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Reference Article: Sun, EC, et al. "Association between concurrent use of prescription opioids and benzodiazepines and overdose: retrospective analysis." *BMJ* 2017;356:j760.
[Http://dx.doi.org/10.1136/bmj.j760](http://dx.doi.org/10.1136/bmj.j760).

Clinical Question: Is there a relationship between the use of opioids and benzodiazepines and do these relationships have an impact on emergency room visits for opioid overdose and hospital admissions?

Introduction: In the US, opioid prescriptions have had a nearly threefold increase over the past 15 years as well as a dramatic increase in opioid related overdoses and deaths. Some international and US Veterans Health Administration studies report that approximately 30% of fatal opioid overdoses involve concurrent use of benzodiazepines. Unfortunately, less attention has been given to benzodiazepines despite their ability to potentiate respiratory depression with concurrent opioid usage.

Methods: Retrospective analysis utilizing a multivariate logistic regression of a US administrative health claims data base from 2001-2013. Overall, 315,428 privately insured people were enrolled ranging in ages of 18 to 64. Participants had to be continuously enrolled in a health plan with medical and pharmacy benefits during the study period and had also filled at least one prescription for an opioid. Concurrent benzodiazepines/opioid use was defined as an overlap of at least one day in the time periods covered by prescriptions for each drug. Participants were stratified into intermittent and chronic opioid users. The main outcomes measured were the annual percentage of opioid users with concurrent benzodiazepine use as well as visits to the ED and inpatient admissions for opioid overdose. Opioid overdose was defined by utilizing ICD-9 codes present on admission or during a visit. Visits were only counted if they fell between the time interval of the day when the prescription was filled and the number of days supplied by the prescription plus 1 week.

Results: Initially, a sample of 595,410 patients were enrolled, however, the analysis was restricted to people that were continuously enrolled from January 2001 to December 2013. Participants were excluded if they died, were unenrolled or had a history of cancer or diagnosis of cancer during the study period. 9% of opioid users also were prescribed benzodiazepines in 2001, increasing to 17% in 2013. Among all opioid users, the annual adjusted incidence of ED visits or inpatient admissions for opioid overdose was 1.16% (95%CI 1.13% to 1.18%) for those not taking concurrent benzodiazepines compared to 2.42% (2.32% to 2.51%) among concurrent users, a significant difference (OR 2.14, 95%CI 2.05 to 2.24; P<0.001).

Discussion: Based on this data, the authors suggest that in a sample of privately insured patients, the incidence of concurrent benzodiazepines/opioid use increased by approximately 80% from 2001 to 2013. In addition, they suggest that opioid users who concurrently use benzodiazepines were at an increased risk of overdose. The authors estimate that eliminating concurrent benzodiazepines/opioid use could decrease the risk of overdose by 15%.

Limitations: Several limitations to the study include: the analysis included participants treated in an ED or hospital that ultimately survived, which may result in underestimating the true risk of overdose. Also

the study did not take into consideration any changes in dosages over time nor did they address illegally acquired drugs.
