Research That Matters

Recovery From Opioid Use Disorder (OUD) After Monthly Long-Acting Buprenorphine Treatment: 12-Month Longitudinal Outcomes From RECOVER, An Observational Study

Authors: Walter Ling, MD; Vijay R. Nadipelli, MS; Arnie P. Aldridge, PhD; Naoko A. Ronquest, PhD; Caitlyn T. Solem, PhD; Howard Chilcoat, ScD; Victoria Albright, MA; Courtney Johnson, MPH; Susan M. Learned, PhD; Vishaal Mehra, MD; Christian Heidbreder, PhD

Full Article: PubMed Central

RECADEMY™

The Academy for Improving Substance Use Disorder Treatment: Making Recovery a Reality™

Research Summary

The RECOVER (Remission from Chronic Opioid Use: Studying Environmental and SocioEconomic Factors on Recovery) study provides longer-term observational data on individuals with moderate-to-severe opioid use disorder (OUD) who had previously participated in clinical trials of monthly extended-release buprenorphine injections (BUP-XR, commercially available as Sublocade).

RECOVER was a 24-month prospective observational study conducted at 35 community-based sites across the United States. This analysis reported outcomes through the first 12 months. The study included 533 participants, of whom 425 completed the 12-month visit. The average age was 42 years, and 66% were male.

Among participants who completed the 12-month visit, 50.8% self-reported sustained opioid abstinence across the observational period, and 68.0% reported past-week abstinence at the 12-month visit. More stringent sensitivity analyses produced lower sustained-abstinence estimates: 45.2% when all available self-reported measures were considered and 32.0% when negative urine drug screens were also required.

Longer BUP-XR exposure during the preceding clinical trials was associated with a greater likelihood of sustained abstinence during RECOVER. After statistical adjustment, the estimated rate of sustained abstinence was 75.3% among participants who had received 12 months of BUP-XR, compared with 24.1% among those who had received no more than two months.

This finding should not be interpreted as demonstrating a causal effect of longer BUP-XR treatment. Treatment duration was not randomized, and participants who continued treatment may have differed from those who discontinued earlier. In addition, 47.7% of participants received some form of substance use disorder treatment during RECOVER, including 38.8% who received pharmacotherapy for OUD.

Participants also reported generally favorable withdrawal, pain, mental health, quality-of-life, and employment outcomes compared with assessments obtained before they entered the preceding BUP-XR trials. These findings broaden the understanding of recovery beyond abstinence alone, while the observational design and continued treatment exposure require careful interpretation.

STUDY DESIGN

- **Design**: Prospective, longitudinal observational study.
- **Study Duration**: RECOVER followed participants for 24 months. This publication reports findings through the 12-month visit.
- **Setting**: 35 community-based sites across the United States.
- **Participants**: 533 individuals enrolled, and 425 completed the 12-month visit. The average age was 42 years, and 66% were male.
- **Population**: Adults with moderate-to-severe OUD who had previously participated in a randomized BUP-XR efficacy trial and/or an open-label BUP-XR safety study. Participants had received between zero and 12 monthly BUP-XR injections before entering RECOVER.
- **Study Entry**: Enrollment in RECOVER occurred at least 28 days after participants completed or discontinued participation in the preceding clinical trials.
- **Treatment During RECOVER**: RECOVER did not assign or provide OUD treatment. Participants could, however, obtain treatment outside the observational study. Some also participated in a separate BUP-XR extension study conducted concurrently with RECOVER.
- **Outcomes Assessed**: Self-reported opioid abstinence, urine drug screening, withdrawal symptoms, pain, physical and mental health-related quality of life, depression, employment, and substance use disorder treatment received during follow-up.
- **Abstinence Measurement**: Sustained abstinence was based primarily on participants' reports of no opioid use during the preceding six months at the 6- and 12-month visits. Urine drug screens and additional self-reported measures were incorporated into sensitivity analyses.

STUDY FINDINGS

Opioid Abstinence

Among participants completing the 12-month visit:

- 50.8% self-reported sustained opioid abstinence throughout the 12-month observational period.
- 68.0% reported past-week opioid abstinence at the 12-month visit.

The estimated sustained-abstinence rate declined when more stringent definitions were applied:

- 45.2% when all available self-reported measures from the quarterly visits were considered.
- 32.0% when participants were also required to have negative urine drug screens.

Self-reported past-month abstinence was 59.2% at RECOVER enrollment and 62.1% at the 12-month visit. The corresponding negative urine drug screen rates were 61.7% and 56.9%.

