OVERVIEW OF PRESCRIPTION DIGITAL THERAPEUTICS (PDTs)

Scott Schepers
Aug 5, 2022
AGENDA

• Digital therapeutics – what are they?

• What are PDTs and how are they different from DTx and drugs?

• Regulatory process to approve PDTs and the requirement of clinical data for authorization

• What PDTs are available to date?

• What is addiction, how is it treated, and what is the current state of research (epidemiology, challenges in field, barriers to access, and new initiatives)

• Example of a PDT for SUD to illustrate supporting evidence for its use -- clinical and real-world experiences

• Conclusions
ADOPTION OF TELEMEDICINE & SOFTWARE-BASED TREATMENTS A POTENTIAL SOLUTION FOR ACCESS & OUTCOMES IN THE TREATMENT OF MENTAL HEALTH AND SUBSTANCE USE

01 Technology is pervasive
Americans spend 5.4 hours on mobile phones daily¹

02 Transition to telemedicine
Telehealth use doubled from 39.4% pre-COVID-19 to 79.5% in 2020²

03 Explosion of digital choices
2021 IQVIA report listed >2500 digital health apps³

04 Mental health provider shortage
There are widespread shortages of mental health providers across the U.S., limiting patient access to CBT.⁴

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

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

1900+ Small Molecules
1980+ Biologics
2000+ Cell/Gene Therapies
2017 Prescription Digital Therapeutics
Pivotal Clinical Trials

- Safety testing
- Efficacy testing

FDA Submission

- FDA Review

- FDA Decision

Post Market Surveillance

**FDA Authorizes PDTs: Pre- and Post-Market Authorization**

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

**For De Novo Currently Authorized Products:**

E.g. in SUD/OUD: 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.

There are currently 9 PDTs authorized by the FDA*

<table>
<thead>
<tr>
<th>PDT Product</th>
<th>Company marketing product</th>
<th>Therapeutic Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDT for SUD¹</td>
<td>Pear Therapeutics</td>
<td>Substance use disorder</td>
</tr>
<tr>
<td>PDT for OUD²</td>
<td>Pear Therapeutics</td>
<td>Opioid use disorder</td>
</tr>
<tr>
<td>Somryst³</td>
<td>Pear Therapeutics</td>
<td>Chronic insomnia</td>
</tr>
<tr>
<td>Nightmare⁴</td>
<td>NightWare</td>
<td>Posttraumatic stress disorder (PTSD)–driven traumatic nightmares</td>
</tr>
<tr>
<td>EndeavorRx⁵</td>
<td>Akili</td>
<td>Attention deficit hyperactivity disorder</td>
</tr>
<tr>
<td>Parallel⁶</td>
<td>Mahana</td>
<td>Irritable bowel syndrome (IBS)</td>
</tr>
<tr>
<td>RelievRx⁷</td>
<td>AppliedVR</td>
<td>Reduction of pain in patients (18 years and over) with chronic lower back pain (indication)</td>
</tr>
<tr>
<td>Luminopia One⁸</td>
<td>Luminopia</td>
<td>Treat amblyopia in children aged 4 to 7 years</td>
</tr>
<tr>
<td>Regulora⁹</td>
<td>metaMe Health</td>
<td>Abdominal pain associated with IBS in adults</td>
</tr>
</tbody>
</table>


For informational purposes only and subject to change.

*As of August 2022.
SUBSTANCE USE DISORDER

Epidemiology and treatment
**SUBSTANCE USE DISORDERS ARE COMMON**

**SAMHSA**
Substance Abuse and Mental Health Services Administration

2020 National Survey on Drug Use and Health

**40.3 Million**
Estimate of people in the U.S. 12 and older with a past year substance use disorder (SUD)¹

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![Chart showing number of people with specific past year substance use disorders](image-url)
Percent Change in Drug Overdose Deaths Between September 2020 and September 2021

12%\(^1\)

99,543 Overdose Deaths Reported Between September 2020 and September 2021\(^1\)

Reported provisional counts for the 12-month ending periods are the number of deaths received and processed for the 12-month period ending in the month indicated. Reported provisional counts may not include all deaths that occurred during a given time period and are subject to change.

