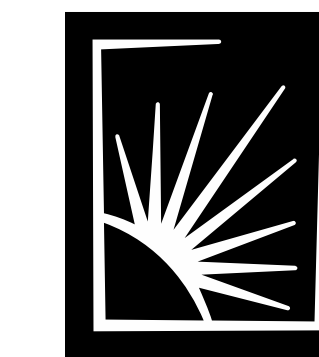




24th Annual
Pain Medicine Meeting
November 13-15, 2025 | Austin, TX



Perioperative Opioid Exposure in Adolescents and Long-Term Psychiatric/Utilization Outcomes: A Real World Cohort Study



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Background

The use of opioids perioperatively, for both analgesia and anesthesia, is being highlighted negatively in the wake of the opioid crisis in the United States. There is evidence that perioperative opioid exposure disrupts the dopamine and serotonin pathways through its effect on the hypothalamic-pituitary-adrenal axis, especially in the pliable adolescent brain. This may lead to the development of long-term psychiatric comorbidity, opioid use disorder, and consequent increased emergency healthcare visits.

Materials and Methods

-- A retrospective cohort study utilizing the TriNetX US Collaborative Network (71 health systems). Adolescents aged 12–19 undergoing common procedures (appendectomy, tonsil/adenoid removal, select orthopedic and dental procedures) were identified..
-The opioid cohort had a perioperative opioid exposure (–3 to +7 days around surgery); the comparison cohort had no perioperative opioid use. Key exclusions at baseline: prior opioid-related disorders (F11), any substance-use disorders (F10–F19), and chronic pain (G89.2). Outcomes (depression, anxiety, PTSD, sleep disorders, suicidal ideation/attempt, ED utilization, opioid poisoning/overdose, long-term opioid therapy [Z79.891], and MOUD/overdose-related medications [buprenorphine, methadone, naltrexone, naloxone]) were assessed from day 1 to 3,650 (~10 years) post-index event.

Table 2. Outcomes (matched cohorts; risk analysis window = day 1 to 10 years)

Outcome	Risk % (opioid)	Risk % (non-opioid)	RR (95% CI)	p
Depression	3.0 (2,328/77,118)	2.5 (1,953/77,330)	1.195 (1.126–1.268)	<0.001
Anxiety	6.8 (5,075/74,234)	5.6 (4,226/75,128)	1.215 (1.168–1.264)	<0.001
PTSD	3.6 (2,703/75,601)	6.2 (4,689/76,151)	0.581 (0.554–0.608)	<0.001
Sleep disorders	7.6 (3,818/49,976)	5.9 (3,166/53,710)	1.296 (1.238–1.356)	<0.001
Suicidal ideation/attempt	1.4 (1,060/77,585)	1.2 (946/77,595)	1.121 (1.027–1.223)	0.010
ED utilization	24.9 (10,471/41,987)	21.0 (10,199/48,525)	1.187 (1.158–1.215)	<0.001
Opioid poisoning/overdose (T40.x)	0.09 (70/77,745)	0.06 (46/77,759)	1.522 (1.049–2.208)	0.026
Long-term opioid therapy (Z79.891)	0.4 (337/77,290)	0.5 (355/77,487)	0.952 (0.820–1.104)	0.514
MOUD/overdose-related meds†	1.3 (914/71,872)	0.4 (338/77,406)	2.912 (2.572–3.298)	<0.001

Discussion:

- In adolescents undergoing common surgical procedures, perioperative opioid exposure was associated with small-to-moderate increases in long-term depression, anxiety, sleep disorders, suicidal ideation/attempt, ED utilization, and opioid overdose, and a large increase in MOUD/overdose-related medication exposure. The null finding for long-term opioid therapy and the inverse association for PTSD warrant cautious interpretation due to possible unmeasured confounding and coding effects. Findings support minimizing perioperative opioid exposure and proactive mental-health surveillance after surgery.

Results

After matching (n=**77,810** per cohort), perioperative opioid exposure was associated with higher risk of depression (RR 1.195, 95%CI 1.126–1.268), anxiety (RR 1.215, 1.168–1.264), sleep disorders (RR 1.296, 1.238–1.356), suicidal ideation/attempt (RR 1.121, 1.027–1.223), ED utilization (RR 1.187, 1.158–1.215), and opioid poisoning/overdose (RR 1.522, 1.049–2.208). Long-term opioid therapy (Z79.891) risk did not increase (RR 0.952, 0.820–1.104). Initiation of MOUD/overdose-related medications was markedly higher (RR 2.912, 2.572–3.298) in the opioid cohort. Notably, PTSD was lower in the opioid group (RR 0.581, 0.554–0.608). Kaplan–Meier results were directionally consistent for most outcomes.

Table 1. Cohorts and matching

Item	Opioid cohort	Non-opioid cohort
N before matching	259,147	78,015
N after matching	77,810	77,810
Age at index (mean ± SD)	6.7 ± 4.1	6.7 ± 4.1
Female (%)	43.7	43.7
Not Hispanic/Latino (%)	56.0	56.0
Propensity score matching on age, sex, ethnicity.		

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