

**Real-world reductions in healthcare resource utilization over 6 months in patients with substance use disorders treated with a prescription digital therapeutic**

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**Abstract** (278 words, limit: 300)

**Background and Aims:** Substance use disorders (SUDs) affect approximately 40.3 million people in the United States, yet only approximately 19% receive evidence-based treatment each year. reSET® is a prescription digital therapeutic (PDT) and the only FDA-authorized treatment for patients with cocaine, cannabis, and stimulant use disorders. This study evaluated real-world healthcare resource utilization (HCRU) and associated costs 6 months after initiation of reSET in patients with SUD.

**Methods:** A retrospective analysis of HealthVerity PrivateSource20 data compared the 6-month incidence of all-cause hospital facility encounters and clinician services in patients treated with reSET (re-SET cohort) before (pre-index period) and after (post-index period) reSET initiation (index). Incidence was compared using incidence rate ratios (IRR). HCRU-related costs were also assessed.

**Results:** The sample included 101 patients (median age 37 years, 50.5% female, 54.5% Medicaid-insured). A statistically significant decrease of 50% was observed in overall hospital encounters from pre-index to post-index (IRR: 0.50; 95% CI: 0.37-0.67;  $P<0.001$ ), which included: inpatient stays (56% decrease; IRR: 0.44; 95% CI: 0.26-0.76;  $P=0.003$ ), partial hospitalizations (57% decrease; IRR: 0.43; 95% CI: 0.21-0.88;  $P=0.021$ ), and emergency department visits (45% decrease; IRR: 0.55; 95% CI: 0.38-0.80;  $P<0.004$ ). Additionally, some clinician services declined significantly including pathology and laboratory services: other (54% decrease; IRR: 0.46; 95% CI: 0.28-0.76;  $P=0.003$ ); pathology and laboratory services: drug assays prior to opioid medication prescription (37% decrease; IRR: 0.63; 95% CI: 0.41-0.96;  $P=0.031$ ); alcohol and drug abuse: medication services (46% decrease; IRR: 0.54; 95% CI: 0.41-0.70;  $P<0.001$ ).

Reductions in facility-encounters drove 6-month reSET per-patient cost reductions of \$3,591 post-index compared to pre-index.

**Conclusions:** Use of reSET by patients with SUD is associated with durable reductions in HCRU and lower healthcare costs over 6 months compared to the 6 months before PDT treatment, after adjusting for covariates, providing an economic benefit to the healthcare system.

**Keywords:** community reinforcement approach; contingency management; healthcare resource utilization; digital therapeutic, DTx, prescription digital therapeutic; PDT; reSET; substance use disorders; SUD.

## Key Summary Points

Why carry out this study?

- Substance use disorders (SUDs) place a heavy cost burden on health care systems and society at large.
- Many barriers to effective treatment of SUDs may be overcome with prescription digital therapeutics (PDTs) delivering evidence-based, FDA-approved treatments to patients via mobile devices.
- This study evaluated the real-world 6-month impact on healthcare resource utilization (HCRU) in 101 patients with SUDs treated with the reSET<sup>®</sup> PDT.

What was learned from this study?

- Comparing the 6 months before treatment to the 6 months after treatment with the PDT, significant decreases were observed in overall hospital encounters, inpatient stays, partial hospitalizations, and emergency department visits.
- Reductions in facility-encounter HCRU drove 6-month per-patient cost reductions of \$3,591 post-treatment compared to pre-treatment.

## DIGITAL FEATURES

This article is published with digital features, including an infographic to facilitate understanding of the article. To view digital features for this article go to <https://doi.org/10.6084/m9.figshare.19950266>

## Introduction

Substance use disorders (SUDs) are highly heterogeneous conditions[1] affecting approximately 40.3 million people in the United States (US), and yet the most recently-available data show that only about 6.5% of these people ever receive SUD treatment[2]. These challenges have been exacerbated during the COVID-19 pandemic[2]. According to the Centers for Disease Control and Prevention, as of June 2020 13% of US adults reported starting or increasing substance use as a way of coping with stress or emotions related to COVID-19[3]. The pandemic has also added an additional layer of challenge for treatment service providers as many have had to quickly adopt an online format to continue operations. Furthermore, although behavioral and psychosocial treatments for SUD have long existed[4], most patients do not receive these therapies due to a lack of specialty facilities and/or trained clinicians or geographical barriers in rural communities[5-7].

