reSET® and reSET-O® as treatments for substance use and opioid use disorders

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- The data presented here includes unpublished “data on file”
- This presentation does not include all the necessary information for the safe and effective use of reSET® or reSET-O®. Disease state information provided is of a general nature regarding disease states and reflects information provided in the referenced publication only
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SUD/OUD Background And Behavioral Treatment Approaches

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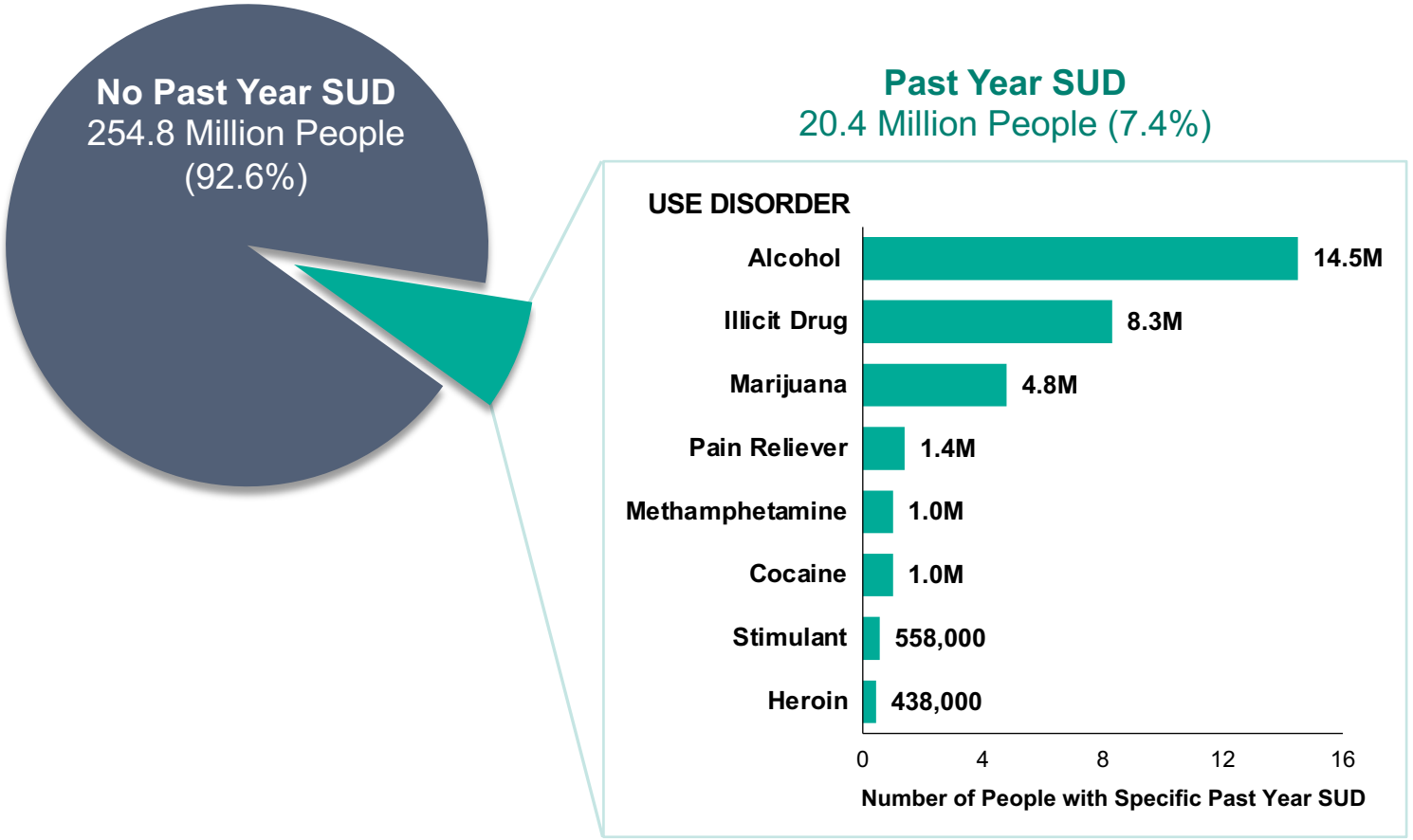
Substance Use Disorder Is Common and Overdose Deaths are Increasing

- **An estimated 20.4 million people in the US had a SUD in 2019[1]**
- **For the year ending in August 2020, provisional data from the Centers for Disease Control and Prevention show that overdose deaths have increased 26.8 percent compared to the previous 12 months, to more than 88,000 deaths[2]**
- **49% increase in psychostimulant overdose deaths in the year ending January 2021 in comparison to the year ending January 2020[3]**
- **11% of individuals 26 years of age or older with a substance use disorder received any substance use treatment in 2019[1]**
- **There are no pharmacological treatments approved for stimulant use disorder**

2019 SAMSHA National Survey on Drug Use and Health



1. Substance Abuse and Mental Health Services Administration. (2019). Results from the 2019 National Survey on Drug Use and Health: Detailed Tables. Rockville, MD: Center for Behavioral Health Statistics and Quality. https://www.samhsa.gov/data/ (Accessed Sep 2021). (https://store.samhsa.gov/system/files/nsduhffr2018.pdf); 2. https://www.federalregister.gov/documents/2021/04/28/2021-08961/practice-guidelines-for-the-administration-of-buprenorphine-for-treating-opioid-use-disorder (accessed Sep 2021) 3. CDC Provisional Overdose Death Counts. https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm. Accessed Aug, 2021

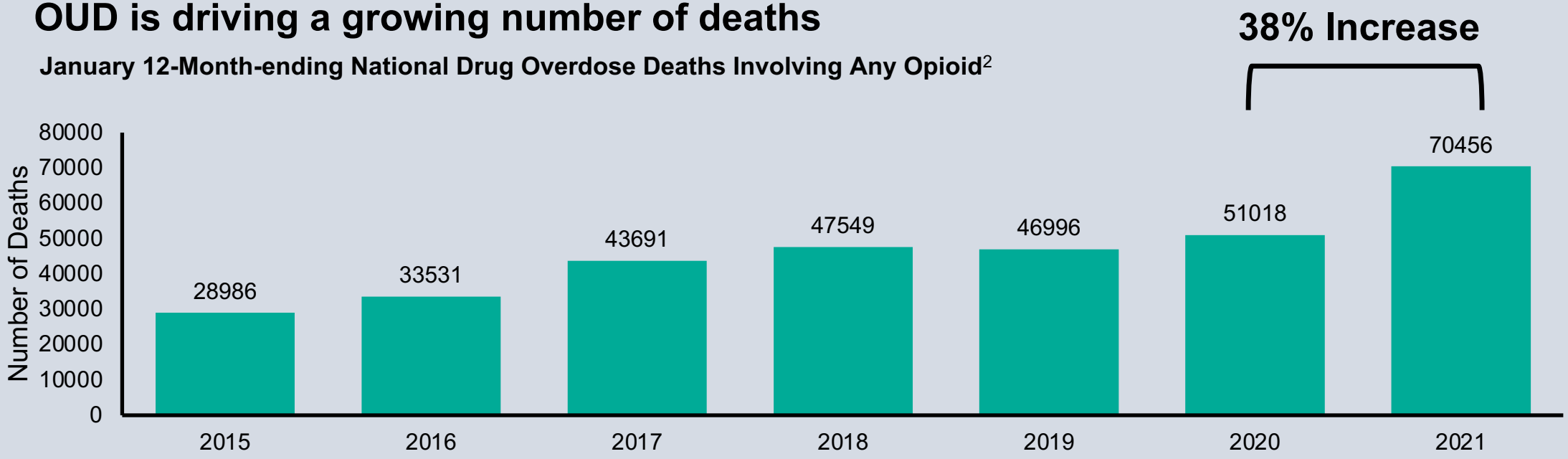
Opioid Use Disorder (OUD) Is An Ongoing Crisis

OUD is an increasingly common condition in the US:

- Approximately 2 million individuals in the US had an OUD in 2019[1]
- Opioid associated deaths increased by 38% in the year ending in January 2021 compared to the year ending in January 2020[2]

OUD is driving a growing number of deaths

January 12-Month-ending National Drug Overdose Deaths Involving Any Opioid[2]



1. Substance Abuse and Mental Health Services Administration. (2020). Key substance use and mental health indicators in the United States: Results from the 2019 National Survey on Drug Use and Health (HHS Publication No. PEP20-07-01-001, NSDUH Series H-55). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://samhsa.gov/data/. Accessed April 2020 2. CDC Provisional Overdose Death Counts. https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm. Accessed Aug, 2021

California faces a serious public health crisis with the opioid epidemic

California Quick Stats[1]

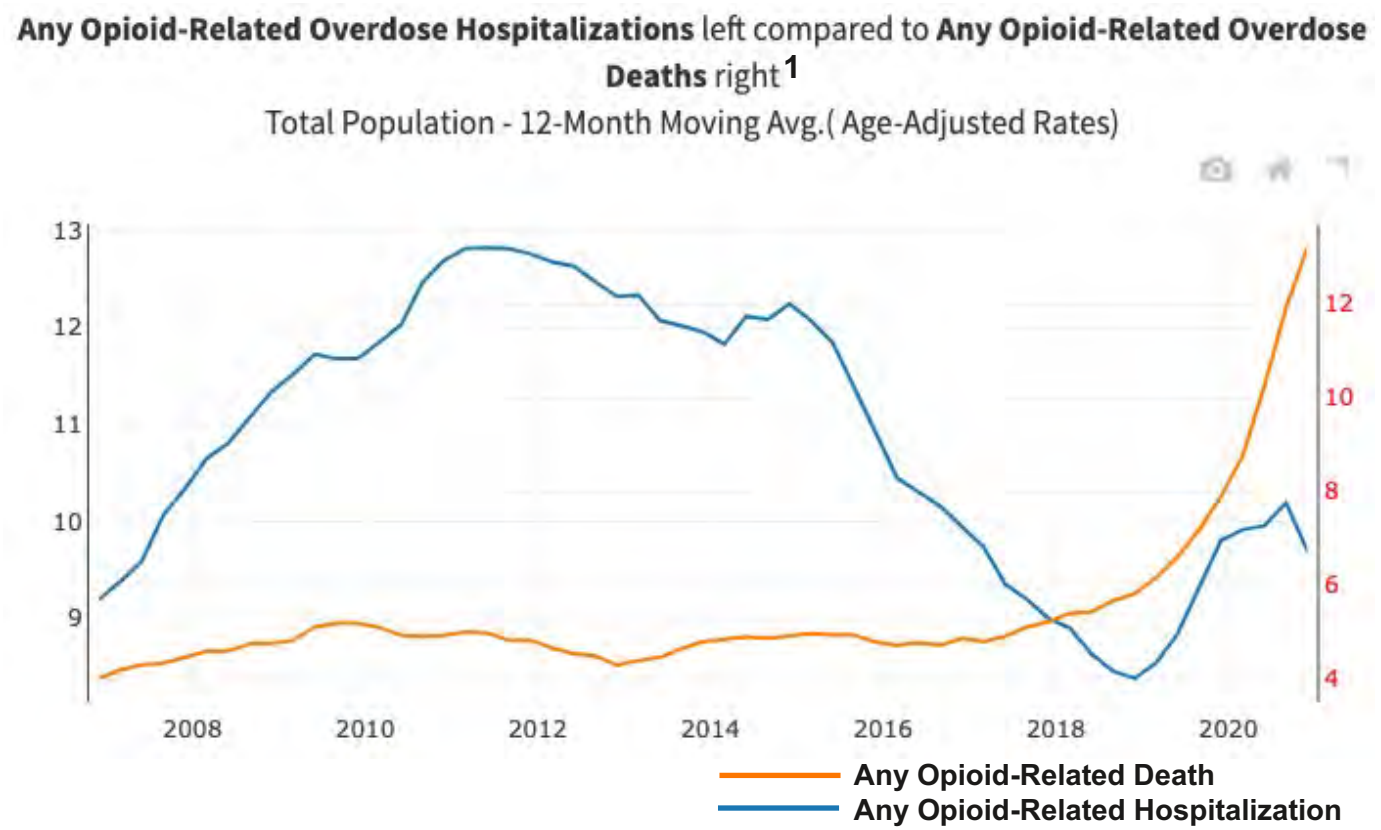
5,363*
Deaths Related to Any Opioid Overdose, 2020

3,857*
Deaths Related to Fentanyl Overdose, 2020

15,664
ED Visits Related to Any Opioid Overdose, 2020

14,867,426
Prescriptions for Opioids, 2020

*Preliminary death data



California's MAT Expansion Efforts

California has included evidence-based behavioral therapy as an integral component of its approach to medication assisted treatment (MAT) expansion[2]

1. California Opioid Surveillance Dashboard. https://skylab.cdph.ca.gov/ODdash/. Accessed Sep, 2021. 2. Ca.gov. https://www.cdph.ca.gov/Programs/CCDPHP/DCDIC/SACB/Pages/MAT-Expansion-Overview.aspx . Accessed Sep. 2021

Behavioral treatment approach landscape

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[2]

Community Reinforcement Approach (CRA):

- Focuses on managing behavior related to substance use, to help patients adopt a healthier lifestyle without alcohol or drug use[3]
- 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 use[4]

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

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

Contingency Management (CM) as a Behavioral Treatment Approach

What is Contingency Management?

