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Association of Opioid Prescriptions From Dental Clinicians for US Adolescents and Young Adults With Subsequent Opioid Use and Abuse

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IMPORTANCE Through prescription writing, dental clinicians are a potential source of initial opioid exposure and subsequent abuse for adolescents and young adults.

OBJECTIVE To examine the association between index dental opioid prescriptions from dental clinicians for opioid-naive adolescents and young adults in 2015 and new persistent use and subsequent diagnoses of abuse in this population.

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study examined outpatient opioid prescriptions for patients aged 16 to 25 years in the Optum Research Database in 2015. Prescriptions were linked by National Provider Identifier number to a clinician category.

EXPOSURES Individuals were included in the index dental opioid (opioid-exposed) cohort if they filled an opioid prescription from a dental clinician in 2015, had continuous health plan coverage and no record of opioid prescriptions for 12 months before receiving the prescription, and had 12 months of health plan coverage after receiving the prescription. Two age- and sex-matched opioid-nonexposed control individuals were selected for each opioid-exposed individual and were assigned a corresponding phantom prescription date.

MAIN OUTCOMES AND MEASURES Receipt of an opioid prescription within 90 to 365 days, a health care encounter diagnosis associated with opioid abuse within 365 days, and all-cause mortality within 365 days of the index opioid or phantom prescription date.

RESULTS Among 754 002 individuals with continuous enrollment in 2015, 97 462 patients (12.9%) received 1 or more opioid prescriptions, of whom 29 791 (30.6%) received prescriptions supplied by a dental clinician. The opioid-exposed cohort included 14 888 participants (7882 women [52.9%], 11 273 white [75.7%], with mean [SD] age, 21.8 [2.4] years), and the randomly selected opioid-nonexposed cohort included 29 776 participants (15 764 women [52.9%], 20 078 [67.4%] white, with mean [SD] age, 21.8 [2.4] years). Among the 14 888 individuals in the index dental opioid cohort, 1021 (6.9%) received another opioid prescription 90 to 365 days later compared with 30 of 29 776 (0.1%) opioid-nonexposed controls (adjusted absolute risk difference, 6.8%; 95% CI, 6.3%-7.2%), and 866 opioid-exposed individuals (5.8%) experienced 1 or more subsequent health care encounters with an opioid abuse–related diagnosis compared with 115 opioid-nonexposed controls (0.4%) (adjusted absolute risk difference, 5.3%; 95% CI, 5.0%-5.7%). There was only 1 death in each cohort.

CONCLUSIONS AND RELEVANCE The findings suggest that a substantial proportion of adolescents and young adults are exposed to opioids through dental clinicians. Use of these prescriptions may be associated with an increased risk of subsequent opioid use and abuse.

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Supplemental content

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Abuse of opioids is a public health crisis in the United States.[1,2] Dentists are the leading source of opioid prescriptions for children and adolescents aged 10 to 19 years, accounting for 31% of opioid prescriptions in this age group in 2009.[3] A recent investigation found that dental opioid prescriptions for 11- to 18-year-old children and adolescents increased from 99.7 per 1000 dental patients in 2010 to 165.9 per 1000 dental patients in 2015,[4] with nearly one-quarter of the first opioid prescriptions in this age group coming from dental clinicians.[5]

A common source of dental opioid exposure is third molar (wisdom teeth) extractions,[6,7] a procedure for which current frequency estimates are unknown but was estimated to have occurred in approximately 5 million Americans per year in 1999.[8,9] Because there is controversy about the risk-benefit profile of third molar extractions,[10,11] which are performed with unexplained variability[12] and have been deemed by some to be unnecessary in the majority of cases,[9] a better understanding of the frequency of this procedure and the use of opioids postoperatively is needed.

The Optum Research Database provides claims information for a large population of privately insured patients in the United States and contains deidentified inpatient, outpatient, and pharmaceutical claims data from approximately 12 million to 14 million privately insured patients per year from across 50 states. The database includes information on prescriptions with a link to the clinician type.

Using the Optum database, this investigation aimed to (1) compare the frequency of opioid use at 90 to 365 days after the index or phantom prescription date and subsequent health care encounters associated with opioid abuse and death within 365 days among patients aged 16 to 25 years with and without an index dental opioid prescription in 2015 and (2) describe the frequency and source of opioid prescriptions among patients aged 16 to 25 years in 2015.

Key Points

Question Are opioid prescriptions from dental clinicians that are written for pain management of third molar extractions from adolescents and young adults associated with subsequent opioid use and abuse?

Findings In this cohort analysis of claims data, index opioid prescriptions in opioid-naive adolescents and young adults compared with age- and sex-matched controls were associated with a statistically significant 6.8% absolute risk increase in persistent opioid use and a 5.4% increase in the subsequent diagnosis of opioid abuse.

Meaning The findings suggest that dental opioid prescriptions, which may be driven by third molar extractions in this age group, may be associated with subsequent opioid use and opioid abuse.

