Northwest (HHS Region 10)
ATTC Addiction Technology Transfer Center Network
Funded by Substance Abuse and Mental Health Services Administration

The Northwest & Pacific Southwest ATTCs and the CTN Western States Node present:

Digital Therapeutics in the Treatment of Substance Use Disorders

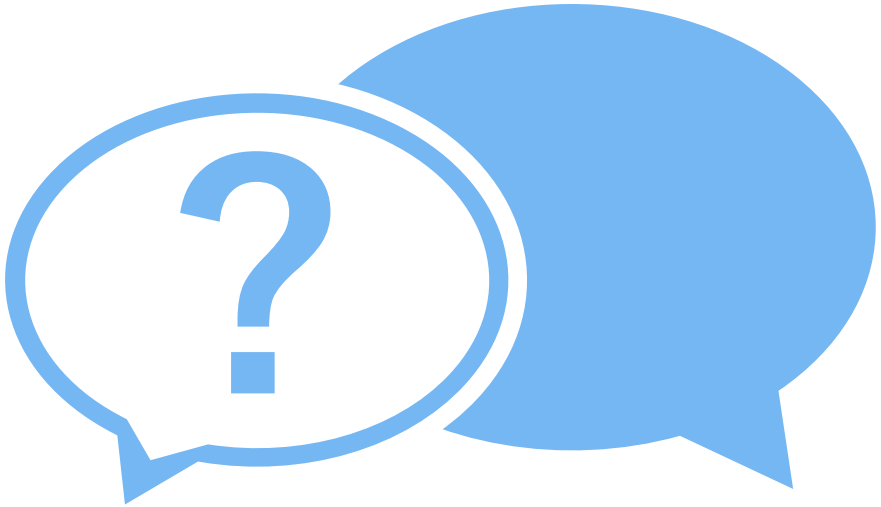
Thank you for joining us! The webinar will begin shortly.

- **You are muted with camera off.** Attendees are automatically muted with their cameras off for the webinar. Please type questions in the chat box!
- **Slides and a recording** of this presentation will be made available on our website at: http://attcnetwork.org/northwest later this week.

SAMHSA
Substance Abuse and Mental Health Services Administration

Q&A

Questions? Please type them in the chat box!



ATTC Survey, Slides, Recording

Look for our survey in your inbox!

We greatly appreciate your feedback!

Every survey we receive helps us improve and continue offering our programs.

A link to the slides and recording will also be provided in this email.

Course Evaluation & Certificates

- Within five (5) business days after the webinar, participants will receive an email to log in to the Stanford CME portal (stanford.cloud-cme.com) and click My CE tab to complete the course evaluation.

- Within the evaluation, you will be asked to attest to your hours of participation. Upon completion of the evaluation and attestation, your transcript will be updated with the appropriate CME/CE credit hours.

CLAIM CME

Questions? Email:
stanfordcme@stanford.edu

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Lisa Marsch, PhD	Royalties, Pear Therapeutics
	Ownership, Square2 Systems
	Consultant, Click Therapeutics

All of the relevant financial relationships listed for these individuals have been mitigated.

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In support of improving patient care, this activity has been planned and implemented by Stanford Medicine and the Northwest Addiction Technology Transfer Center (ATTC). Stanford Medicine is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

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Continuing Education (CE) Credit offered by UCLA Integrated Substance Abuse Programs

- Following the web training, LMFTs, LCSWs, and SUD counselors will receive an email from Victoria Norith with the links to two different brief online CE course evaluations.
- Once you submit your CE evaluation form, a CE Certificate will be emailed to you within 6-8 weeks

- Reach out to Victoria Norith with questions (vnorith@mednet.ucla.edu)

Certificate of Attendance

If you requested a “certificate of attendance” rather than specific CME/CE, you will receive that certificate from the Northwest ATTC automatically via email within a week.

Center for Technology and Behavioral Health

Dartmouth Geisel School of Medicine

DIGITAL THERAPEUTICS IN THE TREATMENT OF SUBSTANCE USE DISORDERS

STATE OF THE SCIENCE AND VISION FOR THE FUTURE

Lisa A. Marsch, PhD

Andrew G. Wallace Professor

Director, Center for Technology and Behavioral Health

Director, Northeast Node of the National Drug Abuse Treatment Clinical Trials Network

Geisel School of Medicine

Dartmouth College, USA

Center for Technology and Behavioral Health | Dartmouth Geisel School of Medicine

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Affiliations with Square2 Systems Inc,
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Click Therapeutics

Digital Health

Use of digital technology to:

- Measure health behavior in daily life
- Provide digital therapeutics accessible anytime and anywhere

Digital Therapeutics

Provide Anytime/Anywhere Science-Based Care

- Digital Therapeutics are clinical-grade software to prevent, treat, or manage a disease/disorder

- They package an entire model of evidence-based care into a seamless, digital delivery platform

Promise of Digital Therapeutics

- Extends the reach and impact of clinicians
- Functions as a virtual therapist in one's pocket that markedly improves patient outcomes
- Delivers treatment with fidelity to best practices
- Virtually any population you can think of has access to mobile devices
- Offers scalable, science-based behavioral healthcare anytime / anywhere
- More timely and significant than ever during global pandemic crisis
- They can have a major impact on health behavior, health costs and health outcomes

Digital Therapeutics for Substance Use Disorders

Research has demonstrated that digital therapeutics, if developed well and in collaboration with the target audience:

1. Are highly useful and acceptable to diverse audiences
2. Have a large impact on health behavior and health outcomes
3. Can produce outcomes compar-able to, or better than, clinicians
4. Increase quality, reach, and personal-ization of care
5. Can be cost-effective
6. Can be responsive to individuals' health behavior trajectory over time

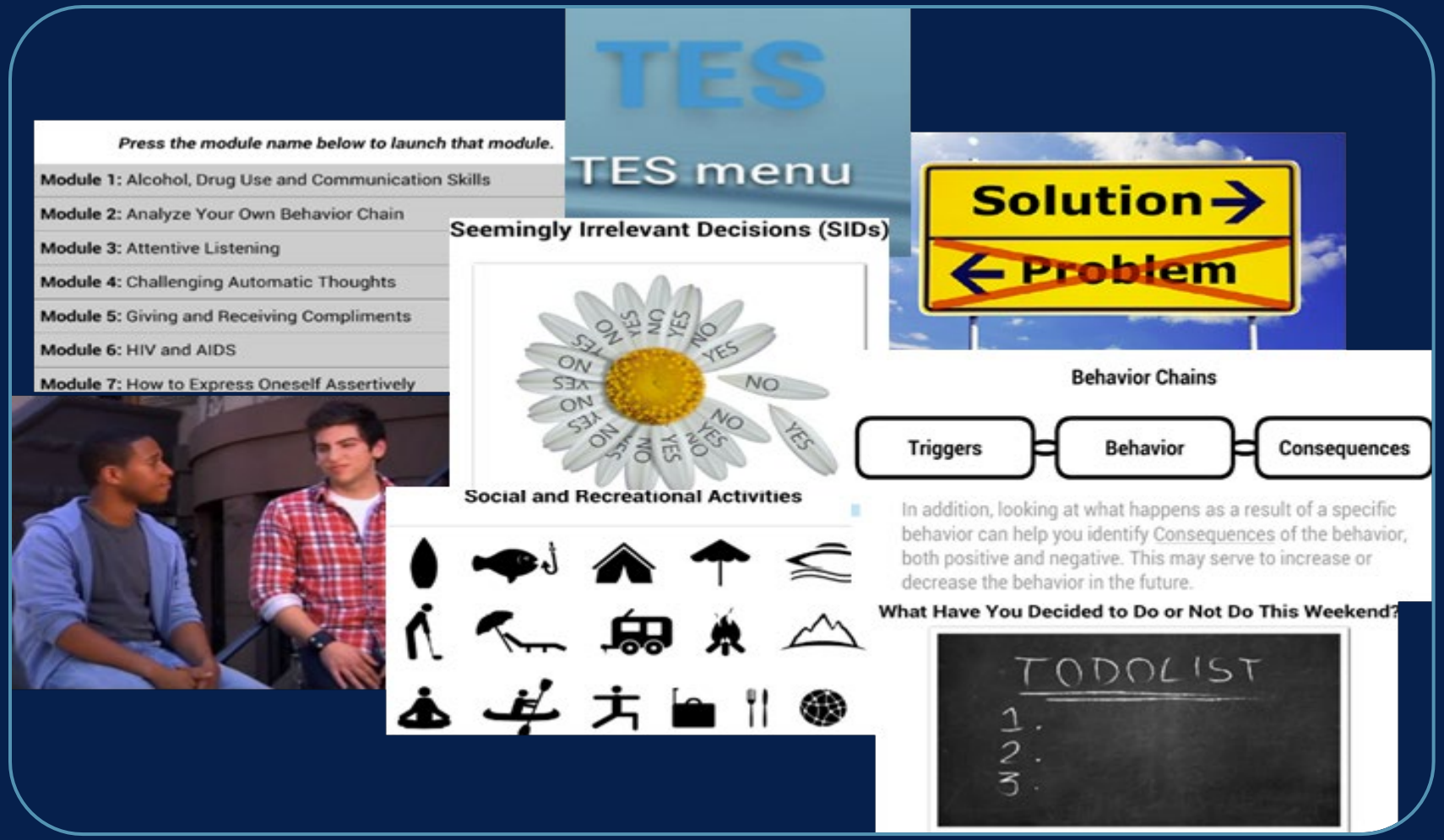
The Therapeutic Education System (TES): Digital Therapeutic for Substance Use Disorders

