



Criminal Justice Presentation

September 2019

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Introduction



Dr. Audrey Kern, MD, FASAM
Global Medical Director, SUD/OUN
Pear Therapeutics®

- The speaker is an employee of Pear Therapeutics®. Information provided constitutes scientific exchange, including information on:
 - reSET® an FDA-authorized prescription digital therapeutic for Substance Use Disorder (SUD) intended to provide cognitive behavioral therapy (CBT) 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-O® an FDA-authorized prescription digital therapeutic (PDT) for Opioid Use Disorder (OUD) intended to increase retention of patient in outpatient treatment by providing cognitive behavioral therapy (CBT), as an adjunct to outpatient treatment that includes transmucosal buprenorphine and contingency management, for patient 18 years of older who are currently under the supervision of a clinician.
- This presentation is not intended to provide medical advice. There are no data on the use of reSET® or reSET-O® in the incarcerated population.

Agenda | Today's Goal and Discussion Topics

Today's Goal

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

Today's Agenda

- 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. population¹

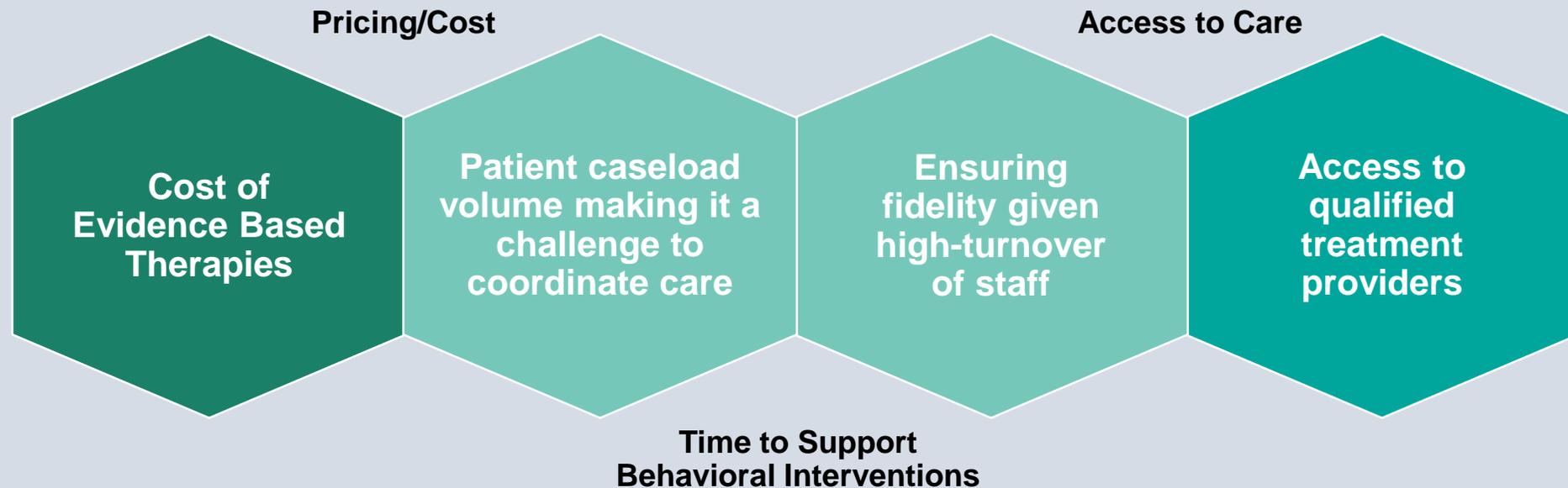


- 83% of prisoners report lifetime drug use and more than two thirds report regular use¹



- **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 20% to 25% of those in need of treatment actually receive it**¹

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



SUD Treatment | Approach Landscape

Some evidence-based practice treatment approaches are difficult to provide for patients in an outpatient setting