Methods

Design and Data Source

This investigation was a retrospective, double cohort study[13] examining opioid prescriptions for patients in the Optum Research Database. Optum provides claims information for a large sample of privately insured patients in the United States and contains deidentified inpatient, outpatient, and pharmaceutical claims data as well as laboratory data for approximately 12 million to 14 million privately insured patients per year from across 50 states. The claims are sourced from Optum's sister company and its affiliates. The database includes demographic and socioeconomic characteristics (ie, age, sex, geographic region, race/ethnicity, and household income), encounter data (ie, hospital admissions, outpatient visits, and associated procedures), pharmaceutical data (ie, filled pharmaceutical claims, number of days' supply, dosage dispensed, medication strength, and method of administration), financial data (ie, total cost, copayment, and deductibles), and laboratory results (test description and results). The Stanford University institutional review board, Stanford, California, determined that this study does not meet the definition of human patient research and was therefore exempt from review.

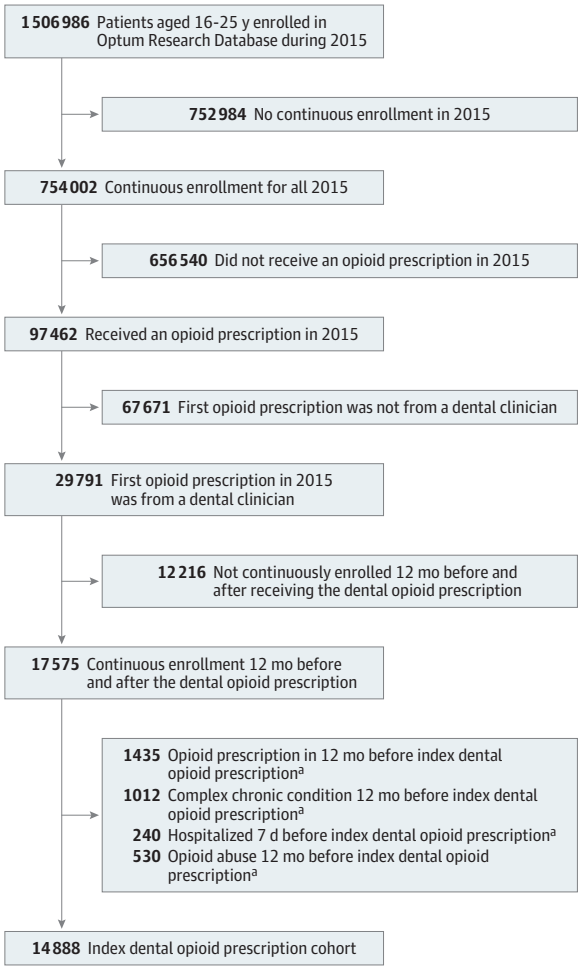
Study Population

Patients were included if their year of birth was from 1990 to 1999, corresponding to an approximate age range of 16 to 25 years in 2015, the common age for eruption and extraction of third molars. Patient flow is depicted in the **Figure**. To analyze the proportion of patients who received at least 1 opioid prescription in 2015, we limited the sample to patients who were enrolled throughout 2015 (the most contemporaneous data available, given the need for 12 months of follow-up data). Counts of opioid prescriptions were calculated per person-year to compare opioid exposure in included and excluded patients.

Claims for outpatient opioid prescriptions were linked using the National Provider Identifier number to a clinician unique number and then its corresponding prescriber category. Dental categories included doctor of medicine in dentistry, doctor of dental surgery, general dentist, general dentist-doctor of medicine in dentistry, general dentist-doctor of dental surgery, or general surgeon-oral/maxillofacial specialist.

The index dental opioid cohort was defined as patients who (1) received an outpatient opioid prescription from a dental clinician in 2015; (2) had evidence of insurance coverage in the Optum database for a minimum of 12 months preceding the opioid prescription without any evidence of opioid prescriptions, opioid abuse (as defined by *International Classification of Diseases, Ninth Revision* [*ICD-9*] and *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* [*ICD-10*] diagnosis codes), or a complex chronic condition, as described by Feudtner et al,[14,15] during that time; and (3) had evidence of continued coverage in Optum for at least 12 months following the prescription. Opioid prescription fills were identified using therapeutic class codes 280808 or 28080800 (opiate agonists). To define index dental opioid exposures, we did not consider opioids that were unlikely to be prescribed by dental clinicians (eg, opioid and caffeine mixtures), whereas the comprehensive list of opioids in the class code was used to define previous and subsequent opioid exposure. We excluded patients who were hospitalized up to 7

Figure. Patient Flowchart



[a] Patients may have had more than 1 exclusion.

days before receiving the index dental opioid prescription to limit the population to patients who were more likely to have undergone elective outpatient procedures.

We created an opioid-nonexposed control cohort as follows. First, we divided patients not in the index dental opioid cohort into 20 discrete age-sex strata (2 strata for each year of age). We randomly assigned phantom prescription dates to patients within each strata that corresponded to the actual prescription dates for the opioid-exposed patients within the same strata. Control patients were similarly required to have continuous health care coverage for 12 months before and after the phantom prescription date, with no complex chronic conditions, no documentation of opioid use or abuse during the 12 months before the phantom prescription date, and no hospitalizations in the previous 7 days. Among patients who fit these criteria, 2 controls were randomly selected per case.