Interactive, self-directed, web-based behavior therapy for substance use disorders (SUDs) based on the science-based, community reinforcement approach to SUD treatment

Interactive modules designed to help people:

- Understand and disrupt harmful behaviors and cognitions leading to self-defeating patterns of drug use
- Leverage personal, social, and vocational resources to help individuals change substance-use
- Sometimes employs motivational incentives

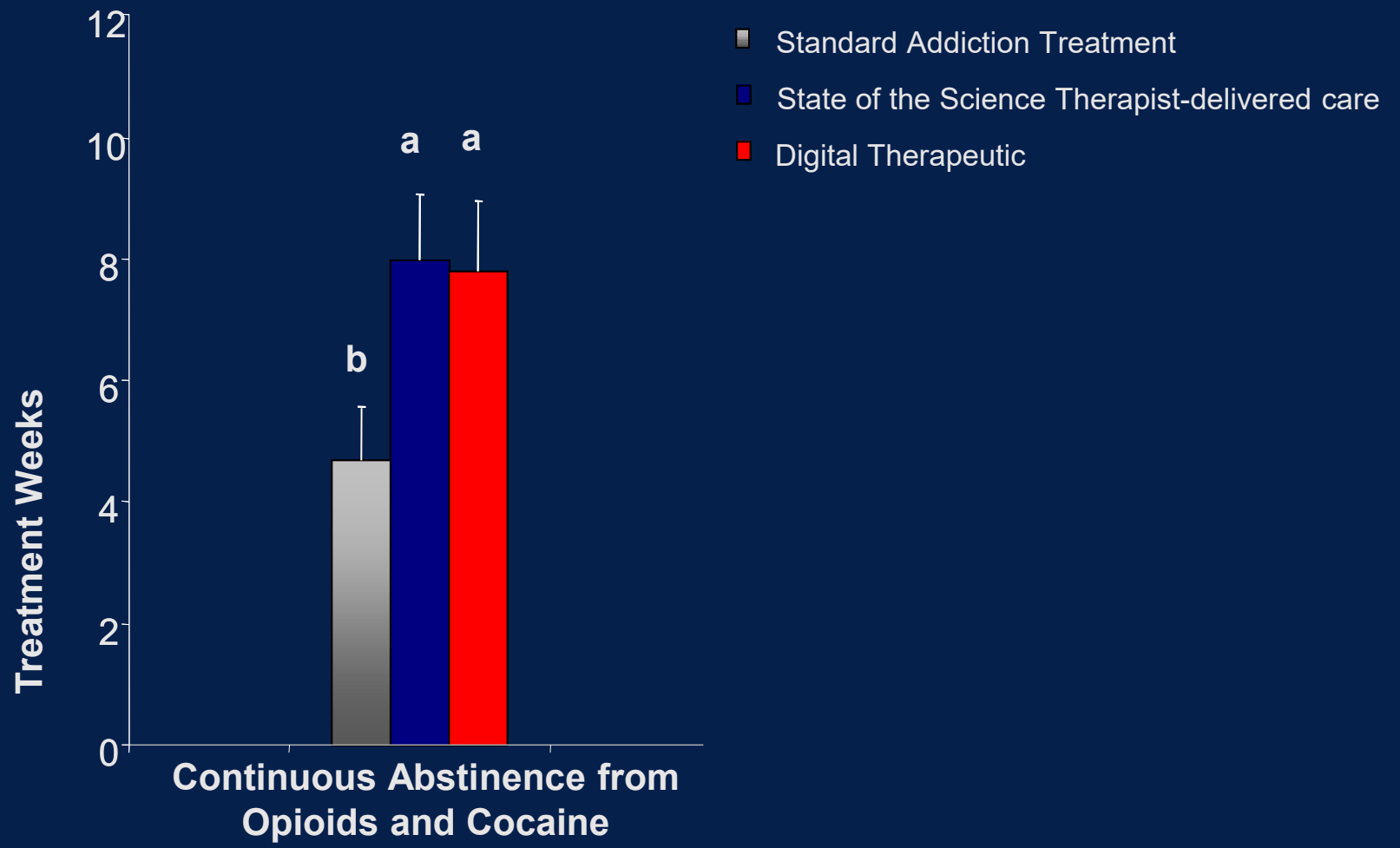
TES Digital Therapeutic for Substance Use Disorders



Digital Therapeutic

is as Effective as "Gold Standard" Clinician-Delivered Treatment in Medication-Treatment for OUD

(n=135)