Positive reinforcement system, in which, financial or non-financial incentives are provided contingent on performing behaviors consistent with treatment

Strong evidence base in stimulant and opioid use disorder

CM has a broad evidence base and support from systematic meta-analyses:

- An analysis of studies using guideline recommended psychosocial interventions for stimulant use disorder found contingency management to be the only intervention associated with a significant reduction in stimulant use[1]
- CM was associated with a medium-large effect size in promoting abstinence from opioid use and medication adherence in treatment as usual controlled trials[2]

Challenges to Implementation

Scaling of CM to the broad treatment community has been challenged by lack of resources and restrictive legislation

- Delivery of CM rewards is resource intensive in community treatment clinics
- Centers for Medicare and Medicaid Services have been reluctant to allow Medicare funds to be used for CM
  - California is seeking to include CM services as a benefit under Medi-Cal in SB-110[3]

1. De Crescenzo et al. Comparative efficacy and acceptability of psychosocial interventions for individuals with cocaine and amphetamine addiction: a systematic review and network meta-analysis. PLoS Med. 2018;15(12). 2. Bolivar et al. Contingency Management for Patients Receiving Medication for Opioid Use Disorder: A Systemic Review and Meta-analysis. JAMA Psychiatry. 2021. 3. https://leginfo.legislature.ca.gov/faces/billTextClient.xhtml?bill_id=202120220SB110

PDTs For The Treatment Of SUD/OUD

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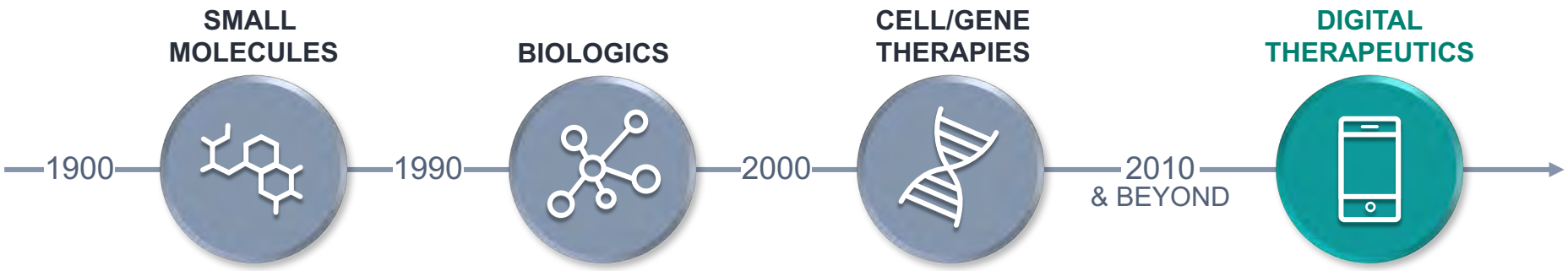
Prescription Digital Therapeutics (PDTs) Are a New Class of Therapies That Treat Serious Diseases



- PDTs meet regulatory requirements related to clinical data for safety and effectiveness and require FDA authorization
- PDTs have the potential to safely expand access to evidence-based therapies, which is highly relevant in the context of limited access to clinicians
- Mental health and wellness apps do not require FDA authorization for use:
  - Lack peer-reviewed evidence of feasibility or efficacy; only 2% supported by original publications[1]
  - Have a median 15-day and 30-day retention rate of 3.9% and 3.3%, respectively[2]

The presentation contains information regarding unapproved uses of a PDT, reSET-O. FDA has not found reSET-O safe or effective for abstinence or for prescriptions beyond the first 12 weeks.

1. Lau N, et al *JMIR Mhealth Uhealth* 2020;8(5); 2. Baumel A, et al. *J Med Internet Res.* 2019;21(9).

reSET and reSET-O are PDTs That Deliver Treatment for Substance Use Disorder and Opioid Use Disorder

reSET Product Description

- reSET® is intended to provide cognitive behavioral therapy, as an adjunct to a contingency management system, for patients ≥18 years of age enrolled in outpatient treatment for substance use disorder (SUD) under the supervision of a clinician
- Based on the Therapeutic Education System (TES)
- Comprised of 61 interactive modules: 31 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 relevant to patients with SUD

reSET-O Product Description

- 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 of age who are currently under the supervision of a clinician.
- 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 relevant to patients with OUD
- Voluntary buprenorphine check-in feature to support buprenorphine use

reSET and reSET-O Clinician Directions for Use. Pear Therapeutics. 2020

reSET and reSET-O Mechanisms of Action: Digital Delivery of Evidence-based Treatment

Community Reinforcement Approach (CRA)[1,2,3]

- A comprehensive CBT package that a special focus on helping people Substance Use Disorders (SUDs) discover and adopt pleasurable and healthy lifestyles that are more rewarding than using alcohol or drugs
- CRA is among the most strongly supported behavioral therapies for SUDs and has been effective in treatment across a variety of different substances of abuse

Fluency Training[4]

- Individually-paced presentation of content and testing to facilitate and confirm mastery of learning
- Demonstrated to promote learning and improve both short-term and long-term retention of material

Contingency Management (CM)[5,6]

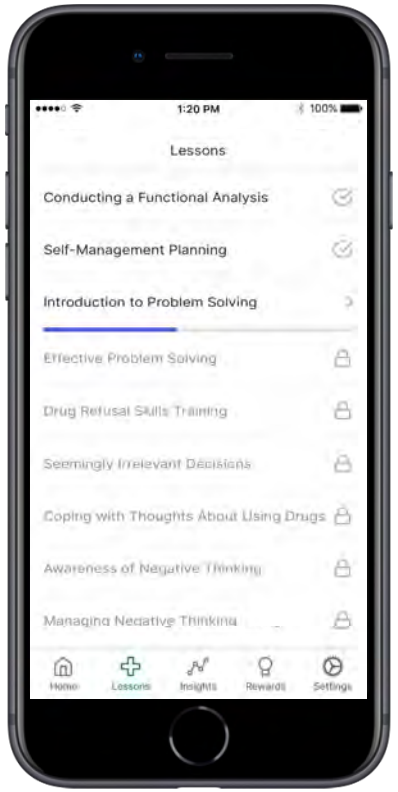
- Evidence-based positive reinforcement system, in which, financial or non-financial incentives are provided contingent on performing behaviors consistent with treatment
- Efficacy of Contingency Management has been demonstrated across a wide range of SUDs

1. Roozen et al. A systematic review of the effectiveness of the community reinforcement approach in alcohol, cocaine and opioid addiction. *Drug Alcohol Depend.* 2004;Apr 9;74(1):1-13. 2. Roozen et al. Contingency management for treatment of substance use disorders: A meta-analysis. *Addiction.* 2006;101(11):1546-1560. 3. Meyers et al. The community reinforcement approach: an update of the evidence. *Alcohol Res Health.* 2011;33(4):380-388; 4. Binder C. Behavioral Fluency: Evolution of a New Paradigm. *Behav Anal.* 1996;19(2):163-197. 5. Stitzer et al. Contingency management: utility in the treatment of drug abuse disorders. *Clin Pharmacol Ther.* 2008;83(4):644-647. 6. Kirby et al. Contingency management works, clients like it, and it is cost-effective. *Am J Drug Alcohol Abuse.* 2016;1-4.

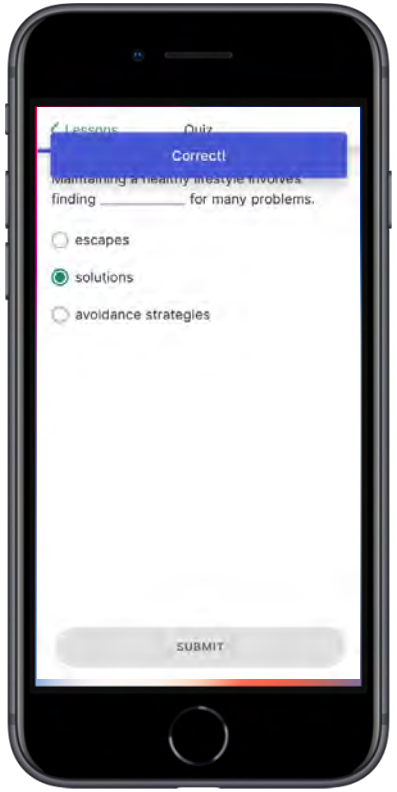
reSET and reSET-O Mechanisms of Action

reSET and reSET-O Have Three Primary Mechanisms of Action

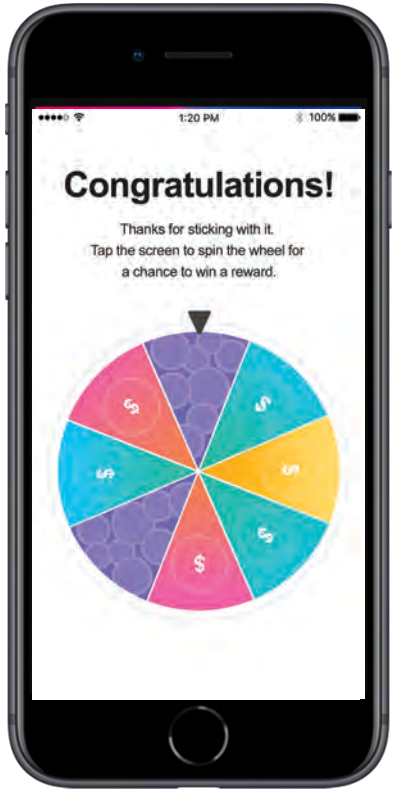
Community Reinforcement Approach (CRA) Lessons



Fluency Training



Contingency Management (CM)



reSET® Clinical Data | Pivotal Trial Summary

Pivotal Trial Overview[1]

399 patients with SUD (alcohol, cannabis, cocaine, stimulants) received either:

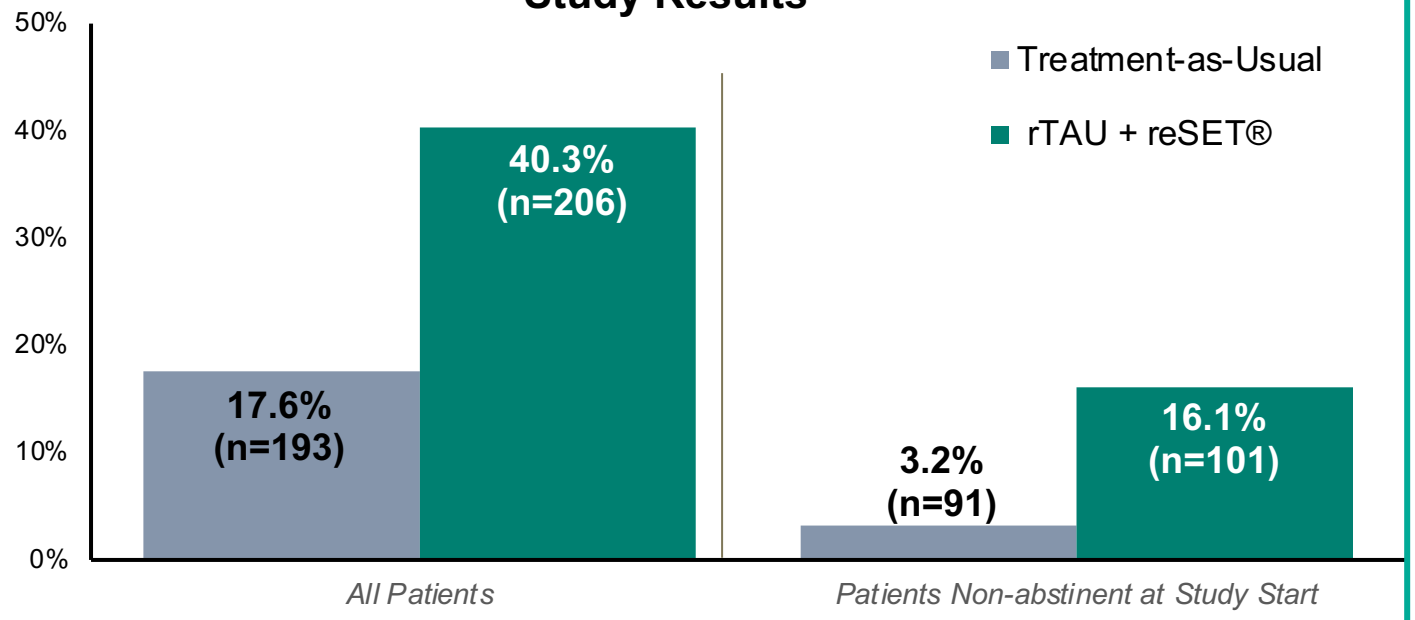
- Treatment-as-Usual **(TAU)**, consisting of intensive face-to-face therapy
- Reduced TAU and reSET (**rTAU+ reSET®**) for 12 weeks[1]

Patients provided urine samples twice per week to objectively monitor abstinence

Co-primary study endpoints

- Abstinence in weeks 9-12
- Retention in treatment

Study Results[2]



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

1. Campbell et al. Internet-delivered treatment for substance abuse: a multisite randomized controlled trial. American Journal of Psychiatry. 2014. 171(6):683-690.2. Pear Internal data and Pear regulatory submission. DEN160018

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 + buprenorphine[1] 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.

