Submission Id: 5300

Title

Mortality risk associated with dose tapering among patients prescribed long-term opioid therapy

Priority 1 (Research Category)

Prescribing and pharmacotherapeutics

Presenters

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Abstract

Context: Studies have shown risks associated with dose tapering and discontinuation among patients prescribed long-term, high-dose opioid therapy, including non-fatal overdose and mental health crisis. It is uncertain if tapering in this population is also associated with fatal events. Objective: To determine the mortality risk associated with opioid dose tapering and tapering rapidity among patients prescribed long-term opioid therapy. Study Design: Retrospective cohort study. Setting: Data from the OptumLabs Data Warehouse,® years 2017-2019, which contains de-identified retrospective administrative data including medical and pharmacy claims and eligibility information as well as electronic health data for commercial and Medicare Advantage enrollees. The database contains longitudinal health information on patients representing a large and diverse sample from across the United States. Population: Adults prescribed stable high-dose opioids (average ≥50 morphine milligram equivalents/day) for 6-month baseline period with ≥2 months follow-up. Exposure: Opioid dose tapering, defined as ≥15% relative reduction in average daily dose during any one of six overlapping 60-day windows within 7 mos of follow-up. Maximum monthly rate of dose reduction was also calculated (Vmax). Outcome: Death during 12-mo follow-up. Negative binomial regression estimated adjusted incidence rate ratios (aIRRs) of death as a function of tapering and maximum rate of dose reduction. Results: We assessed outcomes among 107,931 patients after periods of stable opioid dosing (mean follow-up = 9.11 months). 1,078 deaths occurred across 755,733 person-months of follow-up among non-tapered patients (1.70 deaths/100 person-years). 509 deaths occurred across 250,114 person-months of follow-up after tapering (2.41 deaths/100 person-years). In adjusted models, tapering (as compared to unchanged dose) had aIRR of 1.45 (95% CI: 1.30-1.62) for death. Higher maximum rate of dose reduction was associated with greater mortality risk: Vmax 10-19% aIRR 1.22 (95%CI: 1.05-1.42), Vmax 20-49% aIRR 1.58 (95%CI: 1.37-1.82), Vmax ≥50% aIRR 1.64 (95%CI 1.38-2.02). Conclusions: Among patients prescribed stable, long-term, high-dose opioid therapy, tapering events were significantly associated with increased risk of death. More rapid dose reduction correlated with greater mortality risk. This raises additional concern for potential unintended harms associated with tapering previously stable opioid therapy.