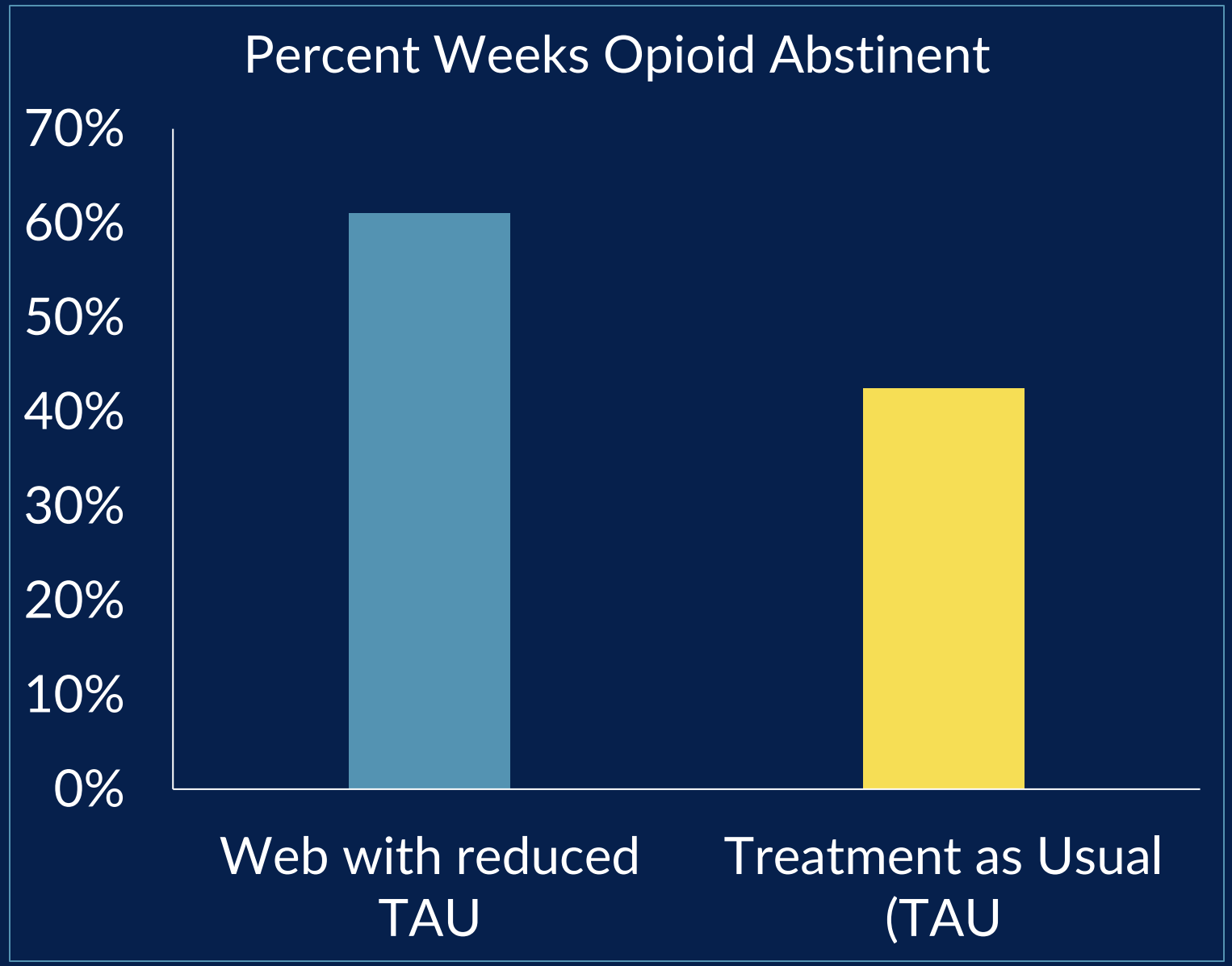


(Bickel, Marsch et al., 2008)

Replacing Half of Clinician-Delivered OUD Treatment with Digital Therapeutic Produces Better Outcomes

than Standard Medication Treatment

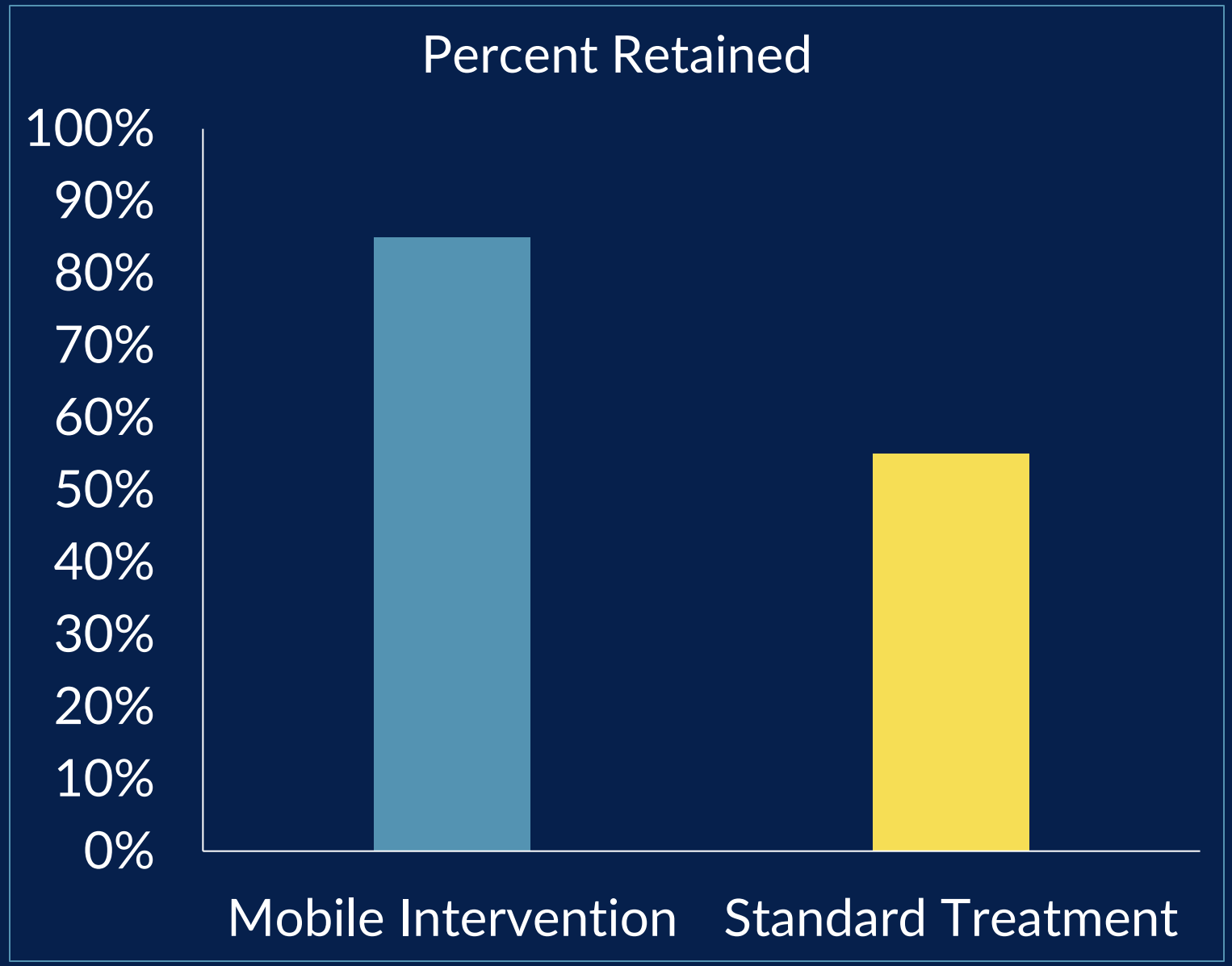
(n=160)



Marsch et al., 2014

Adding Mobile Behavioral Treatment

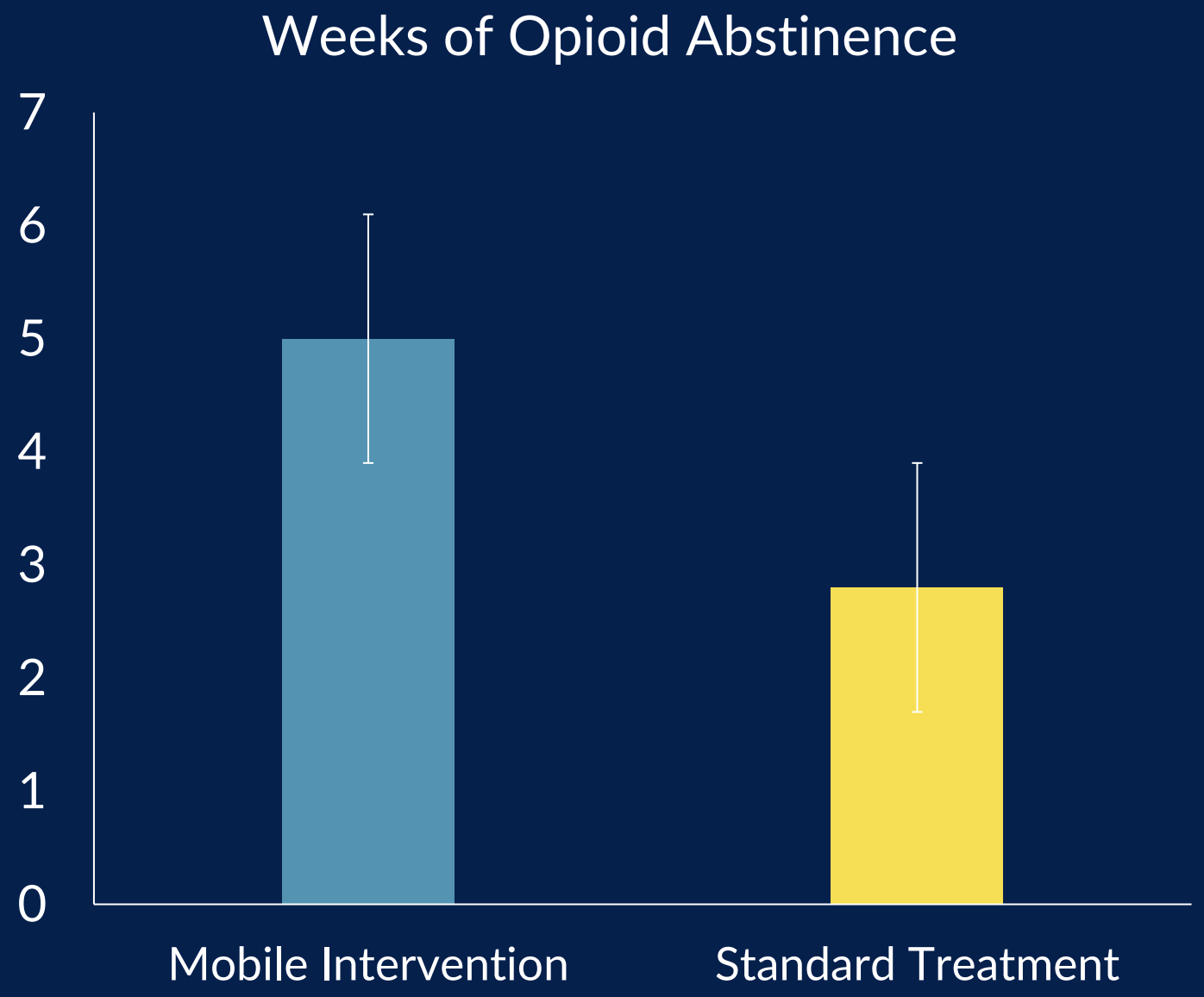
as an Adjunct to Medication Treatment for OUD Greatly Increases Treatment Retention