The authors compared the RECOVER findings with the 18-month follow-up from the Prescription Opioid Addiction Treatment Study (POATS), in which 49.650% of participants reported past-30-day opioid abstinence. Because RECOVER and POATS involved different patient populations, treatments, and follow-up methods, this provides context rather than a direct comparison.

Association With Prior BUP-XR Treatment Duration

Longer participation in the preceding BUP-XR clinical program was associated with a greater likelihood of abstinence during RECOVER.

After adjustment for measured participant and treatment characteristics, the estimated sustained-abstinence rates were:

- 24.1% among participants receiving zero to two months of BUP-XR.
- 29.3% among those receiving three to five months.
- 38.2% among those receiving six to 11 months.
- 75.3% among those receiving 12 months.

These are model-estimated rates, not simply observed percentages. Treatment duration was not randomized, and residual differences between the groups may have affected the results.

The authors also specifically noted that nearly half of the participants in the 12-month BUP-XR exposure group continued receiving BUP-XR through the concurrent extension study. This continued exposure contributed to the abstinence outcomes reported for that group.

Withdrawal, Pain & Quality of Life

Withdrawal and pain scores were lower during RECOVER than before participants entered the BUP-XR clinical trials.

- Average opioid withdrawal scores declined from 17.7 before the trials to 7.3 at RECOVER enrollment and remained at 7.5 at 12 months.
- Average pain scores declined from 4.3 before the trials to 3.0 at RECOVER enrollment and remained at 3.0 at 12 months.

Physical health-related quality-of-life scores remained relatively stable and slightly below the general population reference value. Mental health-related quality-of-life scores improved between the pre-trial assessment and RECOVER enrollment, with much of that improvement maintained at 12 months.

Because the pre-trial and RECOVER assessments used different versions of the health-related quality-of-life measure, these comparisons should be interpreted cautiously.

Depression & Employment

The proportion of participants reporting no or minimal depression increased from 30.2% before the preceding clinical trials to 77.2% at RECOVER enrollment and 74.7% at the 12-month visit.

Employment increased from 20.3% before the clinical trials to 46.7% at RECOVER enrollment and 48.3% at 12 months.

These changes are important patient-centered outcomes. However, RECOVER did not include an untreated or alternative-treatment comparison group, so the changes cannot be attributed to BUP-XR alone.

Continued Treatment During Follow-Up

Nearly half of participants—254 of 533, or 47.7%—received some form of substance use disorder treatment during RECOVER.
- 207 participants, or 38.8%, received pharmacotherapy.
- 196 participants, or 36.8%, received buprenorphine.
- 146 participants, or 27.4%, received BUP-XR through the concurrent extension study.
- Among participants receiving pharmacotherapy, 95% received buprenorphine.

Continued treatment is not a minor qualification. It is central to interpreting the findings. The outcomes reported at 12 months did not occur entirely after medication treatment ended and cannot be understood solely as the lasting effect of prior BUP-XR exposure.

CLINICAL & ADMINISTRATIVE IMPLICATIONS

For Payers

RECOVER adds to the evidence that OUD treatment should be evaluated over longer periods and across multiple domains. Abstinence is important, but mental health, pain, quality of life, employment, and continued engagement in care also matter when assessing recovery.

The study also demonstrates why longer-term outcomes cannot be interpreted without understanding continued treatment exposure. Coverage and quality-measurement approaches should recognize that OUD is a chronic condition and that many individuals require ongoing pharmacotherapy and other services.

RECOVER did not evaluate costs, health care utilization, comparative effectiveness, insurance coverage, prior authorization, or cost-effectiveness. The findings therefore should not be characterized as establishing the actuarial or economic value of BUP-XR or as demonstrating its superiority to other medications for OUD.

For Provider Organizations & Health Systems

Organizations offering monthly BUP-XR need reliable processes for medication acquisition, administration, follow-up, and coordination with pharmacies and payers. RECOVER did not test these operational models, but it illustrates the importance of maintaining continuity after medication initiation.

The study also provides a useful framework for measuring recovery. Organizations may consider tracking:

- Opioid use and abstinence.
- Treatment engagement and continued medication use.
- Withdrawal and pain.
- Depression and mental health-related quality of life.
- Employment and other measures of functioning.

Tracking these outcomes over time can provide a more complete understanding of treatment effectiveness than visit volume, medication administration, or short-term retention alone.

For Clinical Professionals

Monthly extended-release buprenorphine provides another treatment option for individuals with OUD, including patients who prefer less frequent dosing or experience difficulty maintaining a daily medication regimen.