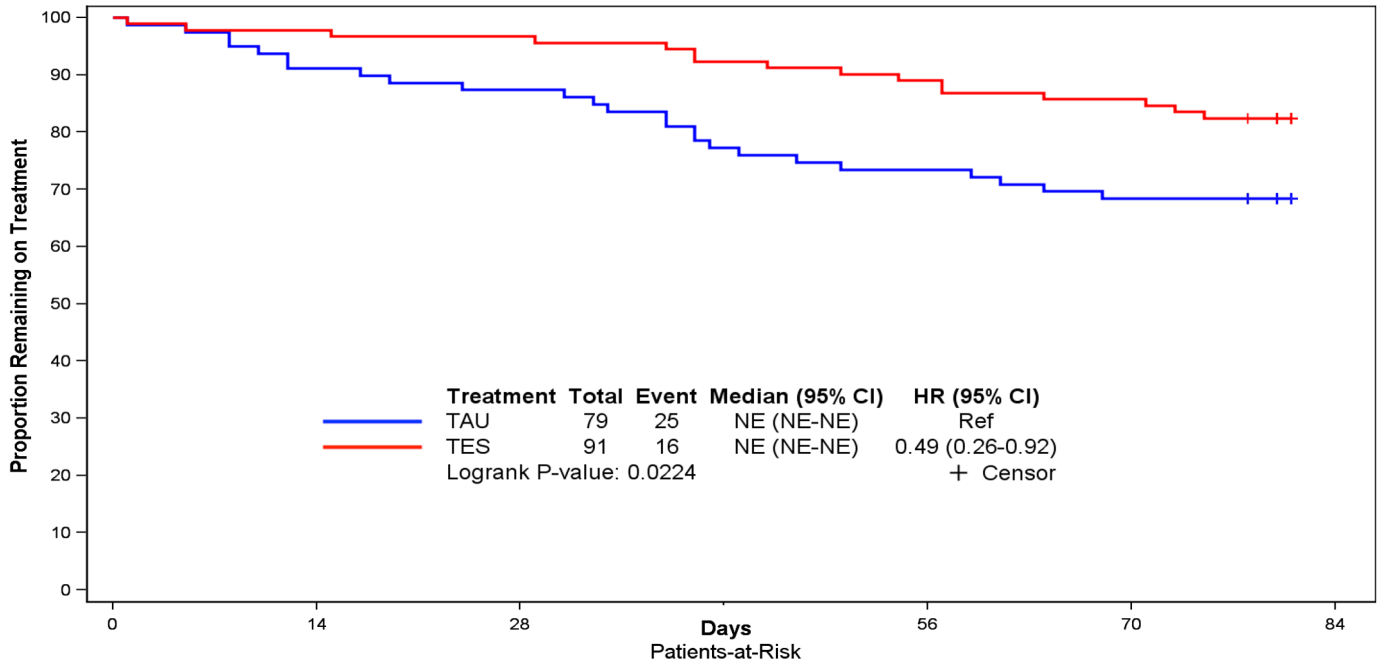
Patients provided urine samples 3x per week to objectively monitor abstinence.

Co-primary endpoint analysis[2]

- Abstinence/Negative urine drug screens in weeks 9-12
- Retention in treatment

Study Results[1]

Retention in Treatment



	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**

1. 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. doi:10.1037/a0037496., and Pear regulatory submission. DEN160018hcf, and reSET-O Clinician Directions for Use. Boston, MA: Pear Therapeutics, Inc; 2020

Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder

Maricich Y, Gerwien R, Kuo A, Malone D, Velez F. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*
https://doi.org/10.1080/21548331.2021.1974243

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Intended Use[1] and Important Safety Information

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. reSET-O is indicated as a prescription-only digital therapeutic.

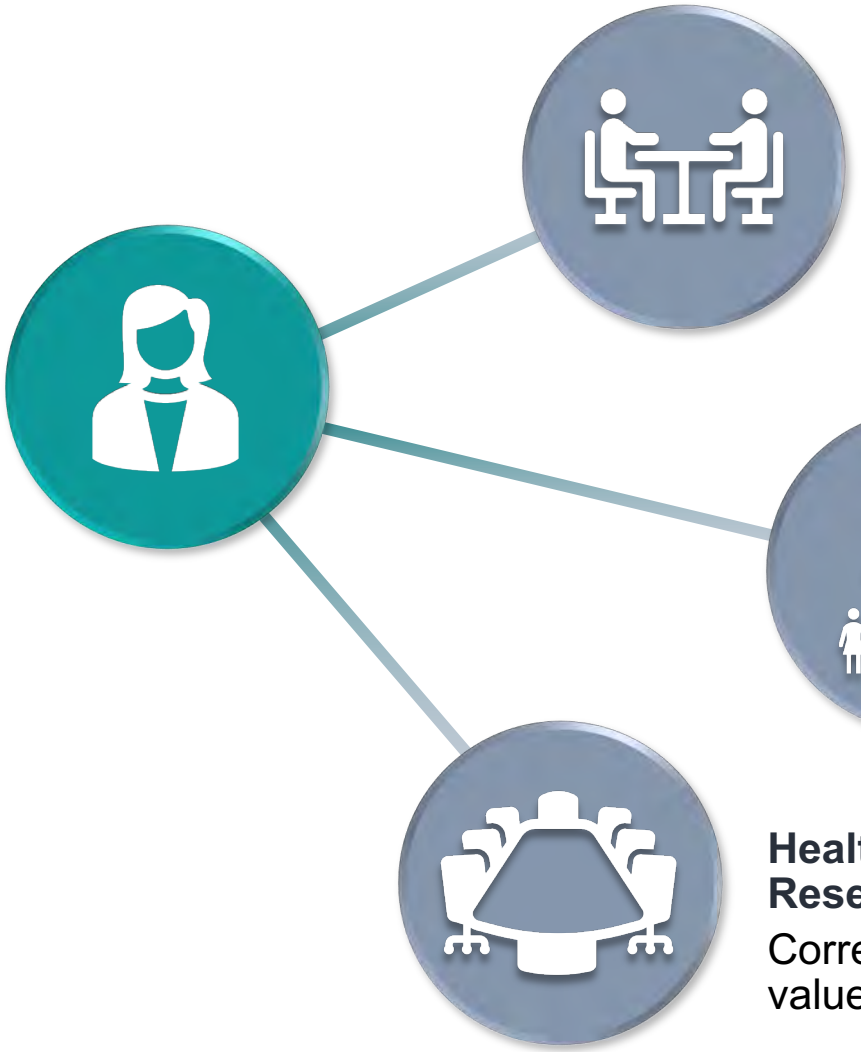
IMPORTANT SAFETY INFORMATION

The duration of the prescription is 12 weeks (84 days). Additional 12-week (84 day) access intervals to the reSET-O prescription digital therapeutic may benefit patients, as OUD is a chronic disease; however, the benefits of prescription extension have not been evaluated.

1. reSET-O Clinician Directions for Use. Pear Therapeutics. 2020

Background and Objectives

A Continuum of Evidence for reSET-O to Support Clinical Use, Policy and Decision Making



Randomized Clinical Trials (RCTs)

Demonstrate gold-standard scientific validity using objective endpoints

Real-World Evidence (RWE)

Confirm generalizability & external validity of RCTs in broad real-world use

Health Economics and Outcomes Research (HEOR)

Correlate economic outcomes with clinical value to support providers and payers

Objectives

Evaluate patient engagement with the PDT as well as rates of opioid use and retention among a geographically diverse population of patients prescribed a second prescription and treated for 24 weeks[1]

The duration of a reSET-O prescription is 12 weeks (84 days). Some providers may opt to prescribe additional 12-week (84 day) access intervals to the reSET-O prescription digital therapeutic, as opioid use disorder is a chronic disease; however, the benefits of prescription extension have not been evaluated.

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

reSET-O Clinician Directions for Use. Pear Therapeutics. 2020

Methods

Population and Data Collection

- Real-world observational evaluation of population who accessed first and subsequent reSET-O prescriptions and completed at least one lesson
  - Under the care of clinicians across 12 states
  - Prescribed reSET-O by their clinician as part of their overall standard of care
    - Completed first prescription between 1/1/2019 and 12/31/2020
  - Broad range of treatment settings and organizations
  - All patients were diagnosed with OUD and were being treated with buprenorphine MOUD at clinician determined doses, routes of administration, and regimens
  - The dose, or unit of treatment, is a module or therapy lesson, with patients instructed to complete four per week
  - Patient interaction with the PDT and other therapeutic use data (de-identified and patient consented via terms of service agreement) were collected and analyzed
  - Substance use was evaluated as a composite of patient self-reports recorded via the PDT, and in clinic urine drug screens (UDS) that were recorded by clinicians

Health Care Resource Utilization (HCRU)

- A retrospective analysis of health insurance claims (HealthVerity PrivateSource 20 claims database) was performed to assess the impact of PDT use among patients who completed a single (12 week) prescription vs. those who completed a second (24 week) prescription

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

Endpoints

Primary Endpoint

- Abstinence over the final 4 weeks of the 12-week reSET-O prescription (weeks 9-12)
  - Defined as no positive urine drug screen (UDS) and/or self-reported use last 4 weeks

Secondary Endpoint

- Treatment Responder Rate
  - Defined as patients with ≥ 80% negative UDS and/or self-reported opioid non-use over the 12-week reSET-O prescription
  - Patients were pushed a self-report assessment every 4 days, but are not required to complete the assessment

Additional Endpoints

- Engagement and use of reSET-O
  - Module completion, active days, activity by week, etc.
  - Activity was defined as patient use of any PDT feature on a given day
- Retention over the last 4 weeks of the 12-week reSET-O prescription (weeks 9-12)
  - Defined as any patient activity in the digital therapeutic over the last 4-weeks of treatment
- Association of abstinence/opioid use and retention outcomes with early therapeutic use (weeks 1-4)

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

Primary Endpoint: Abstinence

- For purposes of the evaluation of the outcome of abstinence in this RWE analysis, abstinence was defined using the endpoints of urine drug screen (UDS) and/or self report, under the approach defined below. As real-world-data, there was no defined schedule for collecting UDS. UDS was collected and entered at the discretion of the clinician. Self-report was collected via pushed assessment in reSET-O.
- Primary Endpoint: Abstinence over the final 4 weeks of the 12-week reSET-O prescription (weeks 9-12) assessed using two imputation methods is reported[1]

Imputation Method

Missing Data Positive	Missing Data Removed
For weeks 9-12: Patients without any data (UDS or self-reports) over the final four weeks of reSET-O prescription assumed non-abstinent/positive in analysis	**For weeks 9-12:** Patients without any data (UDS or self-reports) over the final four weeks of reSET-O prescription removed from analysis population

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

Health Care Resource Utilization

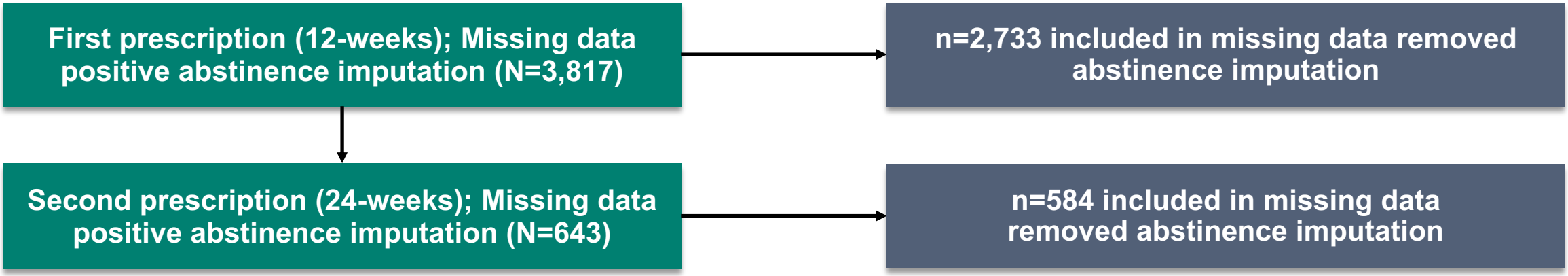
- A retrospective analysis of health insurance claims (HealthVerity PrivateSource 20 claims database) was performed to assess the impact of PDT use among patients who completed a single (12 week) prescription vs. those who completed a second (24 week) prescription
- Evaluated incidence of unique hospital encounters including emergency department, observation, inpatient, intensive care unit, and partial hospitalizations over 9 months following the initiation of the first prescription (index date)
- Incidence and incidence rate ratios were evaluated from a negative binomial model of encounters, with an offset for the number of days in the post-index period and adjusted for age, gender, and pre-index unique hospital encounters
- Minimum of 12 weeks continuous eligibility was required

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

Results

A Large All-comer Population Produced Evaluable Data from First and Second Prescriptions

Real-world observational evaluation of a population that completed at least one lesson of first, and subsequent reSET-O prescriptions

