Research That Matters

Patient-Reported Outcomes Of Treatment Of Opioid Dependence With Weekly & Monthly Subcutaneous Depot Vs. Daily Sublingual Buprenorphine, A Randomized Clinical Trial

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Research Summary

Long-acting injectable buprenorphine provides an alternative to taking buprenorphine every day. Most comparative studies of medications for opioid use disorder (OUD) focus on retention and illicit opioid use. This study asked a different and clinically important question: Do patients experience the treatment itself differently?

Lintzeris and colleagues conducted a 24-week, open-label randomized clinical trial involving 119 adults at six outpatient addiction treatment centers in Australia. All participants were receiving sublingual buprenorphine before enrollment. They were randomized either to continue daily sublingual buprenorphine or to transition to weekly or monthly subcutaneous depot buprenorphine. The primary outcome was global treatment satisfaction at week 24, measured with the Treatment Satisfaction Questionnaire for Medication (TSQM).

Participants assigned to depot buprenorphine reported significantly greater treatment satisfaction and substantially lower treatment burden. They also rated the treatment as more convenient. However, the groups did not differ significantly in illicit opioid use, withdrawal, craving, or treatment retention. Adverse drug reactions were more frequently reported with depot treatment, largely because of generally mild injection-site reactions.

The study therefore supports a focused conclusion: Among patients already stabilized on sublingual buprenorphine, transitioning to this weekly or monthly injectable formulation improved the patient-reported treatment experience over 24 weeks, but it did not demonstrate superior retention or illicit opioid-use outcomes.

STUDY DESIGN

- **Design:** Open-label, randomized, parallel-group, active-controlled clinical trial conducted under naturalistic treatment conditions.
- **Participants:** 119 adults with opioid dependence; 60 received depot buprenorphine and 59 received sublingual buprenorphine.
- **Setting:** Six outpatient addiction treatment centers in Australia.
- **Study Period:** October 2018 through September 2019.
- **Duration:** 24 weeks of treatment, with safety follow-up through week 26.
- Intervention: Weekly or monthly subcutaneous depot buprenorphine. Dosing strength and frequency were selected by the clinician and participant.
- **Comparison:** Daily sublingual buprenorphine, most often buprenorphine-naloxone film, administered under usual Australian practice conditions.
- **Primary Outcome:** TSQM global treatment satisfaction score at week 24. Scores range from 0 to 100, with higher scores indicating greater satisfaction.
- **Other Outcomes:** Treatment burden, convenience, perceived effectiveness, quality of life, recovery measures, illicit opioid use, withdrawal, craving, retention, and safety.

STUDY FINDINGS

Treatment Satisfaction & Burden

At week 24, the adjusted mean TSQM global satisfaction score was:

- Depot buprenorphine: 82.5
- Sublingual buprenorphine: 74.3
- Difference: 8.2 points (95% CI, 1.7–14.6; P=.01)

In a post hoc analysis, 53.3% of participants receiving depot buprenorphine had a satisfaction score of at least 80, compared with 33.9% receiving sublingual buprenorphine. The estimated number needed to treat for one additional participant to reach that threshold was 5.1, although the confidence interval was wide (95% CI, 2.8–61.1).

Treatment burden was also lower with depot buprenorphine. At week 24, the adjusted mean Treatment Burden Questionnaire score was 13.2 with depot treatment and 28.6 with sublingual treatment, a difference of −15.4 points (95% CI, −22.6 to −8.2; P<.001). Lower scores indicate less burden.

Several other patient-reported measures favored depot buprenorphine, including treatment convenience, perceived effectiveness, overall patient satisfaction, the opioid-treatment domain of a quality-of-life measure, fewer aberrant medication-related behaviors as measured by the Opioid-Related Behaviors in Treatment (ORBIT) scale, and physical functioning. Other measures—including general health-related quality of life, mental health functioning, recovery, depression, anxiety, and stress—did not show statistically significant between-group differences.

Retention, Opioid Use, Withdrawal, & Craving

Trial completion was high in both groups:

- **Depot Buprenorphine:** 53 of 60 participants (88.3%)
- **Sublingual Buprenorphine:** 56 of 59 participants (93.3%)

There was no statistically significant difference in treatment retention. At week 24, the combined measure of opioid-negative urine drug screens and self-reports averaged 69.9% in the depot group and 73.5% in the sublingual group, also not a significant difference. Withdrawal and craving were generally well controlled in both groups, without significant between-group differences.

These results are important to interpret correctly. The trial demonstrated a better patient-reported treatment experience with depot buprenorphine; it did not demonstrate better abstinence or retention.