OPIOID USE DISORDER IS AN ONGOING CRISIS

Opioid Use Disorder is driving a growing number of deaths

2.7 Million
Estimate of people in the U.S. 12 and older with a past year Opioid Use Disorder

38%
Increase in opioid associated deaths in the year ending January 2021


January 12-Month-Ending National Drug Overdose Deaths Involving Any Opioid

Number of Deaths

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>28986</td>
</tr>
<tr>
<td>2016</td>
<td>33531</td>
</tr>
<tr>
<td>2017</td>
<td>43691</td>
</tr>
<tr>
<td>2018</td>
<td>47549</td>
</tr>
<tr>
<td>2019</td>
<td>46996</td>
</tr>
<tr>
<td>2020</td>
<td>51018</td>
</tr>
<tr>
<td>2021</td>
<td>70456</td>
</tr>
</tbody>
</table>
DSM-V Diagnostic Criteria: Substance Use Disorder

- A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least 2 of the following, occurring within a 12-month period:
  1. Substance is often taken in larger amounts or over a longer period than was intended.
  2. There is a persistent desire or unsuccessful efforts to cut down or control substance use.
  3. A great deal of time is spent in activities necessary to obtain the substance, use it, or recover from its effects.
  4. Craving, or a strong desire or urge to use the substance.
  5. Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home.
  6. Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance.
  7. Important social, occupational, or recreational activities are given up or reduced because of substance use.
  8. Recurrent substance use in situations in which it is physically hazardous.
  9. Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
  10. Development of tolerance.

- Severity: Mild = 2-3 symptoms; Moderate = 4-5 symptoms; Severe ≥ 6 symptoms
- Additional specifiers: “in early remission,” “in sustained remission,” “on maintenance therapy” for certain substances, and “in a controlled environment.”

ASAM Definition and Treatment Approach

• “Addiction is a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual’s life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences. Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.”

• Treatment goals for SUDs are consistent with those of other chronic disease:
  • Include symptom reduction and improving health and function. Broadly, the key components of care include medications, behavioral therapy, and recovery support services delivered in appropriate treatment setting.

EVIDENCE BASED TREATMENT APPROACHES AND LIMITATIONS

- Medication Management: Evidence suggests that medications can be effective, but are underutilized or not available to treat many types of SUD
  - FDA Approved Medications for OUD: Naltrexone, Buprenorphine, Methadone
  - FDA Approved Medications for AUD: Disulfiram, Naltrexone, Acamprosate
  - There are currently no FDA Approved Medications available to treat marijuana, cocaine, methamphetamine or other SUDs

- Behavioral Therapies have demonstrated effectiveness in treating SUDs, but are limited by access to care and inconsistent treatment fidelity
  - Evidence based behavioral therapies include Cognitive Behavioral Therapy, Contingency Management, Community Reinforcement Approach, Motivational Enhancement Therapy, The Matrix Model and Twelve-Step Facilitation Therapy
  - Combinations of Contingency Management and Cognitive behavioral therapy interventions may be especially effective

- When available, a dual approach including medication management and behavioral therapies may produce optimal outcomes

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.

The COVID-19 pandemic has elucidated the many shortcomings of our healthcare system in its current form. Prescription Digital Therapeutics (PDTs) are uniquely positioned to potentially address barriers to access and treatment inequities by bringing treatments to the patient.

In addition to improving access to treatment, digital health can catalyze and diversify research efforts and expand offerings to underserved populations, including ethnic, racial, and other minority groups.

Diversifying research populations is especially important because it creates treatment options that are appropriate for different populations.

Diversity is excellence. Interpopulation inequities are exacerbated if we do not diversify research and treatment options.

PDTs for SUD and OUD

How they work and how they’ve been studied
Provides intervention
- Cognitive Behavioral Therapy (CBT) Modules
- Fluency Training
- Contingency Management
- Cravings and Trigger Assessment

Provides insight
- Real-world Engagement
- CBT Module Use
- Fluency Training
- Contingency Management
- Cravings and Trigger Assessment
- Urine and Drug Screen Appointments
**Example of PDT Mechanism of Action with Digital Delivery of Evidence-Based Treatment**

<table>
<thead>
<tr>
<th>Community Reinforcement Approach (CRA)(^{1,2,3})</th>
<th>Fluency Training(^4)</th>
<th>Contingency Management (CM)(^{5,6})</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 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</td>
<td>• Individually paced presentation of content and testing to facilitate and confirm mastery of learning</td>
<td>• Evidence-based positive reinforcement system, in which, financial or non-financial incentives are provided contingent on performing behaviors consistent with treatment</td>
</tr>
<tr>
<td>• 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</td>
<td>• Demonstrated to promote learning and improve both short-term and long-term retention of material</td>
<td>• Efficacy of CM has been demonstrated across a wide range of SUDs</td>
</tr>
</tbody>
</table>