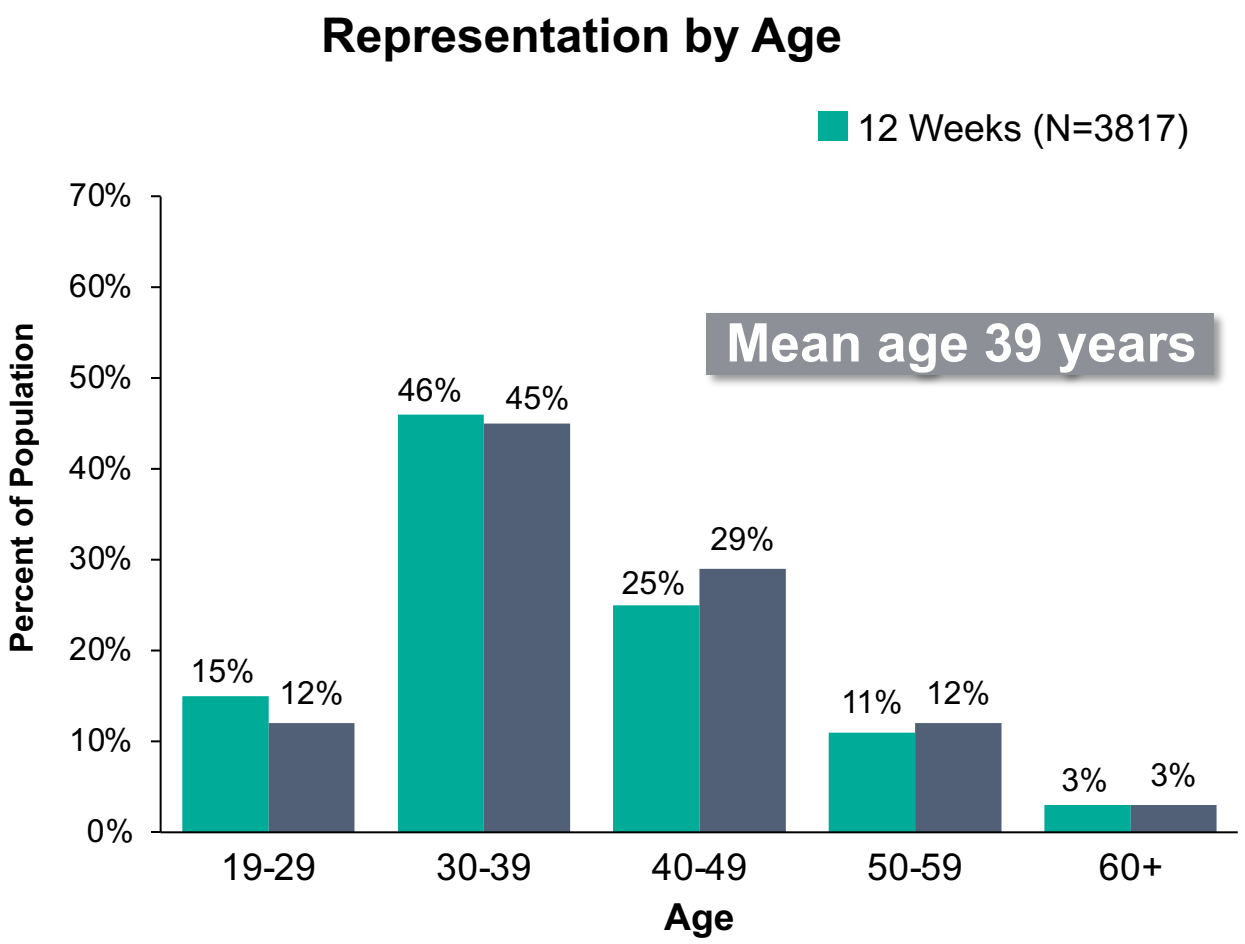


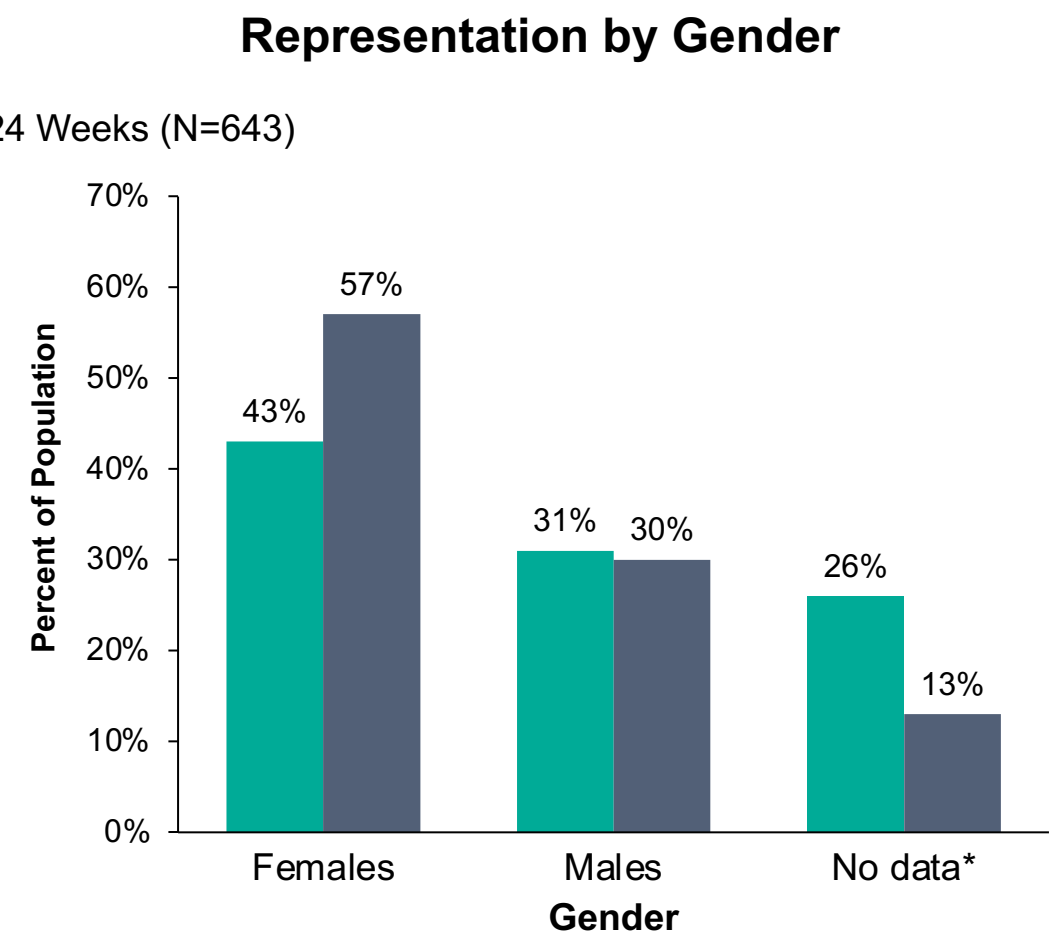
Patients available for health care resource utilization analysis

- ≥12 weeks of pharmacy enrollment before and after the index date (1/1/2019-12/8/2019): N = 424
- Patients with only 1 prescription: N=324
- Patients with only 2 prescriptions: N=103

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

Patients Were Represented Across Age Groups and Gender

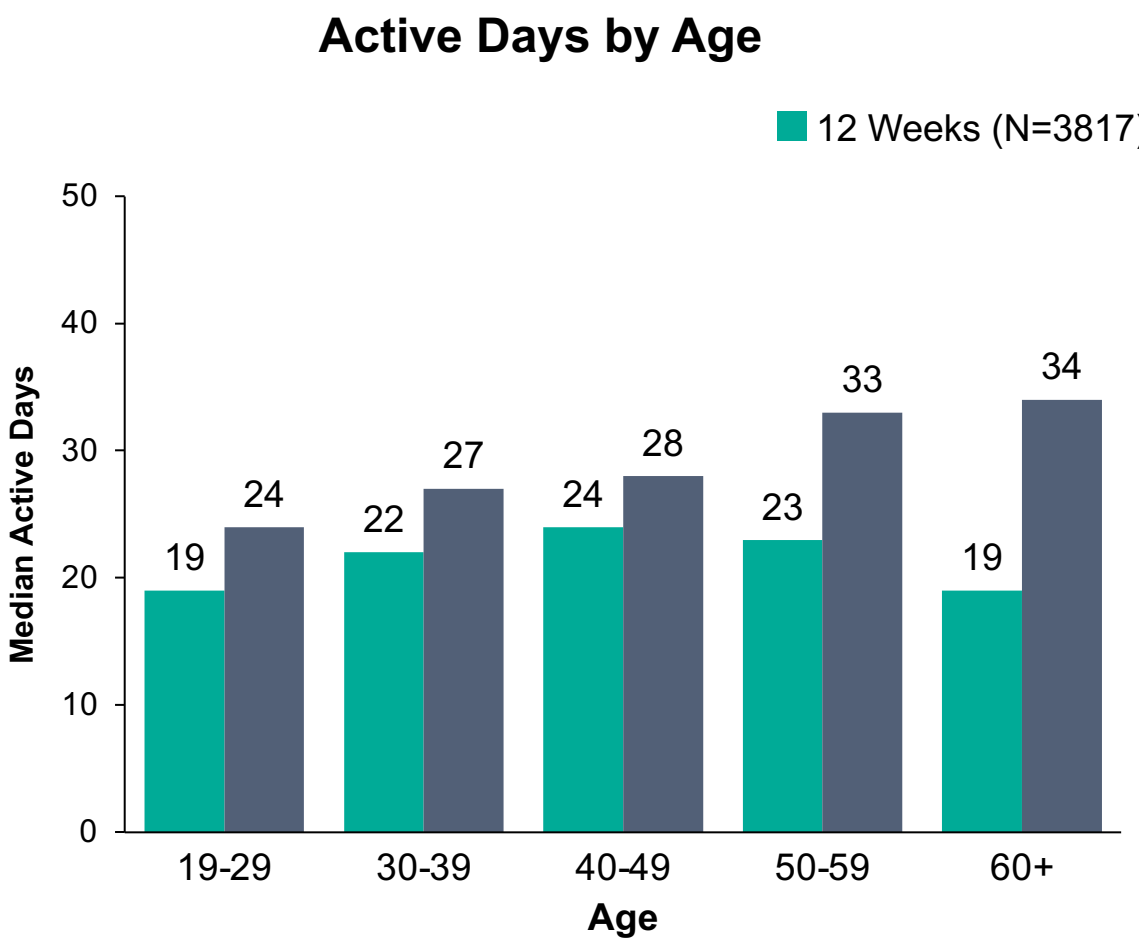


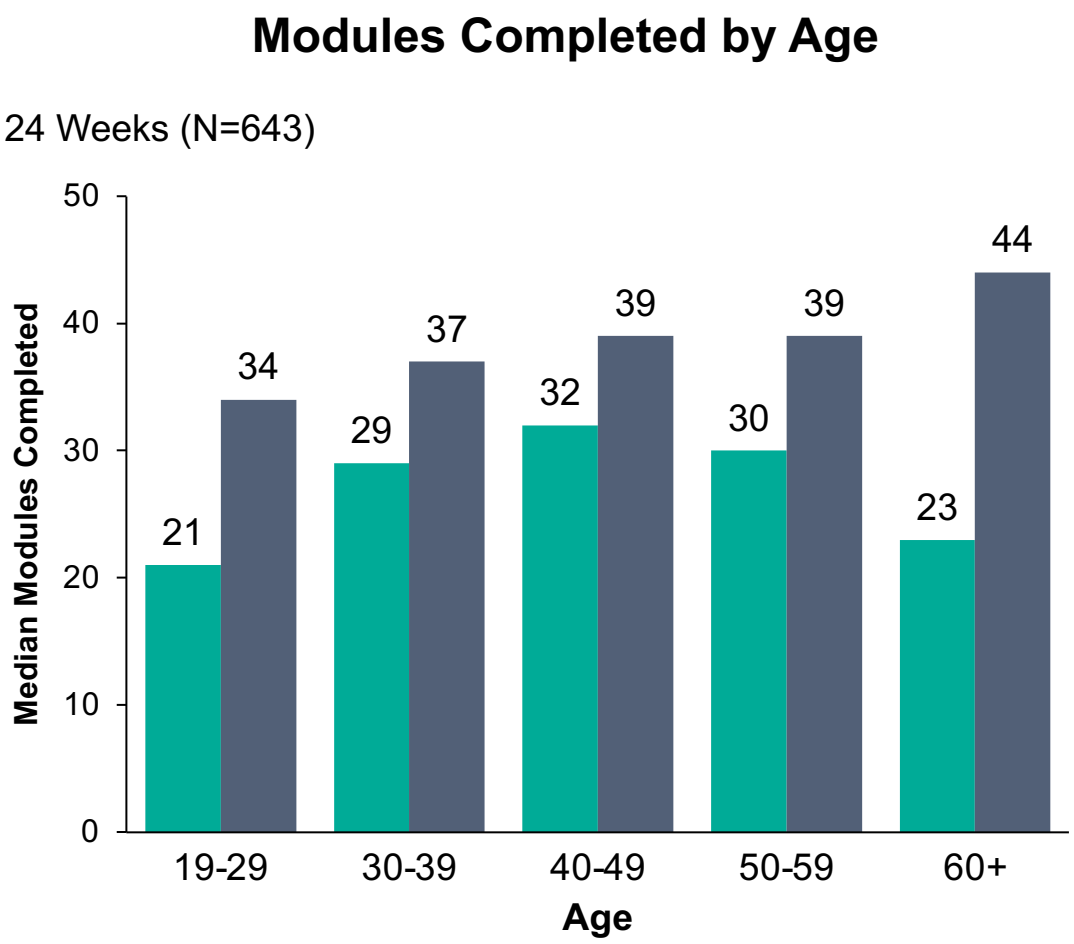


*Proportion of population that did not provide data on gender.

