RESIDENTIAL SUBSTANCE ABUSE TREATMENT (RSAT)

Digital Technology in Treating Opioid Use Disorders in the Criminal Justice System

May 15, 2019

Dr. Audrey Kern, MD, FASAM

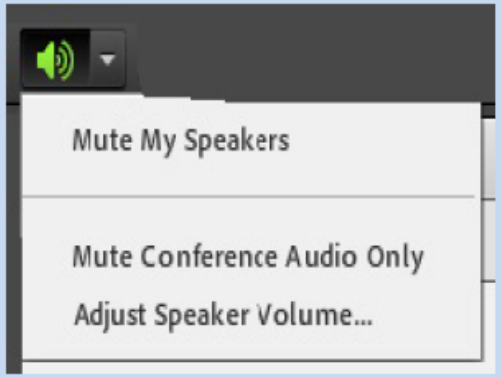
Pear Therapeutics

This project was supported by grant No. 2016-MU-BX-K021 awarded by the Bureau of Justice Assistance. The Bureau of Justice Assistance is a component of the Office of Justice Programs, which also includes the Bureau of Justice Statistics, the National Institute of Justice, the Office of Juvenile Justice and Delinquency Prevention, the SMART Office, and the Office for Victims of Crime. Point of view or opinions in this document are those of the author and do not represent the official position or policies of the United States Department of Justice.

Housekeeping: Functions

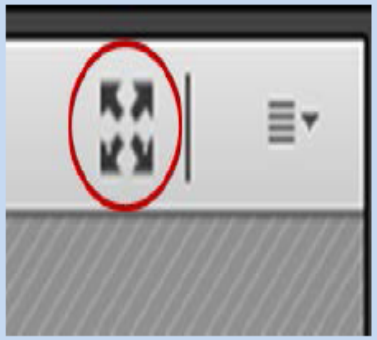
Sound

This webinar will be broadcast through your computer. Please ensure your speakers are on. You can adjust the conference volume with the speaker icon at the top of your screen.



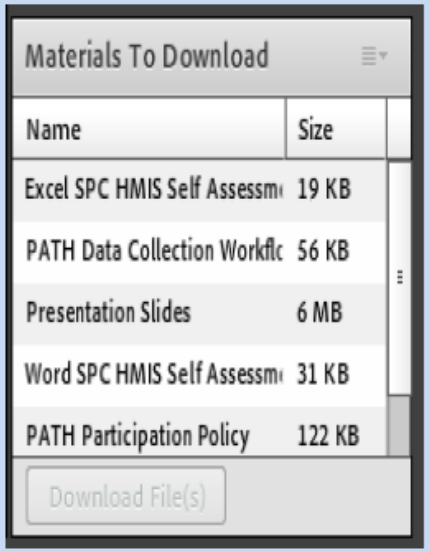
Would you like to enlarge the slide presentation?

You can make the slides larger with the full screen button in the upper right corner of the display pod. To exit full screen, just press the escape key on your keyboard.



Presentation materials!

You can download a PDF version of today's presentation and additional resource materials from the "Materials To Download" box.

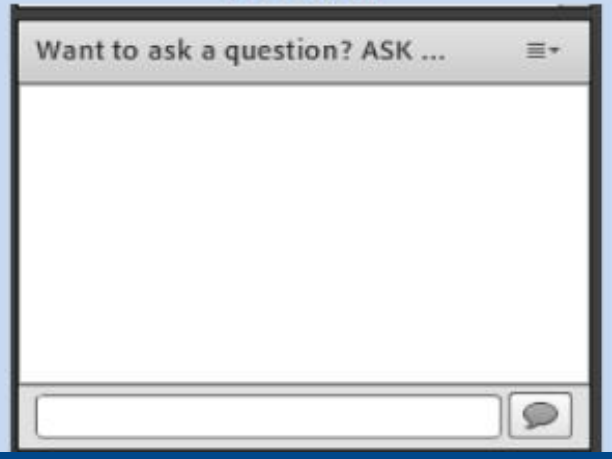


Housekeeping: Communication

Q&A and Technical Issues

If you have questions for either the presenters or our Technical Support Staff, enter them in the Q&A box.

Our support staff will assist you with your technical issues, and our moderator will present as many questions as possible to the presenter.



Chat with us!

If you have general comments, please post them in the participant chat box.

Dr. Audrey Kern, MD, FASAM

Global Medical Director, SUD/OUD

Pear Therapeutics

Learning Objectives:

- Describe the referral and supervisory process of the prescription digital therapeutic, reSET-O
- Identify the collaborative treatment planning between a patient, clinician and prescribing physician
- Understand the intended use of reSET-O as a mobile medical application to increase treatment retention

Digital Technology in Treating Opioid Use Disorders in the Criminal Justice System

Introduction to PDTs, ReSET®, and ReSET-O®

2019

PEAR THERAPEUTICS

Agenda and Goals for Todays Discussion

Goal: understand the potential utility of Prescription Digital Therapeutics for substance use disorder and opioid use disorder in individuals with a history of incarceration

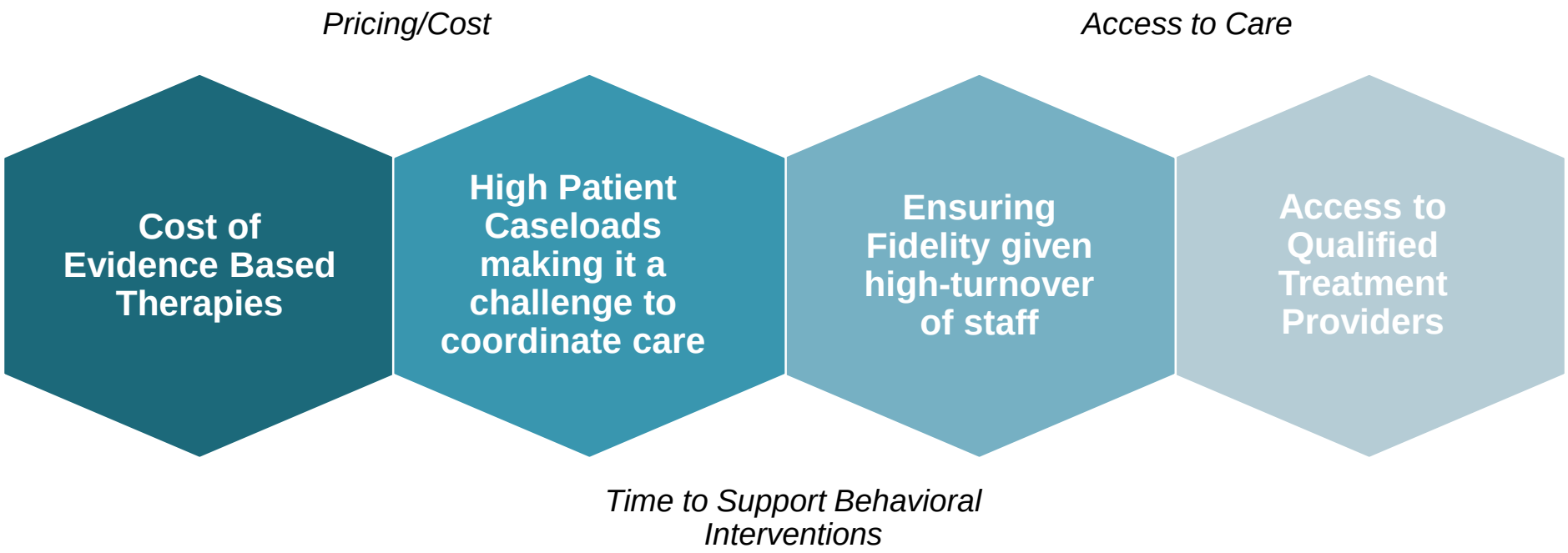
- Introduction
- The Unmet Medical Need in the Incarcerated Population
- Barriers to treatment for Substance Abuse in this population
- Evidence Based Approaches for Effective Treatment
- Prescription Digital Therapeutics
- Clinical Data