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

Study Results²

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>rTAU+TES</th>
<th>TAU</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstinence: all patients</td>
<td>40.3%</td>
<td>17.6%</td>
<td>0.0004</td>
</tr>
<tr>
<td>Abstinence: non-abstinent at study start</td>
<td>16.1%</td>
<td>3.2%</td>
<td>0.0013</td>
</tr>
<tr>
<td>Retention in treatment: all patients</td>
<td>76.2%</td>
<td>63.2%</td>
<td>0.0042</td>
</tr>
</tbody>
</table>

Pivotal Trial Overview

- 170 patients were randomized to receive either:
  - Treatment-as-Usual (TAU), consisting of Contingency Management + buprenorphine
  - TAU + 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
  - Abstinence/Negative urine drug screens in weeks 9-12
  - Retention in treatment

![Study Results](image)

Study Results

REAL WORLD EVIDENCE
A Continuum of Evidence for PDTs 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
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
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 PDT for OUD prescriptions

- First prescription (12-weeks); Missing data positive abstinence imputation (N=3,817)
  - n=2,733 included in missing data removed abstinence imputation
- Second prescription (24-weeks); Missing data positive abstinence imputation (N=643)
  - n=584 included in missing data removed abstinence imputation

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

Patients were represented across age groups and gender.

Representation by Age

Mean age 39 years

Representation by Gender

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

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

A MAJORITY OF PATIENTS REMAIN ACTIVE IN PDT FOR OUD THROUGH WEEK 12 OF FIRST AND SECOND PRESCRIPTIONS

Activity by Week

<table>
<thead>
<tr>
<th>Week</th>
<th>12 Weeks (N=3817)</th>
<th>24 Weeks (N=643)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>2</td>
<td>85%</td>
<td>93%</td>
</tr>
<tr>
<td>3</td>
<td>78%</td>
<td>89%</td>
</tr>
<tr>
<td>4</td>
<td>74%</td>
<td>88%</td>
</tr>
<tr>
<td>5</td>
<td>71%</td>
<td>87%</td>
</tr>
<tr>
<td>6</td>
<td>67%</td>
<td>86%</td>
</tr>
<tr>
<td>7</td>
<td>64%</td>
<td>81%</td>
</tr>
<tr>
<td>8</td>
<td>62%</td>
<td>81%</td>
</tr>
<tr>
<td>9</td>
<td>61%</td>
<td>80%</td>
</tr>
<tr>
<td>10</td>
<td>58%</td>
<td>79%</td>
</tr>
<tr>
<td>11</td>
<td>56%</td>
<td>77%</td>
</tr>
<tr>
<td>12</td>
<td>55%</td>
<td>75%</td>
</tr>
</tbody>
</table>

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

PATIENTS ARE ACTIVE IN PDT FOR OUD THROUGHOUT THE FULL 24-HOUR PERIOD

Activity by Time of Day

- 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
High rates of abstinence were observed in the first and second prescription.

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 PDT for OUD 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 PDT for OUD prescription (weeks 9-12); Patients without any data (UDS or self-reports) over the final four weeks removed from analysis population.

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

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

HEALTH ECONOMICS AND OUTCOMES RESEARCH
The Impact of a PDT for SUD on Healthcare Resource Utilization

6-Month Real-World Claims Analyses

A retrospective analysis of the HealthVerity PrivateSource 20 claims database was performed to assess the impact of PDT for SUD engagement† on HCRU among patients receiving treatment for SUD.

**Patient Identification**
Patients who activated PDT for SUD between 01 January 2019 and 30 October 2020 from a large, nationally representative database*

**Data Collection**

**BASELINE PERIOD**
- 6 Months Pre-index

**STUDY PERIOD**
- 6 Months Post-index

**INDEX DATE**
Date of first prescription for PDT for SUD

**Analysis**
Comparison of HCRU between baseline and study periods, including:
- All facility services
- All clinician services

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*Required medical eligibility is a minimum of 122 days within the 6-months. Mean number of days in the pre-index and post-index period are 181 and 178, respectively.