Guarino, Acosta, Marsch 2016

Adding Mobile Behavioral Treatment

as an Adjunct to Medication Treatment for OUD Greatly Increases Opioid Abstinence



Guarino, Acosta, Marsch 2016

Some Digital Therapeutics can now be prescribed for Substance Use Disorders in the U.S.

- **September 2017.** U.S. Food and Drug Administration (FDA) authorized first "Prescription Digital Therapeutic" for treatment of substance use disorders

- **December 2018.** FDA authorized "Prescription Digital Therapeutic" for opioid use disorder treatment

U.S. FDA Authorization of Rx Digital Therapeutics

- Considered as a type of medical device
- Need to be:
  - *Software Driven*
  - *Evidence-based*
  - *Make a claim to prevent, manage or treat a medical disease or disorder*
- Apps that promote general wellness excluded from regulatory oversight

- Can extend reach of healthcare workforce by overcoming time, place and personnel constraints that limit healthcare delivery
- This process helps clinicians know which apps are safe and effective in the treatment of behavioral health conditions.

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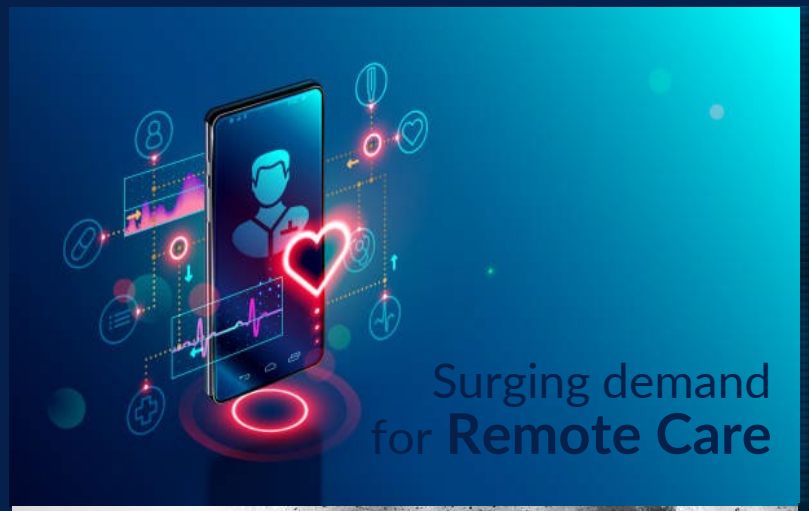
Innovate · Evaluate · Disseminate

GEISEL SCHOOL OF MEDICINE AT DARTMOUTH

We have seen similar robust effects in numerous areas of behavioral health and health behavior

- Reduce **clinical depression**
- Reduce **HIV risk behavior**
- Promote **smoking cessation**
-
- Treat **binge eating disorder**
- Improve functioning among persons with **severe mental illness**
- Reduce problematic **alcohol use among persons with trauma**
- Prevent drug use and risk behavior among **adolescents**
- Treat clinical anxiety
- Promote **medical regimen adherence** among chronic disease patients

The Opportunity



Surging demand for **Remote Care**

Exponential growth in **Digital Health Industry**

Growing global **Behavioral Health Needs**

Multiple paths to **Deployment**

Evolving **Payment Landscape**

SCALING UP SCIENCE-BASED BEHAVIORAL HEALTH CARE
VIA DIGITAL HEALTH

AN EXEMPLAR FROM LATIN AMERICA

Colombia is a part of the world with high mental health burden and limited capacity for mental health care.

Depression and high levels of alcohol use are particularly striking concerns in the region.

This project leveraged digital health solutions to expand access to science-based behavioral health care across Colombia (with expansion to Peru & Chile).

Digitally-Enhanced Model Of **Behavioral Health Care**

Partner with Primary Care Systems across the nation

Leverage Digital Health for:

DIGITAL SCREENING

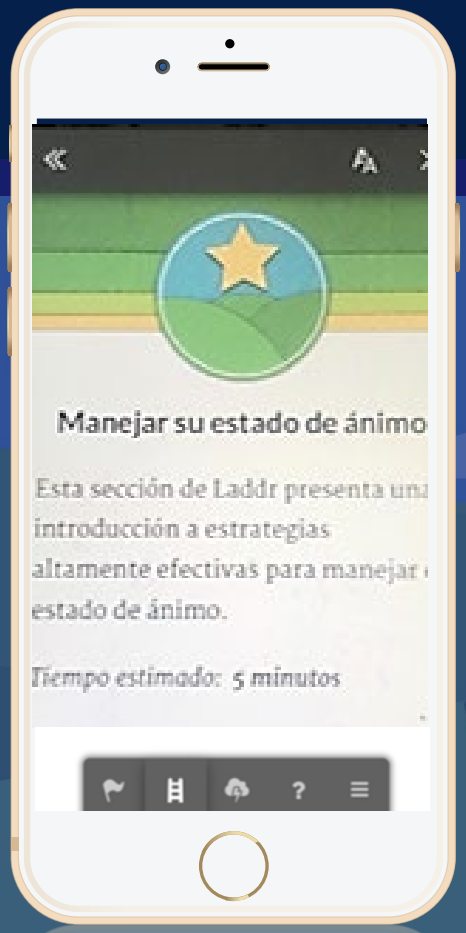
DIGITAL CLINICAL DECISION SUPPORT

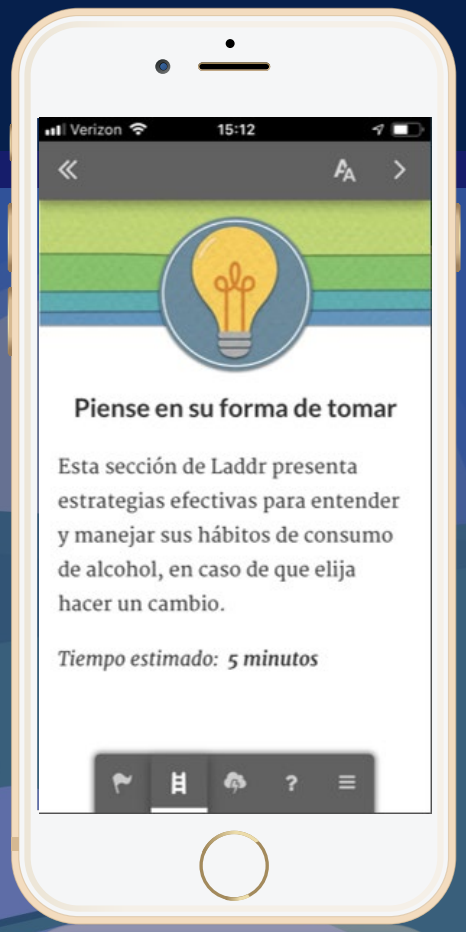
DIGITAL THERAPEUTIC FOR DEPRESSION & PROBLEMATIC ALCOHOL USE

DIGITAL SCREENING

DIGITAL CLINICAL DECISION SUPPORT

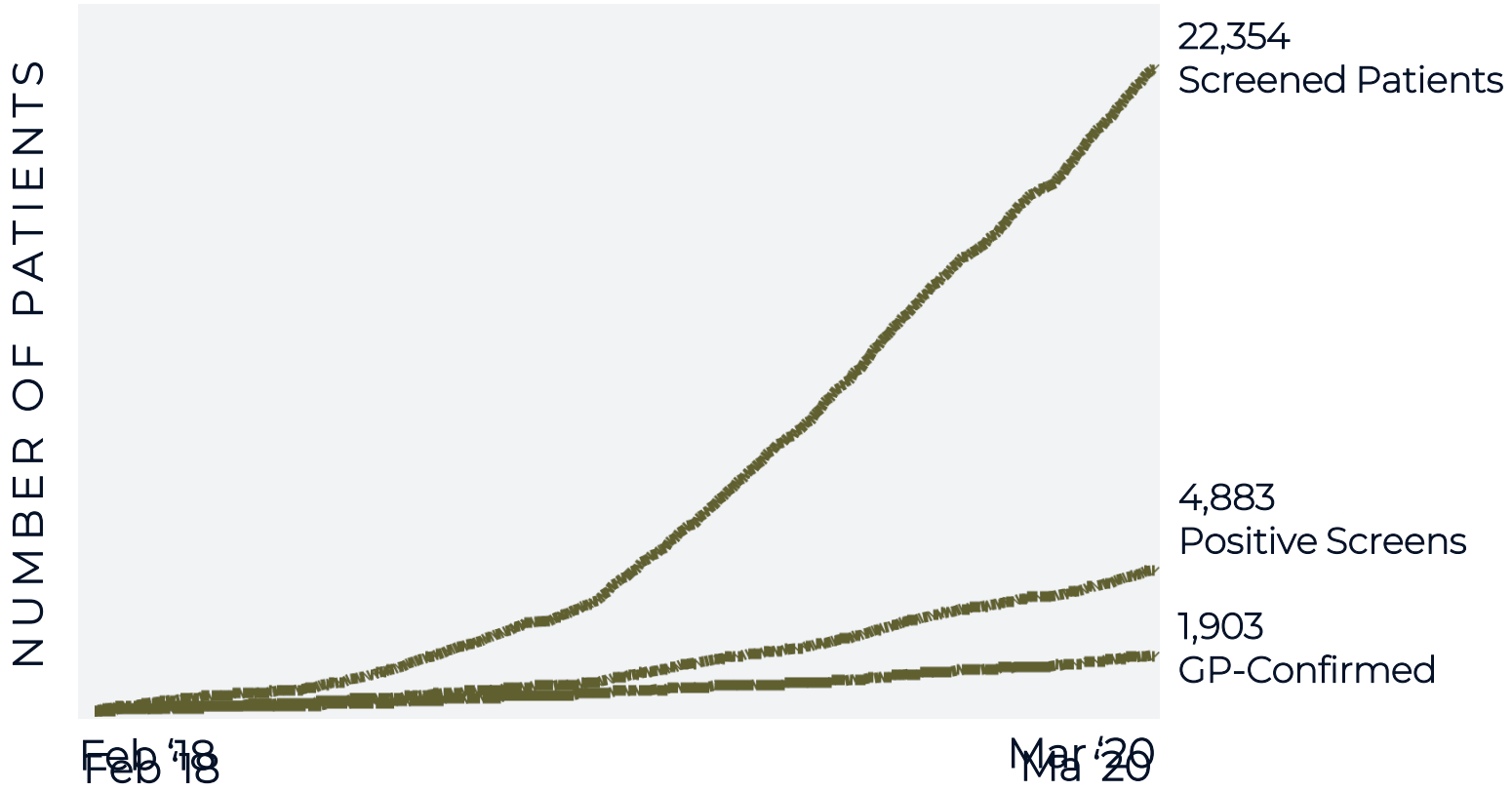
LADDR® DIGITAL THERAPEUTIC





RESULTS

Screening, Positive Screen Rate, and Clinical Diagnosis



22,354
Screened Patients

22%
Positive Screens

8%
Diagnosis
of Depression or
Unhealthy Alcohol Use

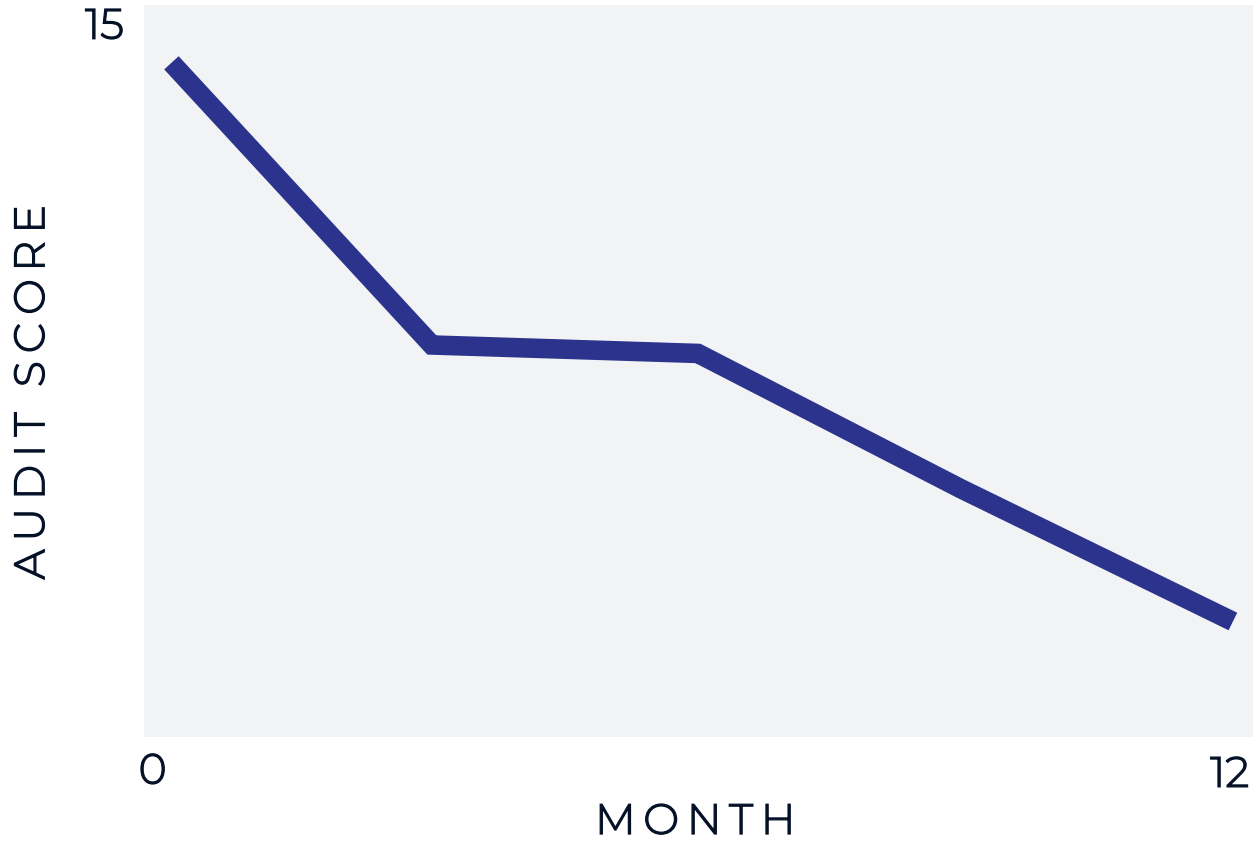
RESULTS

Evolution of Depression Symptoms

RESULTS

Evolution of Depression Symptoms by Severity at Baseline

Evolution of Problematic Alcohol Use



Evolution of Problematic Alcohol Use by Severity at Baseline

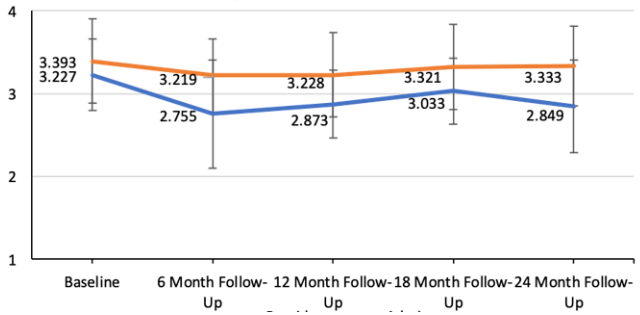
Probable Dependence

Hazardous Consumption

