## Session 2: Presentation of Selected HEAL Program Areas to Improve Prevention and Treatment Strategies for Opioid Addiction





## Optimizing Retention, Duration, and Discontinuation of Medications for Opioid Use Disorder

Betty Tai, PhD Director, Center for Clinical Trials Network

National Institute on Drug Abuse





National Institutes of Health

on Drug Abuse

### National Drug Abuse Treatment Clinical Trials Network (CTN)

*What?* An infrastructure to unite medical and specialty treatment providers, researchers, patients, and NIDA

*Why?* To improve the nation's addiction treatment using science as the vehicle

(Since) When? October 1999 to present

*How?* Conduct rigorous, multi-site clinical trials to determine effectiveness of treatment strategies in broad range of treatment settings and diverse patient populations

Timely transfer of research results to clinicians, providers and their patients



#### National Drug Abuse Treatment Clinical Trials Network (CTN)





### Retention-Discontinuation Study: A Two-Phase Randomized Clinical Trial

- Phase 1: Retention
  - How to reduce dropout from medication (buprenorphine or naltrexone XR) treatment?
  - Outcome measure: Retained in OUD medication treatment for 6 months
- Phase 2: Discontinuation
  - How to discontinue OUD medication treatment?
    - Buprenorphine taper to discontinuation
    - Buprenorphine transition to naltrexone to discontinuation
    - Naltrexone discontinuation
  - Role of supportive counseling (case management; technology-based)
  - Outcome measure: No relapse within 6 months of discontinuation



# Why Study Optimizing Treatment Retention and Discontinuation Instead of Duration?

#### What is the optimal length of medication treatment for OUD?

- Stakeholder Input:
  - RFI on "Optimal Duration of Medication Treatment for OUD" (November 2018)
  - Expert panel consultation (November 2018)
- Key Themes:
  - Medication treatment for OUD is highly effective
  - High drop-out rate (at least 50% in 3-6 months), in practice and in clinical trials
  - Drop-out = high risk for relapse and overdose
  - Ethical challenges (next slide)
  - Limited understanding of how to retain patients in treatment, or how they can successfully discontinue treatment
- Revised Research Questions:
  - How to enhance medication retention-in-treatment?
  - How to safely discontinue medication once a patient has so decided?



#### Safety and Ethical Issues Around Treatment Duration Studies

- High relapse rates (in some cases in excess of 90%) associated with medication discontinuation
- Consequences include overdose, HIV, HCV, and social and CJS consequences
- Little is known about when patients can safely discontinue
- The addiction treatment field largely recognizes that at least 3-5 years of maintained abstinence is necessary before patients are at reduced relapse risk
- Data do not support that it is in patients' interest to recommend discontinuation
- Yet many patients decide to discontinue
- Methods to enhance discontinuation success are lacking and badly needed
- The relationship between duration of medication and successful discontinuation can be studied via data on pharmacy claims, death, and services utilization, without RCTs



#### **Retention Phase: Design**



#### **Discontinuation Phase: Design**



## **Questions/Discussion**





## Behavioral Research to Improve Medication-Based Treatment for Opioid Use Disorder (BRIM)

David Shurtleff, PhD

Deputy Director of the National Center for Complementary and Integrative Health (NCCIH)





### Background and Challenges for MOUD Treatment

- Evidence suggests that access to, and retention on, medication-based treatment for opioid use disorder (MOUD) is protective against mortality
- Adherence to MOUD is a major challenge
- Dropout rate of approximately 50% within the first 6 months (SAMHSA, 2017)
  - Extended time, often years, of MOUD may be needed to stabilize individuals and prevent relapse
  - Contingency management improves adherence, but these effects are not maintained once the reinforcement is removed and do not address comorbid conditions or long-term behavioral change



# Need for Integrative Approach

- ~40-80% of individuals on MOUD experience chronic pain
- Individuals on MOUD receive inadequate evidence-based care for their pain and can experience:
  - Cross-tolerance with other pain medications
  - Increased sensitivity to pain (hyperalgesia)
  - Mental health conditions (e.g., depression) that can exacerbate pain and affect sleep quality
- Treatment for comorbid chronic pain and OUD may require complementary integrative approaches to address mood, anxiety, sleep, and functional difficulties
- Pharmacotherapy can be more effective when combined with behavioral/ social interventions (e.g., smoking cessation)