RECOVER suggests that favorable recovery outcomes can be present well beyond the initial treatment period. It does not, however, establish which patients are most likely to benefit from BUP-XR compared with sublingual buprenorphine, methadone, extended-release naltrexone, or other treatment approaches.

Treatment decisions should continue to reflect clinical needs, patient preferences, prior treatment experience, co-occurring conditions, and the individual's ability to access and remain engaged in care.

Patients should also receive realistic information about the findings. Approximately half of the 12-month completers reported sustained abstinence under the study's primary definition, and the estimate was lower when more stringent measures were applied. Continued treatment remained common and may have contributed substantially to the outcomes.

OTHER CONSIDERATIONS

The Treatment-Access Gap

The authors placed the findings within the broader problem of OUD undertreatment, citing a 2019 National Academies estimate that fewer than 35% of adults with OUD had received OUD treatment in the preceding year.

This is a historical contextual estimate rather than a RECOVER finding or a current prevalence rate. It nevertheless illustrates the scale of the treatment-access gap the authors were addressing and the importance of expanding access to evidence-based OUD treatment options.

Association Is Not Causation

The strong association between longer BUP-XR exposure and sustained abstinence is clinically noteworthy, but it should not be interpreted as proving that 12 months of BUP-XR caused the higher abstinence rate.

Participants were not randomized to treatment duration. Individuals who remained in treatment for 12 months may have differed in motivation, stability, treatment response, access to care, or other characteristics that were not fully captured in the statistical models.

Continued Treatment Is Part Of The Outcome

The study is sometimes described as examining outcomes after BUP-XR treatment. That description is incomplete because a substantial proportion of participants continued receiving pharmacotherapy during RECOVER.

The findings are better understood as longer-term outcomes following participation in a BUP-XR clinical program, with many participants continuing treatment during the observational period.

STUDY LIMITATIONS & FUTURE DIRECTIONS

- **Observational Design**: RECOVER did not randomize treatment during follow-up and did not include a control or comparison group. It cannot establish that BUP-XR caused the outcomes observed.
- **Nonrandomized Treatment Duration**: Participation in the preceding BUP-XR program was voluntary, and participants were not randomly assigned to different treatment durations. Residual confounding may have affected the association between treatment duration and abstinence.
- **Continued Treatment**: Nearly 40% of participants received pharmacotherapy during RECOVER. Some continued receiving BUP-XR through a separate extension study, complicating attribution of the outcomes to prior treatment.
- **Self-Reported Abstinence**: The primary abstinence outcome relied on self-report and may have been affected by recall or reporting bias. Abstinence estimates declined when urine drug screening and additional self-reported measures were incorporated.
- **Participant Attrition**: Although 425 participants completed the 12-month visit, only 339 completed every study visit. Missing data may have influenced the results despite the study's sensitivity analyses.
- **Hawthorne Effect**: Participants knew they were being followed and were questioned regularly about opioid use and recovery. This participation may itself have influenced behavior.
- **Generalizability**: All participants had previously enrolled in BUP-XR clinical trials. They may have been more treatment-engaged than individuals receiving care in routine community settings.
- **Population Characteristics**: Two-thirds of the participants were male, potentially limiting generalizability to women and other populations not well represented in the study.
- **Fentanyl Measurement**: Fentanyl was not specifically included in urine drug screening or explicitly assessed in participant surveys. This is an important limitation when applying the findings in the current fentanyl-dominant environment.

At the time of this publication, additional RECOVER analyses were planned through 24 months. Future research should include more diverse community populations, direct comparisons with other medications for OUD, longer-term follow-up, and evaluations of utilization, costs, treatment access, and patient-reported outcomes.

CONCLUSION

RECOVER provides important longer-term observational information about recovery among individuals who previously participated in BUP-XR clinical trials. At 12 months, participants reported substantial levels of opioid abstinence and generally favorable withdrawal, pain, mental health, quality-of-life, and employment outcomes compared with assessments completed before the preceding trials.

