

## Summary

### WHAT ARE DIGITAL HEALTH TECHNOLOGIES FOR OPIOID USE DISORDER?

Opioid use disorder (OUD) is a public health crisis in the United States. The number of drug overdose deaths in the US increased continuously from 1999 to mid-2017 when it reached a plateau of approximately 70,000 deaths annually, of which 50,000 were from opioids. The number of deaths increased again from 2017-2019. Financial burdens have also been extreme: the White House Council of Economic Advisors estimates that from 2015 to 2018 the opioid epidemic cost the US more than \$2.4 trillion.

Medication assisted treatment (MAT) is the most effective treatment for OUD, but more than half of patients starting MAT drop out of treatment within six months. In-person behavioral therapies have been shown to increase retention, but they are resource intensive. Digital health technologies (DHTs) that provide support for behavioral therapy offer the potential to expand access and reduce the overall cost of providing effective MAT. We examine the evidence for three available DHTs in this review: reSET-O, Connections, and DynamiCare.

### TREATMENT OPTIONS

- **reSET-O**<sup>®</sup> (Pear Therapeutics), a 12-week prescription digital app, used in conjunction with buprenorphine and small rewards, aimed at increasing retention of patients receiving outpatient OUD treatment.
- **Connections** (Chess Health), a digital app that combines communication with addiction experts and support groups, along with a 7-session program that teaches cognitive and behavioral skills, aimed at improving abstinence in patients with substance use disorders.
- **DynamiCare** (DynamiCare Health), a digital app that includes 36 classroom-based training modules, monitoring for substance abstinence, and debit card rewards for negative drug tests and appointment attendance.

### KEY REPORT FINDINGS

- No published randomized trials are available, and the available evidence on the benefits of adding reSET-O, Connections, or DynamiCare to MAT therefore has substantial limitations and can provide no firm estimate of net health benefit for patients compared with MAT alone.
- Cost effectiveness could only be modeled for reSET-O. At its current net price this intervention only aligns with commonly cited cost-effectiveness thresholds when short-term improvements in retention are assumed to persist far beyond the time horizon of the clinical trial. More evidence is needed on the durability of benefit after completion of this program.

### KEY POLICY RECOMMENDATIONS

- MAT saves lives and money, both inside the health system and outside of it. New interventions should be developed, tested, and implemented that can augment the number of individuals who can access MAT, reduce stigma, and ensure that individuals receive care in a format that helps them achieve their goals.
- Manufacturers should provide robust evidence of the clinical effectiveness and broader impact of new DHTs.
- Given the limited evidence supporting the efficacy of DHTs for OUD, alternative payment models may be appropriate (such as outcomes-based payments or subscription models).

## Clinical Analyses

### How strong is the evidence that these therapies improve outcomes in patients using Digital Health Technologies for OUD?

#### ICER EVIDENCE RATINGS

Digital Health Technology	ICER Evidence Rating
reSET-O	C+
Connections	C+
DynamiCare	C+

None of these three digital health technologies has direct randomized trial evidence demonstrating how well it may enhance abstinence or retention in MAT for people with OUD. reSET-O was approved based on its similarity to application of the same educational modules in earlier studies, but those modules were delivered on a computer in the clinic rather than by a smart phone app, and contingency management incentives included as part of the intervention were fundamentally different.

Nonetheless, the use of the DHTs is unlikely to be harmful to patients, so these interventions are, at worst, equivalent to using MAT alone. Given that the limited evidence supporting the underlying training modules and incentives suggests that these DHTs may provide small incremental benefits in retention, ICER gave all three DHTs an ICER evidence rating of “C+”.

#### KEY CLINICAL BENEFITS STUDIED IN CLINICAL TRIALS

##### How effective are these DHTs?

There were no randomized trials, cohort studies or case series that evaluated the DHTs reviewed in this report until after the draft report was released.

