




Prescription
Digital
Therapeutics

Medicine for the Mind, not
the Gut



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Disclosures:

Todd Wurtz is an employee of Coastal Health/Next Step and a Key Opinion Leader and Speaker for Pear Therapeutics (US), Inc. The views and opinions represented in this presentation are solely those of the presenter and are not endorsed by nor necessarily representative of those of their employer.

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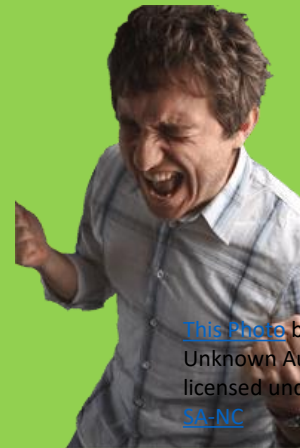
How I got here: The reluctant capitulator



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ADDICTION

Insert whatever other Mental Health
disorder here



20.4 million

Americans living with Substance Use Disorder¹

**ONLY 21% (4.2 MILLION PEOPLE)
RECEIVED FORMAL SUBSTANCE
ABUSE THERAPY**

What we know works



1,3



ASAM Guidelines state **“Participants receiving any psychosocial treatment had better outcomes than participants who did not. Contingency management and the combined CM and CBT intervention produced better outcomes** than the other interventions.”*2 ASAM

VA/DOD Clinical Practice Guidelines list that **the strength of evidence for CBT is "strong" for patients with alcohol, cannabis, and stimulant use disorders.**⁴



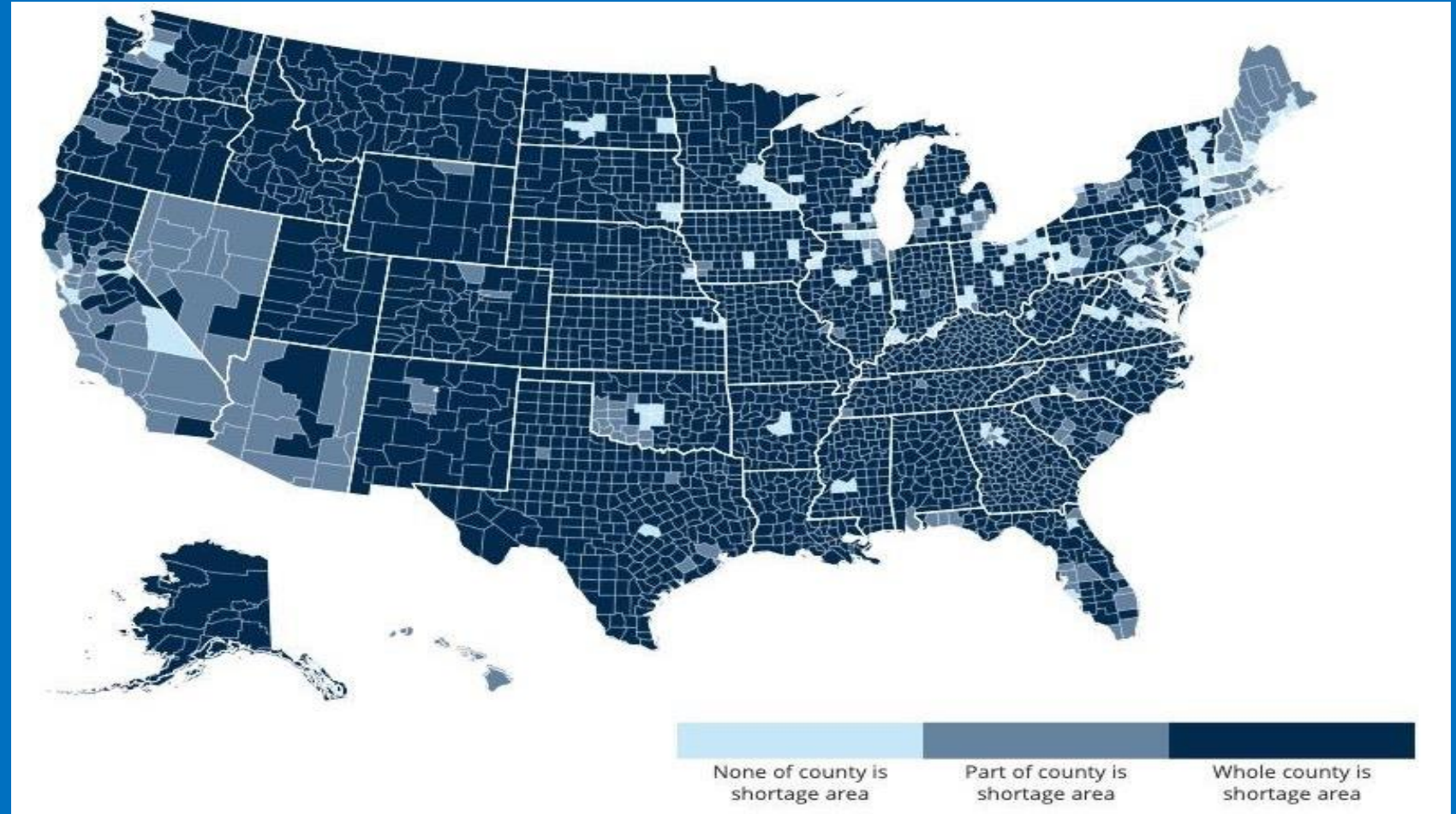
1. Using Technology-Based Therapeutic Tools in Behavioral Health Services. SAMHSA. 2010. 2. ASAM National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. ASAM. 2020. 3. Using Technology-Based Therapeutic Tools in Behavioral Health Services. SAMHSA. 2015. 4. VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders. 2015.