A wider use of behavioral therapies is also impeded by inconsistent delivery, quality, and fidelity across healthcare providers[8], and high attrition rates among providers[9]. It has been suggested that virtual support programs can assist patients in recovery or reduce misuse, especially when access to physicians can be challenging[10-12]. Being forced into isolation, quarantines, curfews, and shutdowns have limited access to in-person supportive programs and have heightened the risk for increased alcohol consumption and drug use, especially among predisposed individuals[13, 14].

The many challenges posed by SUDs fall disproportionately on underserved populations such as older adults, racial/ethnic minorities, rural populations, military veterans, low-income individuals, and sexual and gender minorities[15]. SUDs also place a heavy cost burden on health care systems and society at large. A 2021 study found that the total annual SUD medical

cost in hospitals was \$13.2 billion with annual costs varying by substance type (e.g., \$4 million for inhalant-related disorders and \$7.6 billion for alcohol-related disorders)[16].

Goals of treatment for various SUDs include harm reduction and early intervention with cognitive behavioral therapy (CBT) and/or contingency management (CM)[17]. Harm reduction with CBT can significantly reduce use of substances and the impact of the complex problems associated with use[18, 19]. For example, reduced alcohol consumption is associated with physical and psychological benefits[20], and there is strong empirical support for early intervention (i.e., treatment of lower-severity AUD and those in earlier stages of addiction) using harm reduction strategies[18].

Studies have consistently demonstrated that CM can support engagement and abstinence in patients with SUDs, particularly those with use disorders related to cannabis, cocaine, and stimulants[21] with CM showing the highest individual effect size in a meta-analysis of techniques for treating SUDs[22].

Digital therapeutic approaches have the potential to deliver high-fidelity, evidence-based mechanisms of action, to reach broad patient populations across a variety of diseases, and to tailor treatment to patients' needs, stages of recovery, and clinical trajectories. They can be delivered in a patient-centric manner across diverse care settings and can address variables that constitute social determinants of health[23]. Prescription digital therapeutics (PDTs) are software-based disease treatments evaluated for safety and effectiveness in randomized controlled trials (RCTs) and authorized by the U.S. Food and Drug Administration (FDA). Prescribed by treating physicians, and delivered on mobile devices, PDTs can expand access to evidence-based behavioral therapies across a variety of diseases, including SUDs.

The reSET® PDT is a 12-week therapeutic combining CBT based on the Community Reinforcement Approach (CRA) [24], a CM system providing motivational incentives for lesson completion and abstinence, and fluency training to reinforce concept mastery[25]. It is the only FDA-authorized treatment for adult patients with cocaine, cannabis, and stimulant use disorders.

The clinical effectiveness of reSET was evaluated in a number of RCTs involving approximately 1500 patients with SUDs[26-32], and a real-world study in 602 patients[33]. These studies demonstrated improved rates of abstinence and treatment retention among patients receiving the digital therapy as an adjunct to reduced treatment-as-usual (TAU) compared to those who received treatment-as-usual (TAU) alone.

Real-world data acquired in the context of health care delivery and in the absence of stringent research constraints provides a complementary evaluation of therapeutic performance, including measures of patient engagement and clinical outcomes as well as HCRU and costs-of-care[34, 35]. To date, however, no data have yet been published about the impact of reSET use on HCRU and costs of care.

The objective of this study was to evaluate the real-world HCRU impact in an early cohort of commercially-insured patients treated with the reSET PDT.

## Methods

A 6-month observational retrospective analysis of HealthVerity PrivateSource20 closed-claims data (January 1, 2018 through February 28, 2021) was conducted in adults in the US diagnosed with SUD and prescribed reSET. Patients who filled their reSET prescription (index date) and engaged with the therapeutic for longer than 1 week were included in the reSET cohort (Figure 1). All patients were required to have at least 4 months of enrolment in the pre-index and post-index periods.

All patients had been deemed by their prescribing clinician as being appropriate for the PDT. The incidence of HCRU was compared between the 6-month pre-index period and the 6-month post-index period.