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

Activity and Module Completion Across Age Categories

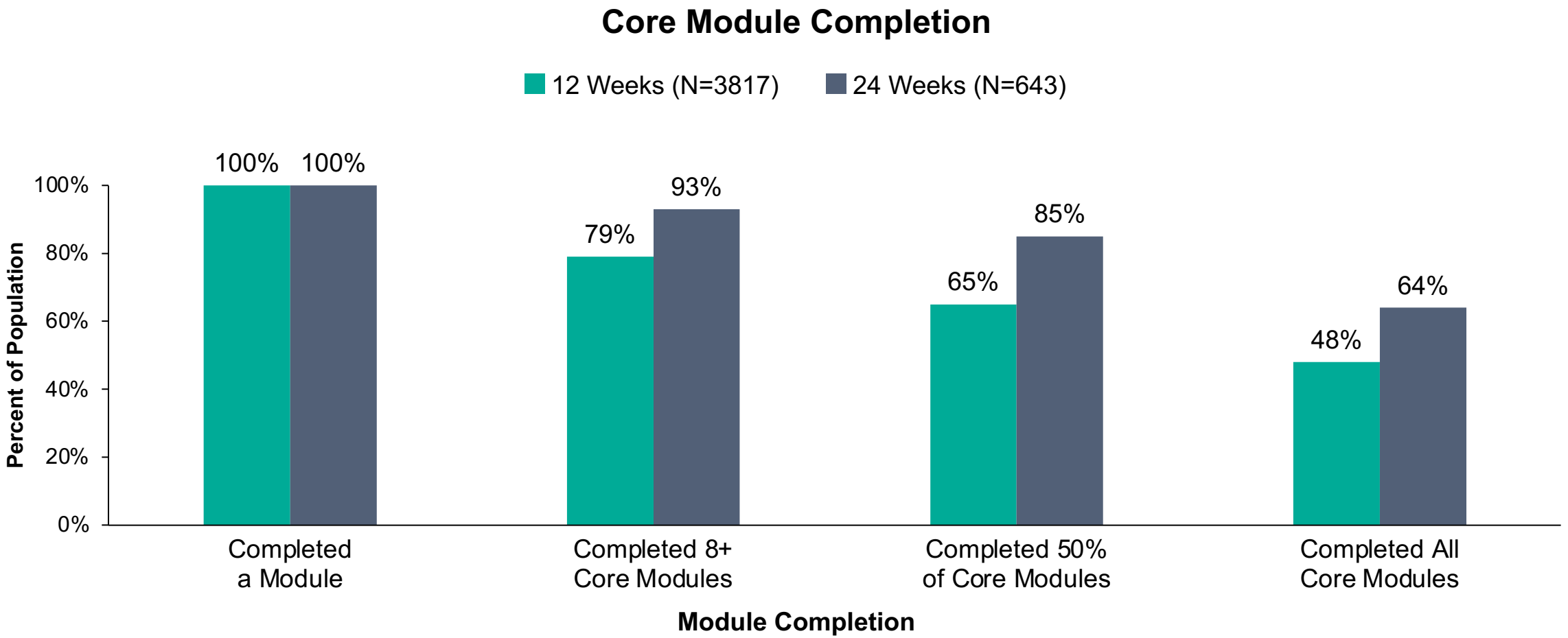




Activity was defined as patient use of any PDT feature on a given day

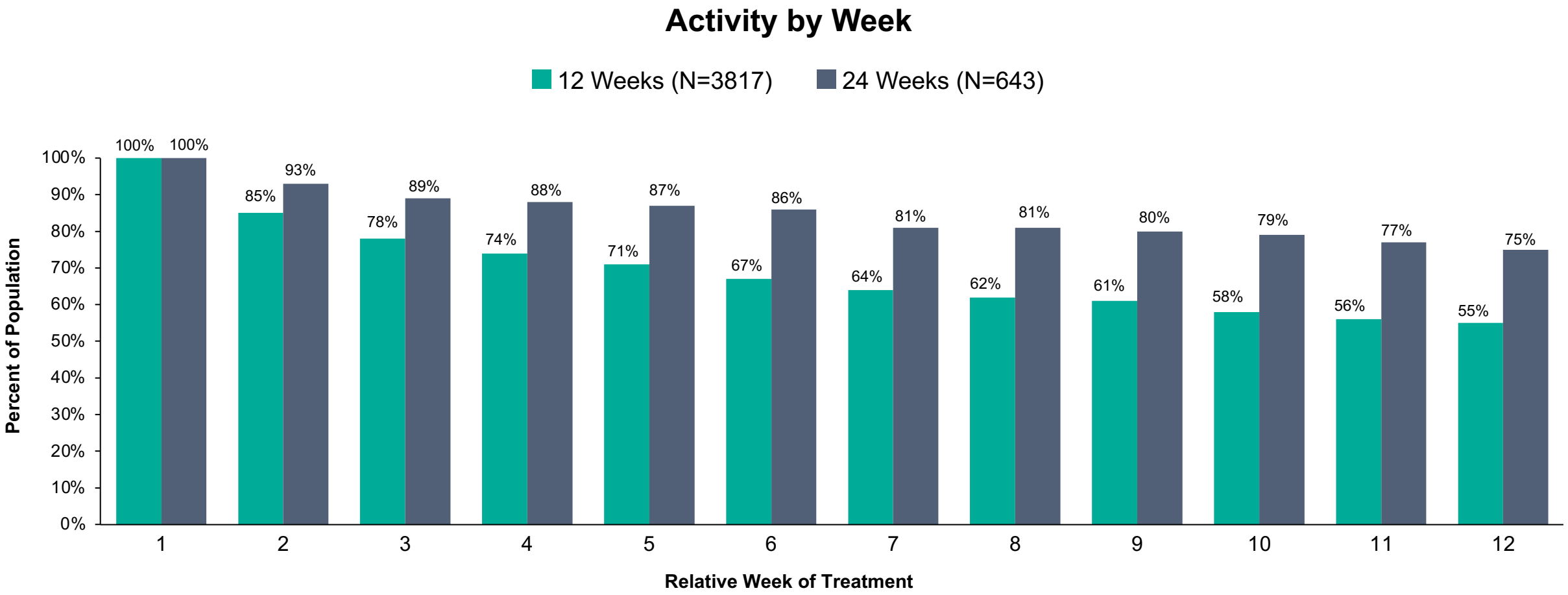
1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

A Majority of Patients Completed at Least Half of Core Modules in First and Subsequent Prescriptions



1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

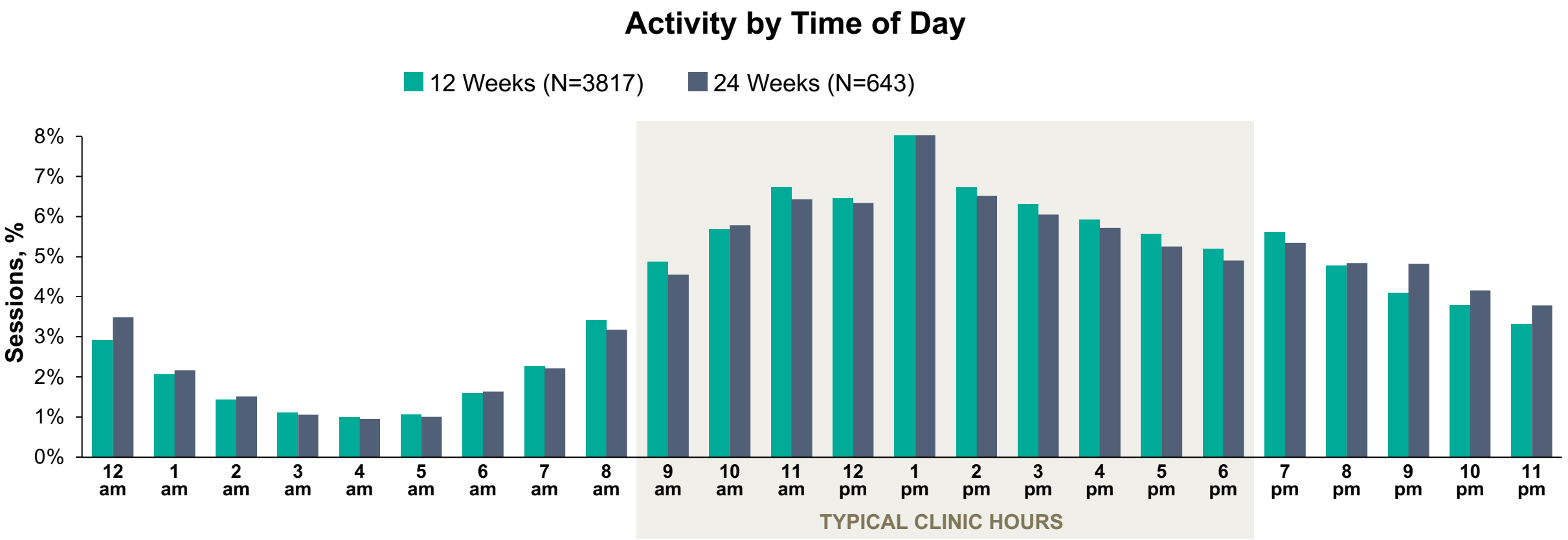
A Majority of Patients Remain Active in reSET-O Through Week 12 of First and Second Prescriptions



Activity was defined as patient use of any PDT feature on a given day

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

Patients are active in reSET-O Throughout the Full 24-hour Period



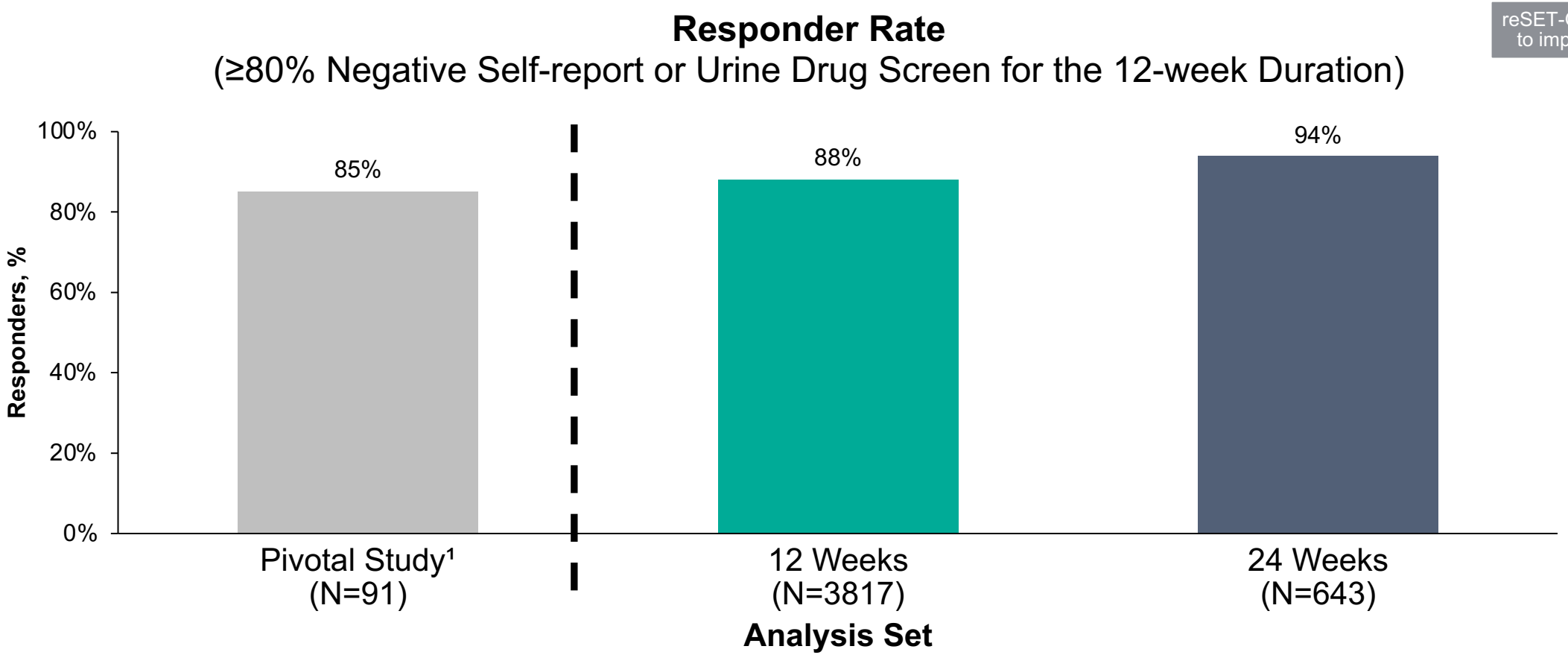
- In each cohort approximately 60% of activity occurred during typical clinic hours
- Approximately 40% of activity occurred when treatment may be otherwise unavailable

Activity was defined as patient use of any PDT feature on a given day

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

Responder Rate of Greater than 80% was Observed in the First and Second Prescription

reSET-O is not authorized to improve abstinence.