The Problem (s)

Despite being highly effective and widely endorsed, access to CBT (and CM) is limited

CBT is provided by mental health professionals (MHPs), but the shortage of MHPs in the U.S. means a lack of access to CBT.

- As of 2014, most individual and small group health insurance plans, including all ACA-compliant plans, are **required to cover mental health and SUD services**.¹ As a form of psychotherapy, CBT is covered under these services.
- But there are **widespread shortages of mental health providers across the U.S.**, limiting patient access to CBT.²
- Given that CBT is a standard of care for many mental disorders, **it is vital that people with these health needs have ready access to CBT** regardless of where they live, their background, or their demographic status.



1. MentalHealth.gov. Health Insurance and Mental Health Services. March 2020. <https://www.mentalhealth.gov/get-help/health-insurance>. 2. Health Resources and Services Administration. Health Professional Shortage Areas. July 2021. <https://www.ruralhealthinfo.org/charts/5>

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Many have burned many bridges because of their mental health and addiction

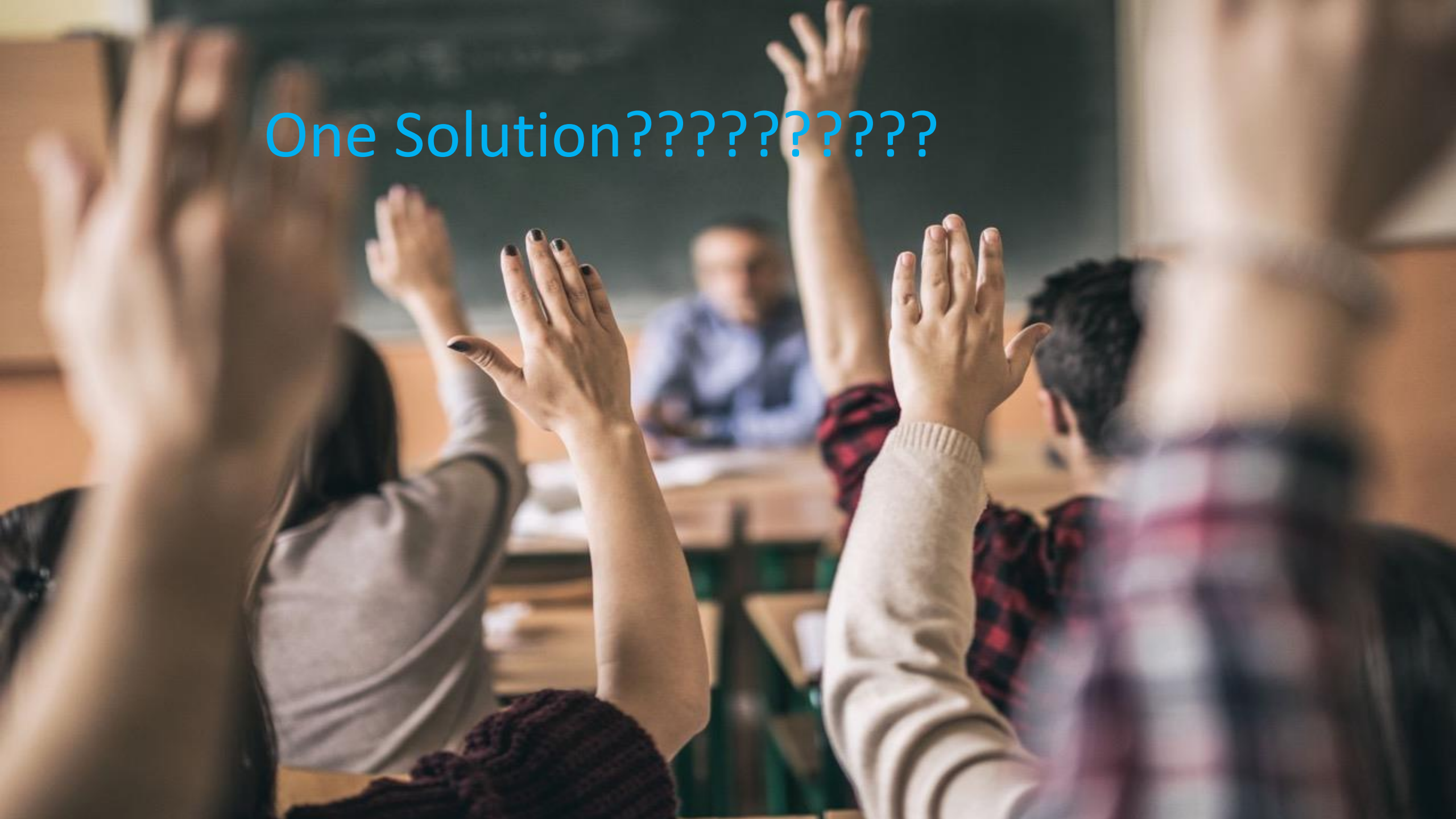
ations

What are we asking these patients to do?