Outcomes

The following outcomes were measured: (1) at least 1 additional filled opioid prescription at 90 to 365 days after the initial prescription or phantom date, (2) at least 1 subsequent health care encounter with an *ICD-9* or *ICD-10* diagnosis code associated with opioid abuse within 365 days, (3) and death within 365 days. The 90-day start time for subsequent prescriptions was decided a priori based on similar investigations of new persistent opioid use[16-18] to examine new prescriptions that were unlikely to be associated with the initial indication. The *ICD* diagnoses (eTable in the Supplement) were derived from previous publications[19-21] assessing opiate overdoses and from querying the complete online list of codes provided by the World Health Organization.[22]

Statistical Analysis

Characteristics and outcomes were described and compared between opioid-exposed and opioid-nonexposed patients using contingency tables, χ^2 tests, and absolute risk differences. Multivariable logistic regression was used to examine potential associations with persistent opioid use and abuse in the index dental opioid cohort: age (stratified as 16-18, 19-21, and 22-25 years), sex, race/ethnicity, geographic region, and previous diagnoses of nonopioid substance abuse. Socioeconomic status information was not included as a covariate because this data field was missing for approximately 15% of the sample and because this variable is derived from other demographics. All associations and potential interactions (defined a priori) between age and race/ethnicity or sex and race/ethnicity were assessed using the likelihood ratio test. Statistical significance was defined at the level of a 2-sided $\alpha = .05$. All analyses were performed using Stata/SE, version 14.2 (StataCorp).

Results

Of 1 506 986 patients aged 16 to 25 years who were enrolled during 2015, 752 984 (50.0%) were not continuously enrolled for the entire year (Figure). For the 754 002 continuously enrolled participants, 97 462 patients (12.9%) received at least 1 opioid prescription, of whom 29 791 (30.6%) received prescriptions supplied by a dental clinician (84.6% from a doctor of medicine in dentistry or doctor of dental surgery, 13.0% from a general dentist, and 2.4% from a general surgeon-oral/maxillofacial specialist). The mean number of opioid prescriptions filled per person-year for excluded patients (those without continuous enrollment in 2015) was 0.19 vs 0.20 for continuously enrolled patients (Figure).

After exclusions for previous complex chronic conditions, hospitalizations within 7 days, and opioid prescriptions or diagnoses of opioid abuse within 12 months of the index opioid prescription, 14 888 individuals were included in the index dental opioid cohort (7882 women [52.9%], 11 273 white [75.7%], with mean [SD] age, 21.8 [2.4] years), and 29 776 randomly selected individuals were included in the opioid-nonexposed control cohort (15 764 women [52.9%], 20 078 white [67.4%], with mean [SD] age, 21.8 [2.4] years). Demographic characteristics of these patients and details of the opioid prescription information are described in **Table 1**. Opioid use at 90 to 365 days occurred among 1021 of 14 888 individuals (6.9%) in the index dental opioid cohort compared with 30

Table 1. Patient Characteristics in the Opioid-Exposed and Opioid-Nonexposed Cohorts[a]

Characteristic	Index Dental Opioid-Exposed Cohort (n = 14 888)	Opioid-Nonexposed Control Cohort (n = 29 776)	*P* Value[b]
Female sex	7882 (52.9)	15 764 (52.9)	NA[c]
Age, mean (SD), y	21.8 (2.4)	21.8 (2.4)	NA[c]
Race/ethnicity			
Asian	593 (4.0)	1324 (4.4)	<.001
Black	939 (6.3)	2772 (9.3)	
Hispanic	1376 (9.2)	4003 (13.4)	
White	11 273 (75.7)	20 078 (67.4)	
Unknown	707 (4.8)	1599 (5.4)	
US Region[d]			
South	6002 (40.3)	11 818 (39.7)	.87
North East	1401 (9.4)	2939 (9.9)	
North Central	4139 (27.8)	8434 (28.3)	
Mountains	1635 (11.0)	3545 (11.9)	
Pacific	1660 (11.1)	2613 (8.8)	
Unknown	51 (0.3)	427 (1.4)	
Index opioid prescription information			
Days' supply, median (IQR)	3 (3-5)	NA	NA
Quantity, median (IQR)	20 (18-30)	NA	
With ≥1 refill, No. (%)	20 (0.1)	NA	
Type of opioid (n = 15 109)[e]			
Hydrocodone/acetaminophen	11 297 (75.9)	NA	NA
Oxycodone HCl/acetaminophen	3173 (21.3)	NA	
Hydrocodone/ibuprofen	259 (1.7)	NA	
Tramadol HCl	216 (1.4)	NA	
Tramadol HCl/oxycodone	99 (0.7)	NA	
Oxycodone	65 (0.4)	NA	
Any diagnosis of nonopioid substance abuse in previous 12 mo[f]	473 (3.2)	834 (2.8)	.03

Abbreviations: HCl, hydrochloride; IQR, interquartile range; NA, not applicable.

[a] Because of rounding, percentages may not total 100. Data are presented as number (percentage) of patients unless otherwise indicated.

[b] *P* values obtained from χ^2 analysis.

[c] Cohorts were matched on age and sex.

