Project: *Novel Digital Health Intervention to Promote Engagement in and Adherence to Medication-Assisted Treatment*

PI: Kirsten Langdon, PhD

The prevalence of opioid use disorders (OUD) has reached epidemic rates in the United States, and opioid-involved overdoses are the country's leading cause of injury deaths.[1] The state of Rhode Island has been especially affected by the opioid crisis, with the rate of overdose deaths rising by 90% from 2011 to 2016.[2] Medication-assisted treatment (MAT), which involves the use of pharmacotherapy in combination with behavioral therapies,[3] is associated with significant reductions in illicit opioid use.[4,5] Buprenorphine, a partial opioid agonist, is one pharmacological option for MAT that is growing in popularity because of its more flexible administration through office-based programs.[6] Despite its advantages, nearly half of participants are unable to achieve stabilization,[7] and many patients lapse or discontinue treatment within the first week.[8,9] Given high rates of nonadherence and/or discontinuation, there have been recent calls to find innovative interventions to enhance motivation, adherence, and retention in MAT.[10]

Individuals use opioids to mitigate aversive internal states such as anxiety and depressive symptoms.[11] Further, negative affect is a primary precipitant of early lapse to opioids.[12] Consistent with this negative reinforcement model of substance use[11], distressing physical and emotional symptoms, that occur in the context of opioid withdrawal and/or early periods of abstinence, may contribute to difficulties with buprenorphine induction (first administration of medication) and stabilization (initial efforts to achieve and maintain abstinence).[13] Distress tolerance (DT), defined as the perceived or actual ability to handle aversive physical or emotional states, is a transdiagnostic vulnerability factor implicated in the development and maintenance of affective symptoms/disorders and substance use.[14] Preliminary work suggests that targeting DT during substance use treatment may improve outcomes by promoting the ability to persist in goal directed activity (e.g., abstinence) even when experiencing distress.[15] Accordingly, an intervention that a) cultivates motivation for abstinence over and above the reinforcing effects of opioids, and b) teaches adaptive strategies for tolerating physical and psychological discomfort, may optimize the induction and stabilization phases of buprenorphine treatment to improve long-term recovery and prevent future incidence of overdose.

Personalized feedback interventions (PFI) represent a promising method to effectively motivate engagement in and adherence to buprenorphine treatment. PFIs involve an evaluation of the advantages/disadvantages of engaging in a certain behavior (e.g., opioid use), compared to the advantages/disadvantages of an alternative behavior (e.g., abstinence), and offer strategies for changing problematic behavior (e.g., DT skills training).[16,17] These interventions are generally brief, individually tailored, and have the potential to be administered via technological platforms. Digital health interventions, such as those delivered via mobile phones, have the capability of efficiently and effectively reaching a variety of patient populations, including those with substance use disorders.[18-20] These interventions offer the advantage of being utilized in everyday settings, and allow for the content, timing, and frequency of messages to be individually tailored to times when certain skills and motivational reminders are most salient. Thus, digital health interventions are well-suited to offer support, skills training, and motivational reminders during times of increased distress that occur in 'real-time' outside of structured treatment settings.

The candidate of this application, Dr. Langdon, serves as the Director of Behavioral Therapy for the Lifespan Recovery Center (LRC) at Rhode Island Hospital. The LRC is a comprehensive outpatient MAT program that offers buprenorphine in combination with ancillary recovery services. In this role, Dr. Langdon is committed to improving clinical outcomes for this at-risk population. The proposed Advance-CTR Mentored Research Award will provide Dr. Langdon with the additional support, protected time, and mentorship necessary to transition into an independent research career focused on the development and evaluation of digital health interventions designed to motivate engagement in and adherence to MAT. <u>Specific aims include</u>: ***Aim 1.*** Develop and refine, through formative evaluation, a combined in-person and text message-delivered PFI, that incorporates DT skills training, for persons actively seeking outpatient MAT at the LRC (PFI-DT). PFI-DT is designed to: (1) enhance motivation to engage in MAT; and (2) increase tolerance of distress to facilitate stabilization. A health education comparison condition (HE) will also be developed and piloted.

Aim 2. Conduct a preliminary randomized controlled trial by recruiting 60 participants entering treatment at the LRC assigned to condition at a 3:1 ratio, with 45 participants assigned to PFI-DT and 15 participants assigned to HE. A 3:1 randomization ratio is proposed to maximize the information gained about the PFI-DT intervention while including a comparison condition. It is hypothesized that the PFI-DT, relative to HE, will result in greater:

Aim 2a. Motivation for treatment and abstinence from illicit substances.

Aim 2b. Likelihood of completing induction and abstinence rates at 1-, 4-, 8- and 12-weeks post-induction.

Aim 2c. Adherence to buprenorphine and treatment retention.

The current proposal has the potential to address a Rhode Island Department of Health priority - the opioid epidemic - by increasing adherence/retention to MAT and preventing future incidence of overdose.