Build a house without a hammer!!!



One Solution??????????



Prescription Digital Therapeutics



Prescription Digital Therapeutics (PDTs) Are a New Category of Therapeutics Defined by Clinical Effectiveness and FDA Market Authorization

	HEALTH AND WELLNESS APPS	PHARMACEUTICALS	PRESCRIPTION DIGITAL THERAPEUTICS
Utilizes digital technology to improve human health	✓		✓
Deliver evidence-based mechanisms of action		✓	✓
Require randomized controlled trials		✓	✓
Authorized or approved as safe and effective		✓	✓
Reimbursement pathways via specific product code		✓	✓
Capability for real-time feedback for clinicians			✓



1900+
Small Molecules



1980+
Biologics



2000+
Cell/Gene Therapies



2017
Prescription Digital Therapeutics

FDA Authorized PDTs: Pre- and Post-Market Authorization



Pivotal Clinical Trials¹



FDA Submission



FDA Review



FDA Decision



Post Market Surveillance

- ⊙ Safety testing
- ⊙ Efficacy testing

De Novo² or Premarket Notification (PMN) 510(k)³ Clearance

⊙ For De Novo Currently Authorized Products:

E.g. in SUD/OD: 21CFR882.5801 class 2 neurological therapeutic device with special controls (includes software verification, validation, and hazard analysis)

Clinical data must be provided to fulfill the following:

- ⊙ Describe a validated model of behavioral therapy for the psychiatric disorder
- ⊙ Validate the model of behavioral therapy as implemented by the device

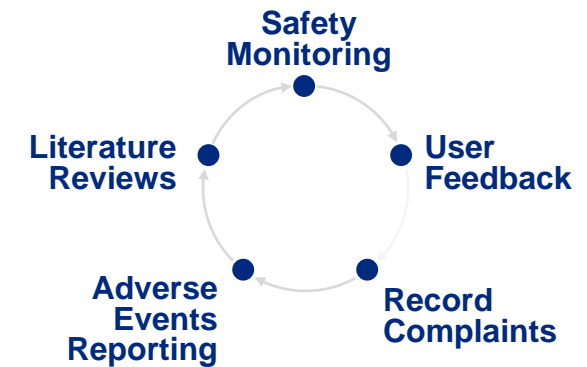
⊙ Requires clinical data to support reasonable assurance of the safety and effectiveness

Sponsors can petition to reclassify low- or moderate-risk devices that do not have predicates as De Novo

Devices approved as De Novo can then be predicates for others

FDA requires the continued monitoring of PDTs⁴

to evaluate the treatments' continued safety, effectiveness, and performance in real-world use.