Unmet Medical Need in Substance Abusing Offenders in the Criminal Justice System

- Offenders engage in disproportionately high rates of substance use while in the community.
- **53% of state and 45% of federal prisoners meet criteria for a substance use disorder** compared with only 3% of the general U.S. population
- 83% of prisoners report lifetime drug use and more than two thirds report regular use
- **50% of male and 33% of female inmates with substance use disorders require substance abuse treatment services in prison; However, the best available estimates show that, while incarcerated, only about 20% to 25% of those in need of treatment actually receive it**

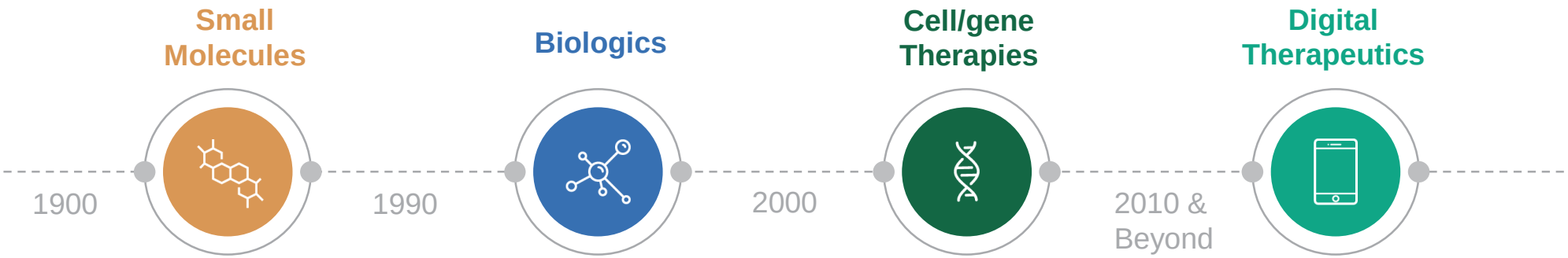
Chaple, M., Sacks, S., McKendrick, K., Marsch, L. A., Belenko, S., Leukefeld, C., … French, M. (2016). A Comparative Study of the Therapeutic Education System for Incarcerated Substance-Abusing Offenders. The Prison Journal, 96(3), 485–508. https://doi.org/10.1177/0032885516636858

Known Barriers to Treatment for Substance Abuse in the Criminal Justice System



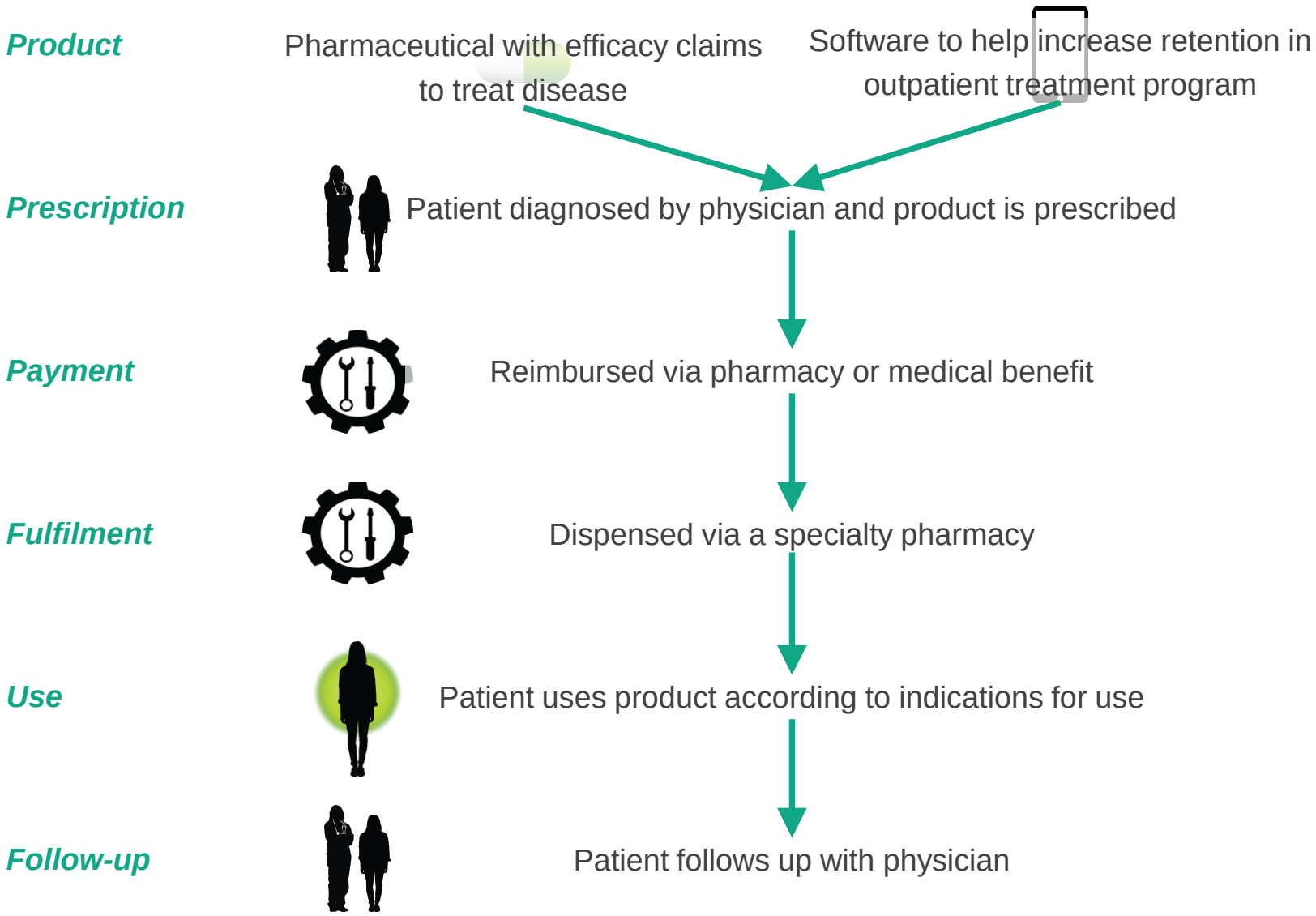
Chaple, M., Sacks, S., McKendrick, K., Marsch, L. A., Belenko, S., Leukefeld, C., … French, M. (2016). A Comparative Study of the Therapeutic Education System for Incarcerated Substance-Abusing Offenders. *The Prison Journal*, *96*(3), 485–508. https://doi.org/10.1177/0032885516636858

Prescription Digital Therapeutics (PDTs) are a new therapeutic class designed to effectively treat disease and leverage mobile technologies



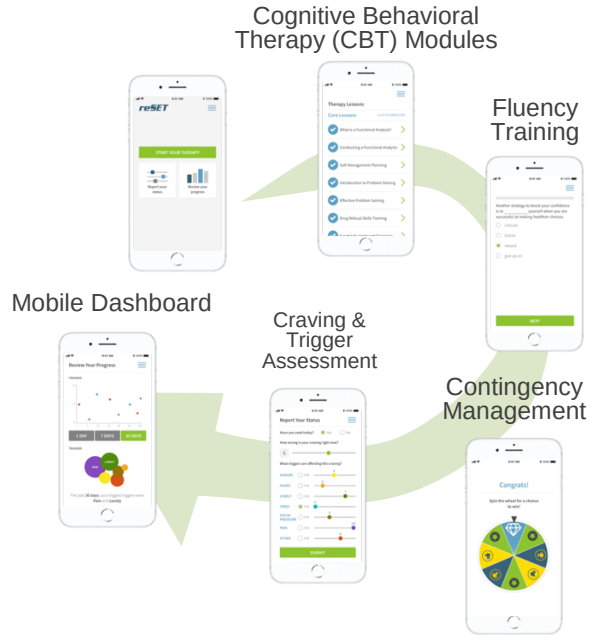
- **"Software as therapeutics"** that treat serious diseases with high unmet medical need
- Evaluated in clinical studies to demonstrate safety and efficacy
- Traditional regulatory pathway for software as a medical device (SaMD)