[d] Middle Atlantic and New England regions were collapsed into Northeast; East North Central and West North Central regions were collapsed into North Central; and East South Central, West South Central, and South Atlantic were collapsed into South.

[e] Patients may have received more than 1 opioid prescription.

[f] Substance abuse consisted of cannabis, sedative, hypnotic, anxiolytic, cocaine, stimulant, hallucinogen, inhalant, alcohol, tobacco, and antidepressant abuse.

of 29 776 individuals (0.1%) in the opioid-nonexposed cohort (adjusted absolute risk difference, 6.8%; 95% CI, 6.3%-7.2%; *P* < .001) (**Table 2**). The second opioid prescription was provided by a dental clinician for 276 of 1021 (27.0%) patients (doctor of dental surgery for 124; doctor of medicine in dentistry, 69; general dentist, 66; endodontist, 11; periodontist, 5; and pedodontist, 1). For the 745 second opioid prescriptions not provided by a dental clinician, the leading clinician-type categories were unknown prescriber (n = 134), emergency medicine physician (n = 132), orthopedic surgeon (n = 69), physician assistant (n = 58), otolaryngologist (n = 55), family practitioner (n = 50), obstetrician/gynecologist (n = 34), general surgeon (n = 25), and general internist (n = 24). A median (interquartile range) of 20 (16-28) pills were dispensed for the second opioid prescription; this number of pills did not differ between dental and nondental clinicians.

Because opioid-exposed patients had initial dental visits and opioid-nonexposed individuals may not have had dental visits, we also examined subsequent opioid prescriptions from nondental clinicians among individuals who received nonopioid prescriptions (eg, antibiotics) from dental clinicians. The results showed that only 0.3% (5 of 1628 patients) of opioid-nonexposed patients who received a dental nonopioid prescription filled opioid prescriptions from nondental clinicians at 90 to 365 days compared with 5.0% (745 of 14 888) of the opioid-exposed patients (*P* < .001).

At least 1 subsequent health care encounter with an *ICD-9* or *ICD-10* diagnosis code associated with opioid abuse within 365 days was documented for 866 patients (5.8%) in the opioid-exposed cohort and 115 (0.4%) in the opioid-nonexposed cohort (adjusted absolute risk difference, 5.3%; 95% CI, 5.0%-5.7%; *P* < .001). For the 866 opioid-exposed patients with a diagnosis of opioid abuse, the first encounter occurred within 90 days for 570 patients (65.8%). Hospitalizations associated with a diagnosis of opioid abuse were more common in the opioid-exposed cohort (74 of 14 888 [0.5%]) than in the opioid-nonexposed cohort (79 of 29 776 [0.3%]) (adjusted absolute risk difference, 0.2%; 95% CI, 0.1%-0.4%; *P* < .001).

For multivariable analysis comparing persistent opioid use at 90 to 365 days and the diagnosis of opioid abuse within 365 days in the opioid-exposed cohort, individuals aged 22 to 25 years were less likely than those aged 16 to 18 years to have persistent opioid use (adjusted odds ratio [aOR], 0.7; 95% CI, 0.6-0.9) and abuse (aOR, 0.8; 95% CI, 0.7-1.0). Female patients were more likely to have persistent use (aOR, 1.2; 95% CI, 1.0-1.4) and abuse (aOR, 11.5; 95% CI, 9.4-14.8), and Asian race/ethnicity was associated with decreased odds of persistent use (aOR, 0.6; 95% CI, 0.4-0.9) and abuse (aOR, 0.3; 95% CI,

Table 2. Outcomes in the Opioid-Exposed and Opioid-Nonexposed Cohorts

Outcome (N = 44 664)	Cohort, No. (%)		P Value[a]	Adjusted Absolute Risk Difference, % (95% CI)[b]
	Opioid-Exposed (n = 14 888)	Opioid-Nonexposed (n = 29 776)		
Opioid prescription at 90 to 365 d	1021 (6.9)	30 (0.1)	<.001	6.8 (6.3 to 7.2)
>1 Opioid prescription	387 (2.6)	3 (0.01)	<.001	2.5 (2.2 to 2.7)
At least 1 diagnosis of opioid abuse in subsequent 365 d	866 (5.8)	115 (0.4)	<.001	5.3 (5.0 to 5.7)
Site of encounter[c]				
Office visit	790 (5.3)	97 (0.3)	<.001	4.9 (4.5 to 5.3)
Emergency department visit	25 (0.2)	24 (0.1)	.005	0.1 (0.02 to 0.2)
Hospitalization	74 (0.5)	79 (0.3)	<.001	0.2 (0.1 to 0.4)
Most common diagnoses of opioid abuse[c]				
Opioid type dependence, unspecified	602 (4.0)	66 (0.2)	<.001	3.8 (3.5 to 4.1)
Poisoning by opium (alkaloids), unspecified	82 (0.6)	8 (0.03)	<.001	0.5 (0.4 to 0.6)
Opioid abuse, unspecified	51 (0.3)	25 (0.08)	<.001	0.3 (0.2 to 0.4)
Death	1 (0.007)	1 (0.003)	.62	0.003 (−0.002 to 0.005)

[a] *P* value obtained from χ^2 analysis.

[b] Adjusted for race/ethnicity and previous nonopioid substance abuse.