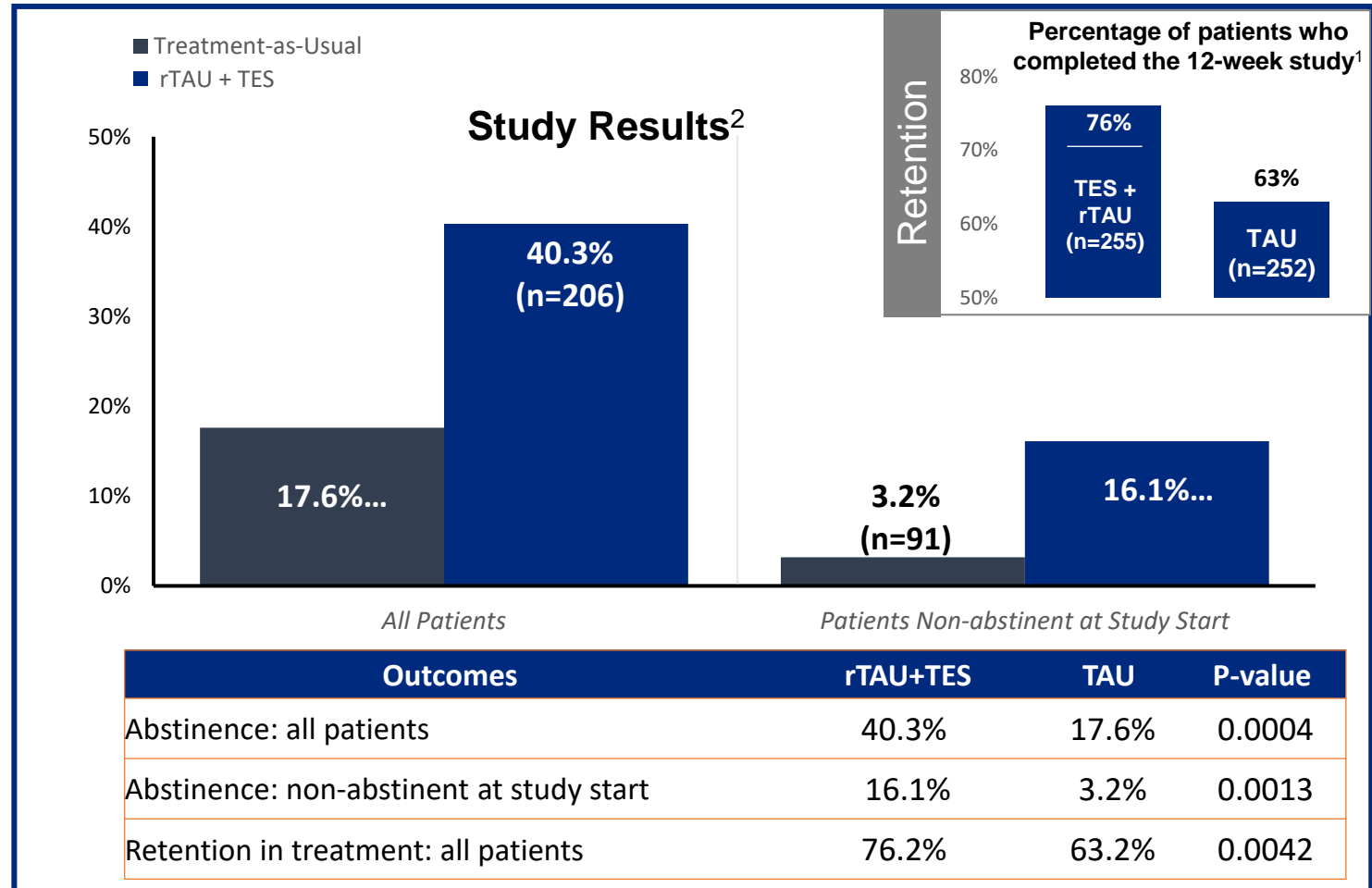


¹ Lee K., Bacchetti P., Sim I. Publication of Clinical Trials Supporting Successful New Drug Applications: A Literature Analysis. <https://doi.org/10.1371/journal.pmed.0050191>. Published September 23, 2008. Accessed September 23, 2021. ² US Food and Drug Administration. De Novo Classification Request. <https://www.fda.gov/medical-devices/premarket-submissions/de-novo-classification-request>. Published November 20, 2019. Accessed September 23, 2021. ³ US Food and Drug Administration. Premarket Notification 510(k). <https://www.fda.gov/medical-devices/premarket-submissions/premarket-notification-510k>. Published March 13, 2020. Accessed September 23, 2021. ⁴ US Food and Drug Administration. Software as a Medical Device (SAMM): Clinical Evaluation. <https://www.fda.gov/media/100714/download>. Published December 8, 2017. Accessed October 2, 2020.

SUD 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 PDT for SUD (rTAU+ TES) 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



1. American Journal of Psychiatry. 2014. 171(6):683-690. 2. Pear regulatory submission. DEN160018; https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN160018.pdf. Accessed Aug 3, 2022. 3. Maricich YA, et al.. Curr Med Res Opin. 2021;37(2):167-173. doi:10.1080/03007995.2020.1846022

Significant Decreases Observed Between Pre-index and Post-index PDT for SUD Cohort¹

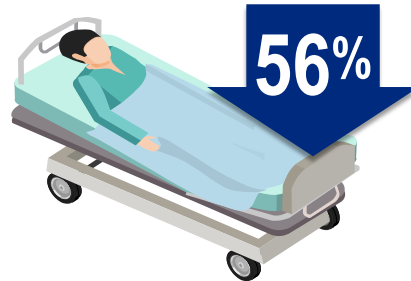
Overall Hospital Encounters

50%



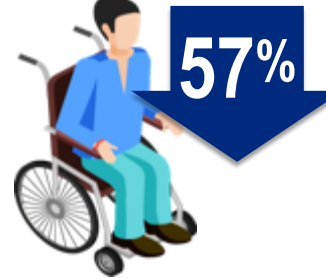
IRR: 0.50;
95% CI: 0.37-0.67; $P < 0.001$

Inpatient Stays



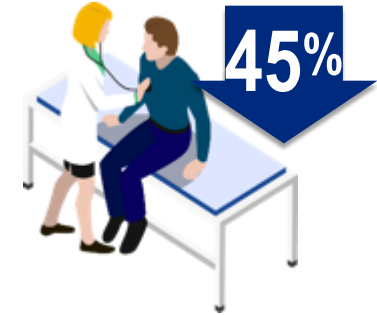
IRR: 0.44; 95% CI: 0.26-0.76; $P = 0.003$