US Treatment Facilities Therapeutic Approach offerings ¹	
Substance abuse counseling	99%
Relapse prevention	96%
Cognitive-Behavioral therapy	94%
Motivational interviewing	93%
Anger Management	83%
Brief Intervention	82%
Trauma Counseling	79%
12-step facilitation	73%
Contingency management	56%
Dialectical behavioral therapy	54%
Rational emotive behavioral therapy	46%

Cognitive-Behavioral Therapy (CBT) for SUD:²

- Helps patients learn to identify and correct behaviors that lead to substance use
- Helps patients learn how to deal with problems related to substance use and teaches strategies to encourage abstinence
- Each lesson ends with Fluency Training to promote learning and improve retention

Community Reinforcement Approach (CRA):

- Focuses on managing behavior related to substance use, to help patients adopt a healthier lifestyle without alcohol or drug use³
- Psychosocial support to support behavioral change and emotional wellbeing

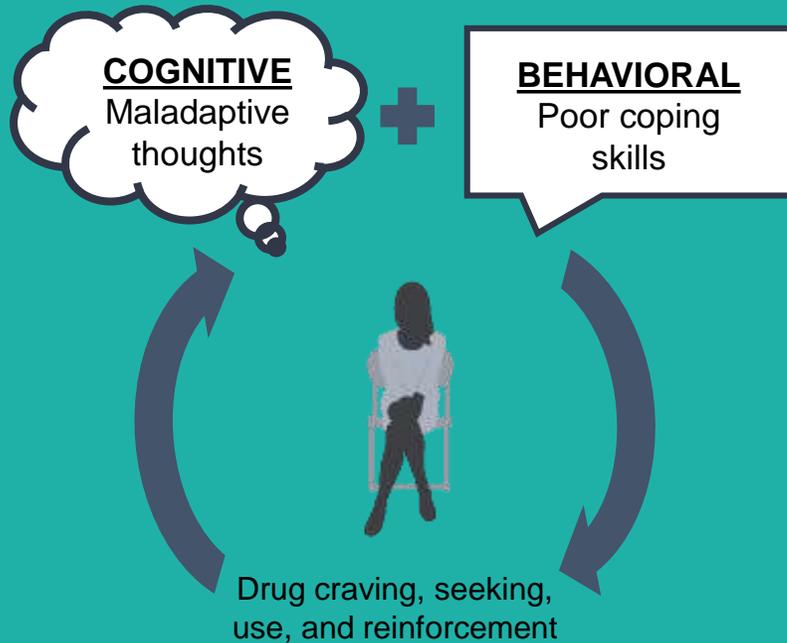
Contingency Management (CM):

- An evidence-based adjunct to counseling that uses positive reinforcement to support treatment goals
- Offers rewards for desired behaviors, designed to weaken drug use by helping replace the 'reward' patients previously received from substance use⁴

1. Source: SAMHSA: National Survey of Substance Abuse Treatment Services (N-SSATS): 2017: Results from the 2017 Survey. https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/2017_NSSATS.pdf
 2. McHough. Cognitive Behavioral Therapy for Substance Use Disorders. Psychiatr Clin N Am 33 (2010) 511–525

3. David, D. The Community Reinforcement Approach An Update of the Evidence Front Psychiatry. 2018
 4. Kellogg et al. 2005, Petry et al, 2005