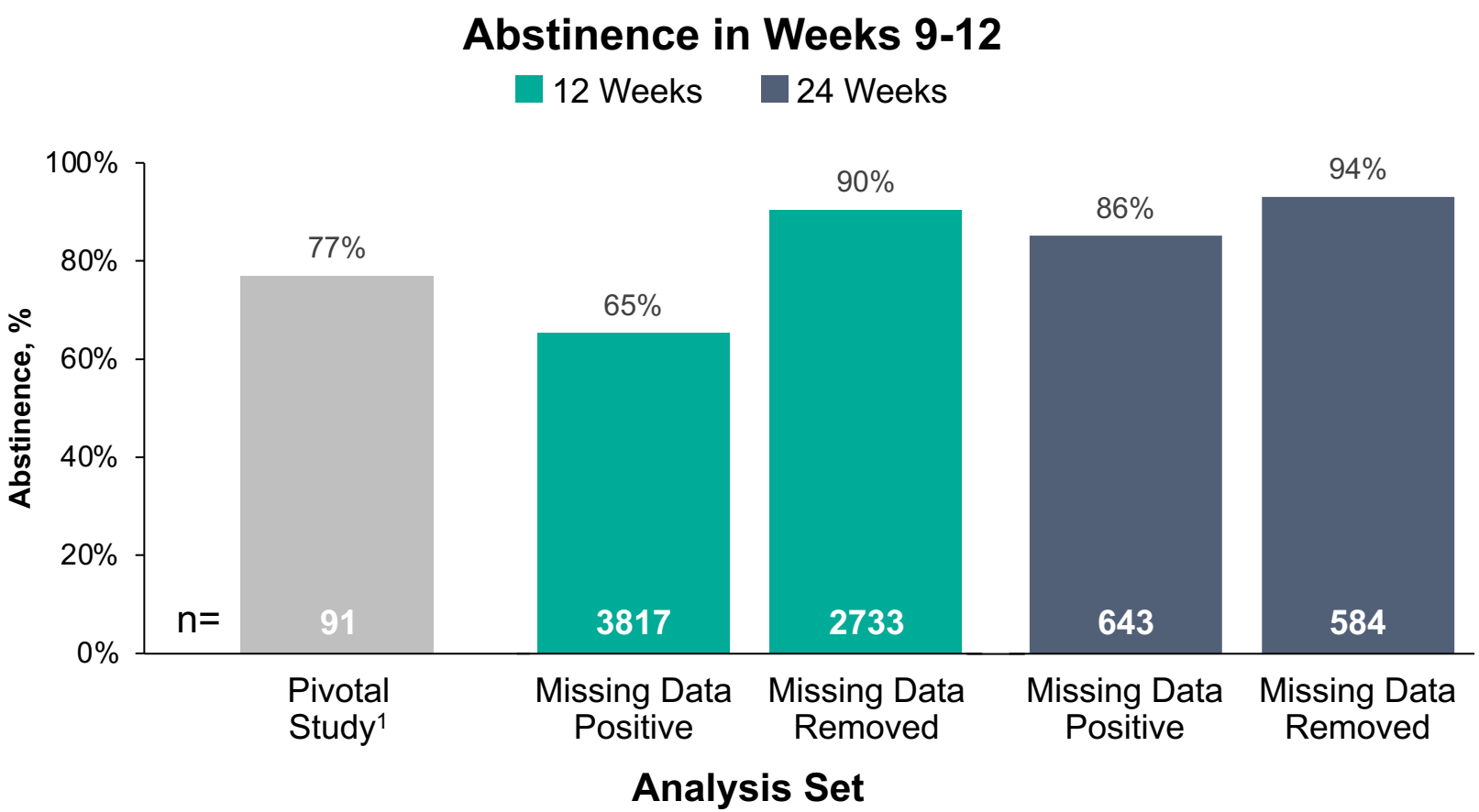
Responder Rate for each group defined as:
Pivotal Study: ≥80% negative UDS and/or self-reported non-use across the 12-week pivotal study
RWE: ≥ 80% negative UDS and/or self-reported non-use over the 12-week reSET-O prescription

Patients are pushed a self report assessment every 4 days, but are not required to complete the assessment

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

High Rates of Abstinence Were Observed in the First and Second Prescription

reSET-O is not authorized to improve abstinence.



Analyses of "Abstinence" for each group:

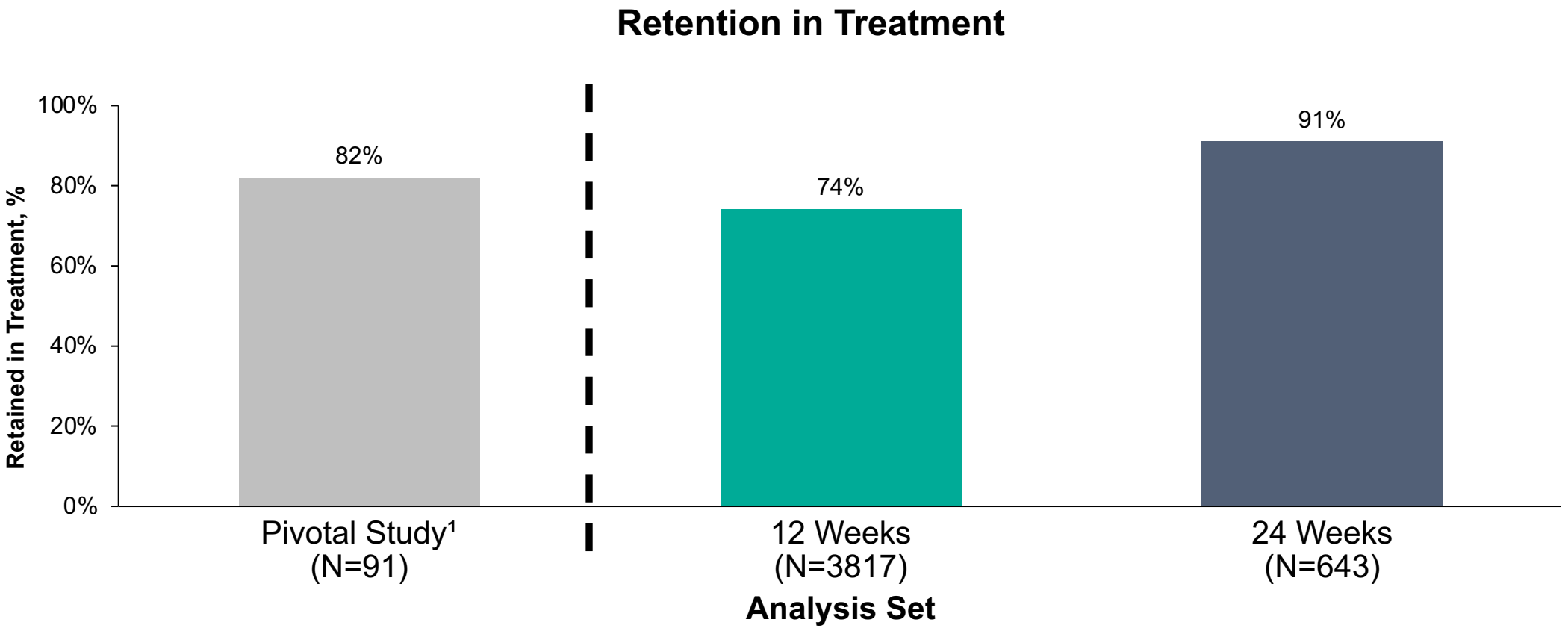
Pivotal Study: Urine drug screen (UDS) for opioids collected 3 days per week over the final four study weeks (weeks 9-12), patients who missed samples assumed positive;

Missing Data Positive: No positive UDS and/or self-reported use over the final 4 weeks of the 12-week reSET-O prescription (weeks 9-12); Patients without any data (UDS or self-reports) over the final four weeks assumed non-abstinent/positive in analysis

Missing Data Removed: No positive UDS and/or self-reported use over the final 4 weeks of the 12-week reSET-O prescription (weeks 9-12); Patients without any data (UDS or self-reports) over the final four weeks removed from analysis population

1. Maricich YA, et al. *Current Medical Research and Opinion*.2020;1-9; 1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

A Majority of Patients Were Retained in Treatment in the First and Subsequent Prescriptions



Retention Rate for each group defined as:

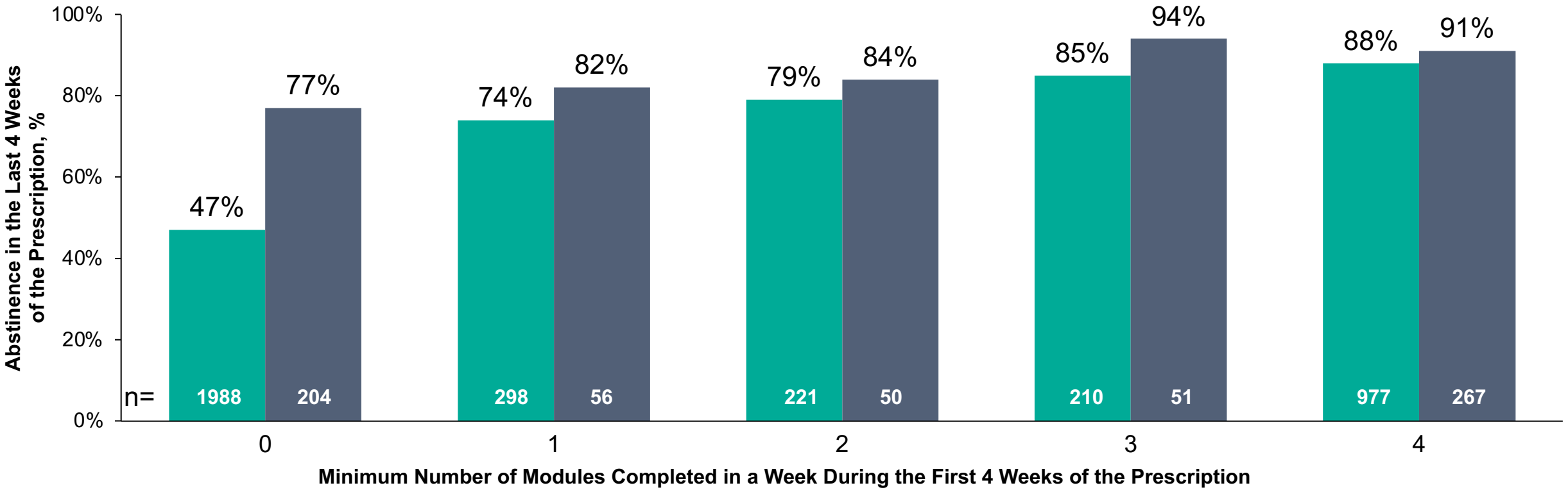
Pivotal Study: Patients remaining in treatment at 12 week study end

RWE: Any patient activity within the digital therapeutic during the last 4-weeks of the prescription

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

Module completion during the first four weeks and abstinence during the last four weeks of the prescription

reSET-O is not authorized to improve abstinence.

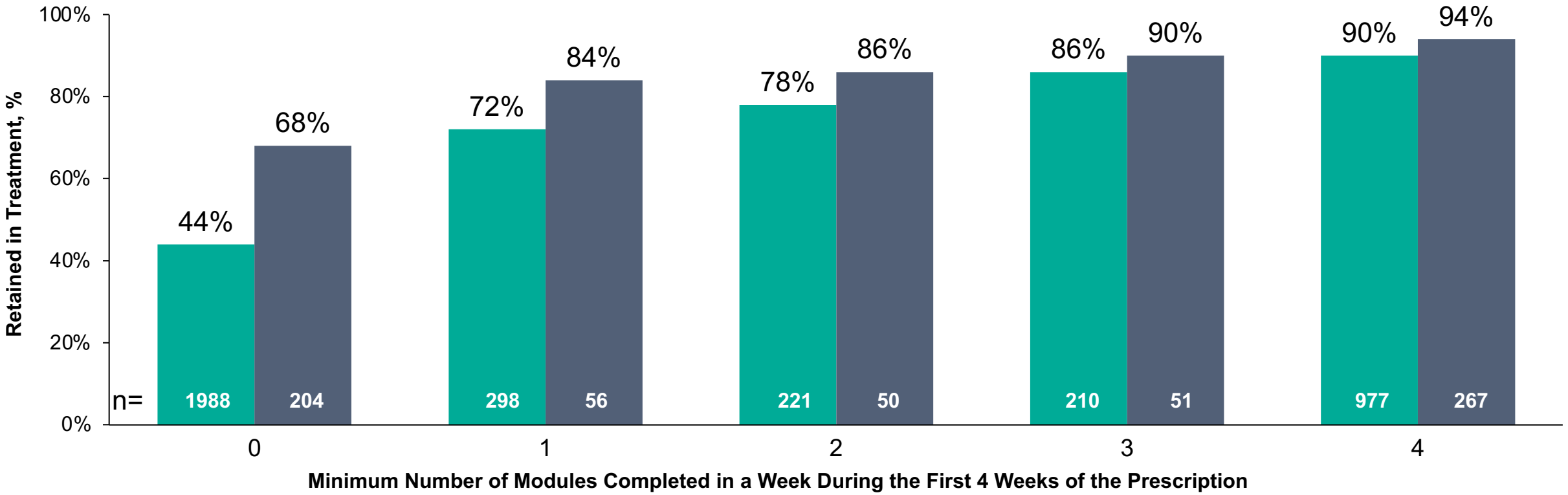


Analyses of "abstinence" conducted with the missing data positive imputation in those completing up to the recommended dose (4 lessons) of therapy in the first 4 weeks of treatment.
Minimum number of modules completed represents the lowest number of lessons a patient completed in a week during weeks 1-4 of the prescription.