Partial Hospitalizations



IRR: 0.43; 95% CI: 0.21-0.88; $P = 0.021$

Emergency Department



IRR: .55; 95% CI: 0.38-0.80; $P < 0.004$

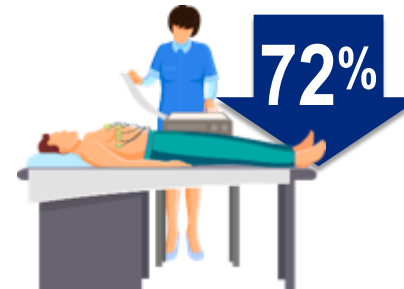
Additional Results

E and M* Consultations



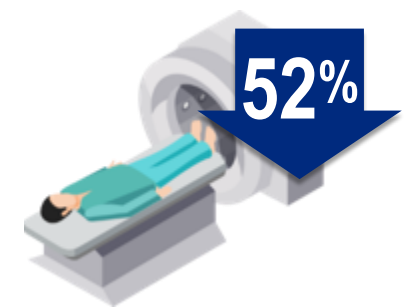
IRR: 0.09; 95% CI: 0.02-0.36, $P < 0.001$

Cardiovascular Procedures



IRR: 0.28; 95% CI: 0.14-0.55, $P < 0.001$

Radiology Services



IRR: 0.48; 95% CI: 0.31-0.76, $P = 0.002$

*Evaluation and Management

1. Median age 37 years, 50.5% female, 54.5% Medicaid-insured

How do they work?



Retrain the Brain

Understand the disease process

Insight into self/Self Awareness

Offers tools



Example of PDT Mechanism of Action with Digital Delivery of Evidence-Based Treatment

Community Reinforcement Approach (CRA)^{1,2,3}

- A comprehensive CBT package that a special focus on helping people with 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 Training⁴

- 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 CM 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.

Example of PDT Capabilities and Functionality and Use

PATIENT

Provides intervention

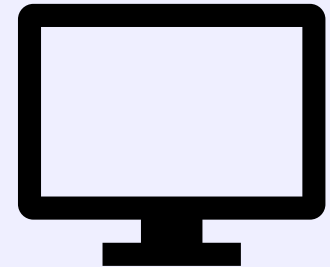
- Cognitive Behavioral Therapy (CBT) Modules
- Fluency Training
- Contingency Management
- Cravings and Trigger Assessment



CLINICIAN

Provides insight

- Real-world Engagement
- CBT Module Use
- Fluency Training
- Contingency Management
- Cravings and Trigger Assessment
- Urine and Drug Screen Appointments



Patient /Provider in office **ENGAGEMENT**

Remember the Road Blocks?

Road Block

PDT

Time From Work
Time From Family
Time Traveling



Can be used
24/7

Transportation



Not Needed

Finances and Costs



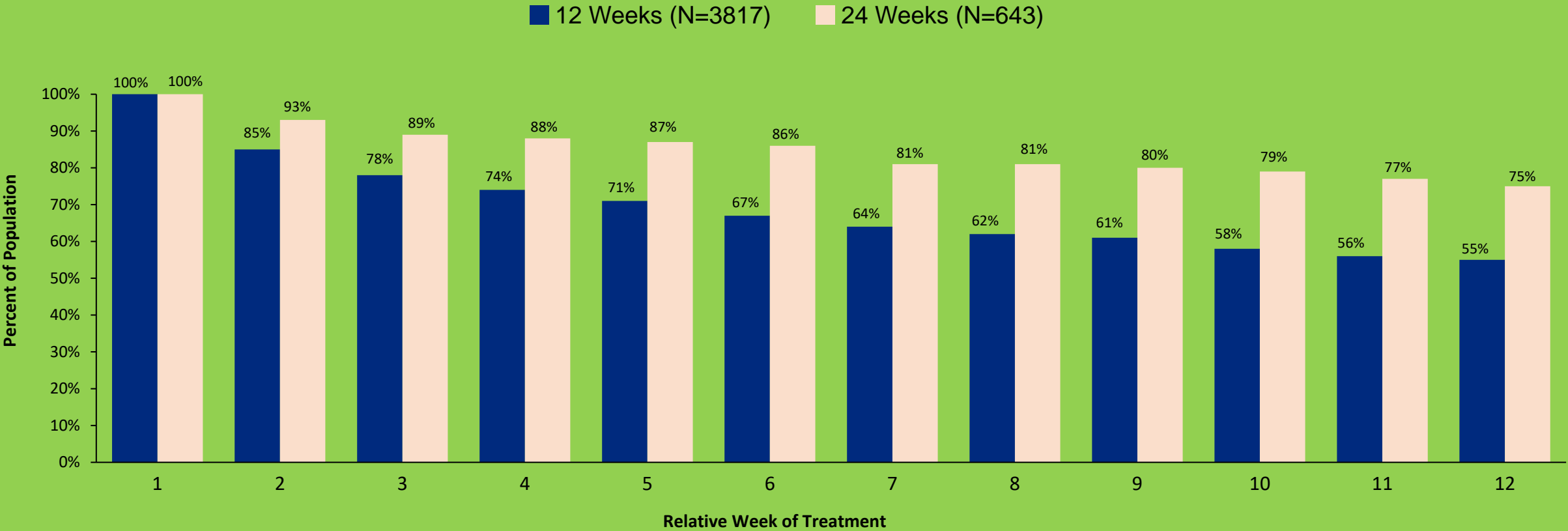
Covered by
Insurance

A photograph showing three healthcare professionals in a clinical setting. A woman in a white lab coat is pointing at a laptop screen, while a man in a white lab coat and a woman in dark scrubs look on. The scene is brightly lit, and a red storage bin is visible in the background.

