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Greetings,

“The ads have been popping up on Facebook” ... what’s the deal with Suboxone and teeth? Back in 2022, during the haze of the pandemic, the FDA issued a warning about dental decay risk from sublingual buprenorphine medications. What is this based on? How likely is this to be a significant risk? Are films worse than tabs? And what do we tell patients about minimizing potential risk? A Google search led me to a bevy of law firm websites with definitive declarations about the dental harms of Suboxone and details about the related class action lawsuits. Might these be the source of our patients’ Facebook ads?

These claims are based on case reports in the setting of reasonable biologic plausibility (low pH of medication, xerostomia). Reviewed here is the only research beyond case studies attempting to characterize the risk. Here, investigators used claims data to compare dental outcomes in patients on buprenorphine/naloxone (bup/nal) to those on naltrexone or transdermal buprenorphine. This brings a significant limitation of confounding by indication, but reviewing it allows us to think more deeply and critically about the claims being made. It also provides an opportunity to consolidate background [information](#) so that we can educate patients about this question and what they can do to best protect their oral health while continuing therapy.

Happy New Year,
Andrea

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Title: Sublingual Buprenorphine-Naloxone Exposure May Be Associated with Dental Disease

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Link: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9856241/>

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BACKGROUND

Case reports raised a signal for dental risk due to sublingual buprenorphine (SL bup) medications. This ultimately led to a 2022 FDA warning on all SL bup containing products. Some of the case reports were in people who were documented to have no dental problems prior to bup initiation. Counter to that, evidence of reporting bias in this group has been documented (Barus, 2023) and a majority of people who take sublingual bup have other risk factors for dental decay complicating the question of causality.

METHODS

This a pharmacoepidemiologic survey using a large pharmacy database (IQVIA) to attempt to characterize the association between buprenorphine-naloxone (bup/nal) prescription and dental disease.

Investigators created a random sample of patients with one year of healthcare contact starting 2006-2020 who were newly exposed to medication for opioid use disorder. The three comparator groups were established: those newly prescribed bup/nal (film or tab), oral naltrexone or transdermal bup brand name, Belbuca (which is lower dose than therapeutic for OUD and indicated for chronic pain, not OUD). Patients were excluded if they had received any of the three drugs in the one year prior to study entry.

The primary outcome was first occurrence of a dental adverse event, defined as any disease of the teeth, gums, or pulp. A secondary outcome of dental caries or tooth loss was also examined. Outcomes were determined via inpatient and outpatient ICD-9 diagnoses (entered by physicians). Patients were followed until event, medication change, loss of insurance or end of follow up (Oct 2020). Adjustments were made for a number of covariates including age, sex, Sjogren's syndrome, inflammatory bowel disease (IFB), DM, HIV, xerostomia, smoking, alcohol use (not further defined), TCAs, previous opioid use (not further defined), chronic pain, illicit drug use (defined as previous use of heroin or cocaine) and mean # dentist visits.

Sensitivity analyses were done that restricted the analyses to various groups including those without opioid or alcohol use, illicit drug use, dm or smoking, history of opioid use or chronic pain. They also examined the risk only in those with at three or more prescriptions.

MAIN RESULTS

Mean fup 2.2-2.6 years

Table 1 describes the participants.

Table 1. Baseline Characteristics of Users of Sublingual Buprenorphine (BPN)/Naloxone, Transdermal BPN, and Oral Naltrexone.

Characteristics	No. (%)		
	Sublingual BPN/naloxone (n = 21 404)	Transdermal BPN (n = 5385)	Naltrexone (n = 6616)
Age, mean (SD), y	35.6 (12.6)	53.0 (15.6)	43.2 (14.4)
Sex			
Men	13 144 (61.4)	1913 (35.5)	3365 (50.9)
Women	8260 (38.6)	3472 (64.5)	3251 (49.1)
Follow-up, mean (SD), y	2.2 (2.4)	2.3 (2.1)	2.6 (2.7)
Comorbidities			
Sjögren syndrome	44.9 (0.21)	93.2 (1.73)	23.2 (0.35)
Inflammatory bowel disease	278.3 (1.3)	150.8 (2.8)	115.1 (1.74)
Diabetes	1586 (7.41)	1361.9 (25.29)	705.9 (10.67)
HIV	51.4 (0.24)	7 (0.13)	11.2 (0.17)
Xerostomia	30 (0.14)	52.2 (0.97)	15.2 (0.23)
Smoking	1406.2 (6.57)	626.8 (11.64)	449.9 (6.8)
Alcohol use	10 098.4 (47.18)	1580 (29.34)	4133 (62.47)
Tricyclic antidepressant use	355.3 (1.66)	315 (5.85)	84 (1.27)
Previous opioid use	11 714.4 (54.73)	710.8 (13.2)	1411.2 (21.33)
Chronic pain	1628.8 (7.61)	1407.1 (26.13)	136.3 (2.06)
Illicit drug use ^a	969.6 (4.53)	18.8 (0.35)	265.3 (4.01)
Dentist visits, mean (SD)	0.38 (2.10)	0.20 (1.51)	0.19 (1.38)

