

Below are the publications of the randomized clinical trials that support the FDA's authorization of reSET and reSET-O:

reSET

reSET is intended to provide cognitive behavioral therapy, as an adjunct to a contingency management system, for patients 18 years of age and older who are currently enrolled in outpatient treatment under the supervision of a clinician. reSET is indicated as a 12-week (90 days) prescription-only treatment for patients with Substance Use Disorder (SUD), who are not currently on opioid replacement therapy, who do not abuse alcohol solely, or who do not abuse opioids as their primary substance of abuse. It is intended to:

- increase abstinence from a patient's substances of abuse during treatment, and
- increase retention in the outpatient treatment program.

The clinical data supporting reSET are:

1. Campbell AN, Nunes EV, Matthews AG, et al. Internet-delivered treatment for substance abuse: a multisite randomized controlled trial. *Am J Psychiatry*. 2014;171(6):683-90. The publication is available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4079279/>
2. Please note that the "all comer patient" population included in Campbell et al., 2014 include some patients that fall out of the reSET indication (specifically: primary opioid users). Therefore a secondary analysis excluding primary opioid users was submitted to the FDA for authorization, and these are included in the attached reSET Clinician Directions For Use which provides a complete overview of the pivotal data and label for reSET.

reSET-O

reSET-O is intended to increase retention of patients with opioid use disorder (OUD) in outpatient treatment by providing cognitive behavioral therapy, as an adjunct to outpatient treatment that includes transmucosal buprenorphine and contingency management, for patients 18 years or older who are currently under the supervision of a clinician. reSET-O is indicated as a prescription digital therapeutic.

The full citations for the reSET clinical data is:

1. Christensen DR, Landes RD, Jackson L, et al. Adding an Internet-delivered treatment to an efficacious treatment package for opioid dependence. *J Consult Clin Psychol*. 2014;82(6):964-72. The publication is available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4244262/>
2. Maricich et al. (2021) Safety and efficacy of a prescription digital therapeutic as an adjunct to buprenorphine for treatment of opioid use disorder, *Current Medical Research and Opinion*, 37:2, 167-173, DOI: 10.1080/03007995.2020.1846022

<https://www.tandfonline.com/doi/pdf/10.1080/03007995.2020.1846022>

3. I am also including the reSET-O Clinician Directions For Use which provides a complete overview of the pivotal data and label for reSET.

Below are the publications of the real-world evidence studies that support reSET-O:

Recently-published real-world evidence studies (available via open access):

- Engagement data from over 3,000 real world reSET-O patients:
 - Maricich et al. (2020): Real-world evidence for a prescription digital therapeutic to treat opioid use disorder, Current Medical Research and Opinion, DOI: 10.1080/03007995.2020.1846023. <https://www.tandfonline.com/doi/pdf/10.1080/03007995.2020.1846023>
- Engagement data and impact of re-prescriptions from over 4,000 real world reSET-O patients:
 - Maricich et al. (2021): Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder, Hospital Practice, DOI: 10.1080/21548331.2021.1974243. <https://www.tandfonline.com/doi/full/10.1080/21548331.2021.1974243?src=recsys>
- Administrative claims data analyses of patients who have been prescribed reSET-O.

Six-month follow-up data showing a reduction in Hospitalizations and emergency department utilization, increased engagement with case management and rehabilitative services, and a net cost reductions of \$2,150/patient.

- Velez et al. (2020) Real-world reduction in healthcare resource utilization following treatment of opioid use disorder with reSET-O, a novel prescription digital therapeutic, Expert Review of Pharmacoeconomics & Outcomes Research, DOI: 10.1080/14737167.2021.1840357. <https://www.tandfonline.com/doi/full/10.1080/14737167.2021.1840357>

Follow-up analysis showing continued effectiveness out to 9 months.

- Velez et al. (2021) Evidence of long-term real-world reduction in healthcare resource utilization following treatment of opioid use disorder with reSET-O, a novel prescription digital therapeutic, Expert Review of Pharmacoeconomics & Outcomes Research, DOI: 10.1080/14737167.2021.1939687. <https://www.tandfonline.com/doi/full/10.1080/14737167.2021.1939687?src=recsys>

Net savings per patient are greater among patients who engage with the therapeutic vs those who don't, and number needed to treat is 4.8.

- Velez et al. (2021) Real-world changes in US health system hospital-based services following treatment with a prescription digital therapeutic for opioid use disorder. Hospital Practice. DOI: 10.1080/21548331.2021.1956256. <https://www.tandfonline.com/doi/full/10.1080/21548331.2021.1956256>

Patients treated with a second prescription for reSET-O experience increased retention, abstinence, and reduced costs compared to patients treated with a single reSET-O prescription.

- Velez et al. (2021) Real-world use and clinical outcomes after 24 weeks of treatment with a prescription digital therapeutic for opioid use disorder. Hospital Practice. DOI: 10.1080/21548331.2021.1974243. <https://www.tandfonline.com/doi/full/10.1080/21548331.2021.1974243>

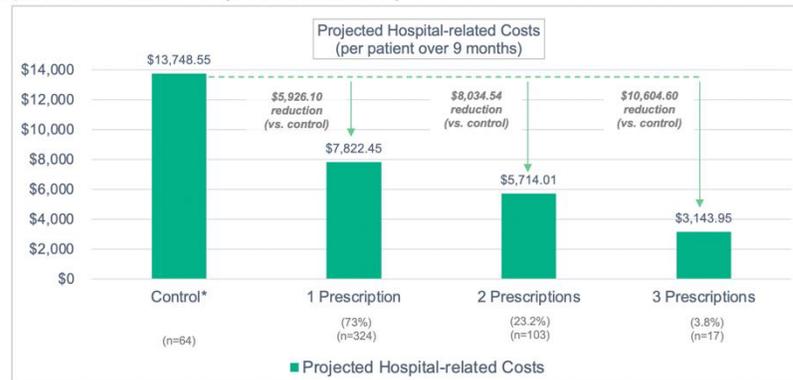
Compared to controls, reSET-O-treated patients experience reduced costs, driven by a reduction in hospital-related utilization.

· Velez et al. (2021) Comparison of Healthcare Resource Utilization Between Patients Who Engaged or Did Not Engage With a Prescription Digital Therapeutic for Opioid Use Disorder. ClinicoEconomics and Outcomes Research. 2021;13:909-916. DOI: 10.2147/CEOR.S334274
<https://www.dovepress.com/comparison-of-healthcare-resource-utilization-between-patients-who-eng-peer-reviewed-fulltext-article-CEOR>

- Data on file:

Each subsequent prescription for reSET-O was associated with a reduction in hospital encounters and related costs compared to controls not treated with reSET-O.

Projected hospital-related costs¹ were lower with initial and subsequent prescriptions of reSET-O (over 9 months)



*Medication Possession Ratio (MPR) for buprenorphine was 0.79 for control, vs 0.81 across all reSET-O arms.

Pear Therapeutics data on file

1. Costs derived from an analysis performed by Premier Inc.: <https://www.premierinc.com/newsroom/press-releases/opioid-overdoses-costing-u-s-hospitals-an-estimated-11-billion-annually>.