ARE PEOPLE
REALLY GOING TO
USE PDTs?

A Majority of Patients Remain Active in PDT for OUD Through Week 12 of First and Second Prescriptions

Activity by Week



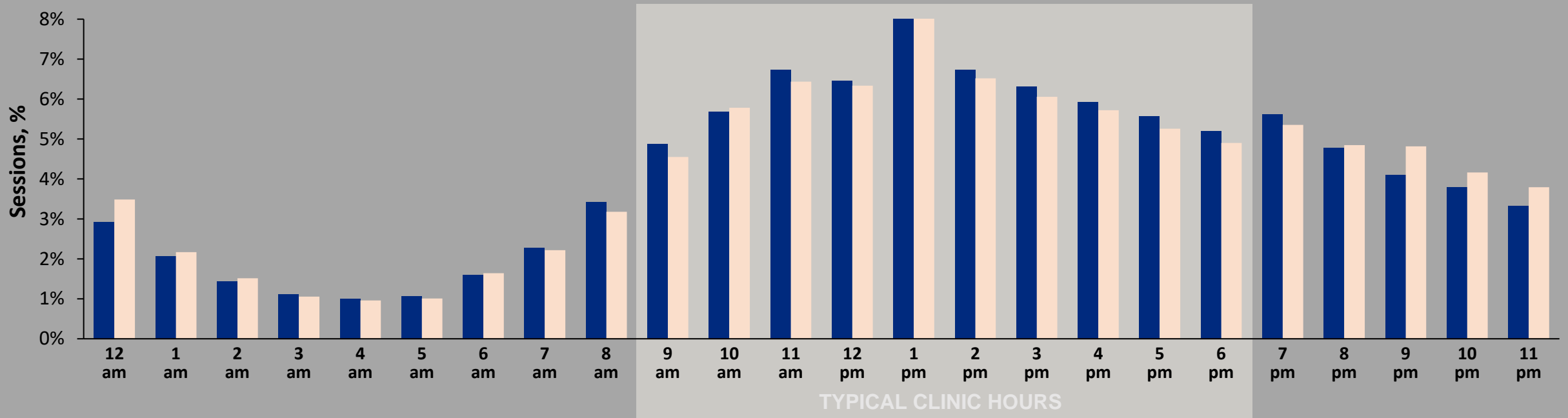
Activity was defined as patient use of any PDT feature on a given day

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 PDT for OUD Throughout the Full 24-hour Period

Activity by Time of Day

■ 12 Weeks (N=3817) ■ 24 Weeks (N=643)



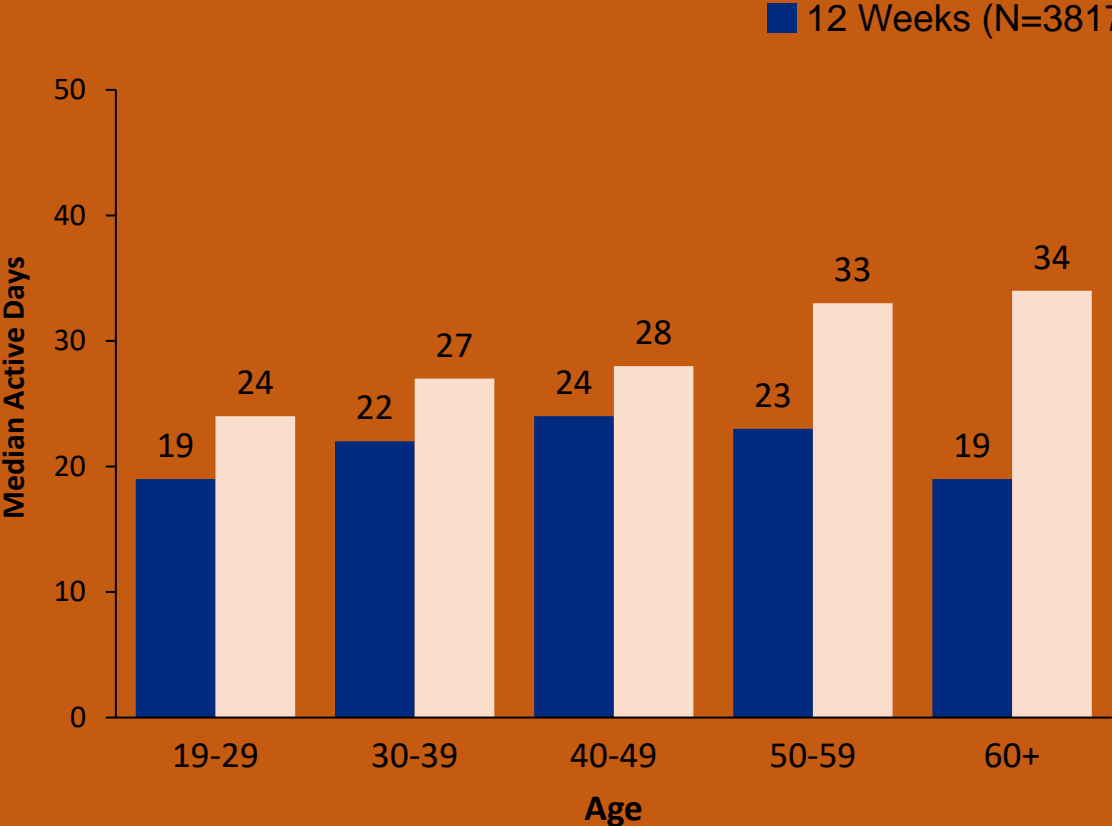
- In each cohort approximately 60% of activity occurred during typical clinic hours
- Approximately 40% of activity occurred when treatment may be otherwise unavailable