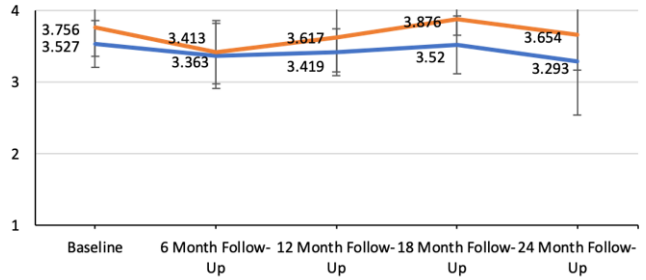
Low Risk Consumption

Clinician and Administrator Data
on Integrated Measure Of Implementation Context And Outcomes

ADOPTION



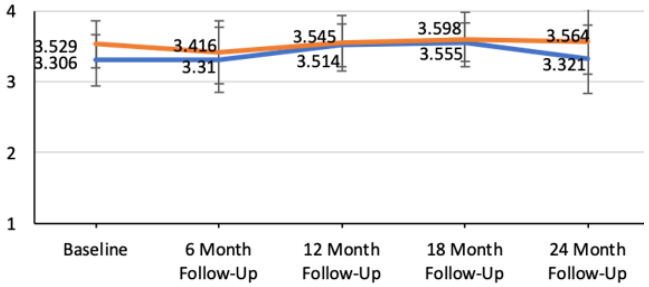
ACCESSIBILITY



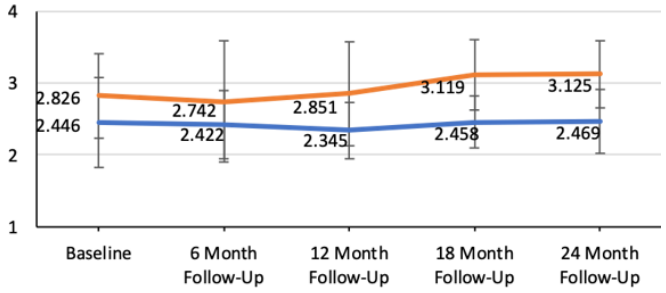
— Admin

— Providers

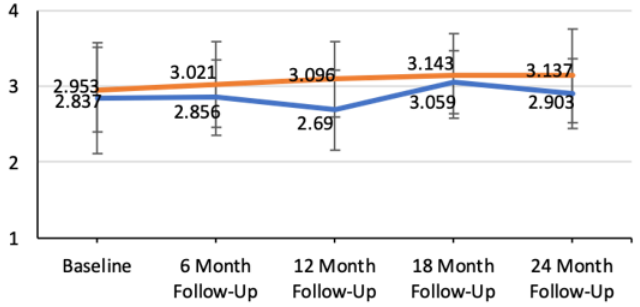
APPROPRIATENESS



FEASIBILITY



SCOPE



IMPLEMENTATION

Implementation Costs

Costs-Based Tool

Time-driven activity-based cost metric

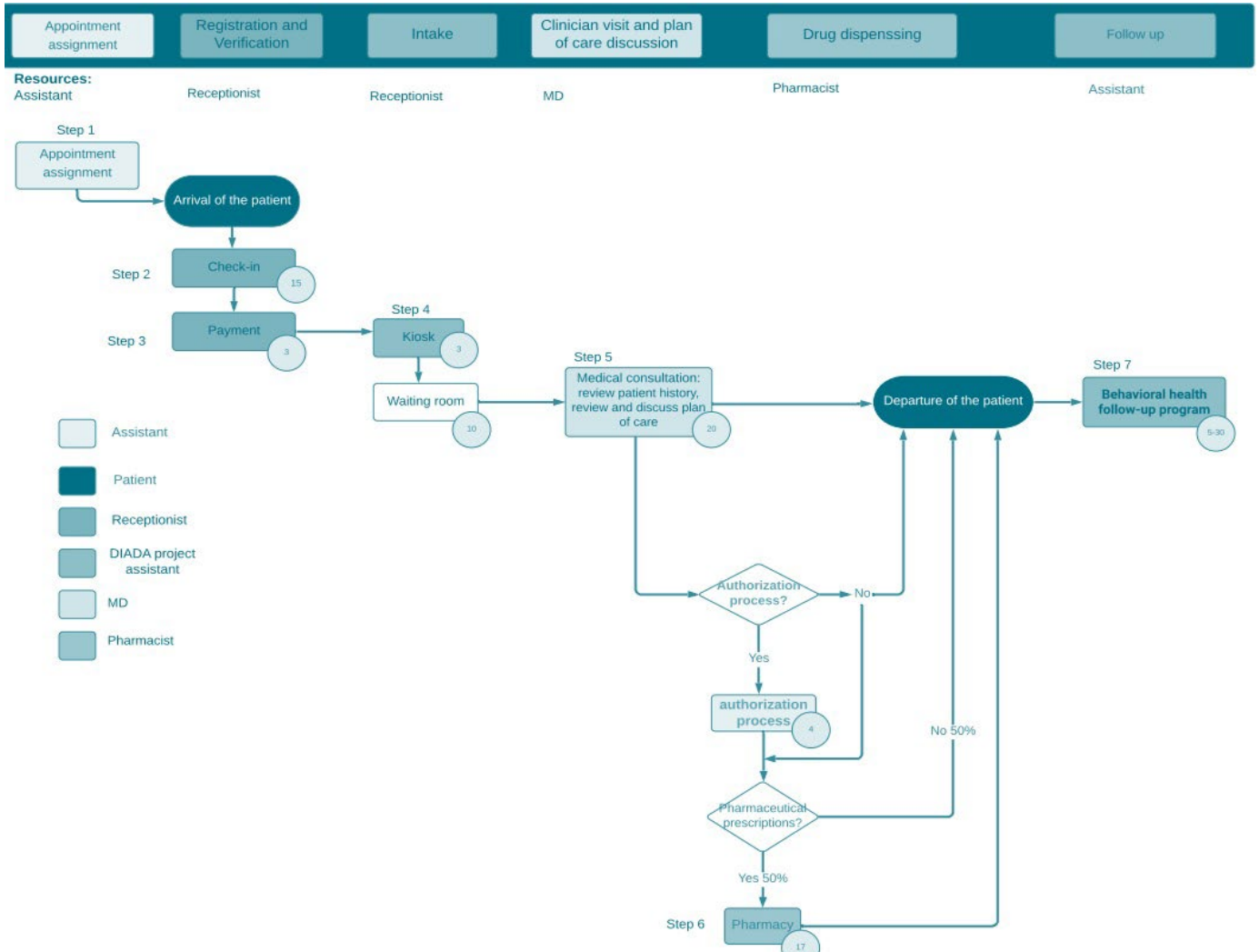
Cost Difference

Before vs after model implementation: $1.89 US dollars

Potential Cost-Effectiveness

Due to early and sustained effects on behavioral health

PROCESS MAP



LESSONS LEARNED

This project has significantly **expanded capacity** for delivering science-based mental health care to meet a large unmet need in Colombia.