[c] Some patients had more than 1 site of encounter or diagnosis of opioid abuse.

0.2-0.6). Previous nonopioid substance abuse was associated with persistent use (aOR, 3.7; 95% CI, 2.9-4.7) and abuse (aOR, 4.5; 95% CI, 3.4-5.9) (**Table 3**). For patients who were prescribed more than 20 pills compared with 20 or fewer pills for the index prescription, persistent use (6.6% vs 7.0%; *P* = .53) and abuse (5.7% vs 5.9%; *P* = .75) were not significantly different.

A sensitivity analysis using a time window of substance abuse at 90 to 365 days instead of 0 to 365 days yielded the following aOR results: lower aOR for female patients (aOR, 3.2; 95% CI, 2.4-4.2) and higher aOR for previous nonopioid substance abuse (aOR, 4.5; 95% CI, 3.4-5.9); aORs for race/ethnicity and geographic region were no longer statistically significant for any subcategory. At 12 months' follow-up of the cohorts, 1 death was reported in each cohort, and this was not significantly different between cohorts (*P* = .62).

Discussion

In this retrospective investigation of a national sample of privately insured adolescents and young adults, the results showed that exposure to opioids through a dental clinician in a population of opioid-naive patients was associated with higher rates of opioid use at 90 to 365 days later and subsequent diagnoses associated with opioid abuse or overdose compared with controls. The results also showed that a substantial proportion of overall opioid exposure in this age group came from dental clinicians, findings that warrant close attention given the current epidemic of opioid abuse.

Several previous investigations have analyzed new persistent opioid use following surgical procedures. Brummett et al[16] noted persistent opioid use at 90 to 180 days in 5.9% of adults who underwent minor surgical procedures and 6.5% of adults who underwent major surgical procedures, compared with 0.4% in a nonoperative control cohort. Clarke et al[17] reported persistent use in 3.1% of opioid-naive elderly patients undergoing major elective surgery but did not include a control group for comparison. Sun et al[23] described a small but significant increase in the risk of chronic use, defined as more than 10 prescriptions, following surgery. In a recent investigation using claims data involving adolescents and young adults, 4.8% of 13- to 21-year-old patients filled opioid prescriptions from 90 to 180 days after a surgical procedure compared with 0.1% of nonsurgical controls.[18] Finally, a recent investigation using a dental claims database showed that 1.3% of patients who filled an opioid prescription after a third molar extraction had new persistent opioid prescription use at 90 days compared with 0.5% of patients who underwent third molar extraction but did not fill an opioid prescription.[24] However, unlike our study results, patients with any subsequent surgery or anesthesia were excluded from that analysis and persistent use was defined as filling a second opioid prescription at 4 to 90 days and a third opioid prescription at 90 to 365 days.

Although we were unable to discern whether repeated opioid prescriptions were provided for new, painful medical conditions, there is no reason why the probability of these indications would vary by index opiate prescription. In addition, the higher probability of abuse diagnoses in the exposed cohort suggests that many of the repeated opioid prescriptions in this cohort were related to substance abuse.

Similar to the results of our study, several other investigations have identified female sex as a risk factor for opioid exposure or persistent use.[18,24-26] In our study, the aOR for subsequent abuse among women was 11.5 (95% CI, 9.4-14.8). That this aOR was higher than that for persistent use (aOR, 1.2;

Table 3. Multivariable Model for Opioid Use at 90 to 365 Days and Diagnosis of Opioid Abuse in the Opioid-Exposed Cohort

Variable	Opioid Use at 90 to 365 d			Diagnosis of Opioid Abuse Within 365 d		
	No. (%)	aOR (95% CI)	LRT *P* Value	No. (%)	aOR (95% CI)	LRT *P* Value
Age, y						
16-18 (n = 1814)	171 (9.4)	1 [Reference]	<.001	115 (6.3)	1 [Reference]	<.001
19-21 (n = 3969)	300 (7.6)	0.8 (0.6-1.0)		291 (7.3)	1.1 (0.9-1.4)	
22-25 (n = 9105)	550 (6.0)	0.7 (0.6-0.9)		460 (5.1)	0.8 (0.7-1.0)	
Sex						
Male (n = 7006)	440 (6.3)	1 [Reference]	.01	69 (1.0)	1 [Reference]	<.001
Female (n = 7882)	581 (7.4)	1.2 (1.0-1.4)		797 (10.1)	11.5 (9.4-14.8)	
Race/ethnicity						
White (n = 11 273)	768 (6.8)	1 [Reference]	.01	680 (6.0)	1 [Reference]	<.001
Asian (n = 593)	23 (3.9)	0.6 (0.4-0.9)		11 (1.9)	0.3 (0.2-0.6)	
Black (n = 939)	78 (8.3)	1.2 (0.9-1.5)		62 (6.6)	1.0 (0.7-1.3)	
Hispanic (n = 1376)	101 (7.3)	1.1 (0.9-1.3)		70 (5.1)	0.9 (0.7-1.1)	
Unknown (n = 707)	51 (7.2)	1.1 (0.8-1.5)		43 (6.1)	1.0 (0.8-1.5)	
US Region[a]						
South (n = 6002)	432 (7.2)	NA[b]	.28	334 (5.6)	1 [Reference]	.006
Northeast (n = 1401)	83 (5.9)	NA[b]		88 (6.3)	1.1 (0.9-1.4)	
North Central (n = 4139)	298 (7.2)	NA[b]		277 (6.7)	1.2 (1.0-1.4)	
Mountains (n = 1635)	94 (5.7)	NA[b]		66 (4.0)	0.8 (0.6-1.0)	
Pacific (n = 1660)	114 (6.9)	NA[b]		101 (6.1)	1.2 (0.9-1.5)	
Unknown (n = 51)	3 (5.9)	NA[b]		0	NA[c]	
Previous nonopioid substance abuse						
Yes (n = 473)	100 (21.1)	3.7 (2.9-4.7)	<.001	87 (18.4)	4.5 (3.4-5.9)	<.001
No (n = 14 415)	921 (6.4)	1 [Reference]		779 (5.4)	1 [Reference]	