A scenario analysis of the cost impact of changes in facility and clinical service encounters was conducted using published facility costs for patients with OUD: \$19,023 for inpatient (IP) stays[36], \$124,419 for intensive care unit (ICU) stays(24), \$1,969 for emergency department (ED) visits)[16], and 2020 Medicare reimbursement rates for remaining facility and clinician services, as has been performed in previous analyses[37]. These costs were multiplied by the number of events in each category and averaged by patient to derive the net cost reductions/increases.

#### Data sources and statistical analyses

The PrivateSource20 data source includes closed medical claims for approximately 70 million commercial, 60 million Medicaid, and 15 million Medicare Advantage enrollees across 150 payers since 2015. All US census regions and states, Washington DC, and Puerto Rico are represented. The data include enrollment history and healthcare claims for both pharmacy and medical benefits from all settings of care. Medical claims include diagnoses and procedures for exact dates of service. Pharmacy claims include prescribed medications, prescription date, days' supply, and quantity dispensed.

The analysis will examine the differences in the incidence of HCRU encounters between the pre-index and post-index periods. The incidence for each HCRU encounter type will be calculated using a repeated measures (pre and post) negative binomial model. An incidence rate ratio (IRR) will be calculated as the incidence in the post-index period relative to the incidence in the pre-index period, and will be used to compare the pre-index and post-index incidence (e.g.,

an IRR < 1 indicates lower HCRU in the post-index period compared to the pre-index period). The 95% confidence intervals for the incidences and the IRR will also be calculated along with the IRR P-value. Analyses were performed using SAS statistical software (SAS Institute Inc. Cary, North Carolina, U.S.)

This study received a waiver of authorization for the use and disclosure of protected health information (PHI) and a determination of exempt status under 45 CFR § 46.104(d)(4) from Western Institutional Review Board on October 21, 2021.

#### PDT Description

The reSET CBT content consists of a series of interactive, on-demand audio, text, and video modules that are sequentially unlocked as patients progress through the program with CM providing motivational incentives for lesson completion and abstinence. Patients are instructed to complete 4 modules per week starting with the 31 core modules and then, when those are completed, an additional 30 supplemental modules.

Core modules teach basic cognitive behavioral and relapse prevention skills, and provide education about behavioral risk reduction for infections related to sex or shared needles. Supplemental modules target improved psychosocial functioning (e.g., managing relationships, building communication skills, and improving time management) and provide in-depth training on preventing or living with infections. Upon successful completion of each module the patient undergoes fluency training via a quiz and they have a chance to “spin” the digital CM wheel to be eligible for either virtual rewards (e.g., a “thumbs up” icon) or digital gift certificates ranging in value from \$5 to \$100, with the odds of winning a certificate higher for lower-value certificates. Patient-reported outcomes can be recorded in the PDT, and the clinical care team can



enter urine drug screen results, with negative results allowing providing the patient with another CM wheel spin.

### Study Measures

This study evaluated patient demographic characteristics including age, sex, geographic region, and payer type. Claims in the pre-index and post-index period were identified as facility claims or clinician service claims in order to characterize patients' HCRU. All-cause hospital facility encounters were evaluated overall and individually for IP stays, ED visits, partial hospitalizations (PH), and hospital outpatient department (HOPD) surgical visits. Among the inpatient stays, intensive care unit (ICU) stays were examined. Clinician services included categories of Current Procedure Terminology (CPT) codes identified from clinician claims such as evaluation and management (E&M), specific medical services (e.g., cardiovascular, psychiatry, neurology), pathology and laboratory, and rehabilitative services. Costs associated with facility encounters were evaluated.

### **Results**

The study included 101 patients who were prescribed and using reSET with a median age of 37 years, 50.5% female, 54.5% Medicaid-insured, and 37.6% commercially-insured (Table 1). Approximately 71.4% of patients had an alcohol-related disorder, 41.6% had a nicotine-related disorder, 38.% had an opioid-related disorder, 33.7% had a cannabis-related disorder, 29.7% had a cocaine-related disorder, and 10.9% had a disorder related to a stimulant other than cocaine. (Percentages don't add to 100% because patients often have multiple substance disorders).

Approximately one-quarter of patients (N=24) were prescribed naltrexone in either the pre-index or post-index periods.