PDTs are developed, approved, prescribed, and may be reimbursed via the traditional therapeutics model



Patient and clinician engagement to address Substance Use Disorder and Opioid Use Disorder

Patient-Facing Product



+

Clinician Dashboard

Module Use

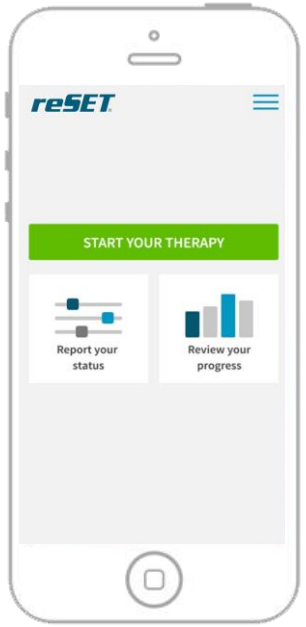
Cravings and Triggers

Contingency Management

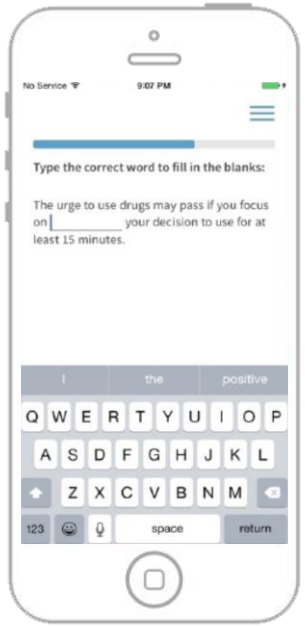
Abstinence and Appointments

Prescription Digital Therapeutics

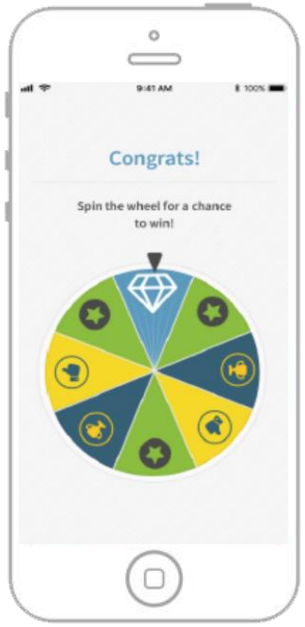
Cognitive Behavioral Therapy (CBT) Lessons



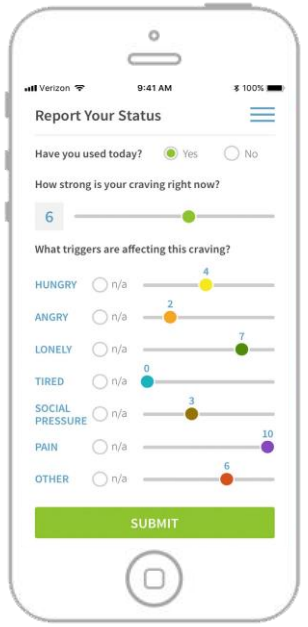
Fluency Training



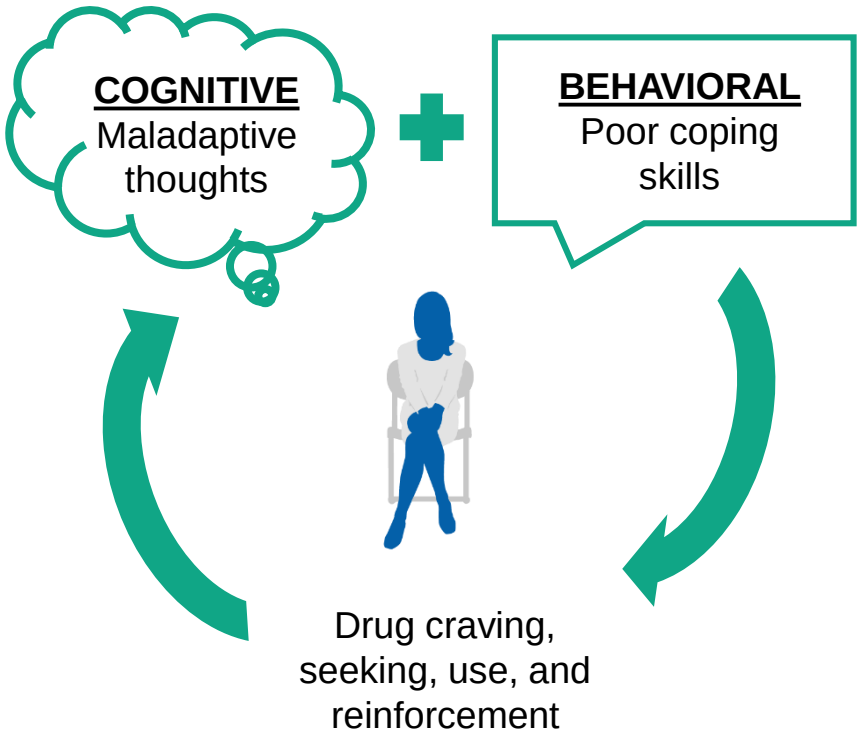
Contingency Management



Craving & Trigger Assessment



Cognitive Behavioral Therapy (CBT) for SUD



CBT is intended to treat SUD by

- Understanding the connection between thoughts and behaviors
  - Functional analysis to identify triggers and understand consequences of use
  - Identify factors that promote/maintain use
- Modifying cognitive barriers to change
  - Identify rationalizing, giving up, overgeneralizations, or personalizing in thinking
  - Use cognitive restructuring to evaluate and alter negative thinking
- Improving behavioral strategies
  - Enhanced coping skills
  - Drug refusal skills
  - Problem solving skills
  - Enhanced social experiences

Calkins AW, et al. (2016) Basic Principles and Practice of Cognitive Behavioral Therapy. In: Petersen T., E. Sprich S., Wilhelm S. (eds) The Massachusetts General Hospital Handbook of Cognitive Behavioral Therapy. Current Clinical Psychiatry. Humana Press, New York, NY.

McHugh, KW et al. (2010). Cognitive Behavioral Therapy for Substance Use Disorders. *Psychiatric Clinics of North America, 33,* 511-525.

Data on File: reSET-O Lesson Content. Boston, MA: Pear Therapeutics, Inc; 2017.

