating ongoing study activities with community partners, tracking progress toward study completion, and assisting with data programming and analysis. Dr. Easter also collaborated on a series of analyses of mandated outpatient treatment in New York City with Duke colleagues, Drs. Swartz, Swanson, and Robertson.

Our community partners include personnel from the Wake County drug court and staff from Fellowship Health Resources, a community-based, private, not-for-profit behavioral health treatment agency that provides a range of substance abuse treatment services, including Vivitrol, and contracts with Wake County drug court to provide court clients' treatment. Fellowship partners include **Brandon Robinson, LCAS, LPC, CCS**, Director of SA and Corrections Services, and **Mary Ann Johnson**, Region Director. Wake County drug court partners include **Nicole Singletary**, Drug Court Administrator, and presiding Wake County **District Court Judges Robert Rader** and **Judge Craig Croom**.

Letters of support from our two community partner agencies are included in this application. We also include a letter of support from Alkermes, the company that manufactures Vivitrol, indicating its commitment to donating 12 months of medication for 10-20 participants in this feasibility study (with market value of approximately $240,000).

STRATEGY FOR FOLLOW-UP RCT

The next-stage RCT will include three to five county-level drug courts in North Carolina, including Wake County drug court where the feasibility study will take place. Three other drug courts in North Carolina that were recommended by our Wake County partner, Ms. Singletary, and are enthusiastic about incorporating MAT into their scope of treatment include Brunswick County, Guilford County, and Mecklenburg County. With Ms. Singletary as our liaison, we will approach each of these courts as leading prospects for partnering in the multi-site RCT. Other potential partner courts for the RCT include Robeson County, which is very enthusiastic about MAT, and Orange and Durham Counties, which currently do not allow MAT but are giving it strong consideration.

At each study site, eligible drug court participants will be randomized to either (1) Vivitrol plus the court-arranged treatment plan (e.g., individual and/or group therapy, 12-step meetings), or (2) the court-arranged treatment plan, for a 12-month course of treatment. Eligibility criteria will include: being 18 years or older, able to provide informed consent, detoxified from opioids, not pregnant or breastfeeding, and no medical contraindications for Vivitrol. Data will be collected at baseline, 3 months, 6 months, and 1 year follow-up. Proximal outcomes to be measured will include: number of missed court appointments, positive drug screens, and sanctions imposed. These data will come directly from drug court records for each participant. Treatment-related proximal outcome will include number of missed treatment appointments, and number of missed Vivitrol treatments for the intervention arm. Ultimate outcomes of interest will include (1) all new arrests, by type (e.g., violent, non-violent, drug, felony, misdemeanor), collected from the publicly available North Carolina Automated Criminal Infraction System (ACIS) and drug court records, and new convictions, identifying the new arrests that result in a conviction from the drug court records; (2) new incarcerations, including categorized as serious or non-serious as described above, collected from drug court and treatment agency records; and (3) brief client interviews to yield outcomes related to client preferences regarding treatment, including Vivitrol for intervention group; level of functioning and stability; quality of life; and employment/education engagement.

We will also build a preliminary cost analysis into the RCT, drawing on estimates from the scientific literature, including our group's previous cost research on behavioral health disorders and criminal justice involvement, and where possible, administrative budget and expense reports to monetize the key study outcomes (namely, arrest and incarceration) and also crisis-driven health care service use (e.g., emergency department visits, hospitalizations) in order to estimate the net costs or savings associated with Vivitrol as it relates to changes in recidivism. The methods and results from our Connecticut criminal justice cost study will heavily guide the cost work in the next-stage RCT. This cost analysis will offer early information about potential cost savings to the justice and healthcare systems to inform a future, larger-scale cost-effectiveness analysis if Vivitrol is demonstrated to improve drug court clients' outcomes in the RCT.

CONCLUSION

Drug courts are a unique and successful approach to breaking the link between addiction and criminal justice involvement, connecting clients to treatment, often for a first time. Conclusive evidence is needed to understand the extent to which MAT like Vivitrol reduce reoffending among drug court clients. Building this evidence base is especially important now, when federal policy change is building momentum for increased access to MAT in drug courts. Our feasibility study will identify and address considerations unique to conducting a Vivitrol RCT in the drug court setting, as well as generating preliminary data necessary to power the multi-site RCT. This feasibility study and next-stage RCT will produce important, but not yet available evidence that can heavily influence drug court practice and policy on MAT.