A statistically significant decrease of 50% was observed in overall hospital facility encounters from the pre-index period (incidence=1.326) to the post-index period (incidence=0.661) (IRR: 0.50; 95% CI: 0.37-0.67;  $P<0.001$ ) (Table 2). Statistically significant decreases were observed for inpatient stays (56% decrease; IRR: 0.44; 95% CI: 0.26-0.76;  $P=0.003$ ), PHs (57% decrease; IRR: 0.43; 95% CI: 0.21-0.88;  $P=0.021$ ), and ED visits (not admitted) (45% decrease; IRR: 0.55; 95% CI: 0.38-0.80;  $P<0.002$ ). Decreases in HPOD surgical visits were not significant (50% decrease; IRR: 0.50; 95% CI: 0.12-2.04;  $P<0.335$ ).

Significant changes were observed in the use of a number of clinician services. The top 4 service categories with the largest changes, in terms of number of events in the observational periods included pathology and laboratory services: other (54% decrease; IRR: 0.46; 95% CI: 0.28-0.76;  $P=0.003$ ); pathology and laboratory services: drug assays prior to opioid medication prescription (37% decrease; IRR: 0.63; 95% CI: 0.41-0.96;  $P=0.031$ ); alcohol and drug abuse: medication services (46% decrease; IRR: 0.54; 95% CI: 0.41-0.70;  $P<0.001$ ); and alcohol and drug abuse: treatment program (11% decrease; IRR: 0.89; 95% CI: 0.61-1.30;  $P=0.552$ ) (see supplementary Table 1 for a complete listing of clinician and facility services data).

Reductions in hospital facility HCRU drove 6-month, per-patient net cost reductions of \$3,591 in the post-index period.

## Discussion

Acute healthcare utilization attributed to SUD is continuing to rise, particularly among patients with stimulant use disorder[38, 39], and in minority populations[2]. This is the first real-world evaluation to describe the economic and clinical effectiveness of the only SUD treatment

intervention currently FDA-authorized for patients with cocaine, cannabis, and stimulant use disorders. Expansion of the Affordable Care Act's SUD services to Medicaid recipients as well as to young adults between the ages of 18 and 23 may have resulted in an increase in treatments for these patients[40, 41], but the efficacy of these treatments and the net benefit has yet to be determined. No other treatment intervention for SUD to our knowledge has exhibited real-world effectiveness and net monetary benefit to the health system.

This study showed that within-patient hospital encounters dropped by 50%, and ED visits by 45% in the 6 month period after treatment with reSET compared to a similar baseline period. Patients with SUDs often seek care in the ED, and overuse of services in this setting unnecessarily burdens the health care system. The situation is complicated for patients with ED presentations related to cocaine and psychostimulants because such visits may not be identified as related to drug toxicity/withdrawal and, instead, be described by the interventions used, such as acute cardiopulmonary services or psychiatric interventions[38].

The reductions in service usage we observed are particularly significant in the context of reported increases in service usage during the COVID-19 pandemic among patients with SUDs. Although hospitalization rates for certain disease states declined during the pandemic (e.g., acute cardiovascular disease,[42] and stroke/TIAs[43]), several published datasets and analyses show that among patients with existing SUDs the rate of ED visits and hospitalizations increased during the pandemic. This may partially be due to an increased susceptibility to COVID among people with SUDs. For example, a 2022 study found that people with SUDs or alcohol use disorders have a greater probability of being hospitalized for COVID-19 infections compared to the general population.[44] Regardless of the cause, however, a 2021 report by Holland et al., in *JAMA Psychiatry* found that, compared to pre-pandemic rates in 2019, rates of ED visits related to all-drug overdoses rose from 12,891 to 14,959 per 100,000 ED visits, and the rates of visits related to opioid-related overdoses rose from 3940 to 5075 per 100,000 ED visits.[45]

We were unable to perform subgroup analyses by gender, race, and insurance status due to small sample sizes. Evidence in the literature clearly reveals a significant unmet need for SUD treatments among racial minorities, reproductive age women, and veterans, all of whom are

disproportionately vulnerable to SUD and its deleterious effects[46-48]. Future investigations should focus on these populations.

### Limitations

Potential limitations exist that are common with all healthcare claims-based analyses. For instance, mortality cannot be assessed using claims data and it is possible that some patients may have died in the post-index period. Another limitation of claims data is the potential for data entry errors, as well as the absence of medical history context (which can affect the interpretability of the observed trends). Cost calculations are limited to estimates derived from the published literature, therefore they may not be representative of actual costs, which will vary across different healthcare plans. A limitation of a pre/post design is that the potential impact of secular trends is limited by the period (e.g., 6 months) over which incidence is assessed and compared pre/post. It is important to note that observational research complements the evidence from randomized controlled trials on which FDA authorization decisions are made because real-world, post-authorization studies provide evidence from all-comer populations being treated in a wide range of locations and settings, which is much different from the selected populations being treated in highly controlled environments typical of clinical trials.