Contingency management (CM) and the community reinforcement approach (CRA)

CM: Contrived Contingencies[1,2]

- Promote initial abstinence
- Put in place explicitly and exclusively for therapeutic purposes; Monetary/other gift tied to defined abstinence endpoints
- Allows time for the therapist and patient to work toward reestablishing naturalistic contingencies

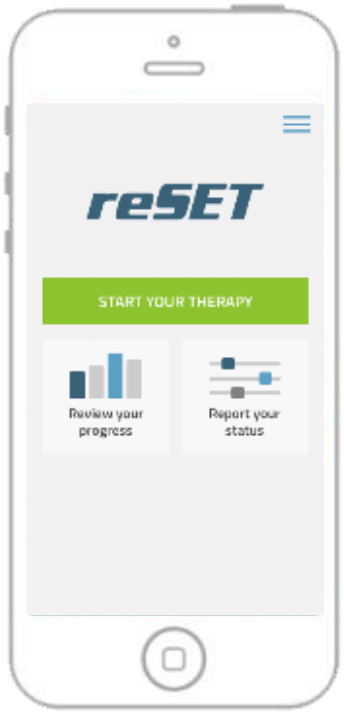
CRA: Naturalistic Contingencies[1,2]

- Promote sustained long-term abstinence once the contrived reinforcers are discontinued
- Systematically increasing the availability and frequency of alternative reinforcing activities (stable family life, job, participation in self-help, etc.)
- Use aversive events or the loss of reinforcing event as a consequence of drug use

1. Higgins ST, Redner R, White TJ. Contingency management and the community reinforcement approach. In: Ries RK et al, eds. *Principles of Addiction Medicine.* Philadelphia, PA: Wolters Kluwer; 2014:877-893.

2. Higgins ST, Budney AJ, Bickel WK, Foerg FE, Donham R, Badger GJ. Incentives improve outcome in outpatient behavioral treatment of cocaine dependence. *Arch Gen Psychiatry*. 1994;51(7):568-576. doi:10.1001/archpsyc.1994.03950070060011.

FDA-authorized Prescription Digital Therapeutic (PDT) for Substance Use Disorder (SUD):
Indication for Use and Population Definition



INDICATION:
"reSET® is intended to provide cognitive behavioral therapy, as an adjunct to a contingency management system, for patients 18 years of age and older who are currently enrolled in outpatient treatment under the supervision of a clinician. reSET® is indicated as a 12-week (90-day) prescription only treatment for patients with substance use disorder (SUD), who are not currently on opioid replacement therapy, or abuse alcohol solely, or whose primary substance of abuse is opioids": reSET® is intended to:

➢ Increase abstinence from a patient's substance of abuse during treatment,
➢ Increase retention in the outpatient treatment program

FDA-authorized PDT to Treat SUD for patients not on opioid replacement therapy: Overview

Product Profile	▪ Delivers addiction-specific form of cognitive behavioral therapy (CBT), fluency training, and contingency management for patients with substance use disorder (SUD)[3]
Indication(s)	▪ Monotherapy with labeled claims to increase retention and abstinence in patients with SUD ▪ 12-week prescription duration[3]
Clinical	▪ 2 randomized controlled trials (RCTs) demonstrating safety and efficacy in >1,000 SUD patients (alcohol, cannabis, cocaine, stimulants)[1-3]
Regulatory	▪ 1st-ever PDT to achieve FDA marketing authorization with medical claims to treat disease[3]
Commercial	▪ Reimbursement code (UDI) issued ▪ Novartis/Sandoz launched in H2 2018

1. Campbell et al., American Journal of Psychiatry. 2014. 171(6):683-690.
2. Chaple et al. 2016. The Prison Journal. 96(3):485-508.
3. DEN 160018 FDA Decision Summary.

FDA-authorized PDT to Treat SUD for patients not on opioid replacement therapy: Overview

Mechanisms of Action

- Delivers:
  - Community Reinforcement Approach (CRA), an intensive form of validated neurobehavioral cognitive behavioral therapy for SUD
  - Contingency management
  - Fluency training to enhance learning.

Product Description

- Based on the Therapeutic Education System (TES)[1]
- Comprised of 62 interactive modules: 32 core modules and 30 supplemental modules
- Core modules focus on key CRA concepts, building skills to support behavior change and prevent relapse
- Supplemental modules provide more in-depth information on specific topics such as relationship skills or living with Hepatitis
- Each module is lasts approx. 10-20 minutes

1. Bickel et al. Computerized behavior therapy for opioid-dependent outpatients: a randomized controlled trial. *Experimental and Clinical Psychopharmacolog. 2008; 16*(2), 132–43.

PDT to treat SUD: Pivotal Clinical Study Design

Background & Objectives

- NCT01104805 was designed to evaluate the effectiveness of a digital version of cognitive behavioral therapy called the Therapeutic Education System (TES), which is the academic version of reSET®, as part of community-based, outpatient substance abuse treatment

Trial Design

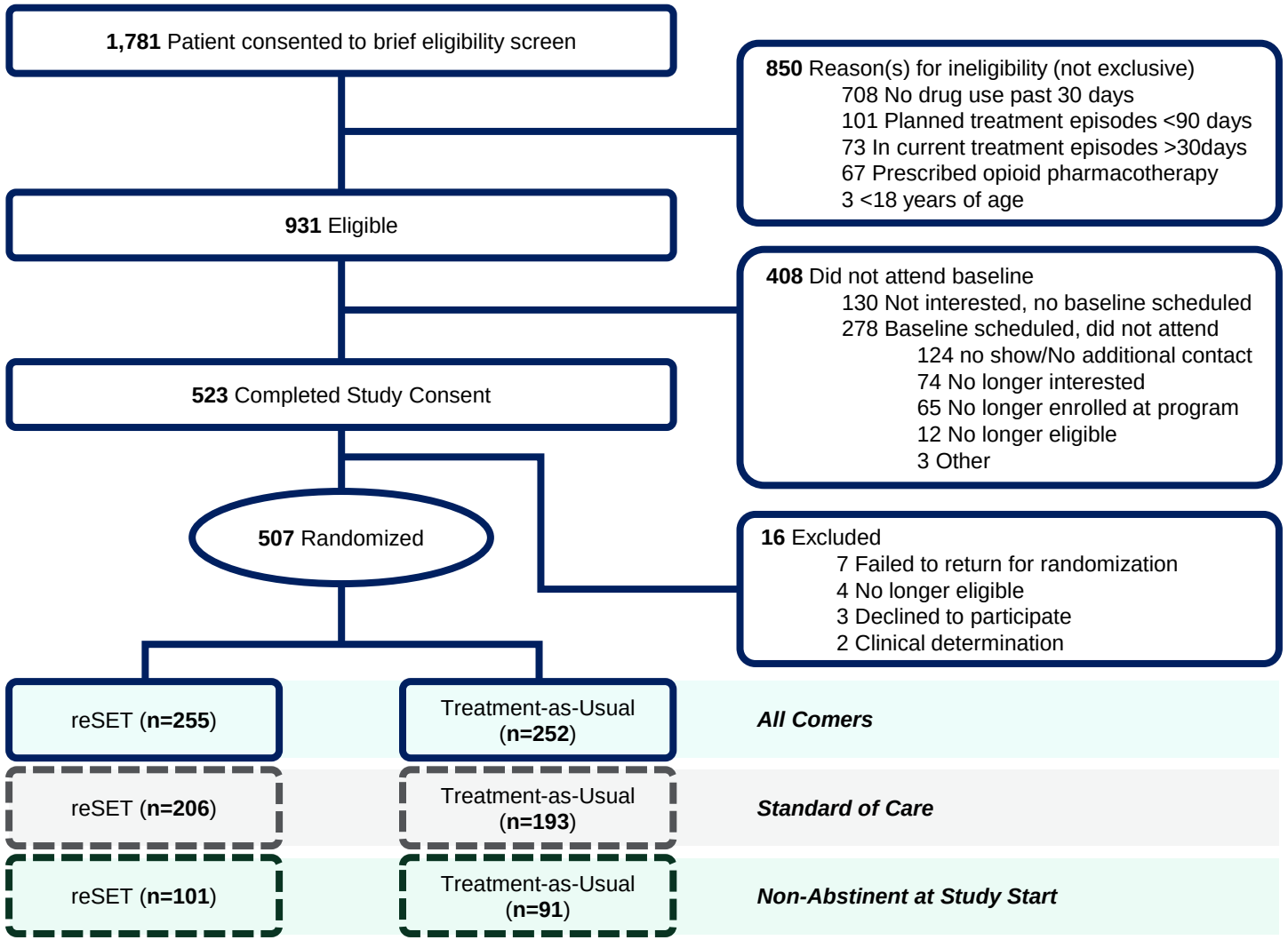
- 507 participants w/ Substance Use Disorders related to Opioids, Cannabis, Alcohol, Stimulants, and/or Cocaine were enrolled and randomized to receive either;
  - Treatment as Usual (TAU) - standard treatment offered and prescribed, as usual, in the outpatient substance abuse treatment program consisting of 4-6hrs per week of face-to-face treatment
  - reSET® substituted for ~2hrs per week of standard face to face treatment at each site