Abbreviations: aOR, adjusted odds ratio; LRT, likelihood ratio test; NA, not applicable.

[a] Middle Atlantic and New England regions were collapsed into Northeast; East North Central and West North Central regions were collapsed into North Central; and East South Central, West South Central, and South Atlantic were collapsed into South.

[b] Not included in final regression model given LRT *P* > .05.

[c] CIs not calculated because of group size and zero numerator.

95% CI, 1.0-1.4) may in part be explained by the time windows for exposure being different for these 2 outcomes. In addition, this discrepancy suggests that perhaps women were using opiates obtained from nonprescription sources. One investigation suggested that women are more likely than men to misuse opioids for nonanalgesic purposes (ie, anxiety or tension).[26] It is possible that increased subsequent use of opioids and diagnoses of substance abuse among women is partly explained by increased overall utilization of health care services by women compared with men.

Our investigation adds several new dimensions to the existing literature. Because dental procedures are largely not covered by medical insurance, most previous studies using claims databases have been unable to quantify persistent opioid use when the index prescription follows a dental procedure. By linking the prescriptions to clinician categories, we were able to gain insight into the contribution of dental care to overall and persistent opioid use. The proportion of patients (6.9%) with new persistent opioid use in our study was slightly higher than that reported in other studies,[16,17,23] which may reflect the vulnerable age range of patients that we analyzed and/or different time windows for evaluation. We showed that only 27% of the second opioid prescriptions came from dental clinicians, indicating that many subsequent opioid prescriptions were likely written for new, nondental issues rather than subsequent molar removals.

In addition, unlike previous studies, we identified diagnoses associated with opioid abuse and found that a concerning proportion of patients exposed to opioids had at least 1 subsequent diagnosis of opioid abuse. By limiting our cohort to patients with no filled opioid prescriptions and no diagnoses of abuse in the 12 months preceding the opioid prescription, we attempted to create an opioid-naive cohort. However, especially given the relatively high proportion of patients who were given an abuse diagnosis within 90 days of the index prescription, it is likely that some patients had preexisting opioid abuse not documented in the claims database during the study period.

Although the indication for these opioid prescriptions is not obtainable in the Optum database, given the available data on the frequency of third molar extractions[8,9,27] and subsequent opioid prescriptions,[6,7,24] it is likely that this procedure is responsible for most of these prescriptions. Because of the multiple additional potential risks beyond opioid exposure associated with this procedure,[28,29] anesthesia[30] (including sporadic deaths[31-34]), and prescribed prophylactic antibiotics,[35,36] updated population-level estimates for the frequency of this procedure and associated complications are needed.

One proposed solution to limit opioid exposure following dental procedures has been to use nonopioid alternatives such as nonsteroidal anti-inflammatory medications or long-acting local anesthesia.[37] Another solution is to limit the quantity of opioids dispensed. Some pills may be given to friends or family,[38] and many of these pills remain unused,[39] indicating that similar to other common surgical procedures, the quantity prescribed is excessive (the median number dispensed in our study was 20).[40] If third molar extractions are the primary source of exposure to opioids, given that the potential risks and complications of the procedure extend beyond the potential for opioid use and abuse and given the lack of evidence supporting removal of asymptomatic third molars,[11] there is also a need to focus on potentially unnecessary procedures. More studies are needed to understand when benefits are likely to exceed risks and costs.

Limitations

This investigation has several limitations. We relied on *ICD-9* and *ICD-10* diagnosis codes for the diagnosis of opioid abuse and used previous similar investigations[19-21] and a direct search of diagnosis codes to construct a comprehensive list. However, the full list of codes has not been validated with medical record review; thus, misclassification may have occurred. The database only includes privately insured patients. Although the demographics (Table 1) of our sample reasonably reflect the US population in terms of geographic and racial/ethnic diversity, our findings may not be generalizable to other privately insured or publicly insured patients. At least 1 publication has reported higher use of opioids among Medicaid-enrolled women compared with privately-insured women.[41]

Last, because of our attempt to analyze patients with continued insurance coverage, there was fallout of patients from the original sample, which is likely explained by frequent shifts in insurance coverage in this age range. Although fallout poses a potential threat to generalizability of the findings, these concerns are partially mitigated by the fact that the mean opioid prescription fill count in person-years was similar between patients included and excluded from the study.