†Those who redeemed PDT for SUD and demonstrated any activity within the therapeutic after the first week of the 12-week prescription
## 6-Month Pre-Post Demographics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>n=101</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age on Index Date</strong></td>
<td></td>
</tr>
<tr>
<td>Mean, (SD)</td>
<td>38.3 (11.34)</td>
</tr>
<tr>
<td>Median, (range)</td>
<td>37.0 (19–67)</td>
</tr>
<tr>
<td><strong>Age on Index Date, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>9 (8.9%)</td>
</tr>
<tr>
<td>25-34</td>
<td>34 (33.7%)</td>
</tr>
<tr>
<td>35-44</td>
<td>30 (29.7%)</td>
</tr>
<tr>
<td>45-54</td>
<td>17 (16.8%)</td>
</tr>
<tr>
<td>55-64</td>
<td>10 (9.9%)</td>
</tr>
<tr>
<td>65-74</td>
<td>1 (1.0%)</td>
</tr>
<tr>
<td><strong>Sex, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>51 (50.5%)</td>
</tr>
<tr>
<td>Male</td>
<td>50 (49.5%)</td>
</tr>
<tr>
<td><strong>Payer on Index Date, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Commercial</td>
<td>38 (37.6%)</td>
</tr>
<tr>
<td>Medicaid</td>
<td>55 (54.5%)</td>
</tr>
<tr>
<td>Medicare Advantage</td>
<td>3 (3.0%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>5 (5.0%)</td>
</tr>
</tbody>
</table>

### Clinical Characteristics

<table>
<thead>
<tr>
<th>Substance Use Disorder in the Pre-Index Period*, n (%)</th>
<th>n=101</th>
</tr>
</thead>
<tbody>
<tr>
<td>F10.20 Alcohol dependence, uncomplicated</td>
<td>41 (40.6%)</td>
</tr>
<tr>
<td>F11 with any other substance F10, F12 F19</td>
<td>30 (29.7%)</td>
</tr>
<tr>
<td>F11.20 Opioid dependence, uncomplicated</td>
<td>27 (26.7%)</td>
</tr>
<tr>
<td>F17.210 Nicotine dependence, cigarettes, uncomplicated</td>
<td>22 (21.8%)</td>
</tr>
<tr>
<td>F10.10 Alcohol abuse, uncomplicated</td>
<td>18 (17.8%)</td>
</tr>
<tr>
<td>F14.20 Cocaine dependence, uncomplicated</td>
<td>18 (17.8%)</td>
</tr>
<tr>
<td>F17.200 Nicotine dependence, unspecified, uncomplicated</td>
<td>18 (17.8%)</td>
</tr>
<tr>
<td>F12.20 Cannabis dependence, uncomplicated</td>
<td>17 (16.8%)</td>
</tr>
<tr>
<td>F19.20 Other psychoactive substance dependence, uncomplicated</td>
<td>16 (15.8%)</td>
</tr>
<tr>
<td>F12.10 Cannabis abuse, uncomplicated</td>
<td>15 (14.9%)</td>
</tr>
<tr>
<td>F19.10 Other psychoactive substance abuse, uncomplicated</td>
<td>12 (11.9%)</td>
</tr>
<tr>
<td>F15.20 Other stimulant dependence, uncomplicated</td>
<td>9 (8.9%)</td>
</tr>
<tr>
<td>F11.10 Opioid abuse, uncomplicated</td>
<td>8 (7.9%)</td>
</tr>
<tr>
<td>F14.10 Cocaine abuse, uncomplicated</td>
<td>8 (7.9%)</td>
</tr>
<tr>
<td>F10.21 Alcohol dependence, in remission</td>
<td>7 (6.9%)</td>
</tr>
<tr>
<td>F11.21 Opioid dependence, in remission</td>
<td>6 (5.9%)</td>
</tr>
<tr>
<td>F15.10 Other stimulant abuse, uncomplicated</td>
<td>5 (5.0%)</td>
</tr>
<tr>
<td>No substance use diagnosis code in the pre-index period</td>
<td>15 (14.9%)</td>
</tr>
</tbody>
</table>

*Characteristics presented for indications ≥5% of study population. Percentages may add to more than 100% as patients claims may be indicated for different opioid use disorder indications.

MPR, medication possession ratio; SD, standard deviation
Pear Therapeutics Data on File
**Significant Decreases Observed Between Pre-index and Post-index PDT for SUD Cohort**

**Overall Hospital Encounters**
- 50%
- IRR: 0.50; 95% CI: 0.37-0.67; *P*<0.001

**Inpatient Stays**
- 56%
- IRR: 0.44; 95% CI: 0.26-0.76; *P*=0.003

**Partial Hospitalizations**
- 57%
- IRR: 0.43; 95% CI: 0.21-0.88; *P*=0.021

**Emergency Department**
- 45%
- IRR: 0.55; 95% CI: 0.38-0.80; *P*<0.004

**Additional Results**
- **E and M**<sup>*</sup> Consultations
  - 91%
  - IRR: 0.09; 95% CI: 0.02-0.36; *P*<0.001

- **Cardiovascular Procedures**
  - 72%
  - IRR: 0.28; 95% CI: 0.14-0.55; *P*<0.001