Endpoints

- Patients visited clinics 2x per week for Urine Drug Screen (UDS) and Breath Alcohol Screen with reduced substance use (measured by a combination of self-report confirmed by urine toxicology) and better retention in treatment serving as co-primary endpoints

1. Campbell et al. Am J Psychiatry. 2014 and DEN160018 FDA Submission and Pear Internal Data: Publication in-Process.

PDT to treat SUD: Pivotal Clinical Study Patient Flow



1. Campbell et al. Am J Psychiatry. 2014 and DEN160018 FDA Submission and Pear Internal Data: Publication in-Process.

PDT to treat SUD: Enhances abstinence and retention*

Pivotal Study Overview

- 399 patients with SUD (alcohol, cannabis, cocaine, stimulants) received either best-of-breed face-to-face therapy or reduced face-to-face therapy + reSET for 12 weeks[1]
- Patients provided urine samples 2x per week to objectively monitor abstinence
- Co-primary endpoints
  - Abstinence in weeks 9-12
  - Retention in treatment

Study Results[1,2]

	reSET +Therapy	Therapy only	P-value
Abstinence (All)	**40.3%**	**17.6%**	0.0004
Abstinence (Refractory)	**16.1%**	**3.2%**	0.0013
Retention (SUD)	**76.2%**	**63.2%**	0.0042

Labeled Indication

- Monotherapy, to increase retention & abstinence in patients with SUD
- 12-week prescription duration[3]

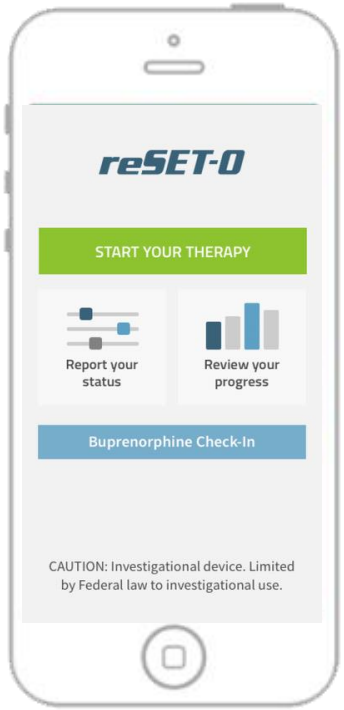
Commercial Launch Nov 2018

- Reimbursement codes issued
  - UDI: 10851580008026
  - NDC: 51580000802
- Novartis/Sandoz field force

* The long-term benefit of treatment with this PDT on abstinence has not been evaluated in studies beyond 12 weeks and the ability to prevent relapse has not been studied.

[1]American Journal of Psychiatry. 2014. 171(6):683-690.
[3]DEN 160018 FDA Decision Summary

FDA-authorized PDT for Opioid Use Disorder (OUD): Indication for Use Statement



INDICATION:
reSET-O® is intended to increase retention of patients with opioid use disorder (OUD) in outpatient treatment by providing cognitive behavioral therapy, as an adjunct to outpatient treatment that includes transmucosal buprenorphine and contingency management, for patients 18 years or older who are currently under the supervision of a clinician.

PDT for OUD: Safety Information/Warnings

reSET-O® is intended for patients whose primary language is English and who have access to an Android/iOS tablet or smartphone. reSET-O® is intended only for patients who own a smartphone and are familiar with use of smartphone apps (applications).

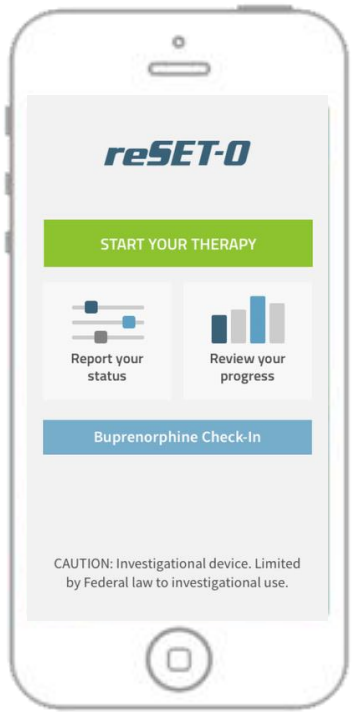
Clinicians should not use reSET-O® to communicate with their patients about emergency medical issues. Patients should be clearly instructed not to use reSET-O® to communicate to their clinician any urgent or emergent information. In case of an emergency, patients should dial 911 or go to the nearest emergency room.

reSET-O® is not intended to be used as a stand-alone therapy for Opioid Use Disorder (OUD). reSET-O® does not replace care by a licensed medical practitioner. reSET-O® does not represent a substitution for a patient's medication. Patients should continue to take their medications as directed by their healthcare provider. The ability of reSET-O® to prevent potential relapse after therapy discontinuation has not been studied.

reSET-O [clinician directions for use]. Boston, MA: Pear Therapeutics, Inc; 2018.

PDT for OUD: Overview

Product Profile	▪ Delivers addiction-specific form of CBT, fluency training, and contingency management for opioid use disorder (OUD)
Indication(s)	▪ Used in combination with buprenorphine to treat OUD[1] ▪ 12-week prescription duration
Clinical	▪ 3 RCTs in >450 OUD patients demonstrating safety and efficacy: 2 with reSET-O® + buprenorphine and 1 with reSET-O® + methadone[1,2,3]
Regulatory	▪ First PDT to receive Breakthrough Designation ▪ FDA Market authorization received H2 2018
Commercial	▪ Reimbursement code (UDI) issued ▪ Launched in Q1 2019



1. Christensen et al. J Consult Clin Psychol. 2014;82(6):964-972.
2. Bickel et al. Exp Clin Psychopharmacol. 2008;16(2):132-143.
3. Marsch et al. Subst Abuse Treat. 2014;46(1):43-51.

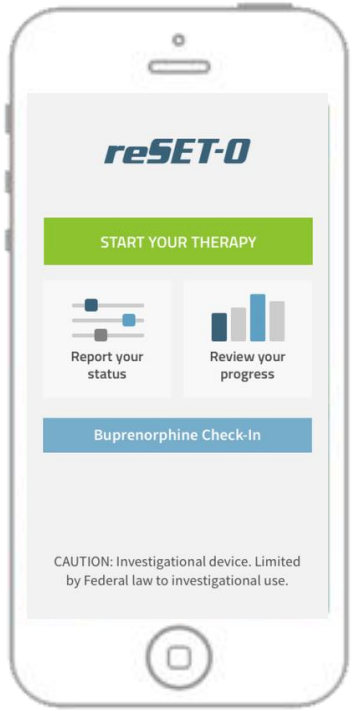
PDT for OUD: Overview

Mechanism of Actions

- Delivers:
  - Community Reinforcement Approach (CRA), an Addiction-specific form of CBT
  - Fluency training
  - Contingency management