The groups were large (n=21,404 bup/nal, transdermal bup n=5385, and naltrexone n=6616) and very different. In particular transdermal bup had more women, older age (mean age 53yrs compared with 35 in bup/nal, 43 in naltrexone), more dm, IFB, chronic pain, xerostomia and smoking. Alcohol use was more common in the naltrexone group (63%) than in bup/nal (47 %), and the naltrexone group had much less previous opioid use (21%) than bup/nal (55%).

Of note, the rate of smoking captured in the bup/nal group was a mere 6.6%. Also note that in the bup/nal group previous opioid use is only 55%, chronic pain 7.6%.

Outcomes were as follows:

	Adjusted HR for dental adverse event	Adjusted HR for caries or tooth loss
Bup/nal vs transdermal bup	1.42 (1.17-1.73)	1.57 (1.11-2.23)

Bup/nal vs naltrexone	1.67 (1.41-1.98)	1.71 (1.29-2.27)
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Sensitivity analysis for dental adverse events showed a slight increase in the effect when restricted to those receiving 3 or more prescriptions (HRs 1.8-2.0) and no significant change when removing those with prior opioid use, prior alcohol use, illicit use, dm and smoking (HRs 1.6-1.7)

CONCLUSION

The risk of dental events was 1.4-1.7 times higher for patients taking bup/nal compared to transdermal bup and oral naltrexone, but the likely residual confounding in this study limits conclusions about the true presence and degree of dental risk posed by SL bup.

COMMENTARY

This study was a responsive attempt to go beyond case reports to answer the question raised about SL bup induced dental problems. A related editorial highlights the study's defining limitation: "In this study, use of buprenorphine-naloxone identified people with opioid use disorder, while the other medications identified people much less likely to have opioid use disorder. These groups differ in multiple ways not captured by administrative data, including experiences of stigma, poverty, and access to health care." (Brothers et al. 2023). Other factors found commonly in patients with OUD that may or may not be similarly present in these comparison groups are use of tobacco, marijuana, suboptimal oral hygiene practices sometimes from a young age, limited access to dental care, history of full agonist opioid use, other substance use, dietary factors including high soda intake, mood disorders and medications for it→bruxism, dry mouth.

The study essentially compares people with OUD (on bup/nal) to those with AUD (and maybe concomitant OUD) (on naltrexone), and to those with chronic pain (on transdermal bup). Though there is overlap in these groups they are quite different as evidenced even in the limited data available to describe them. The attempt to adjust for these large differences cannot be sufficient given how limited this administrative data appears to be. For example, smoking was documented at a prevalence of 7% in those on bup/nal, though smoking in people with OUD is widely documented as being on the order of 80-90%, and 'previous opioid use' was documented at 55% in the bup/nal group though the only indication -and usual practice for prescribing that medication- is OUD.

In addition, though it was not the authors intent to describe the absolute risk, it is important not to try to use this data to understand the absolute risk of dental decay in these populations as dental claims documented by a physician are likely to miss a great number of events. And with mean follow up of 2.2-2.6 years, important clinical risk is missed, particularly as average time to development of decay in one case series was 46 months (range 5-77months), (Suzuki, et al 2013).

So what can we say? The question remains. A prospective comparison of medications for OUD among patients with OUD, such as injectable versus SL bup would allow for a better understanding of the presence and degree of risk without the significant confounding by indication present in this study.

In the meantime, the question of risk remains, and given co-occurring dental risk factors, people with OUD would be more susceptible to such a risk. This does not mean stopping medication but it does call for informing patients of the potential risk and ways that they can protect their dental health while they continue medication. Please follow [this link](#) for more on that!

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