CONCLUSION CONTINUED

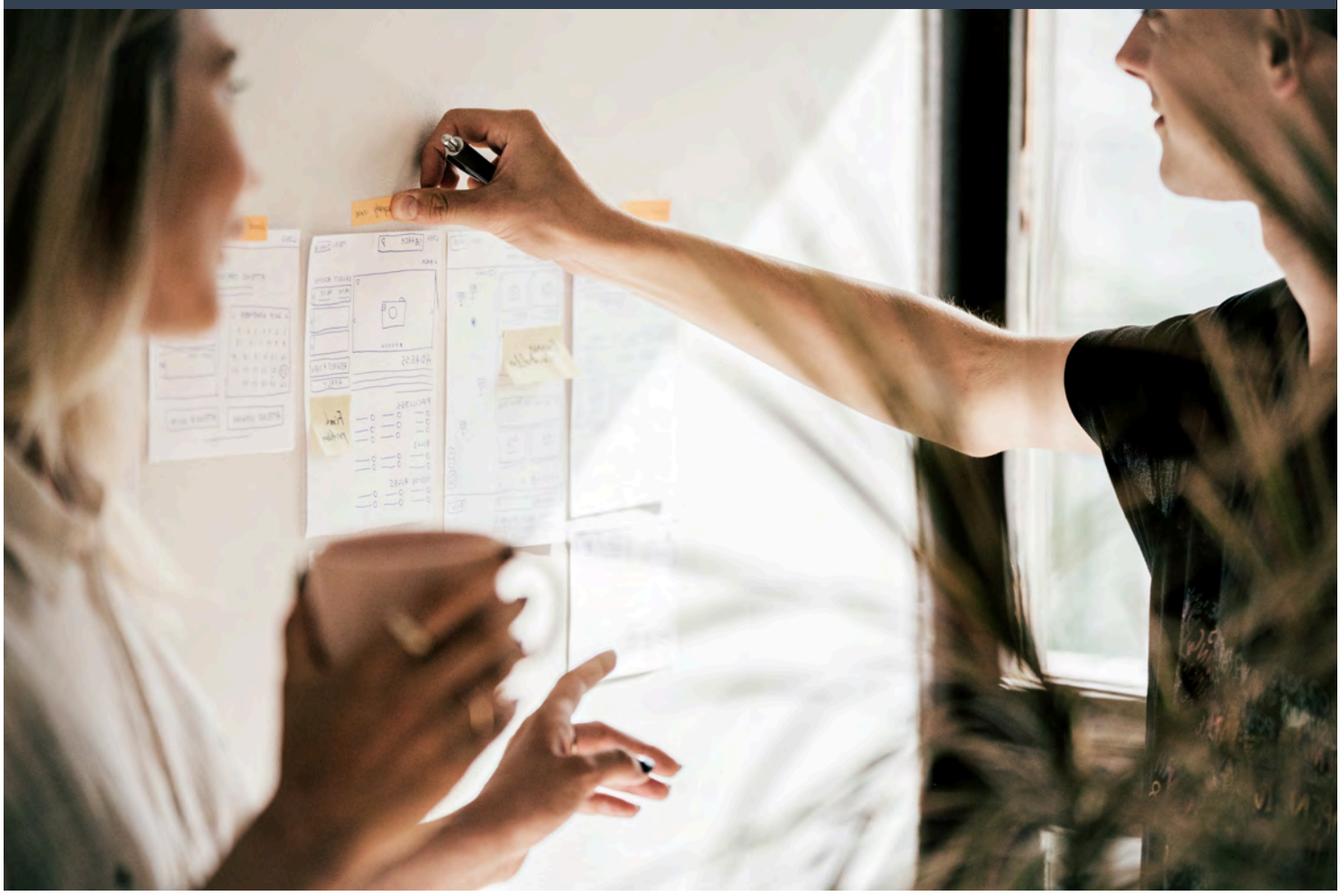
Longer prior BUP-XR exposure was strongly associated with sustained abstinence, but treatment duration was not randomized and many participants continued receiving pharmacotherapy during RECOVER. The findings therefore should not be interpreted as proving that BUP-XR alone caused the outcomes or that it is more effective or cost-effective than other medications for OUD.

The study's most important contribution may be its demonstration that recovery should be measured over time and across multiple dimensions. Abstinence remains important, but so do mental health, physical well-being, employment, functioning, and continued engagement in treatment.

FUNDING & DISCLOSURES

The RECOVER study was sponsored by Indivior Inc., the manufacturer of Sublocade.

Several authors were Indivior employees and owned Indivior stock. Other authors reported employment or consulting relationships with Indivior, and the lead author reported consulting relationships with Indivior and other pharmaceutical companies. These relationships should be considered when interpreting the study and its conclusions.



RECADEMY™

The Academy for Improving Substance Use Disorder Treatment:
Making Recovery a Reality™

CITATION

Ling W, Nadipelli VR, Aldridge AP, et al. Recovery From Opioid Use Disorder (OUD) After Monthly Long-Acting Buprenorphine Treatment: 12-Month Longitudinal Outcomes From RECOVER, an Observational Study. Journal of Addiction Medicine. 2020;14(5):e233–e240. doi:10.1097/ADM.0000000000000647.