Product Description

- Based on the Therapeutic Education System (TES)[1]
- Comprised of 67 interactive modules: 31 core modules and 36 supplemental modules
- Core modules focus on key CRA concepts, building skills to support behavior change and prevent relapse
- Supplemental modules provide more in-depth information on specific topics such as relationship skills or living with Hepatitis
- Each module lasts approx. 10-20 minutes
- Buprenorphine check-in feature to support buprenorphine use



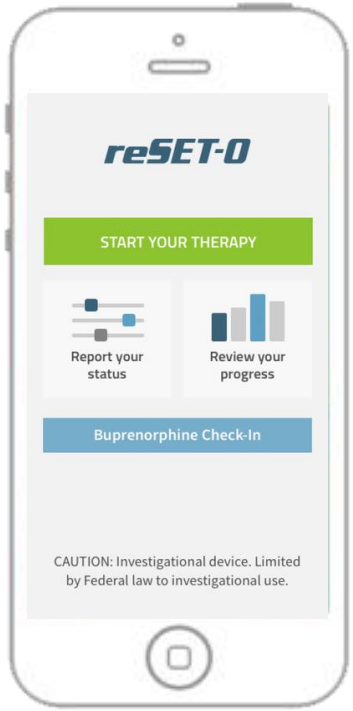
1. Bickel et al. Exp Clin Psychopharmacol. 2008;16(2):132-143.

2. reSET-O Directions for Use 2018

PDT for OUD: Overview

Indication(s)

- reSET-O® is intended to increase retention of patients with opioid use disorder (OUD) in outpatient treatment by providing cognitive behavioral therapy, as an adjunct to outpatient treatment that includes transmucosal buprenorphine and contingency management, for patients 18 years or older who are currently under the supervision of a clinician.
- Intended for use in combination with buprenorphine pharmacotherapy
- 12-week prescription duration



Clinical Data

- Pivotal study demonstrating safety and efficacy[1]

1. Christensen et al. J Consult Clin Psychol. 2014;82(6):964-972.

PDT for OUD: Pivotal Trial: Study Objectives and Endpoints

Primary Objective:

- To examine the effects of combined buprenorphine and voucher incentive to promote abstinence from illicit opiate use and retention in treatment, along with or without the prescription digital therapeutic (PDT) during treatment of opioid use disorder

Primary Endpoints:

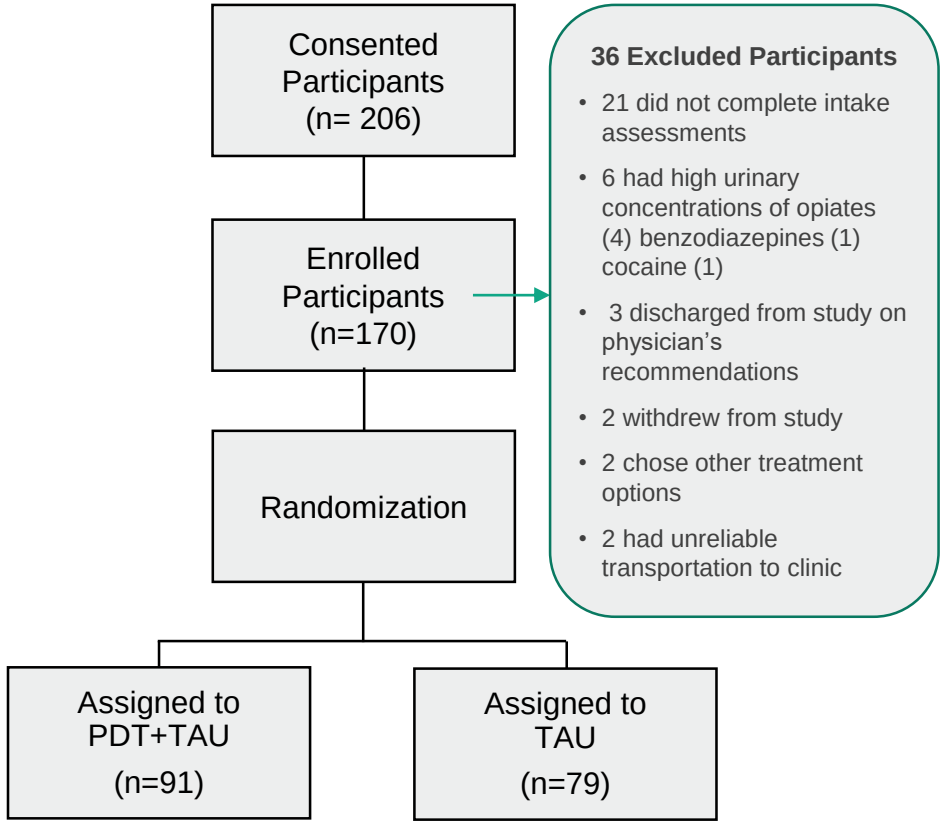
- Retention: as Measured by Time to Dropout
- Abstinence: as measured by urine drug screens during the last 4 weeks of treatment[1]

Secondary Objectives and Endpoints:

- Abstinence: urine drug screens during the Last 6 Weeks and Last 8 Weeks
- Total Abstinence: total number of urine drug screens (UDS)
- Continuous Abstinence: longest-period of consecutive negative UDS
- Safety: to measure the number of patients reporting adverse events between the therapeutic and treatment as usual (TAU) groups