Missing Data Positive: No positive urine drug screen (UDS) and/or self-reported use over the final 4 weeks of the 12-week reSET-O prescription (weeks 9-12); Patients without any data (UDS or self-reports) over the final four weeks assumed non-abstinent/positive in analysis

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

Module Completion During The First Four Weeks And Retention During The Last Four Weeks Of The Prescription



Retention Rate in those completing up to the recommended dose (4 lessons) of therapy in the first 4 weeks of treatment.

Minimum number of modules completed represents the lowest number of lessons a patient completed in a week during weeks 1-4 of the prescription.

Retention defined as any patient activity within the digital therapeutic during the last 4-weeks of treatment.

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

Incidence of Unique Hospital Encounters Was Observed to be Lower in Patients With a Second reSET-O Prescription

Unique Hospital Encounters

- Inpatient stays
- ICU stays
- Emergency department visits
- Partial hospitalizations
- Observation visits

	reSET-O	
	1 Script (n=324)	2 Scripts (n=103)
Incidence Rate (95% CI)	0.63 (0.49, 0.80)	0.46 (0.29, 0.73)
% Reduction	Reference	27%

FDA has not found reSET-O® safe or effective for prescriptions beyond the first 12 weeks
reSET-O® has not been shown to impact patient and health system costs in prospective, randomized, clinical trials

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

Limitations and Conclusions

Limitations

- Evaluation of real-world data is collected in an environment that is not as stringently controlled as a randomized controlled trial derived data
- Data is derived from a mixed population of patients who were at various stages of treatment
- Abstinence outcomes are based on composite of patient self-reports and/or objective urine drug screens (UDS)
- Activity in the application may not reflect full engagement with the therapeutic content of reSET-O

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

Conclusions

reSET-O is not authorized to improve abstinence.

First published data on real-world clinical outcomes over a 24-week period:

- Patients with opioid use disorder had higher engagement with a second prescription of a PDT in comparison to patients with first prescription
- Patients with 24 weeks of reSET-O treatment showed durable and high levels of self-reported abstinence and treatment retention
- Patients with 24 weeks of reSET-O treatment had a lower rate of unique hospital encounters compared to those treated for 12 weeks

1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. https://doi.org/10.1080/21548331.2021.1974243

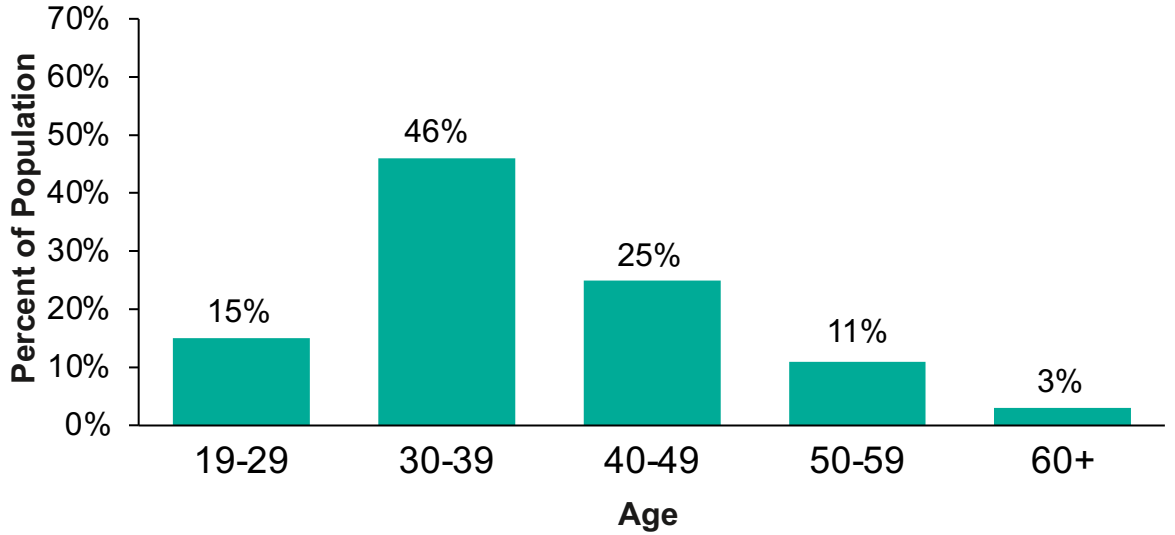
Therapeutic use of reSET-O in California

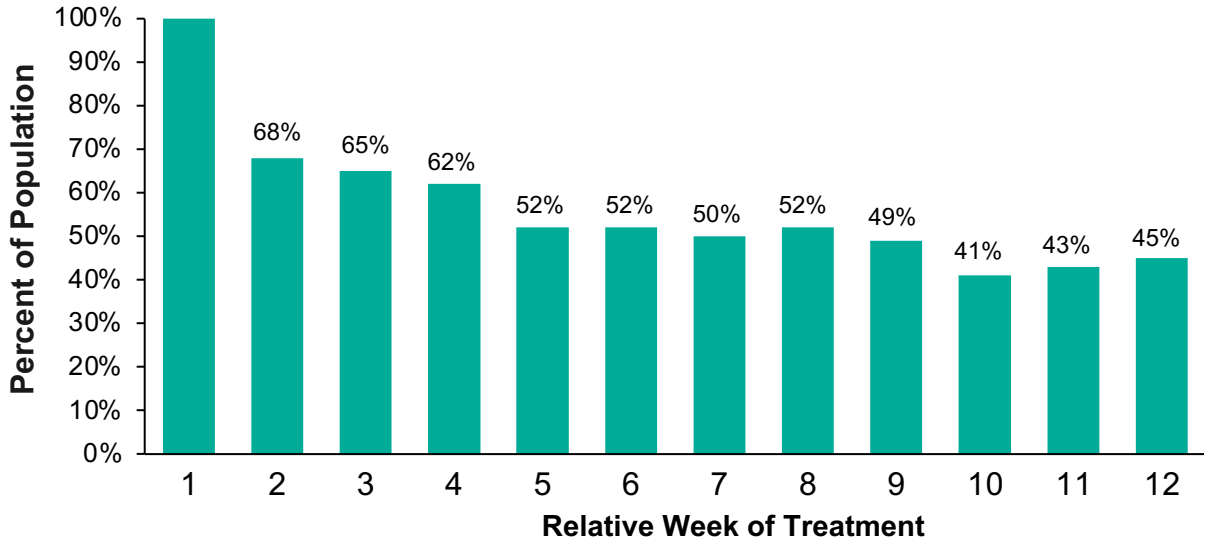
PEAR THERAPEUTICS

What has been done in California to date?

- Demonstrated provider and patient demand for reSET-O within California
  - 174 patients have used reSET-O
  - 11 providers writing prescriptions

- Demonstrated strong engagement with reSET-O
  - Data from California patients at completion of their first prescription (N=174)
    - 45% of patients were active in the therapeutic in week 12
    - 86% of patients engaged during non-clinic hours (7pm-9am)
    - 30% of patients completed all core treatment modules





Data from patients that were prescribed reSET-O prescription between 1/1/2019 and 9/1/2021 and completed at least 1 lesson

reSET-O® Health Care Resource Utilization and Cost Impact Analysis

A 6-month and 9-month Claims Analysis

PEAR THERAPEUTICS

Objective

Utilize a retrospective study design to understand the impact of reSET-O prescribing on healthcare resource utilization in patients with opioid use disorder

- The retrospective design allows patients exposed to reSET-O to act as their own controls
- Gaining an understanding of the population impact of reSET-O under usual care conditions

Limitations

- Real world evidence lacks randomization and therefore may produce results influenced by selection bias
- The majority of patients identified were Medicaid patients; thus, the results may not generalize to all populations
- Health care resource utilization in the pre-index period may be increased prior to intensification of treatment with reSET-O
- The pre-index and post-index period differed substantially in assessed duration

A 6-month Claims Database Analysis of Healthcare Resource Utilization Before and After reSET-O in Patients With Opioid Use Disorder

A retrospective analysis of the HealthVerity PrivateSource 20 claims database was performed to assess the impact of reSET-O initiation on healthcare resource utilization among patients receiving treatment for opioid use disorder

Patient Identification

Patients who activated reSET-O between January 2019 and October 2019 from a large, nationally representative database

Data Collection

INDEX DATE

Date of first prescription for reSET-O

Analysis

Comparison of HRU between baseline and study periods, including:

- All facility services
- All clinician services

reSET-O has not been shown or indicated to impact patient and health system cost in prospective, randomized, clinical trials.

Pear Therapeutics data on file

Patients Were Largely Buprenorphine Adherent Medicaid Recipients

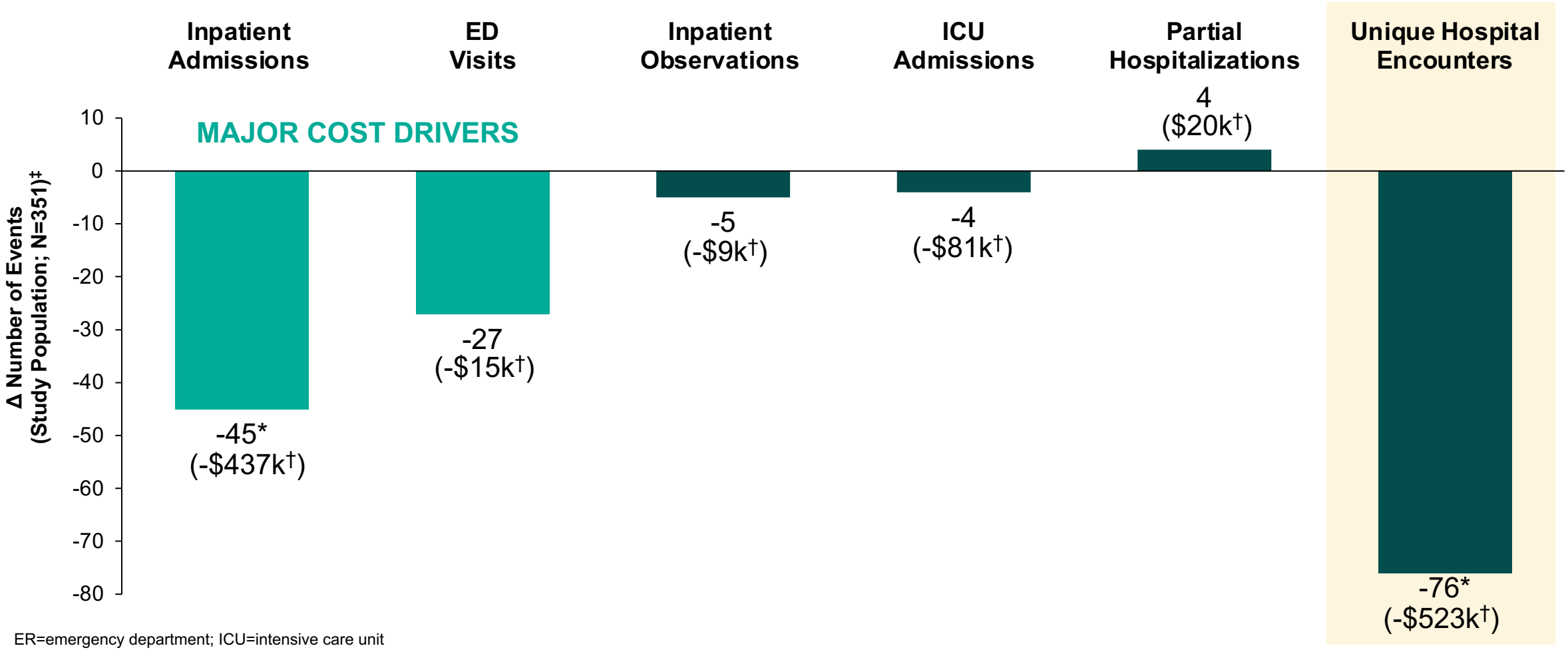
Demographics	N=351
Age on Index Date	
Mean, (SD)	**37.0 (8.64)**
Median, (range)	36.0 (20–67)
Age on Index Date, n (%)	
18-24	15 (4.3%)
25-34	**134 (38.2%)**
35-44	**145 (41.3%)**
45-54	39 (11.1%)
55-64	16 (4.6%)
65-74	2 (0.6%)
Sex, n (%)	
Female	**209 (59.5%)**
Male	142 (40.5%)
Payer on Index Date, n (%)	
Commercial	45 (12.8%)
Medicaid	**290 (82.6%)**
Medicare Advantage	8 (2.3%)
Unknown	8 (2.3%)