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

Cognitive Behavioral Therapy (CBT) for SUD

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}

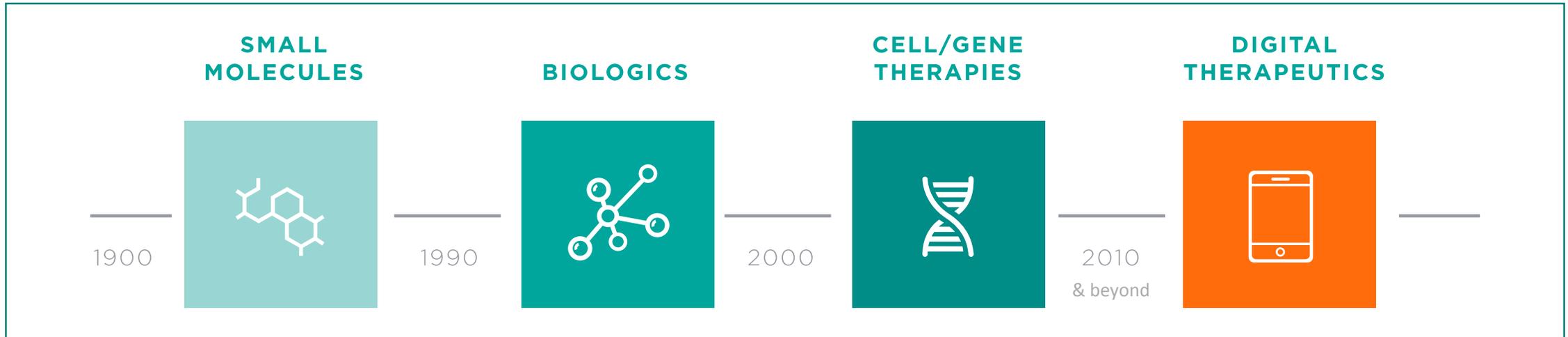
- Promote sustained long-term abstinence once the contrived reinforcers are discontinued
- Systematically increasing the availability and frequency of alternative reinforcing activities (stable family life, job, participation in self-help, etc.)
- Use aversive events or the loss of reinforcing event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

8
1. 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.

2. 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.

Prescription Digital Therapeutics (PDTs)

A new class of therapies that are being integrated into standard of care



“Software as therapeutics” that treat serious diseases with high unmet medical need

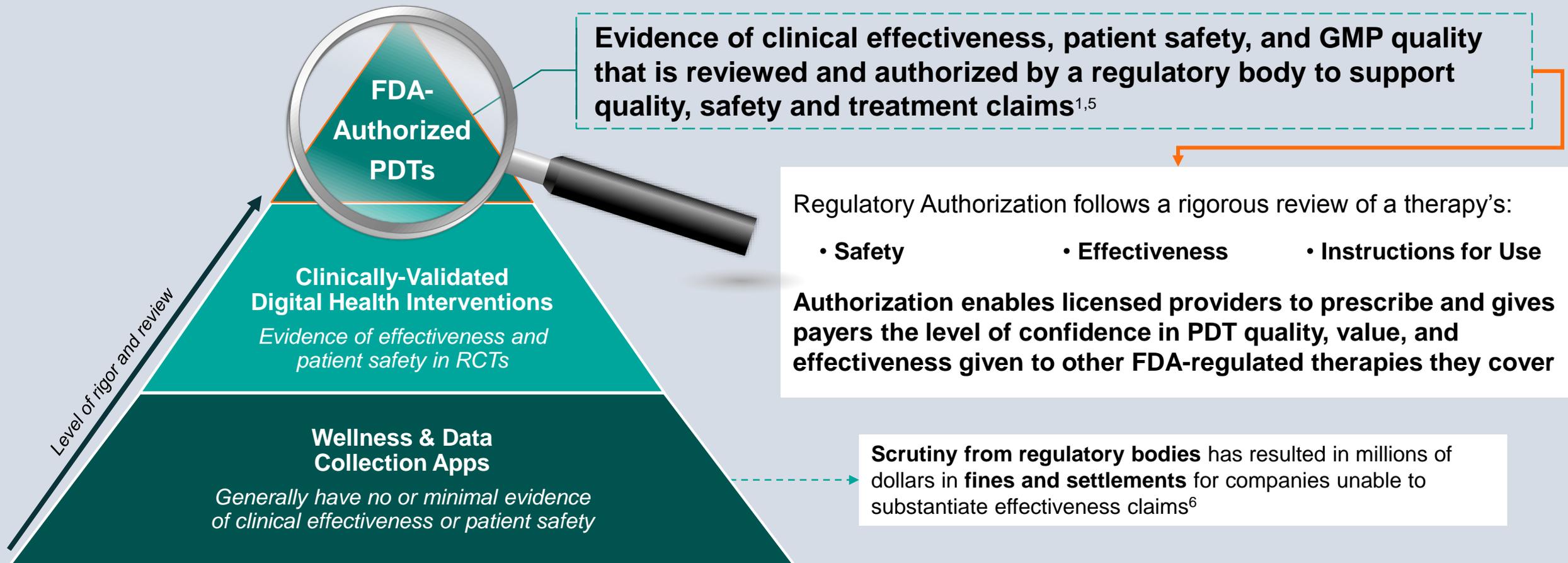
PDTs meet stringent regulatory requirements related to:

- Safety and effectiveness clinical data ^{1,2}
- Regulatory labeling³
- Payers to evaluate coverage based on traditional therapeutic coverage mechanisms

1. Campbell ANC, Nunes EV, Matthews AG, et al. Internet-delivered treatment for substance abuse: a multisite randomized controlled trial. *Am J Psychiatry*. 2014;171(6):683-690.
2. Christensen DR, Landes RD, Jackson L, et al. Adding an internet-delivered treatment to an efficacious treatment package for opioid dependence. *J Consult Clin Psychol*. 2014;82(6):964-972.

3. Federal Drug Administration permits marketing of mobile medical application for substance use disorder [press release]. FDA News Release; Site <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm576087.htm> Published September 14, 2017. Accessed July 2019

What Does Regulatory Authorization Mean in The Context of Digital Therapeutics?



FDA: Food and Drug Administration PDT: Prescription Digital Therapeutic GMP: Good Manufacturing Practice

reSET[®] | Mechanism of Action

An FDA-authorized Prescription Digital Therapeutic (PDT) for SUD

Mechanism of Action

- Delivers therapy based on the community reinforcement approach (CRA), an intensive form of validated neurobehavioral therapy for SUD, along with contingency management and fluency training to enhance learning.

Product Description

- Based on the Therapeutic Education System (TES)
- 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 C
- Each module can be completed in approximately 10-20 minutes



reSET[®] | Indications for Use

reSET[®] is the only therapy approved for marijuana and stimulant patients

Indication(s)

- reSET[®] is intended to provide cognitive behavioral therapy, as an adjunct to a contingency management system, for patients 18 years of age and older, enrolled in outpatient treatment under the supervision of a clinician
- 12-week prescription duration
- Patient population: Patients with SUD, under treatment for the following:
 - Stimulants
 - Alcohol + another substance
 - Marijuana
 - Cocaine
 - Opioids (when not primary substance of abuse)
 - All other substances
- Not indicated for patients who are on opioid replacement therapy, or abusing alcohol solely, or abusing opioids as their primary substance

Effectiveness Data

- Pivotal study demonstrated significant improvements in abstinence and treatment retention^{1,2}



reSET[®] | Safety Information

An FDA-authorized PDT for SUD

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

Clinicians should not use reSET to communicate with their patients about emergency medical issues. Patients should be clearly instructed not to use reSET to communicate to their clinician any urgent or emergent information.

reSET[®] is not to be used for emergencies. In case of an emergency, patients should dial 911 or go to the nearest emergency room.

The long-term benefit of treatment with reSET on abstinence has not been evaluated in studies lasting beyond 12-weeks in the Substance Use Disorder (SUD) population. The ability of reSET to prevent potential relapse after treatment discontinuation has not been studied.