The key study supporting the 510(k) application to the FDA of reSET-O included participants who met the DSM-4 criteria for opioid dependence and the FDA qualification criteria for buprenorphine treatment. There was no significant difference in the primary outcome: number of days of continuous abstinence, and therefore any other significant findings should be considered hypothesis generating. The study did find a reduced likelihood of dropping out of treatment at 12 weeks in patients who received reSET-O as compared to those who only received contingency management (CM) plus MAT. However, a study of the same intervention found no difference in drop-out rates at 1 year. Two recently published observational studies of reSET-O suggested potential benefits, but the study designs left room for significant bias.

## Clinical Analyses

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### HARMS

The use of the DHTs is unlikely to be harmful to patients, but there is the potential for loss of privacy.

### SOURCES OF UNCERTAINTY

**Lack of peer-reviewed data:** the primary source of uncertainty in the clinical evidence for these DHTs is the complete lack of peer-reviewed data on the impact of their use for patients with OUD treated with MAT.

**Lack of long-term follow-up:** the trials that demonstrated some efficacy for the behavioral components implemented in the DHTs had only short-term outcomes. Clinical experts testified that the minimum follow-up to demonstrate a meaningful impact on adherence would be six months, and 12 to 24 month data would be more convincing.

**Lack of data on patient-important outcomes:** no data were reported on key health outcomes that matter to patients like ER visits, hospitalizations, return to work, and improved relationships with family and friends.

## Economic Analyses

### LONG-TERM COST-EFFECTIVENESS

Do these therapies meet established thresholds for long-term cost-effectiveness?

Treatment	Incremental Cost per Life Year Gained	Incremental Cost per QALY Gained	Incremental Cost per evLYG	Incremental Cost per Additional MAT Year
reSET-O vs. SoC	\$48,449,000	\$121,500	\$121,400	\$10,000

As a best-case scenario, and only with the assumption that short-term improvement in retention in MAT persists far beyond the term of the available studies, the reSET-O arm has an incremental cost-effectiveness ratio of approximately \$121,500 per QALY gained. Results were similar when compared to outcomes of evLYG due to the very small mortality benefit associated with reSET-O given the fewer days of illicit opioid use assumed while using the DHT/MAT.

### HEALTH-BENEFIT PRICE BENCHMARKS

What is a fair price for these DHTs based on its value to patients and the health care system?

	List Price	Net Price	Price at \$100,000 Threshold	Price at \$150,000 Threshold	Discount from WAC to Reach Threshold Prices
reSET-O	\$1,665	\$1,219	\$1,080	\$1,400	16%-35%

With the favorable assumptions noted above, the health benefit price benchmark for reSET-O ranges from \$1,080 to \$1,400. A discount of 16-35% off the list price would be needed to reach these prices. The manufacturer provided an average net price estimate of \$1,219, which is a 27% discount from the list price.

The HBPB is a price range suggesting the highest US price a manufacturer should charge for a treatment, based on the amount of improvement in overall health patients receive from that treatment, when a higher price would cause disproportionately greater losses in health among other patients in the health system due to rising overall costs of health care and health insurance. In short, it is the top price range at which a health system can reward innovation and better health for patients without doing more harm than good.

## Economic Analyses (continued)

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### POTENTIAL SHORT-TERM BUDGET IMPACT

#### How many patients can be treated before crossing ICER's budget impact threshold?

**reSET-O:** the annual potential budgetary impact of treating 20% of the eligible population was \$117.2 million, assuming the WAC download price for one-time treatment (\$1,665). We do not provide a reference threshold to a potential budget impact for non-drugs per ICER's Value Assessment Framework. The annual potential budget impact of treatment for 20% of the estimated eligible population at the \$100,000 per QALY threshold price was \$61.4 million, and \$91.9 million at the \$150,000 per QALY threshold price.

## Voting Results

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The Midwest CEPAC deliberated on key questions raised by ICER’s report at a public meeting on November 18, 2020. The results of the votes are presented below, and focus on reSET-O. More detail on the voting results is provided in the [full report](#).

### CLINICAL EVIDENCE

- A majority of panelists found that the evidence is not adequate to demonstrate a net health benefit for patients treated with reSET-O plus the standard of care compared to standard of care alone.
- All panelists found that the evidence is not adequate to demonstrate a net health benefit of treatment with the Connections app added to standard care compared to standard of care alone.
- All panelists found that the evidence is not adequate to demonstrate a net health benefit for patients treated with the DynamiCare app plus standard of care compared to standard of care alone.

