A Single-site Retrospective Cohort Study of Oral & Dental Disease Associated with Buprenorphine Use in Patients with Opioid Use Disorder

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Introduction

- In 2022, the FDA issued a warning to prescribers regarding potential increased risk of tooth decay, cavities, oral infections and tooth loss associated with sublingual buprenorphine. This warning was based on 305 cases of dental adverse events reported via the FDA Adverse Event Reporting System (FAERS) or in the medical literature.[1]
- Since then, there have been limited studies on the association between sublingual buprenorphine and dental adverse events.
- One retrospective cohort study of 33,405 participants examined dental effects of sublingual buprenorphine/naloxone versus transdermal buprenorphine or oral naltrexone in patients with. They found a statistically significant increase in both any dental adverse effects involving the teeth, gums, or pulp and dental caries or tooth loss when compared to both transdermal buprenorphine and oral naltrexone.[2] Of note, transdermal buprenorphine and oral naltrexone are not approved for treatment of OUD; indeed, patients with OUD, who are likely to be at increased risk for dental disease,[3] may have been overrepresented in the group receiving sublingual buprenorphine.

The objective of this study was to evaluate whether patients with opioid use disorder (OUD) who are prescribed sublingual buprenorphine have increased rates of oral and dental diseases compared to patients with opioid use disorder who are not prescribed any buprenorphine.

Methods

Study Design

- This study was a retrospective cohort study using routinely collected data from the Stanford Health Care electronic medical record from 2010 - April 2023. Data was extracted and mapped to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) Version 5.3 and subsequently analyzed by Atropos Health.
- The cohort was identified as patients aged 18-90 with opioid use disorder (ICD-9: 304.0*, 305.5*, and ICD-10: F11*) who had never been previously prescribed buprenorphine or previously had oral or dental issues. Patients were required to have a minimum history of 90 days and minimum follow up for 6 months for inclusion in the cohort.
- The intervention group then included patients who were prescribed sublingual buprenorphine and the control group included patients who were not prescribed buprenorphine but were prescribed other medications to control for attrition bias.
- Patients receiving transdermal buprenorphine were excluded.
- Outcomes included new diagnosis of any diseases of the oral cavity, salivary glands, and jaws (ICD10: K00-K14, ICD9: 520-529.99) within 6 months of initial prescription and within 12 months of initial prescription.
- Stanford IRB determined this study was not human subjects research.

Statistical Analysis

- For confounder matching, pre-exposure confounders include demographics, Charlson comorbidities[4], diagnostic, procedure and medication codes and number of encounters observed in the 90 days before treatment initiation.
- To control for confounders, the treated group was matched with the untreated group using 1:1 matching on age and sex, or high dimensional propensity score (hdPS)[5] considering all baseline confounders listed above.
- Odds ratios were reported for both matching scenarios and when unmatched.
- A two-sided *p*-value of 0.05 was considered statistically significant. Analyses were performed using R version 4.2 on the Atropos Health's platform. 95% Confidence Intervals are provided after each statistic.

Results

	No Buprenorphine	Sublingual Buprenorphine
N	1728	197
Female (%)	855 (49.5%)	95 (48.2%)
Mean age (sd)	50.3 (16.3%)	50.4 (16.5%)
Race (%)		
White	1206 (69.8%)	147 (74.6%)
Other	310 (17.9%)	39 (19.8%)
Black	160 (9.3%)	7 (3.6%)
Asian	52 (3.0%)	4 (2.0%)
Hispanic (%)	250 (14.5%)	26 (13.2%)
Comorbidity score (sd)	2.4 (SD = 2.8)	2.2 (SD = 2.5)

Table 1: Demographics of study cohort

- 1,925 patients met criteria for inclusion. The intervention group contained 197 patients who were prescribed sublingual buprenorphine and the control group included 1,728 patients who were never prescribed buprenorphine.
- At 6 months, the OR for oral and dental issues among patients prescribed sublingual buprenorphine versus no buprenorphine was 2.62 (1.11, 6.15, p=0.03) for an unmatched analysis and 0.71 (0.17, 2.64, p=0.77) for a propensity score analysis.
- At 12 months, the OR for oral and dental issues among patients prescribed sublingual buprenorphine versus no buprenorphine was 2.4 (1.08, 5.30, p=0.03) for an unmatched analysis and 0.74 (0.25, 2.18, p=0.59) for a propensity score analysis.

	Unmatched Analysis				Propensity Score Matched			
	N	% Oral and Dental disease	OR (95% CI)	p-value	N	% Oral and Dental disease	OR (95% CI)	p-value
At 6 months								
No Buprenorphine	1704	1.39			178	3.78		
SL Buprenorphine	190	3.55	2.62 (1.11, 6.15)	0.03	180	2.79	0.71 (0.17, 2.64)	0.77
At 12 months								
No Buprenorphine	1704	1.74			178	4.32		
SL Buprenorphine	190	4.06	2.40 (1.08, 5.30)	0.03	180	3.24	0.74 (0.25, 2.18)	0.59

Table 2: risk of new diagnosis of oral or dental disease in the study population at 6 and 12 months after initiation of sublingual buprenorphine.

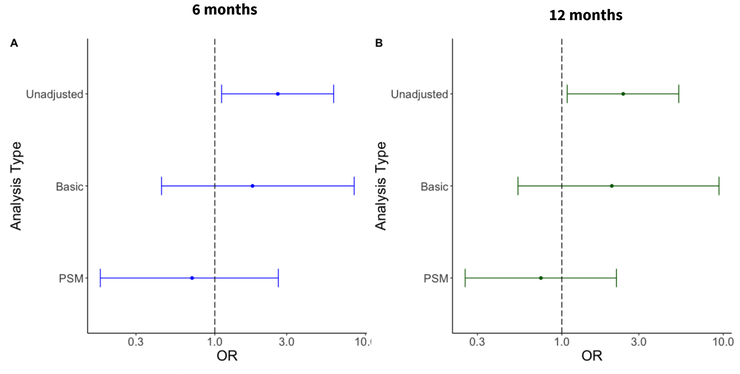

Figure 1: Odds ratio for diagnosis of new oral or dental issues at 6 months (A) and 12 months (B)

Discussion

- Buprenorphine/naloxone is a commonly prescribed treatment for Opioid Use Disorder.
- Sublingual buprenorphine is posited to lead to adverse dental effects including caries, tooth decay, and tooth loss through decreased salivary production and immunosuppressive effects which are also seen with use of other opioids, however most of the available data on the dental and oral effects of sublingual buprenorphine comes from isolated case reports.[1,6]
- In this retrospective cohort study, a greater proportion of patients on sublingual buprenorphine had dental and oral issues documented at 6 and 12 months in an unmatched analysis; after adjusting for visible confounders, this finding was not statistically significant.
- This study did not compare oral and dental health outcomes associated with sublingual buprenorphine to outcomes associated with other formulations of buprenorphine such as extended-release injection formulations or transdermal formulations.
- Limitations of this study include uncaptured data from outpatient dental office visits, uncaptured data from participants with dental effects not severe enough to present to a physician or participants who do not have regular dental screening, and potentially unmeasured confounders including oral hygiene, other medications, and regular dental care.

Conclusions

- More research is needed to understand the effect of sublingual buprenorphine on oral and dental health.
- Clinicians should continue to encourage regular dental care among patients with OUD who are receiving sublingual buprenorphine.
- The FDA continues to recommend that the benefits of sublingual buprenorphine/naloxone for the treatment of opioid use disorder outweigh the potential dental and oral health risks.

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