Hidden Risk: Antidepressant Users Face 5-Fold Higher Opioid Abuse After THA Despite Almost Similar Opioid Prescribing

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INTRODUCTION: Antidepressants, including SSRIs, tricyclics, MAO inhibitors, and related agents, are commonly prescribed in patients undergoing total hip arthroplasty (THA). These medications may alter platelet function, immune responses, and pain perception—factors potentially influencing perioperative outcomes. Moreover, there is growing concern that patients on chronic antidepressants may require prolonged pain control, increasing the risk of opioid overprescription and dependence postoperatively. While antidepressant use has been widely studied in other surgical fields, its impact on THA outcomes remains underexplored. This study aimed to evaluate short- and long-term surgical and systemic complications—including opioid-related outcomes—among THA patients with versus without perioperative antidepressant use.

METHODS:

We conducted a retrospective cohort study using the TriNetX Research Network (2005–2025). Adult patients undergoing elective, non-traumatic primary THA were identified via ICD-10 and CPT codes. Patients were stratified based on perioperative exposure (within 3 months of surgery) to antidepressants under ATC code N06AA, including SSRIs and related agents.

Cohorts were matched 1:1 using propensity scores based on demographics, comorbidities, BMI, and medication use. Outcomes were assessed at 90 days and 5 years postoperatively.

Short-term outcomes included opioid prescription and abuse, mortality (see table 1).

Long-term outcomes included revision THA, periprosthetic fracture, prosthetic joint infection, mechanical loosening, osteolysis, and mortality. Statistical tests included chi-square and t-tests, with odds ratios (OR) and 95% confidence intervals (CI); significance threshold was $P < 0.01$.

RESULTS:

After matching, 46,227 patients were included in each cohort for the 90-day analysis and 16,019 for the 5-year analysis. Baseline demographics were balanced between groups (mean age 63.9–66.4 years, 63% female, BMI ~30.6; $P > 0.05$).

At 90 days, patients on antidepressants were significantly more likely to receive opioid prescriptions (25% vs. 14.8%; OR 1.7; $P < 0.001$) and be diagnosed with opioid abuse (0.12% vs. 0.02%; OR 5.7; $P < 0.001$). Mortality was also higher in the antidepressant group (0.25% vs. 0.15%; OR 1.6; $P = 0.001$). Additionally, elevated rates of complications were observed—including pulmonary embolism, infection, transfusion, and myocardial infarction (see Table 1).

At 5 years, antidepressant users demonstrated increased risk of prosthetic joint infection (0.75% vs. 0.52%; OR 1.4; $P = 0.01$), THA dislocation/instability (0.80% vs. 0.43%; OR 1.8; $P < 0.001$), and periprosthetic fracture (0.31% vs. 0.17%; OR 1.8; $P = 0.01$). No significant differences were found in revision THA, THA osteolysis, mechanical loosening, or long-term mortality ($P > 0.05$).

Long-term opioid abuse remained significantly higher in antidepressant users (0.42% vs. 0.09%; OR 4.5; $P < 0.001$), despite only modestly increased rates of opioid prescription (50% vs. 43.2%; OR 1.14; $P < 0.001$).

Notably, although the increase in opioid prescription rates among antidepressant users was relatively modest—approximately 10% higher than controls at both time points—the rate of documented opioid abuse was disproportionately elevated, with odds ratios ranging from 4.5 to 5.7. This discrepancy suggests a heightened vulnerability to opioid misuse in this population that is not explained by prescription volume alone, indicating potential neuropsychological or pharmacologic susceptibility.

DISCUSSION AND CONCLUSION:

Antidepressant use in patients undergoing total hip arthroplasty is associated with a striking increase in the risk of postoperative opioid abuse—despite only slightly higher rates of opioid prescribing. This mismatch underscores the need for more nuanced pain management protocols and closer postoperative monitoring in this vulnerable population. Additionally, antidepressant users experienced higher complication rates in both the short- and long-term, including thromboembolic events, prosthetic joint infections, and dislocations. These findings call for interdisciplinary approaches integrating orthopedic, psychiatric, and pain management teams to reduce postoperative morbidity and mitigate the risk of opioid misuse. Future research should explore biologic and behavioral mechanisms underlying this susceptibility and evaluate targeted interventions to support safer recovery in this high-risk group.

Table 1. 90 days outcomes

OUTCOME	ANTIDEPRESSANT GROUP (%)	CONTROL GROUP (%)	ODDS RATIO (95% CI)
DVT	0.56	0.45	1.2 (P value = 0.02)
PE	0.68	0.51	1.3 (P value < 0.001)
IFP +	0.48	0.20	2.4 (P value < 0.001)
TRANSFUSION	0.37	0.20	1.8 (P value < 0.001)
SEPSIS	0.47	0.23	2.0 (P value < 0.001)
MI	0.53	0.36	1.4 (P value < 0.001)
STROKE	0.73	0.42	1.7 (P value < 0.001)
ANEMIA	6.1	4.1	1.5 (P value < 0.001)

+ IFP; Infection Following Procedure