Conclusions

Many adolescents and young adults are exposed to opioids from prescriptions given by dental clinicians. The findings of our study suggest that opioid-naive patients who receive an opioid prescription from a dental clinician may be at risk for persistent opioid use and abuse. Given the potential contribution of third molar extractions to the opioid epidemic, heightened scrutiny regarding this procedure and opioid prescriptions associated with postoperative care is warranted.

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REFERENCES

1. Manchikanti L, Helm S II, Fellows B, et al. Opioid epidemic in the United States. *Pain Physician*. 2012;15(3)(suppl):ES9-ES38.

2. O'Donnell JK, Gladden RM, Seth P. Trends in deaths involving heroin and synthetic opioids excluding methadone, and law enforcement drug product reports, by census region - United States, 2006-2015. *MMWR Morb Mortal Wkly Rep*. 2017;66(34):897-903. doi:10.15585/mmwr.mm6634a2

3. Volkow ND, McLellan TA, Cotto JH, Karithanom M, Weiss SR. Characteristics of opioid prescriptions in 2009. *JAMA*. 2011;305(13):1299-1301. doi:10.1001/jama.2011.401

4. Gupta N, Vujicic M, Blatz A. Opioid prescribing practices from 2010 through 2015 among dentists in the United States: What do claims data tell us? *J Am Dent Assoc*. 2018;149(4):237-245.e6. doi:10.1016/j.adaj.2018.01.005

5. Gupta N, Vujicic M, Blatz A. Multiple opioid prescriptions among privately insured dental patients in the United States: evidence from claims data. *J Am Dent Assoc*. 2018;149(7):619-627 e1. Medline: 29656805 doi:10.1016/j.adaj.2018.02.025

6. Moore PA, Nahouraii HS, Zovko JG, Wisniewski SR. Dental therapeutic practice patterns in the US II. analgesics, corticosteroids, and antibiotics. *Gen Dent*. 2006;54(3):201-207; quiz 208, 221-222. Medline:16776415

7. Weiland BM, Wach AG, Kanar BP, et al Use of opioid pain relievers following extraction of third molars. *Compend Contin Educ Dent*. 2015;36(2):107-111; quiz 112, 114. Medline:25822637

8. American Dental Association. 1999 survey of dental services rendered [unpublished report]. In: SDSR-1999. 1999.

9. Friedman JW. The prophylactic extraction of third molars: a public health hazard. *Am J Public Health*. 2007;97(9):1554-1559. doi:10.2105/AJPH.2006.100271

10. Boughner JC. Maintaining perspective on third molar extraction. *J Can Dent Assoc*. 2013;79:d106.

11. Ghaeminia H, Perry J, Nienhuijs ME, et al. Surgical removal versus retention for the management of asymptomatic disease-free impacted wisdom teeth. *Cochrane Database Syst Rev*. 2016;(8):CD003879.

12. Eklund SA, Pittman JL. Third-molar removal patterns in an insured population. *J Am Dent Assoc*. 2001;132(4):469-475. doi:10.14219/jada.archive.2001.0209

13. Hulley SB, Cummings SR, Browner WS, Grady DG, Newman TB. *Designing Clinical Research*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013.

14. Feudtner C, Feinstein JA, Zhong W, Hall M, Dai D. Pediatric complex chronic conditions classification system version 2: updated for *ICD-10* and complex medical technology dependence and transplantation. *BMC Pediatr*. 2014;14:199. doi:10.1186/1471-2431-14-199

15. Feudtner C, Hays RM, Haynes G, Geyer JR, Neff JM, Koepsell TD. Deaths attributed to pediatric complex chronic conditions: national trends and implications for supportive care services. *Pediatrics*. 2001;107(6):E99. doi:10.1542/peds.107.6.e99

16. Brummett CM, Waljee JF, Goesling J, et al. New persistent opioid use after minor and major surgical procedures in US adults. *JAMA Surg*. 2017;152(6):e170504. doi:10.1001/jamasurg.2017.0504

17. Clarke H, Soneji N, Ko DT, Yun L, Wijeysundera DN. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. *BMJ*. 2014;348:g1251. doi:10.1136/bmj.g1251

18. Harbaugh CM, Lee JS, Hu HM, et al. Persistent opioid use among pediatric patients after surgery. *Pediatrics*. 2018;141(1):e20172439. doi:10.1542/peds.2017-2439

19. Kane JM, Colvin JD, Bartlett AH, Hall M. Opioid-related critical care resource use in US children's hospitals. *Pediatrics*. 2018;141(4):e20173335. doi:10.1542/peds.2017-3335

20. Stevens JP, Wall MJ, Novack L, Marshall J, Hsu DJ, Howell MD. The critical care crisis of opioid overdoses in the United States. *Ann Am Thorac Soc*. 2017;14(12):1803-1809. doi:10.1513/AnnalsATS.201701-022OC

21. Unick GJ, Rosenblum D, Mars S, Ciccarone D. Intertwined epidemics: national demographic trends in hospitalizations for heroin- and opioid-related overdoses, 1993-2009. *PLoS One*. 2013;8(2):e54496. doi:10.1371/journal.pone.0054496