- **Radiology Services**
  - 52%
  - IRR: 0.48; 95% CI: 0.31-0.76; *P*=0.002

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*Evaluation and Management
1. Median age 37 years, 50.5% female, 54.5% Medicaid-insured
THE IMPACT OF PDT FOR OUD ON HEALTHCARE RESOURCE UTILIZATION

12-MONTH REAL-WORLD CLAIMS ANALYSES

A retrospective analysis of the HealthVerity PrivateSource 20 claims database was performed to assess the impact of PDT for OUD engagement† vs. non-initiation* (control group) on HCRU among patients receiving treatment for OUD.

Patient Identification
Patients who activated PDT for OUD between 01 January 2019 and 30 June 2020‡ from a large, nationally representative database

INDEX DATE
Date of first prescription for PDT for OUD

STUDY PERIOD (12 Months Post-Index)
12 Months Post-Index PDT for OUD
12 Months Post-Index Controls

Data Collection
Analysis
Comparison of HCRU between baseline and study periods, including:
• All facility services
• All clinician services

†Those who redeemed PDT for OUD and demonstrated any activity within the therapeutic after the first week of the 12-week prescription

*Non-initiation is defined as a PDT for OUD prescription that was not redeemed.

‡Required medical eligibility is a minimum of 244 days within the 12-months. Mean number of days in the pre-index and post-index period are 351 and 349, respectively
# 12-Month Case-Control Demographics

## Demographics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>PDT for OUD (n=901)</th>
<th>Control (n=978)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age on Index Date</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean, (SD)</td>
<td>37.9 (8.84)</td>
<td>39.2 (10.18)</td>
</tr>
<tr>
<td>Median, (range)</td>
<td>36.0 (19–68)</td>
<td>38.0 (18-71)</td>
</tr>
<tr>
<td><strong>Age on Index Date, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>21 (2.3%)</td>
<td>43 (4.4%)</td>
</tr>
<tr>
<td>25-34</td>
<td>347 (38.5%)</td>
<td>305 (31.2%)</td>
</tr>
<tr>
<td>35-44</td>
<td>359 (39.8%)</td>
<td>372 (38.0%)</td>
</tr>
<tr>
<td>45-54</td>
<td>113 (12.5%)</td>
<td>155 (15.8%)</td>
</tr>
<tr>
<td>55-64</td>
<td>55 (6.1%)</td>
<td>93 (9.5%)</td>
</tr>
<tr>
<td>65-74</td>
<td>6 (0.7%)</td>
<td>10 (1.0%)</td>
</tr>
<tr>
<td><strong>Sex, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>562 (62.4%)</td>
<td>539 (55.1%)</td>
</tr>
<tr>
<td>Male</td>
<td>339 (37.6%)</td>
<td>439 (44.9%)</td>
</tr>
<tr>
<td><strong>Payer on Index Date, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commercial</td>
<td>96 (10.7%)</td>
<td>137 (14.0%)</td>
</tr>
<tr>
<td>Medicaid</td>
<td>666 (73.9%)</td>
<td>640 (65.4%)</td>
</tr>
<tr>
<td>Medicare Advantage</td>
<td>17 (1.9%)</td>
<td>25 (2.6%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>122 (13.5%)</td>
<td>176 (18.0%)</td>
</tr>
</tbody>
</table>