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

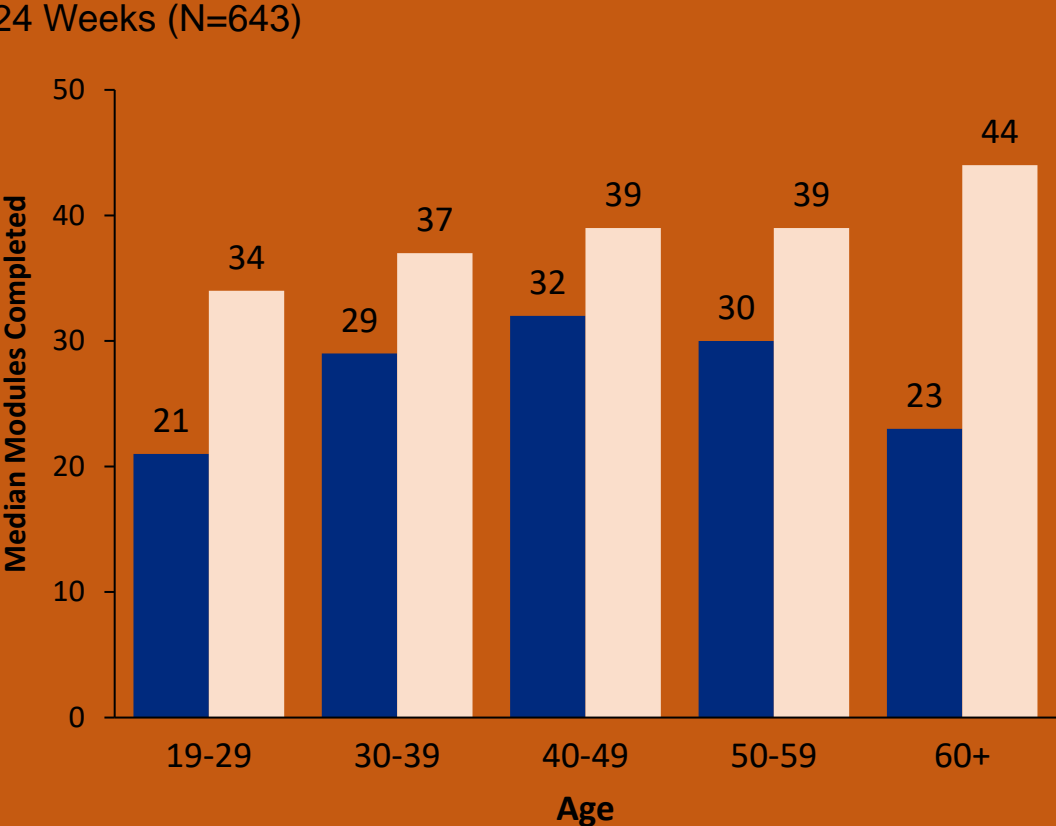
1. Maricich Y et al. Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. *Hospital Practice*. 2021. <https://doi.org/10.1080/21548331.2021.1974243>

Activity and Module Completion Across Age Categories

Active Days by Age



Modules Completed by Age



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>

Other Disease States



Clinical Studies Evaluating Digital Interventions for Mental Health Conditions

Adults with Major Depression ¹

Improved sustained attention as measured by a continuous performance task modeled after T.O.V.A.® (Test of Variables of Attention)

Reduced depression severity over time as measured by the Patient Health Questionnaire-9

Children with Intellectual and developmental Disabilities ^{2,3}

Significant short- and long-term improvements in selective attention performance as measured by the Wilding Attention battery

Enhanced numeracy skills

as assessed by the Test of Early Mathematics Ability-Third Edition 3 months postintervention

Reduced behavioral and emotional problems as assessed by a parent-rated developmental behavior checklist

Adults with PTSD ⁴

Marked reduction in severity of PTSD symptoms as measured by the Clinician Administered PTSD Scale

Sustained mental and physical health improvements 6 months postintervention

Adults with Post-Partum Depression ⁵

Significant reduction in symptoms of depression and anxiety as measured by the Patient Health Questionnaire-9 and General Anxiety Disorder-7 assessment, respectively

1. Gunning FM, Anguera JA, Victoria LW, Areán PA. A digital intervention targeting cognitive control network dysfunction in middle age and older adults with major depression. *Transl Psychiatry*. 2021;11(1):269.