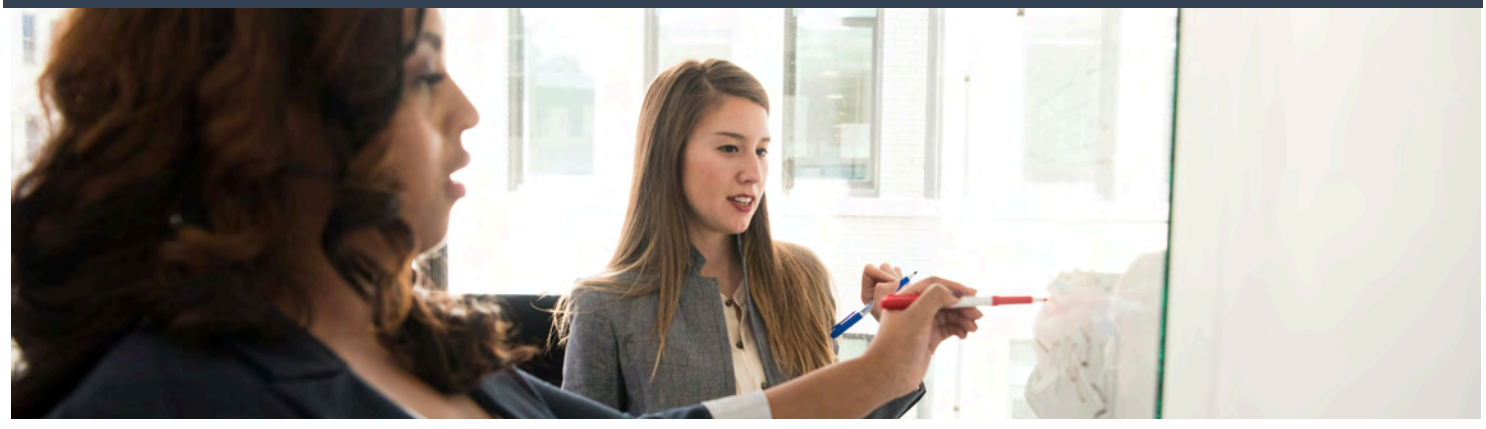
Safety & Tolerability

Adverse drug reactions were reported by 65.0% of participants receiving depot buprenorphine and 20.3% receiving sublingual buprenorphine. The difference was largely attributable to injection-site reactions, most of which were mild.

Treatment-emergent adverse events occurred in 90.0% of the depot group and 83.1% of the sublingual group. Severe treatment-emergent adverse events were reported by 5.0% and 6.8%, respectively. One severe event in the depot group—suicidal ideation—was considered possibly related to the medication; the event resolved after the dose was increased.

Serious adverse events occurred at similar rates—15.0% with depot buprenorphine and 15.3% with sublingual buprenorphine. One participant in the depot group had a serious adverse drug reaction; none occurred in the sublingual group. “Severe” describes the intensity of an event, whereas “serious” reflects specific regulatory criteria; the two classifications are not interchangeable.

No deaths occurred, and no participant discontinued trial medication or withdrew from the trial because of an adverse event.



CLINICAL & OPERATIONAL IMPLICATIONS

For Payers

The study supports including patient-reported outcomes—particularly treatment satisfaction, convenience, and treatment burden—alongside traditional measures such as retention and opioid use when evaluating OUD treatment options. It does not establish reduced health care utilization, lower total cost of care, improved adherence in routine practice, or better long-term clinical outcomes. Those questions require additional evidence.

For Clinical Professionals

For patients already receiving sublingual buprenorphine, weekly or monthly injectable treatment may offer a more satisfactory and less burdensome experience. The findings support shared decision-making rather than a one-size-fits-all treatment hierarchy. Patients should understand that the trial did not find better retention or illicit opioid-use outcomes and that injection-site reactions were common, although generally mild.

LIMITATIONS & OTHER CONSIDERATIONS

- **Open-Label Design:** Participants and clinicians knew which treatment was assigned. Because the primary outcome was self-reported satisfaction, expectations about a newer formulation may have influenced the findings.
- **Established-Treatment Population:** All participants in the primary analysis were already receiving sublingual buprenorphine. The study therefore compared continuing sublingual treatment with transitioning to depot treatment; it does not establish what newly initiating patients would experience.
- **No Weekly-Versus-Monthly Comparison:** Participants were randomized to depot or sublingual treatment, but not separately randomized to weekly or monthly depot dosing. The study cannot determine whether one depot schedule produced better outcomes than the other.
- **Sample Size & Duration:** The trial was powered for treatment satisfaction, not for smaller differences in illicit opioid use or other secondary outcomes. It included 119 treated participants and lasted 24 weeks.
- **Multiple Comparisons:** Secondary outcomes were not adjusted for multiple comparisons and should be interpreted as supportive rather than definitive.
- **Generalizability**: Australian medication-dispensing and supervision practices differ from those in the United States. Trial participants did not pay medication or dispensing fees, which may also have affected satisfaction and retention.
- **Funding & Sponsor Role**: Camurus AB, the manufacturer of the depot formulation, funded the trial. The company participated in study design, management, data analysis and interpretation, manuscript preparation and review, and the decision to submit the manuscript. Several authors were employees of or had financial relationships with Camurus and other pharmaceutical companies.

CONCLUSION

This randomized clinical trial found that adults already receiving sublingual buprenorphine who transitioned to weekly or monthly depot buprenorphine reported higher treatment satisfaction and lower treatment burden than those who continued daily sublingual treatment. Traditional clinical outcomes—including retention, illicit opioid use, withdrawal, and craving—were similar between groups.

The practical lesson is not that one formulation is universally superior. It is that treatment experience matters and can differ substantially even when conventional clinical outcomes do not. Offering appropriate patients a choice of formulations—and measuring satisfaction and burden as well as retention and opioid use—can support more patient-centered OUD care.

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CITATION

Lintzeris N, Dunlop AJ, Haber PS, et al. Patient-Reported Outcomes of Treatment of Opioid Dependence With Weekly and Monthly Subcutaneous Depot vs Daily Sublingual Buprenorphine: A Randomized Clinical Trial. JAMA Network Open. 2021;4(5):e219041. doi:10.1001/jamanetworkopen.2021.9041.