This approach could be expanded to **include other areas** of mental health, chronic disease management, and preventive health-promoting interventions.

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LESSONS LEARNED

An important demonstration project on **how to leverage digital health in low-resource contexts globally** to tackle the significant burden of mental disorders and scale up access to evidence-based models of mental health service delivery.

Won National Academy of Medicine **Award**

Now **scaling** across Latin America

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The Opportunity

Digital technologies enable an entirely new offering of tools:

Collecting rich data about people's behavior, health, and environment

Providing personalized interventions and resources based on individuals' needs and preferences

Enabling dynamic computational models to predict and respond to people's changing needs, goals, and health trajectories over time.

Digital Health Measurement

Novel Digital Biomarkers

Digital tools and analytics to measure an individual's behavior, health and context "in vivo".

Captures richness/granularity in behavior, confluence of factors that impact behavior in the moment, and within-individual

To understand the full range of human behavior in environmental and neuro-developmental contexts

Marsch, LA. 2021. Digital Health Data-Driven Approaches to Understand Human Behavior. *Neuropsychopharmacology*

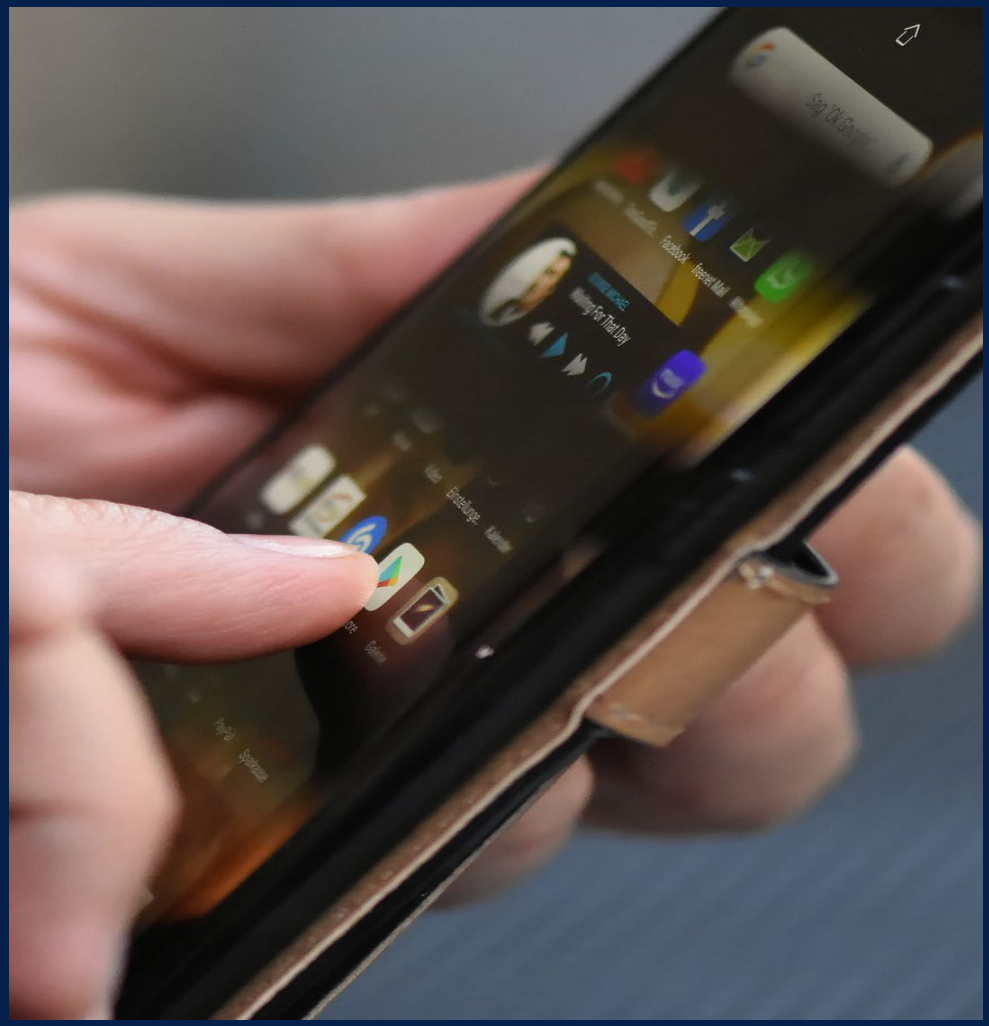
Digital Health Measurement

Digital Phenotyping: Allows for moment-by-moment quantification of individual-level data collected via digital devices

Ecological Momentary Assessment (EMA) and passive sensing

May inform the confluence of factors that predict clinically meaningful events

May inform the delivery of the right intervention at the right time



Digital Biomarkers have shown promise in the field of substance use disorders.

e.g.,

Lapses to smoking among smokers trying to quit were associated with increases in negative mood for many days (not just hours) before a smoking lapse event *(Shiffman & Waters, 2004)*.

Craving predicted imminent drug use, but self-reported stress was much less predictive than craving *(Preston et al., 2018)*.

Drug triggers (e.g., exposure to drug cues or mood changes) increased for hours before cocaine use events but not before heroin use events *(Epstein et al, 2009)*.

Personalized Interventions

Tailored messages responsive to an individual's smoking risk (e.g., advised to chew a piece of nicotine gum) was more engaging and effective than usual care *(Hebert et al., 2020)*.

Adaptively tailored advice intervention for managing nicotine withdrawal symptoms and medication side-effects was used more often and more acceptable among smokers seeking to quit vs. usual care *(McClure et al, 2016)*.

Digital interventions that can impact momentary self-regulation (e.g., emotion regulation; perseverance) can impact health behavior across populations (Marsch, Poldrack et al.)

Digital Phenotyping of Opioid Use Disorder (OUD)

Marsch, Campbell et al.

- First study to employ:
  - passive mobile sensing
  - social media data
  - active responses to queries on mobile devices

to obtain moment-by-moment quantification of individual-level data that may predict retention in treatment, opioid use and medication adherence outcomes in a population of persons in medication treatment with OUD

Ambulatory Physiological Assessment using Mobile Sensors

Sensors	Smartphone	Smartwatch
Accelerometer	✓	✓
Activity/Steps	✓	✓
App Usage	✓	
Audio (characteristics)	✓	
Call/Text	✓	
GPS	✓	✓
Screen On/Off	✓	
Phone Lock/Unlock	✓	
Phone Notification Information	✓	
Wi-Fi & Bluetooth Logs	✓	
Heart Rate		✓
Sleep	✓	✓
Ambient Light	✓	
Proximity	✓	

Ecological Momentary Assessments

- Sleep
- Stress
- Pain severity, interference, & catastrophizing
- Craving
- Withdrawal
- Substance Use Risk Context
- Mood
- Context
- Substance Use
- Self Regulation
- OUD Medication Treatment Adherence

Social Media Data

- For participants who consent, data will be extracted from Twitter, Facebook and/or Instagram
  - Images/texts of postings and comments
  - Date/time and the number of reaction responses (e.g., Like, Sad, Angry) per posting and per comment
  - Extraction will occur when participant joins the study and retroactively at the end of the 12-week study time period

Feasibility

Participants:

- Carried phone on 94% of days
- Wore watch 74% of days
- Mean EMA response rate = 70%
- 88% agreed to share social media data

Utility

- EMA and random forest models, we predicted next-day opioid use (AUC = 0.97, sensitivity = 93%, specificity = 98%) using data from the previous week

- Wearable heart rate and smartphone conversation detection data forecasted next-day opioid use using data from the previous week (AUC = 0.72, sensitivity = 65%, specificity = 65%)