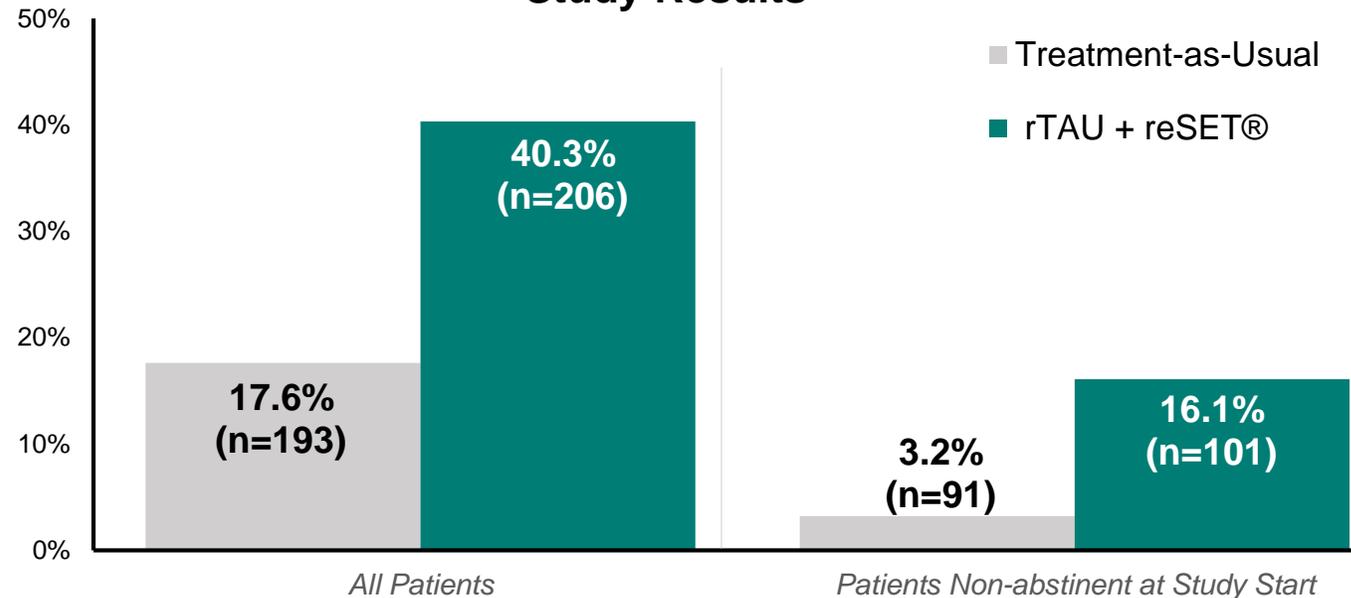


reSET[®] Clinical Data | Pivotal Trial Summary

Pivotal Trial Overview¹

- 399 patients with SUD (alcohol, cannabis, cocaine, stimulants) received either:
 - Treatment-as-Usual (TAU), consisting of intensive face-to-face therapy
 - Reduced TAU and reSET (rTAU+ reSET[®]) for 12 weeks¹
- Patients provided urine samples twice per week to objectively monitor abstinence
- Co-primary study endpoints
 - Abstinence in weeks 9-12
 - Retention in treatment

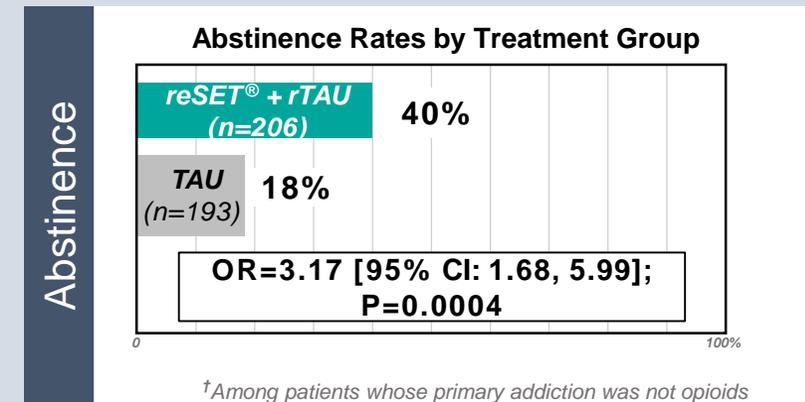
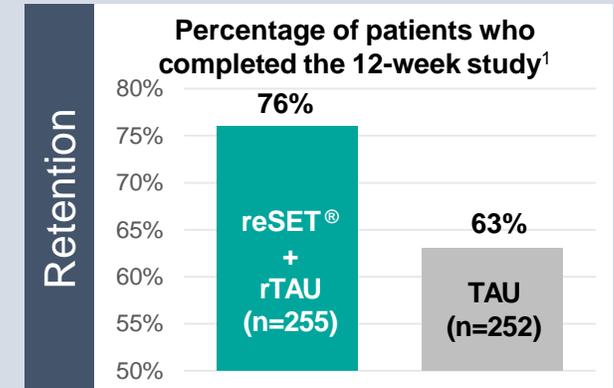
Study Results²