### LONG-TERM VALUE FOR MONEY

- Given the available evidence on comparative effectiveness and incremental cost effectiveness, and considering other benefits, disadvantages, and contextual considerations, the majority of panelists believed that reSET-O represented **low** long-term value for money at its current price.

### OTHER BENEFITS AND CONTEXTUAL CONSIDERATIONS

ICER asks panelists to vote on whether specific potential other benefits, disadvantages, and contextual considerations are important to weigh in judging the long-term value for money of the intervention. For reSET-O:

- Approximately half of the panelists found that it (and other DHT modalities) DHTs will differentially benefit a historically underserved or disadvantaged community.
- Approximately one-third of panelists thought that economic model assumptions were too optimistic.
- Approximately one-third voted that reSET-O offered a new mechanism of action compared to that of other treatments.

## Policy Recommendations

### General Policy Recommendations

- MAT saves lives and money, both inside the health system and outside of it. New interventions should be developed, tested, and implemented that can augment the number of individuals who can access MAT, reduce stigma, and ensure that individuals receive care in a format that helps them achieve their goals.
  - DHTs may be important aids in improving care for many individuals, but it is vital that adequate evidence be generated to evaluate the relative effectiveness of different options so that each person can receive effective treatment tailored to maximize their health.
  - Poor evidence that leads to ineffective use of DHTs represents a health risk to individuals, a financial risk to the health system, and a moral risk for us all that society will fail in its responsibility to use its resources to the greatest effect in combatting an ongoing national epidemic.
- Manufacturers should be prepared to provide a full dossier of evidence to payers and providers that includes robust information on 1) the durability of beneficial clinical effects; 2) the impact on health care utilization; 3) the impact on clinician productivity; 4) the usability as measured by clinician and patient experience; 5) the security of IT components; 6) the generalizability of results to diverse patient populations and health systems; and 7) the scalability to larger populations.
- Manufacturers and researchers should design trials of DHTs to be able to identify potential subgroups of patients who benefit most from a DHT and those who are less likely to benefit. Existing evidence may also be reanalyzed for this purpose.

### For Researchers and Manufacturers

- Manufacturers should provide robust evidence of the clinical effectiveness and broader impact of new DHTs. For DHTs like those featured in this report that have a function of guiding or enhancing treatment outcomes, a minimum evidence requirement is high-quality observational or quasi-experimental studies with an appropriate comparator and relevant patient outcomes. However, many DHTs should undergo formal evaluation through randomized controlled trials to minimize the risk of bias in trial results.

### For Payers

- Given the limited evidence supporting the efficacy of DHTs for OUD, alternative payment models may be appropriate if coverage is provided (such as outcomes-based payment or subscription models).

### For Regulators

- The FDA should develop a clear taxonomy of DHTs, with different levels of risk and other factors, and clarify evidence requirements that are robust enough to inform patients, clinicians, health systems, and payers regarding the safety and comparative effectiveness of their use in representative patient populations.

## About ICER

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The Institute for Clinical and Economic Review (ICER) is an independent nonprofit research institute that produces reports analyzing the evidence on the effectiveness and value of drugs and other medical services. ICER's reports include evidence-based calculations of prices for new drugs that accurately reflect the degree of improvement expected in long-term patient outcomes, while also highlighting price levels that might contribute to unaffordable short-term cost growth for the overall health care system.

ICER's reports incorporate extensive input from all stakeholders and are the subject of public hearings through three core programs: the California Technology Assessment Forum (CTAF), the Midwest Comparative Effectiveness Public Advisory Council (Midwest CEPAC) and the New England Comparative Effectiveness Public Advisory Council (New England CEPAC). These independent panels review ICER's reports at public meetings to deliberate on the evidence and develop recommendations for how patients, clinicians, insurers, and policymakers can improve the quality and value of health care.

For more information about ICER, please visit ICER's website ([www.icer.org](http://www.icer.org)).