2 Kirk HE, Gray KM, Ellis K, Taffe J, Cornish KM. Computerised attention training for children with intellectual and developmental disabilities: a randomised controlled trial. *J Child Psychol Psychiatry*. 2016;57(12):1380-1389.

3. Kirk H, Gray K, Ellis K, Taffe J, Cornish K. Impact of attention training on academic achievement, executive functioning, and behavior: a randomized controlled trial. *Am J Intellect Dev Disabil*. 2017;122(2):97-117.

4. Ostacher MJ, Fischer E, Bowen ER, Lyu J, Robbins DJ, Suppes T. Investigation of a capnometry guided respiratory intervention in the treatment of posttraumatic stress disorder. *Appl Psychophysiol Biofeedback*. 2021;46(4):367-376.

5.. Darcy A, Beaudette A, Chiauzzi E, et al. Anatomy of a Woebot® (WB001): agent guided CBT for women with postpartum depression. *Expert Rev Med Devices*. 2022;19(4):287-301.

There Are Currently 9 PDTs Authorized by the FDA*

PDT Product	Company marketing product	Therapeutic Area
reSET ¹	Pear Therapeutics	Substance use disorder
reSET-O ²	Pear Therapeutics	Opioid use disorder
Somryst ³	Pear Therapeutics	Chronic insomnia
Nightware ⁴	NightWare	Posttraumatic stress disorder (PTSD)—driven traumatic nightmares
EndeavorRx ⁵	Akili	Attention deficit hyperactivity disorder
Parallel ⁶	Mahana	Irritable bowel syndrome (IBS)
RelieVRx ⁷	AppliedVR	Reduction of pain in patients (18 years and over) with chronic lower back pain (indication)
Luminopia One ⁸	Luminopia	Treat amblyopia in children aged 4 to 7 years
Regulora ⁹	metaMe Health	Abdominal pain associated with IBS in adults

For informational purposes only and subject to change.

*As of August 2022.
 1. Pear Therapeutics. Pear obtains FDA clearance of the first prescription digital therapeutic to treat disease. Accessed January 11, 2022. <https://peartherapeutics.com/fda-obtains-fda-clearance-first-prescription-digital-therapeutic-treat-disease/> 2. Pear Therapeutics. Pear Therapeutics receives expedited access pathway designation from FDA for PDT for OUD™ prescription digital therapeutic to treat opioid use disorder. Accessed January 11, 2022. <https://peartherapeutics.com/pear-therapeutics-receives-expedited-access-pathway-designation-fda-pdt-for-oud-prescription-digital-therapeutic-treat-opioid-use-disorder/> 3. Pear Therapeutics. Pear Therapeutics launches Somryst™ for chronic insomnia via an end-to-end virtual care experience. Accessed January 11, 2022. <https://peartherapeutics.com/pear-therapeutics-launches-somryst-for-chronic-insomnia-via-an-end-to-end-virtual-care-experience/> 4. Truong K. Nightware receives breakthrough designation for its PTSD nightmare therapy technology. Accessed January 11, 2022. <https://medcitynews.com/2019/05/nightware-receives-breakthrough-designation-for-its-ptsd-nightmare-therapy-technology/> 5. Akili Interactive. Akili announces FDA clearance of EndeavorRx™ for children with ADHD, the first prescription treatment delivered through a video game. Accessed January 11, 2022. <https://www.akiliinteractive.com/news-collection/akili-announces-endeavorm-attention-treatment-is-now-available-for-children-withattention-deficit-hyperactivity-disorder-adhd-al3pw> 6. Mahana Therapeutics. Mahana Therapeutics obtains FDA marketing authorization for the first prescription digital therapeutic to treat irritable bowel syndrome. Accessed January 11, 2022. <https://www.mahanatx.com/press/parallel-fda-authorization> 7. US Food and Drug Administration. FDA authorizes marketing of virtual reality system for chronic pain reduction. Accessed December 15, 2021. <https://www.fda.gov/news-events/press-announcements/fda-authorizes-marketing-virtual-reality-system-chronic-pain-reduction> 8. US Food and Drug Administration. FDA device classification under section 513(f)(2)(de novo). Accessed January 11, 2022. <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm?id=DEN210005> 9. metaMe Health. metaMe Health receives FDA clearance for Regulora®, the first FDA-authorized treatment specifically for abdominal pain due to irritable bowel syndrome (IBS). Accessed January 11, 2022. <https://www.metamehealth.com/press/metame-health-receives-fda-clearance-for-regulora-the-first-fda-authorized-treatment-specifically-for-abdominal-pain-due-to-irritable-bowel-syndrome-ibs>

Digital Diagnostics

- Able to Accurately offer Diagnosis using established Scales and Diagnostic Tools
- Uses Algorithms
- Done on patient's time and in privacy
- Can be done before in clinic appointment saving Clinician Time
- Can be done throughout the course of care to assess changing conditions

Thank you!!!!!!!!!!

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