Outcomes	rTAU+reSET [®]	TAU	P-value
Abstinence: all patients	40.3%	17.6%	0.0004
Abstinence: non-abstinent at study start	16.1%	3.2%	0.0013
Retention in treatment: all patients	76.2%	63.2%	0.0042

reSET® | Additional Clinical Data Highlights

Highlights	Clinical Outcomes Summary
Abstinence	<ul style="list-style-type: none"> Among patients whose primary addiction was not opioids, adding reSET® to outpatient therapy more than doubled abstinence rates (40% vs. 18%)
Retention Rates	<ul style="list-style-type: none"> Among all patients, adding reSET® to outpatient therapy improved rates of retention (76% vs. 63%) Patients who adhered to reSET® module completion in the first six weeks of the trial were 7x more likely to complete treatment than those who did not
Treatment Attendance	<ul style="list-style-type: none"> Clinical trial data revealed a positive correlation between module completion and appointment attendance¹
Safety	<ul style="list-style-type: none"> reSET® did not demonstrate a significant difference in unanticipated adverse events¹
Module Completion	<ul style="list-style-type: none"> Average Core Modules Completed: 38² (of 48) Number of reSET® modules completed correlated with abstinence ($R^2=0.21$, $p<.001$ with $n=206$)²



15 1. Pear Internal data and Pear regulatory submission. DEN160018
 2. Luderer HF, Campbell ANC, Nunes EV, Maricich YA. A Digital Therapeutic for SUD, reSET®, Demonstrates a Correlation Between Dose and Treatment Outcomes. Poster presented at: 29th Annual Meeting of the American Academy of Addiction Psychiatry; December 6-9, 2018; San Diego, CA.

reSET-O[®] | Capabilities and Functionality

Used in conjunction with Medication Assisted Treatment, under clinician supervision

ENTER drug and alcohol screen results, to guide conversation and inform clinicians

SEE the intensity of patient-reported cravings and triggers. Each metric can be expanded for greater detail— increasing transparency in patient-HCP dialogue

FOLLOW patient-reported cravings, triggers, buprenorphine use, and substance use; track lesson completion, progress over time, and appointment compliance

VIEW patient summary, personal information, prescription status, and drug screen results

Intervention

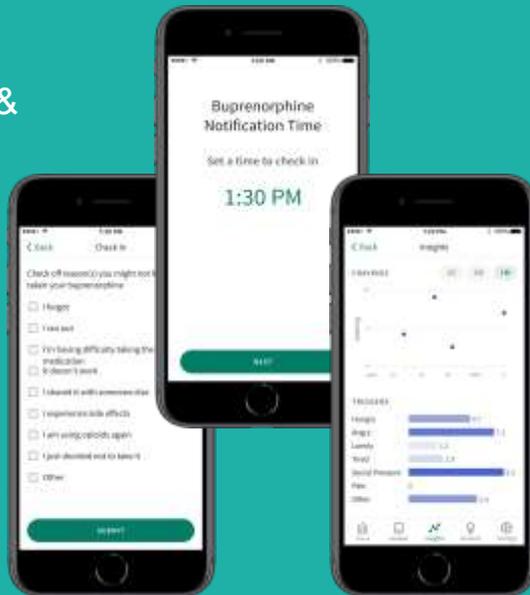
Medication Reminders & Tracking

Craving & Trigger Assessment

CBT Module Delivery

Fluency Training

Contingency Management



Insight

Abstinence & Appointment Attendance Tracking

CBT Module Completion Tracking

Fluency Training

Contingency Management

Cravings & Triggers Reporting



PATIENT

CLINICIAN

reSET-O[®] | Mechanism of Action

An FDA Cleared Digital Therapy for OUD

Mechanism of Action

- Delivers addiction-specific form of CBT, fluency training, and contingency management for opioid use disorder (OUD)