## Clinical Characteristics

<table>
<thead>
<tr>
<th>Opioid use disorder in the pre-index period, n (%)</th>
<th>PDT for OUD (n=901)</th>
<th>Control (n=978)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F11.10 Opioid abuse, uncomplicated</td>
<td>115 (12.8%)</td>
<td>113 (11.6%)</td>
</tr>
<tr>
<td>F11.11 Opioid abuse, in remission</td>
<td>35 (3.9%)</td>
<td>28 (2.9%)</td>
</tr>
<tr>
<td>F11.14 Opioid abuse with opioid-induced mood disorder</td>
<td>1 (0.1%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>F11.19 with unspecified opioid-induced disorder</td>
<td>2 (0.2%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>F11.20 Opioid dependence, uncomplicated</td>
<td>690 (76.6%)</td>
<td>762 (77.9%)</td>
</tr>
<tr>
<td>F11.21 Opioid dependence, in remission</td>
<td>117 (13.0%)</td>
<td>100 (10.2%)</td>
</tr>
<tr>
<td>F11.23 Opioid dependence with withdrawal</td>
<td>55 (6.1%)</td>
<td>61 (6.2%)</td>
</tr>
<tr>
<td>F11.288 Opioid dependence with other opioid-induced disorder</td>
<td>7 (0.8%)</td>
<td>10 (1.0%)</td>
</tr>
<tr>
<td>F11.29 Opioid dependence with unspecified opioid-induced disorder</td>
<td>6 (0.7%)</td>
<td>4 (0.4%)</td>
</tr>
<tr>
<td>F11.90 Opioid use, unspecified, uncomplicated</td>
<td>32 (3.6%)</td>
<td>33 (3.4%)</td>
</tr>
<tr>
<td>F11.988 Opioid use, unspecified with unspecified opioid-induced disorder</td>
<td>1 (0.1%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>F11.99 Opioid use, unspecified with other opioid-induced disorder</td>
<td>20 (2.2%)</td>
<td>24 (2.5%)</td>
</tr>
<tr>
<td>No opioid use diagnosis code</td>
<td>192 (21.3%)</td>
<td>196 (20.0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Buprenorphine treatment Pre-Index or Post-Index, n</th>
<th>PDT for OUD (n=901)</th>
<th>Control (n=978)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine treated Pre-Index, n (%)</td>
<td>647 (97.3%)</td>
<td>686 (95.8%)</td>
</tr>
<tr>
<td>Buprenorphine treated Post-Index, n (%)</td>
<td>637 (95.8%)</td>
<td>680 (95.0%)</td>
</tr>
</tbody>
</table>

| 12-month Buprenorphine adjusted adherence         |                     |                |
| Pre-Index (MPR), mean (SE)                        | 0.65 (0.01)         | 0.63 (0.01)    |
| Post-Index (MPR), mean (SE)                       | 0.85* (0.01)        | 0.76 (0.01)    |

SD=standard deviation; *P = 0.0001; 1 Fulton F. Velez, Kathryn Anastassopoulos, resource utilization in patients with opioid use disorder in the 12 months after initiation of a prescription digital therapeutic. Advances in Therapy. 2022; https://doi.org/10.6084/m9.figshare.20013323.v1.
SIGNIFICANT DECREASES OBSERVED BETWEEN PDT FOR OUD\(^1\) (n=901) AND THE CONTROL COHORT\(^2\) (n=978)

**Overall Inpatient Stays**
- 28% decrease
  - IRR: 0.72; 95% CI: 0.55-0.96; \(P=0.026\)

**ICU Stays**
- 30% decrease

**Hospital Readmissions**
- 56% decrease
  - IRR: 0.44; 95% CI: 0.20-0.93; \(P=0.033\)

**Emergency Department**
- 7% increase
  - IRR: 0.93; 95% CI: 0.79-1.09; \(P=0.386\)

**Additional Results**
- Fewer unique hospital encounters:
  - 145 per 1,000 patients vs control
- Case Management Services:
  - 106%
- Buprenorphine Adherence:
  - 9%
- Total clinician services increased by:
  - 1,391 events vs controls

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1. Median age of 36 years; 62.4% were female, 73.9% were Medicaid recipients, and 93.1% were treated with buprenorphine in both the pre-index and post-index periods.
2. Median age of 38 years; 54.9% were female, 66.0% were Medicaid recipients, and 91.2% were treated with buprenorphine in both the pre-index and post-index periods.
CONCLUSIONS
CONCLUSIONS

- PDTs are regulatory-authorized products. 9 PDTs are already FDA-authorized, more PDTs are currently in development
  - PDTs enable the delivery of evidence-based treatment regardless of geographic barriers -- at home, off-hours, offline if needed

- Three types of evidence can be used to support the use of PDTs across disease areas
  - Randomized Clinical Trials (RCTs), demonstrating gold-standard scientific validity using objective endpoints
  - Real-World Evidence (RWE), confirming generalizability & external validity of RCTs in broad real-world use
  - Health Economics and Outcomes Research (HEOR), correlating economic outcomes with clinical value to support providers and payers

- Additional considerations for the use of PDTs
  - PDTs enable access to care in various patient populations, across socioeconomic states and other healthcare inequities
  - PDTs have an additional impact on society – effective treatment can produce additional benefits in decreasing/improving comorbidities, absenteeism/presenteeism, workplace and other injuries, caregiver burden etc.