22. World Health Organization. http://www.who.int/classifications/icd/en/. Accessed November 15, 2017.

23. Sun EC, Darnall BD, Baker LC, Mackey S. Incidence of and risk factors for chronic opioid use among opioid-naive patients in the postoperative period. *JAMA Intern Med*. 2016;176(9):1286-1293. doi:10.1001/jamainternmed.2016.3298

24. Harbaugh CM, Nalliah RP, Hu HM, Englesbe MJ, Waljee JF, Brummett CM. Persistent opioid use after wisdom tooth extraction. *JAMA*. 2018;320(5):504-506. doi:10.1001/jama.2018.9023

25. Janakiram C, Chalmers NI, Fontelo P, et al. Sex and race or ethnicity disparities in opioid prescriptions for dental diagnoses among patients receiving Medicaid. *J Am Dent Assoc*. 2018;149(4):246-255. doi:10.1016/j.adaj.2018.02.010

26. McHugh RK, Devito EE, Dodd D, et al. Gender differences in a clinical trial for prescription opioid dependence. *J Subst Abuse Treat*. 2013;45(1):38-43. doi:10.1016/j.jsat.2012.12.007

27. Cunha-Cruz J, Rothen M, Spiekerman C, Drangsholt M, McClellan L, Huang GJ; Northwest Practice-Based Research Collaborative in Evidence-Based Dentistry. Recommendations for third molar removal: a practice-based cohort study. *Am J Public Health*. 2014;104(4):735-743. doi:10.2105/AJPH.2013.301652

28. Kunkel M, Kleis W, Morbach T, Wagner W. Severe third molar complications including death-lessons from 100 cases requiring hospitalization. *J Oral Maxillofac Surg*. 2007;65(9):1700-1706. doi:10.1016/j.joms.2007.04.014

29. Bouloux GF, Steed MB, Perciaccante VJ. Complications of third molar surgery. *Oral Maxillofac Surg Clin North Am*. 2007;19(1):117-128, vii. doi:10.1016/j.coms.2006.11.013

30. Mehrabi M, Allen JM, Roser SM. Therapeutic agents in perioperative third molar surgical procedures. *Oral Maxillofac Surg Clin North Am*. 2007;19(1):69-84, vi. doi:10.1016/j.coms.2006.11.010

31. Byrne M. Love, sorrow, questions after Cheverus student's death. 2014; https://www.pressherald.com/2014/02/25/cheverus_senior_budding_musician_dies_after_routine_oral_surgery_/. Accessed March 6, 2018.

32. Cobler N. Hours before dental surgery, Dallas teen who died wrote: 'The Lord will take care of me'. 2017; https://www.dallasnews.com/news/lake-highlands/2017/06/20/hours-dental-surgerydallas-teen-died-wrotethe-lord-will-take-care. Accessed March 6, 2018.

33. D'eramo EM, Bookless SJ, Howard JB. Adverse events with outpatient anesthesia in Massachusetts. *J Oral Maxillofac Surg*. 2003;61(7):793-800. doi:10.1016/S0278-2391(03)00238-6

34. Narins E. 17-Year-Old Girl Dies After Getting Her Wisdom Teeth Removed. 2015; https://www.cosmopolitan.com/health-fitness/news/a41983/17-year-old-girl-dies-after-getting-her-wisdom-teeth-removed/. Accessed March 6, 2018.

35. Lodi G, Figini L, Sardella A, Carrassi A, Del Fabbro M, Furness S. Antibiotics to prevent complications following tooth extractions. *Cochrane Database Syst Rev*. 2012;11:CD003811.

36. Lang MS, Gonzalez ML, Dodson TB. Do antibiotics decrease the risk of inflammatory complications after third molar removal in community practices? *J Oral Maxillofac Surg*. 2017;75(2):249-255. doi:10.1016/j.joms.2016.09.044

37. Lieblich SE, Danesi H. Liposomal bupivacaine use in third molar impaction surgery: INNOVATE study. *Anesth Prog*. 2017;64(3):127-135. doi:10.2344/anpr-64-02-03

38. Ashrafioun L, Edwards PC, Bohnert AS, Ilgen MA. Nonmedical use of pain medications in dental patients. *Am J Drug Alcohol Abuse*. 2014;40(4):312-316. doi:10.3109/00952990.2014.930152

39. Maughan BC, Hersh EV, Shofer FS, et al. Unused opioid analgesics and drug disposal following outpatient dental surgery: a randomized controlled trial. *Drug Alcohol Depend*. 2016;168:328-334. doi:10.1016/j.drugalcdep.2016.08.016

40. Hill MV, McMahon ML, Stucke RS, Barth RJ Jr. Wide variation and excessive dosage of opioid prescriptions for common general surgical procedures. *Ann Surg*. 2017;265(4):709-714. doi:10.1097/SLA.0000000000001993

41. Ailes EC, Dawson AL, Lind JN, et al; Centers for Disease Control and Prevention (CDC). Opioid prescription claims among women of reproductive age–United States, 2008-2012. *MMWR Morb Mortal Wkly Rep*. 2015;64(2):37-41.