Product Description

- Based on the Therapeutic Education System (TES)
- 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 is lasts approx. 10-20 minutes
- Voluntary buprenorphine check-in feature to support buprenorphine use



reSET-O[®] | Indications for Use

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.
- 12-week prescription duration
- indicated as a prescription-only Mobile Medical Application

Intended Use

- Intended for use in combination with buprenorphine pharmacotherapy

Effectiveness Data

- Pivotal study demonstrated significant improvements in retention in treatment²



reSET-O[®] | Safety Information

An FDA Cleared Digital Therapy for OUD

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.

The long-term benefit of treatment with reSET-O[®] on abstinence has not been evaluated in studies lasting beyond 12-weeks in the Opioid Use Disorder (OUD) population. The ability of reSET-O to prevent potential relapse after treatment discontinuation has not been studied.

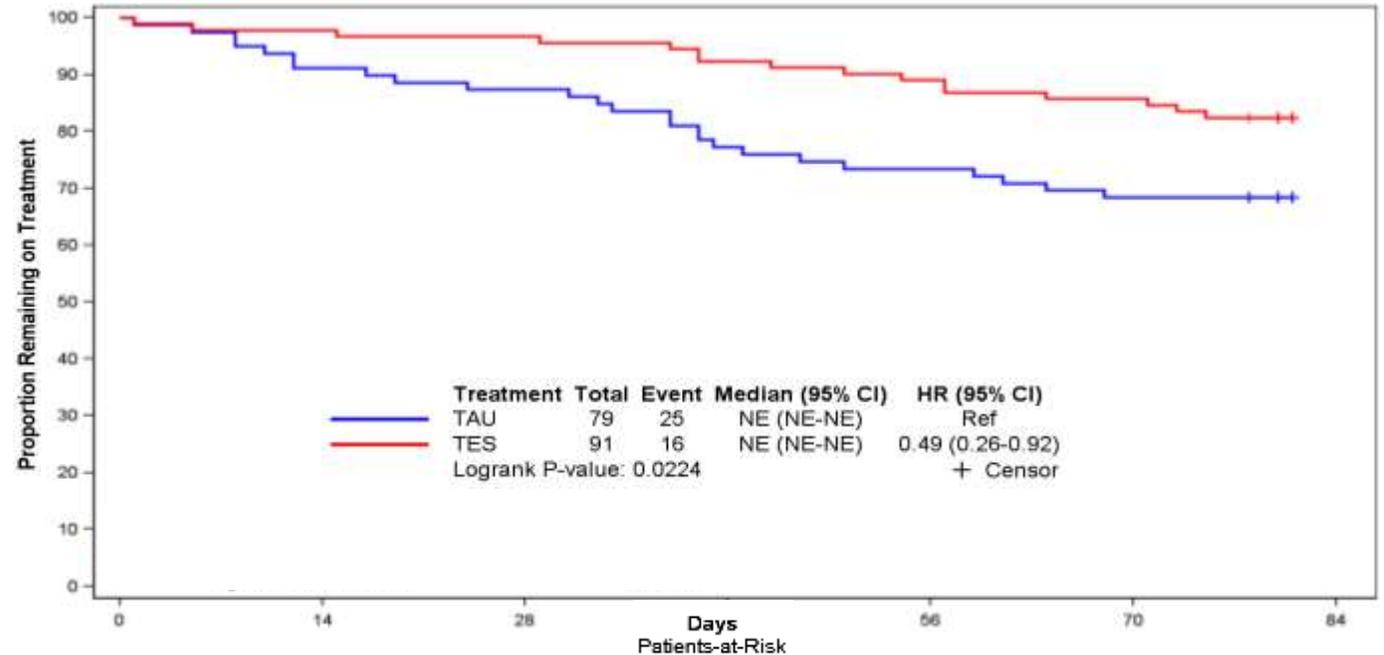


reSET-O[®] Clinical Data | Pivotal Trial Summary

Pivotal Trial Overview

- 170 patients were randomized to receive either:
 - Treatment-as-Usual (**TAU**), consisting of Contingency Management + buprenorphine¹ or
 - TAU + reSET-O[®]** (academic name Therapeutic Education System, or TES) + Contingency Management + buprenorphine
- All patients received 30 mins. of face-to-face counseling every other week.
- Patients provided urine samples 3x per week to objectively monitor abstinence.
- Co-primary endpoint analysis²
 - Abstinence/Negative urine drug screens in weeks 9-12
 - Retention in treatment