### **Conclusions**

This real-world evaluation in diverse patients with SUD treated with the reSET PDT showed significant decreases in unique hospital encounters and ED visits 6 months after initiation of the PDT compared to the 6 months before treatment. The observed per-patient cost reduction of \$3,591 in the pre-post analysis suggests that treating patients with reSET may lower overall costs of care, which may be relevant to payors at all levels of the healthcare system.

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297 **Authorship**

298 All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria  
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302 **Author contributions**

303 All authors contributed to the study conception and design. Material preparation, data  
304 collection, and analysis were performed by Samuel Colman, Laura Kauffman, Charles Ruetsch,  
305 and Kathryn Anastassopoulos. The first draft of the manuscript was written by Neel Shah, and all  
306 authors commented on subsequent versions of the manuscript. All authors read and approved the  
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308 **Disclosures**

309 Neel Shah, Fulton Velez, and Yuri Maricich are employees of Pear Therapeutics (US), Inc.  
310 Samuel Colman, Laura Kauffman, and Kathryn Anastassopoulos are employees Market Access  
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312 Pear Therapeutics (US), Inc. Charles Ruetsch is an employee of Health Analytics, which  
313 participated in this study under contract with Pear Therapeutics (US), Inc.

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315 **Compliance with Ethics Guidelines**

316 This study received a waiver of authorization for the use and disclosure of protected health  
317 information (PHI) and a determination of exempt status under 45 CFR § 46.104(d)(4) from  
318 Western Institutional Review Board on October 21, 2021.

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321 **Figure and Table Titles**

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323 **Figure 1. CONSORT diagram for reSET 6-month pre/post analyses**

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**Table 1. Patient demographics and characteristics**

Demographic/characteristic	reSET cohort (N = 101)
Median age	37
Female sex	50.5%
Mean Charlson comorbidity score	0.802
Payer, n (%)	
Commercial	38 (37.6%)
Medicaid	55 (54.5%)
Medicare Advantage	3 (3.0%)
Unknown	5 (5.0%)
Census region, n (%)	
Middle Atlantic	41 (40.6%)
East North Central	17 (16.8%)
South Atlantic	12 (11.9%)
Other	31 (30.7%)

**Table 2. reSET cohort pre/post analysis of incidence of hospital facility services over 6 months**

Resource	Pre-index period (N=101)			Post-index period (N=101)			IRR	95% CI	p-value
	n (%)	Incidence	95% CI	n (%)	Incidence	95% CI			
6-month									
Unique hospital encounters	46 (45.5%)	1.326	(0.974, 1.805)	31 (30.7%)	0.661	(0.456, 0.959)	0.50	(0.37, 0.67)	<0.001
Inpatient stays	22 (21.8%)	0.320	(0.209, 0.488)	12 (11.9%)	0.142	(0.081, 0.248)	0.44	(0.26, 0.76)	0.003
ICU stays	0 (0.0%)	0.000	(0.000, 0.030)	2 ( 2.0%)	0.020	(0.005, 0.081)	NA	NA	NA
Readmissions	6 ( 5.9%)	0.080	(0.035, 0.182)	1 ( 1.0%)	0.010	(0.001, 0.071)	0.13	(0.02, 1.07)	0.058
Partial hospitalizations	9 ( 8.9%)	0.278	(0.130, 0.595)	6 ( 5.9%)	0.120	(0.053, 0.269)	0.43	(0.21, 0.88)	0.021
ED visits - not admitted	35 (34.7%)	0.710	(0.497, 1.013)	22 (21.8%)	0.391	(0.244, 0.627)	0.55	(0.38, 0.80)	0.002
HOPD visits	2 ( 2.0%)	0.020	(0.005, 0.079)	1 ( 1.0%)	0.010	(0.001, 0.072)	0.50	(0.12, 2.04)	0.335
CI, confidence interval; ED, emergency department; HOPD, hospital outpatient department; IRR, incidence rate ratio; NA, not applicable									
n=number of patients with at least 1 encounter									

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