Clinical Characteristics	N=351
Opioid use disorder in the pre-index period, n (%)	
F11.10 Opioid abuse, uncomplicated	19 (5.4%)
F11.11 Opioid abuse, in remission	5 (1.4%)
F11.14 Opioid abuse with opioid-induced mood disorder	1 (0.3%)
F11.19 with unspecified opioid-induced disorder	1 (0.3%)
F11.20 Opioid dependence, uncomplicated	**290 (82.6%)**
F11.21 Opioid dependence, in remission	38 (10.8%)
F11.23 Opioid dependence with withdrawal	16 (4.6%)
F11.288 Opioid dependence with other opioid-induced disorder	1 (0.3%)
F11.29 Opioid dependence with unspecified opioid-induced disorder	1 (0.3%)
F11.90 Opioid use, unspecified, uncomplicated	8 (2.3%)
F11.988 Opioid use, unspecified with other opioid-induced disorder	1 (0.3%)
F11.99 Opioid use, unspecified with unspecified opioid-induced disorder	1 (0.3%)
No opioid use diagnosis code	46 (13.1%)
Buprenorphine treated Pre-Index, n (%)	249 (76.7%)
Buprenorphine treated Post-Index, n (%)	240 (72.8%)
Buprenorphine adherence Pre-Index (MPR) , adjusted mean (SE)	**0.73 (0.21)**
Buprenorphine adherence Post-Index (MPR), adjusted mean (SE)	**0.82 (0.21)**

MPR=medication possession ratio; SD=standard deviation

Pear Therapeutics data on file

reSET-O Prescription May Be Associated With Reduced Utilization of Major Cost Drivers



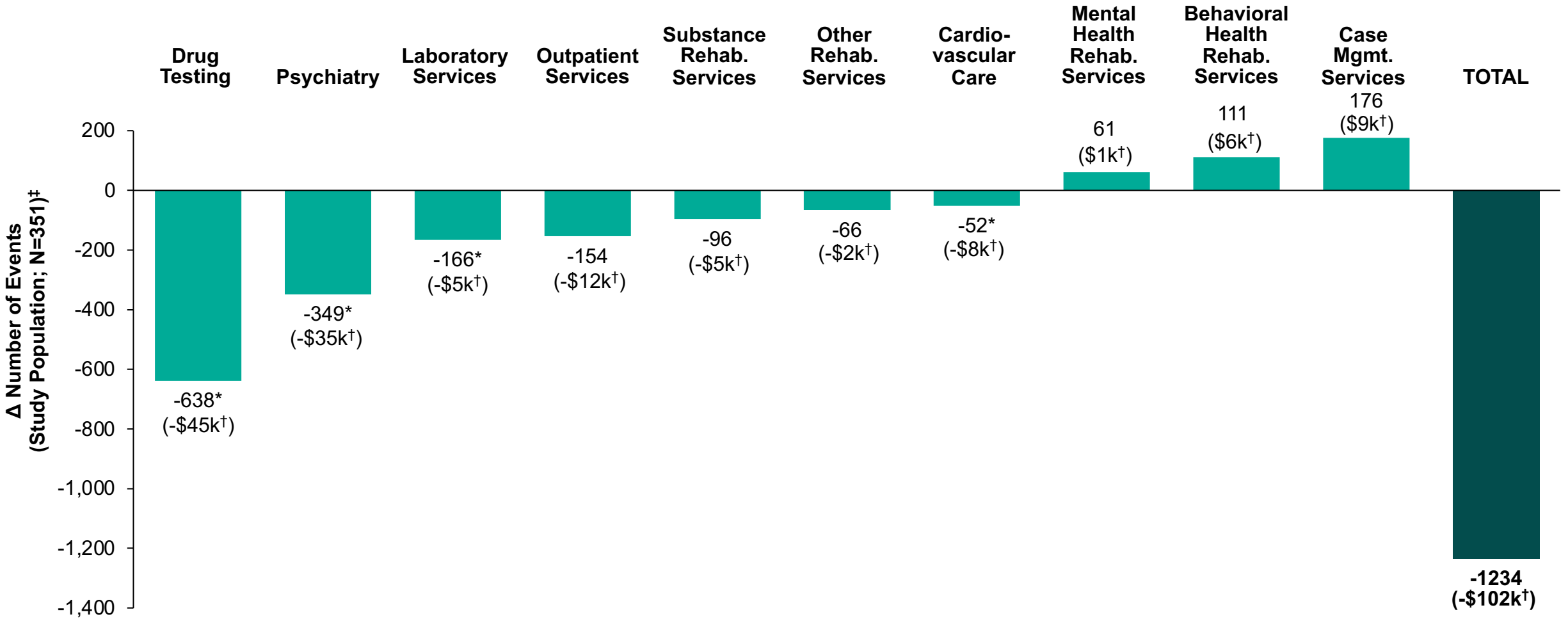
ER=emergency department; ICU=intensive care unit

*p<0.05; †projected cost; ‡Mean number of days in the pre-index and post-index period are 180.0 and 104.0, respectively. Incidence and IRR are evaluated from a repeated measures (ie, pre- and post-index for each patient) negative binomial model of count of stays/visits, with an offset for the number of days in each period

Category costs were derived from published Medicare reimbursement costs

Pear Therapeutics data on file

reSET-O Prescribing May Be Associated With an Increase in Rehabilitation Visits



*p<0.05; †projected cost; ‡Mean number of days in the pre-index and post-index period are 180.0 and 104.0, respectively. Incidence and IRR are evaluated from a repeated measures (ie, pre- and post-index for each patient) negative binomial model of count of stays/visits, with an offset for the number of days in each period

Pear Therapeutics data on file

reSET-O Prescribing May Be Associated With Reduced Resource Utilization and Projected Cost

		Number of Episodes (Study Population; N=351)	Projected Cost of Episodes (Study Population; N=351)	Cost Change per Patient
Utilization Reduced	Facility Encounters	-81	-$627,868.20	-$1,788.80
	Clinician Encounters	-1760	-$172,779.99	-$492.25
	Subtotal	-1841	-$800,648.19	-$2,281.05
Utilization Increased	Facility Encounters	25	$23,903.10	$68.10
	Clinician Encounters	537	$22,088.37	$62.93
	Subtotal	562	$45,991.47	$131.03
	NET IMPACT	**-1279**	**-$754,656.71**	**-$2,150.02**

reSET-O has not been shown or indicated to impact patient and health system cost in prospective, randomized, clinical trials.

Pear Therapeutics data on file

9-month Analysis of Healthcare Resource Use Before and After reSET-O in Patients With Opioid Use Disorder

A retrospective analysis of the HealthVerity PrivateSource 20 claims database was performed to assess the impact of reSET-O initiation vs. non-initiation/non-engagement* (control group) on healthcare resource utilization among patients receiving treatment for OUD.

Patient Identification

Patients who activated reSET-O between January 2019 and October 2019 from a large, nationally representative database

Data Collection

STUDY PERIOD (9 Months Post-index)

9 Months Post-index reSET-O

9 Months Post-index Controls

INDEX DATE

Date of first prescription for reSET-O

Analysis

Comparison of HRU between baseline and study periods, including:

- All facility services
- All clinician services

reSET-O has not been shown or indicated to impact patient and health system cost in prospective, randomized, clinical trials.

HRU=healthcare resource use; OUD=opioid use disorder

*Non-initiation is defined as a reSET-O prescription that was never activated. Non-engagement is defined as an activated prescription in which patients do not complete any lessons after week 1.

Pear Therapeutics data on file

Patients Were Largely Buprenorphine Adherent Medicaid Recipients

Demographics	reSET-O N=444	Control N=64
Age on Index Date		
Mean, (SD)	**37.5 (8.75)**	**39.5 (10.13)**
Median, (range)	36.0 (20–68)	38.5 (21-69)
Age on Index Date, n (%)		
18-24	14 (3.2)	3 (4.7)
25-34	**166 (37.4)**	**19 (29.7)**
35-44	**188 (42.3)**	**24 (37.5)**
45-54	48 (10.8)	13 (20.3)
55-64	24 (5.4)	4 (6.3)
65-74	4 (0.9)	1 (1.6)
Sex, n (%)		
Female	**280 (63.1)**	**21 (32.8)**
Male	164 (36.9)	43 (67.2)
Payer on Index Date, n (%)		
Commercial	50 (11.3)	14 (21.9)
Medicaid	**373 (84.0)**	**47 (73.4)**
Medicare Advantage	13 (2.9)	1 (1.6)
Unknown	8 (1.8)	2 (3.1)

Clinical Characteristics	reSET-O N=444	Control N=64
Opioid Use Disorder in the Pre-index Period, n (%)		
F11.10 Opioid abuse, uncomplicated	53 (11.9)	11 (17.2)
F11.11 Opioid abuse, in remission	14 (3.2)	1 (1.6)
F11.14 Opioid abuse with opioid-induced mood disorder	1 (0.2)	0 (0.0)
F11.19 with unspecified opioid-induced disorder	1 (0.2)	0 (0.0)
F11.20 Opioid dependence, uncomplicated	**398 (89.6)**	**54 (84.4)**
F11.21 Opioid dependence, in remission	58 (13.1)	7 (10.9)
F11.23 Opioid dependence with withdrawal	33 (7.4)	8 (12.5)
F11.288 Opioid dependence with other opioid-induced disorder	1 (0.2)	0 (0.0)
F11.29 Opioid dependence with unspecified opioid-induced disorder	5 (1.1)	0 (0.0)
F11.90 Opioid use, unspecified, uncomplicated	17 (3.8)	3 (4.7)
F11.988 Opioid use, unspecified with other opioid-induced disorder	2 (0.5)	1 (1.6)
F11.99 Opioid use, unspecified with unspecified opioid-induced disorder	9 (2.0)	0 (0.0)
No opioid use diagnosis code	38 (8.6)	8 (12.5)
Buprenorphine treated Pre-Index, n (%)	345 (97.7)	43(100.0)
Buprenorphine treated Post-Index, n (%)	332 (94.1)	42 (97.7)
Buprenorphine Adherence	**N=324**	**N=42**
Pre-Index (MPR) , adjusted mean (SE)	**0.69 (0.02)**	**0.62 (0.06)**
Post-Index (MPR), adjusted mean (SE)	**0.81 (0.02)**	**0.79 (0.06)**

MPR=medication possession ratio; SD=standard deviation

Pear Therapeutics data on file

reSET-O May Be Associated With Cost Savings in the 9-months Following Prescription

Inpatient	Cost/Patient reSET-O (n=444)	Cost/Patient Control (n=64)	Difference (Control minus reSET-O)
Facility Services	$2,693	$6,130	($3,437)
Clinician services	$6,040	$5,311	$729
		Net Cost Difference	**($2,708)**

- Control Patients were observed to have more costs than reSET-O patients in the 9 months following prescription of reSET-O
- There was a 46% lower rate of observed hospitalizations per patient (0.14 vs. 0.26), despite an increase in clinician services following prescription fo reSET-O

reSET-O has not been shown or indicated to impact patient and health system cost in prospective, randomized, clinical trials.

Pear Therapeutics data on file

Conclusions

- reSET-O prescription may be associated with reduced utilization of major cost drivers in the healthcare system
- reSET-O prescription may be associated with an increase in utilization of rehabilitation services
- Findings may indicate a potential for near-term total cost reduction

reSET®

INDICATIONS FOR USE:

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 days) prescription only treatment for patients with Substance Use Disorder (SUD), who are not currently on opioid replacement therapy, who do not abuse alcohol solely, or who do not abuse opioids as their primary substance of abuse. reSET is intended to increase abstinence from a patient's substances of abuse during treatment and increase retention in the outpatient treatment program.

IMPORTANT SAFETY INFORMATION

Warnings: reSET is intended for patients whose primary language is English with a reading level of 7th grade or above, 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. In case of an emergency, patients should dial 911 or go to the nearest emergency room.

The long-term benefit of reSET has not been evaluated in studies lasting beyond 12 weeks (90 days) in the substance use disorder population. The ability of reSET to prevent potential relapse after therapy discontinuation has not been studied.

Please see the Clinician Brief Summary Instructions for reSET.

reSET-O®

INDICATIONS FOR USE:

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. reSET-O is indicated as a prescription-only digital therapeutic.

IMPORTANT SAFETY INFORMATION

Warnings: reSET-O is intended for patients whose primary language is English with a reading level of 7th grade or above, 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 and is not intended to reduce the frequency or duration of in-person therapy. 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.

Patients with opioid use disorder experience mental health disease and co-morbid medical problems at higher rates than the general population. Patients with opioid use disorder have higher baseline rates of suicidal ideation, and suicide attempts, and suicide completion. Clinicians should undertake standard of care to monitor patients for medical problems and mental health disease, including risk for harming others and/or themselves.

The long-term benefit of reSET-O has not been evaluated in studies lasting beyond 12 weeks (84 days) in the OUD population. The ability of reSET-O to prevent potential relapse after therapy discontinuation has not been studied.

Please see the Clinician Brief Summary Instructions for reSET-O.