1. NIDA CTN Guidelines
2. Presented at American Academy of Addiction Psychiatry (AAAP), December 2018

PDT for OUD: Pivotal Trial: Patient Flow

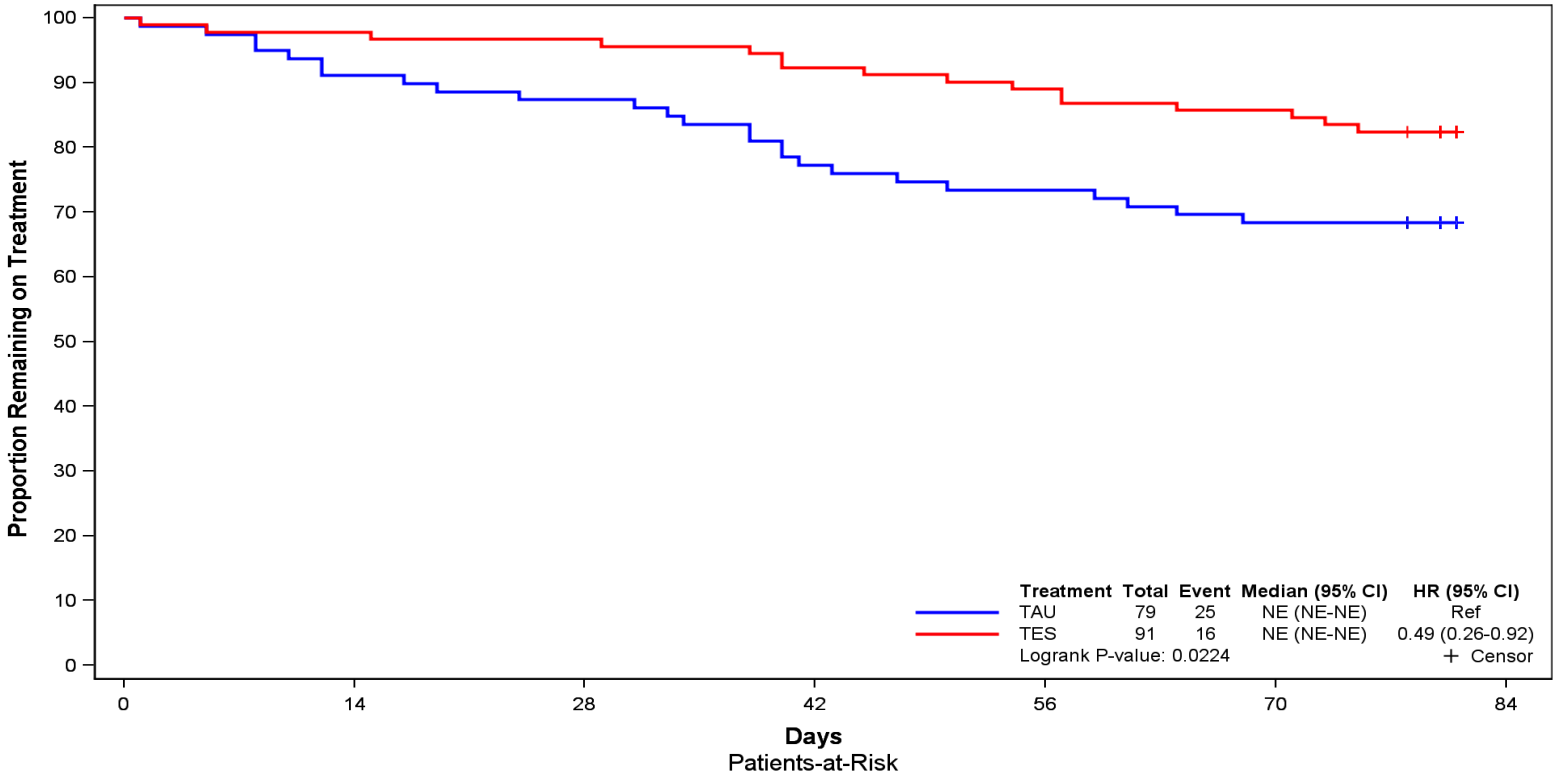


Presented at American Academy of Addiction Psychiatry (AAAP), December 2018

PDT for OUD: Pivotal Trial Results: Retention – time to drop out (study withdrawal) endpoint

Number and % of Participants Who Prematurely Withdrew from the Study for the Treatment Group Indicated

Treatment Group	Total number	Number of Dropouts	% dropout	p-value
TAU	79	25	31.6%	0.0224
TES	91	16	17.6%	



Presented at American Academy of Addiction Psychiatry (AAAP), December 2018

*Retention was analyzed using the Kaplan-Meier method with probability of retention estimated at weeks 2, 4, 6, 8, 10 and 12. Retention distribution between groups were compared using a log-rank test

PDT for OUD: Pivotal Trial Results: Urine Drug Screen (UDS) Endpoint

National Institute of Drug Abuse Recommends the last 4 weeks of treatment as the primary abstinence endpoint[1]: as most relevant and meaningful, thus the last 4 weeks: weeks 9-12 is the primary endpoint for Substance Use

Primary Endpoint: Urine Drug Screens Negative for Opioids (Weeks 9-12)

Assessment	TAU (n=79)	PDT +TAU (n=91)	Odds Ratio (95% CI)	p-value*
Week 9-12	62.1%	77.3%	2.08 (1.10, 3.95)	0.0248

Missing data treated as failures.

Odds ratio of > 2 means patients randomized to PDT + TAU have greater than 2 times the odds of being abstinent during weeks 9-12 compared to TAU

Rates were determined for weeks 9-12 using repeated measures logistic Generalized Estimating Equations (GEE) model with factors for treatment time and treatment*time interaction.

Secondary Endpoint: Total One-Third Weeks UDS (Entire 12-Week Duration = 36 UDS Total)

Endpoint	Treatment Group	Number of Subjects	Mean	SD	p-value*2
Total One-Third Weeks Abstinent	TAU	79	24.06	11.89	
	PDT + TAU	91	27.97	8.17	0.0152

Missing data treated as failures.

Total, One-Third Weeks, is the sum of all urine drug screens. It compares total abstinence for the entire duration. In other words, it measures *substance use across all weeks as well as total use.*

1. NIDA Clinical Trial Network Guidelines: Treatment Effect & Assessment Measures (TEAM) Task Force Recommendations; 2010. http://ctndisseminationlibrary.org/PDF/522.pdf
2. Presented at American Academy of Addiction Psychiatry (AAAP), December 2018

PDT for OUD: Pivotal Trial: Secondary/Additional Urine Drug Screen Endpoints

Secondary/Additional Endpoint: Urine Drug Screens Negative for Opioids (Weeks 5-12)[1]

Assessment	TAU (n=79)	PDT + TAU (n=91)	Odds Ratio (95% CI)	p-value*
Week 5-12	66.3%	81.5%	2.23 (1.20, 4.17)	0.0117

Missing data treated as failures.

Odds ratio of > 2 means patients randomized to PDT + TAU have greater than 2 times the odds of being abstinent during weeks 5-12 compared to TAU

Secondary/Additional Endpoint: Urine Drug Screens Negative for Opioids (Weeks 7-12)[1]

Assessment	TAU (n=79)	PDT + TAU (n=91)	Odds Ratio (95% CI)	p-value*
Week 7-12	62.6%	77.%	2.00 (1.07, 3.76)	0.0305

Missing data treated as failures.

Odds ratio of > 2 means patients randomized to PDT + TAU have greater than 2 times the odds of being abstinent during weeks 7-12 compared to TAU

Secondary Endpoint: Longest Consecutive Negative UDS

Endpoint	Treatment Group	Number of Subjects	Mean	SD	p-value*2
Longest Consecutive Negative UDS	TAU	79	13.47	8.60	
	PDT + TAU	91	14.71	6.78	0.3010

Missing data treated as failures.

1. Rates were determined for weeks 9-12 using repeated measures logistic Generalized Estimating Equations (GEE) model with factors for treatment time and treatment*time interaction
2. Presented at American Academy of Addiction Psychiatry (AAAP), December 2018

PDT for OUD: Pivotal Trial: Safety and Adverse Events

- Adverse events were collected throughout the study.
- Adverse events analyses were performed by summarizing the number of patients with any AEs, grade 3/4/5 AEs and suicide related events.
- The null hypothesis (H0: TAU AE Rate = PDT AE Rate was tested using a Fischer's Exact Test for each case

	TAU (n=79)	PDT + TAU (n=91)	Total	p-value*
Number of Patients with at least one AE	55 (69.6%)	57 (62.6%)	112 (65.9%)	0.4176
Number of Patients with a Grade 3/4/5 Adverse Events	1 (1.3%)	3 (3.3%)	4 (2.4%)	0.6243
Number of Patients with Suicide Related Events	0	0	0	

- The observed AEs were of type and frequency as anticipated in a large population of patients with OUD or associated with buprenorphine pharmacotherapy, particularly during the induction phase
- AEs observed were not adjudicated to be device (therapeutic) related
- The AE data did not demonstrate statistically significant differences in the AE rate between PDT+TAU and the TAU groups

Clinical Data | Technology Enabled Behavioral Therapy in Incarcerated Substance Abuse Offenders*

Study Design:

- **Randomized into two study groups**: Standard of care (C) (n=255) and E-TES (n=258)
- Study focuses on outcomes post prison release (endpoints):
  - Self-reported crime
  - Drug use
  - HIV risk at 3 and 6 months and re-incarceration at 12 months.
- **Treatment** conditions included 48 interactive modules: once a week for two hours or twice a week for one hour
- **Standard of care**: group activities 1 day per week for 2 hours a day over 8-12 weeks.
- No significant differences across facilities.
- Although the study was open to all substance-abusing inmates in need of treatment, both the treatment interventions (E-TES and C) targeted inmates with low to moderate severity of substance abuse.
- **Objective:** comparing TES with standard care in a sample of substance-abusing offenders in prison

*There are no data on the use of reSET® or reSET-O® in the incarcerated population.