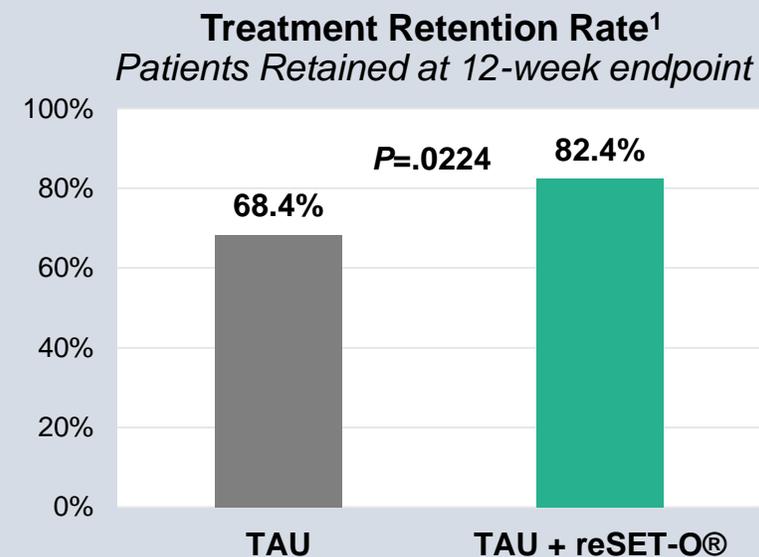
Study Results¹



	TAU + reSET-O [®]	TAU	P-value
Abstinence (Opioids)	77.3% (n=91)	62.1% (n=79)	0.0248
Retention (All)	82.4%	68.4%	0.0224

reSET-O[®] | Additional Clinical Data Highlights

Highlights	Clinical Outcomes Summary
Retention Rates	<ul style="list-style-type: none">Adding reSET-O[®] to outpatient treatment using buprenorphine increased retention of patients with OUD almost 15%
Safety	<ul style="list-style-type: none">The observed adverse events (AE) 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.The AEs observed were not adjudicated to be device related.
Module Completion	<ul style="list-style-type: none">reSET-O[®] vs TAU did not demonstrate any significant safety differences between the cohorts



Technology Enabled Behavioral Therapy¹

Clinical Data in Incarcerated Substance Abuse Offenders

A Comparative Study of the Therapeutic Education System for Incarcerated Substance-Abusing Offenders:

• Objectives and Design

- Study compared the effectiveness of the Therapeutic Education System (TES) vs. Standard of Care on measures of crime (including re-incarceration at 12 months), drug use, and HIV risk behavior 3 and 6 months after prison release.
- Participants were randomized into two study groups, Standard of Care (C) (n=255) and E-TES (n=258)
- *Note: These data were not the basis for reSET® or reSET-O® FDA review/authorization. The incarcerated population were not specifically studied in the pivotal trials used as the basis for authorization. There are no data on the use of reSET® or reSET-O® in the incarcerated population.*

• Randomized into two study groups: Standard of Care (C) (n=255) and E-TES (n=258)

• 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.

• Outcomes: Results showed TES and standard treatment were equally effective across facilities in reducing criminality, relapse to drug use, and HIV risk behavior.

- In prisons, where a majority of substance-using offenders do not receive treatment, identifying an equally effective high-volume alternative such as TES can greatly expand access to quality psychosocial interventions.

• Objective: comparing TES with standard care in a sample of substance-abusing offenders in prison

Technology Enabled Behavioral Therapy

Clinical Data 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.

Thank You!

Dr. Audrey Kern

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