  - Similar results for predicting future stress, craving, pain, and anxiety

- Social media data and deep learning models predicted next-day opioid use (AUC = 0.74, sensitivity = 86%, specificity = 62%) using data from the previous week

Implications

This study may inform:

- which subset(s) of digitally-derived data may be most useful to employ as part of outcome measurement in clinical trials

- when an individual may be most receptive to real-time intervention delivery (to provide the right type/amount of therapeutic support at the right time by adapting to an individual's changing internal and contextual state)

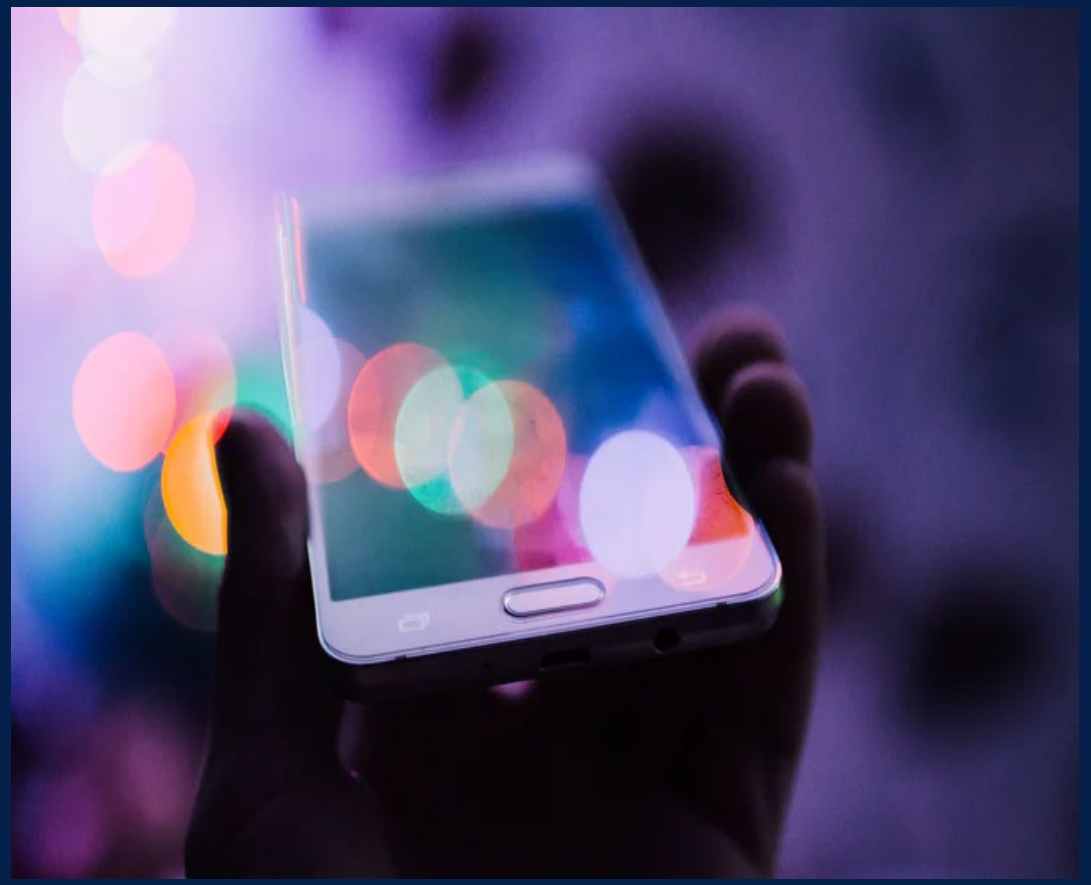
Digital Health Measurement Concluding Comments

Discovery Science to Translational Science
Informs a full spectrum ranging from digital biomarkers-- to clinical outcomes -- to personalized intervention delivery responsive to the dynamic nature of health behavior

Overall, the literature to date provides a compelling “proof of concept”.

More focus needed on validation of measures, rigorous trials, and reproducibility of results

Opportunity to transcend disease-specific models of behavior to embrace, understand and treat the complexity and interrelatedness of clinical disorders.



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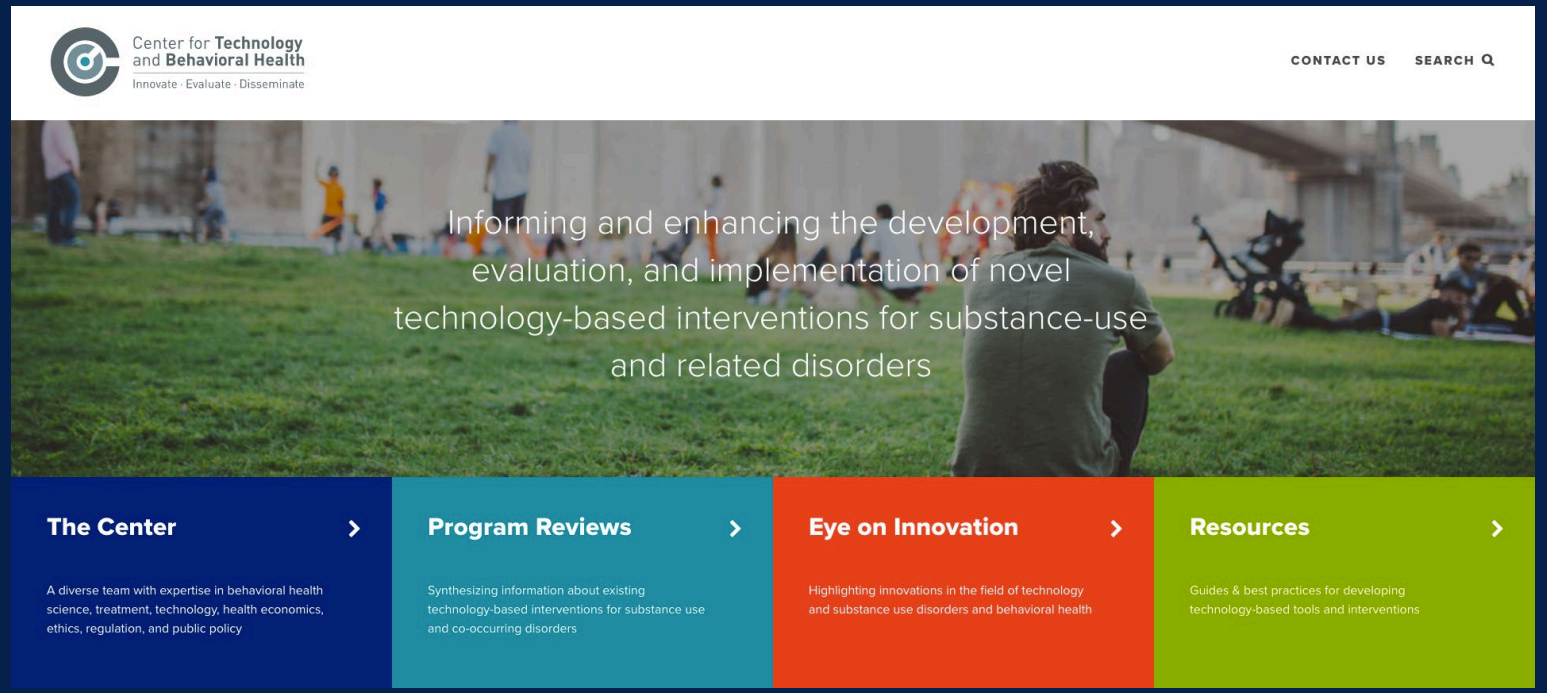
Use science to inform the development, evaluation, & implementation of digital therapeutics for health behavior

Bring science to people's daily lives



Sample of Current Research Directions at CTBH

- Transdiagnostic Digital Therapeutics
- Adaptive Digital Therapeutics (Momentary Interventions)
- Expand research and resources on digital health ethics
- Increase training, mentorship and representation of underrepresented minorities in digital health research
- Markedly enhance collaborative work with a wide array of scientific, clinical, industry, and governmental partners to scale access to science-based digital therapeutics globally

Thank you!

Lisa.a.marsch@dartmouth.edu

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