Chaple, M., Sacks, S., McKendrick, K., Marsch, L. A., Belenko, S., Leukefeld, C., … French, M. (2016). A Comparative Study of the Therapeutic Education System for Incarcerated Substance-Abusing Offenders. *The Prison Journal*, *96*(3), 485–508. https://doi.org/10.1177/0032885516636858

Clinical Data | Technology Enabled Behavioral Therapy in Incarcerated Substance Abuse Offenders*

Clinical Outcomes:

- Analysis indicated similar rates of re-incarceration for the two groups overall and separately for new offenses or for re-incarceration; no statistical significance (181.8 days for E-TES vs 225.1 days for C)

- The degree of change was statistically similar for drug use (54% E-TES; 54% C) and alcohol intoxication (54% E-TES; 57% C) fell more than half and the number of days of abstinent increased by nearly 3 months (80 E-TES; 85 C)

- Computer-based treatment required much less therapist time

Key Takeaway: There was no significant difference between groups, indicating that E-TES is equally effective compared with standard of care.

*There are no data on the use of reSET® or reSET-O® in the incarcerated population.

Chaple, M., Sacks, S., McKendrick, K., Marsch, L. A., Belenko, S., Leukefeld, C., … French, M. (2016). A Comparative Study of the Therapeutic Education System for Incarcerated Substance-Abusing Offenders. *The Prison Journal*, *96*(3), 485–508. https://doi.org/10.1177/0032885516636858

Thank You!

Dr. Audrey Kern
Audrey.Kern@peartherapeutics.com

Questions?

Type your questions in the Q&A box on your screen

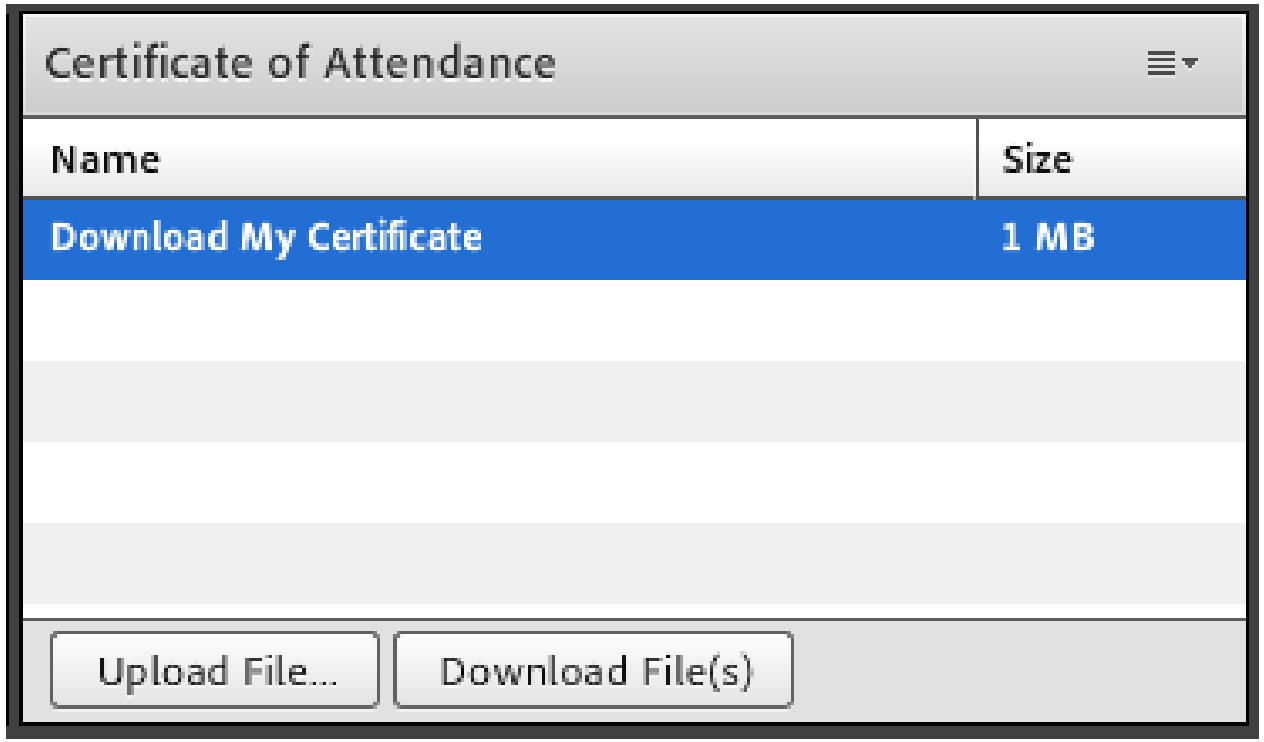
Speaker Contact Info:

Dr. Audrey Kern

audrey.kern@peartherapeutics.com

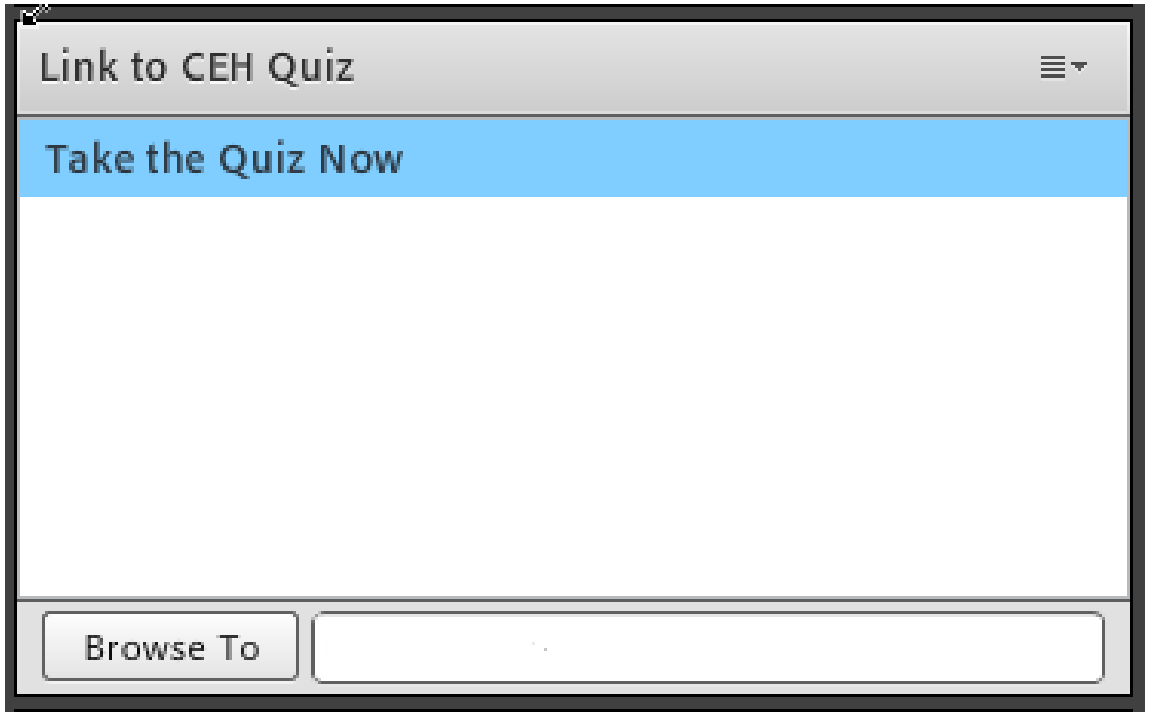
Certificate of Attendance

Download Now!



Certificate of Continuing Education

- **1 NAADAC CEH**
- **Pass 10-question quiz with 7 correct answers**
- **Download certificate upon completion**



For more information on RSAT training and technical assistance please visit:

http://www.rsat-tta.com/Home

Stephen Keller
RSAT TTA Coordinator

skeller@ahpnet.com