### Mindfulness-Based Interventions for Substance Abuse Treatment and Pain Management

- Promote cognitive control
- Enhance interoceptive awareness
- Restructure reward
- Decrease stress reactivity and enhance emotional control and coping
- Facilitate extinction to drug cues
- Reduce pain catastrophizing
- Increase psychological flexibility, acceptance, and sensory discrimination of pain-evoking sensations
- Enhance top-down modulation of ascending nociceptive input

Adapted from Garland, E, Ann NY Acad Sci. 2016 Jun;1373(1):25-37; McClintock, AS et. al., J Alt Complement Med. 2018 Dec 5.



#### Mindfulness-Based Interventions and Neural Networks





## Purpose of the BRIM Program

- Test behavioral and/or social interventions (e.g., mindfulness meditation, CBT, or multi-disciplinary rehabilitation) to:
  - Improve adherence to MOUD
  - Prevent OUD relapse
  - Improve abstinence for persons engaged in OUD treatment
- Applicants encouraged to leverage funding under SAMHSA 21st Century Cures Act "State Targeted Response (STR) to the Opioid Crisis"
  - RFA-AT-18-001 Behavioral Interventions for Prevention of Opioid Use Disorder or Adjunct to Medication Assisted Treatment - SAMHSA Opioid STR Grants
  - RFA-AT-18-002 Clinical Trials or Observational Studies of Behavioral Interventions for Prevention of Opioid Use Disorder or Adjunct to Medication Assisted Treatment - SAMHSA Opioid STR Grants



## Additional Goals of BRIM

- Applicants encouraged to propose studies that consider:
  - Co-occurring conditions such as chronic pain
  - Stress-reduction
  - Multilevel interventions that target individuals, families, caregivers, health care providers, communities, and/or health care system delivery methods



# FY18 HEAL Supported BRIM Projects

=

AT009932	C. Price	Mindful Body Awareness Training as an Adjunct to Medication Assisted Treatment for Opioid Use Disorder
AT010106	M. Ilgen	Psychosocial Pain Management to Improve Opioid Use Disorder Treatment Outcomes
AT010109	Cooperman & Kline	Mindfulness-Oriented Recovery Enhancement as an Adjunct to Methadone Treatment for Opioid Use and Chronic Pain Management
AT010125	Schuman-Olivier	Effect of Mindfulness Training on Opioid Use and Anxiety During Primary Care Buprenorphine Treatment
AT010117	Lord & Goodman	Mindful Moms in Recovery: Yoga-based mindfulness relapse prevention for pregnant women with opioid disorder
AT010118	Kawasaki & Nunes	Comprehensive CBT via reSET for a Hub and Spoke MAT System of Care

### Behavioral and Social Interventions to Improve Adherence to Medication-Based Treatment for OUD

- RFA-AT-19-006: New applications to examine the impact of behavioral and social interventions designed to improve adherence to medication-based treatment for opioid use disorder
- Phased award total of 5 years
  - R61 provides 1 to 2 year milestone-driven planning period
  - R33 provides up to 4 years to implement the trial
- Participating ICOs:
  - NCCIH, NIDA, NIA, NIMH, NIAAA, NICHD, NIMHD, OBSSR
- Applications submitted on February 8, 2019
- Anticipate funding 6 to 8 awards



#### Limited Competition: Ancillary Studies to Improve Adherence to Medication Assisted Treatment for OUD

- RFA-AT-19-007: Allows expansion of currently funded projects under RFA-AT-18-001, RFA-AT-18-002, and RFA-DA-18-005
  - Increase total sample size for fully powered efficacy
  - Add new sites to improve generalizability
  - Add evidence-based behavioral or social interventions to studies that are only expanding medication availability or access
  - Increase efforts to increase recruitment of under-represented populations
  - Increase data collection, follow-up time, and add new outcome measures
- Applications due March 15, 2019



## **Questions/Discussion**

