

This Common Combo Raises the Risk of Lethal Overdose 5-Fold

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✓ Fact Checked

May 01, 2023

STORY AT-A-GLANCE

- › Drug overdoses are the leading cause of death among Americans. Opioids are responsible for nearly two-thirds of these deaths, but benzodiazepine (“benzos”) overdoses are also on the rise
- › Benzo prescriptions tripled from 1996 to 2013, but this doesn't fully account for the uptick in overdoses, which quadrupled during that time
- › A number of studies have highlighted the deadly risks you take when combining opioids with benzos. During the first 90 days of concurrent use, your risk of a deadly overdose rises fivefold, compared to taking an opioid alone
- › The combination of opioids and benzos is the most common drug combination in cases where an overdose death involved two or more drugs; more than 30% of opioid overdoses also involve benzos
- › The ratio of patients using opioids and benzos concurrently rose from 9% in 2001 to 17% in 2013; concurrent use for at least one day doubled the odds of an opioid overdose compared to taking opioids alone

Editor's Note: This article is a reprint. It was originally published July 19, 2018.

Drug overdoses are now the leading cause of death among Americans.¹ Preliminary data for 2016 reveals the death toll may be as high as 65,000² — a 19% increase in a single year. Opioids, narcotic pain killers, are responsible for nearly two-thirds, about 42,000, of

these deaths.³ Between 2002 and 2015, more than 202,600 Americans died from opioid overdoses.⁴

While such statistics are sobering enough, recent research⁵ suggests the death toll may still be underestimated due to incomplete drug reporting of overdose deaths.

The researchers believe upward of 70,000 opioid overdose deaths were excluded from national estimates between 1999 and 2015, for the simple reasons that coroners routinely fail to specify opioid use as a contributing cause of death. According to lead author Jeanine Buchanich, research associate professor at University of Pittsburgh School of Public Health:⁶

"Proper allocation of resources for the opioid epidemic depends on understanding the magnitude of the problem. Incomplete death certificate reporting hampers the efforts of lawmakers, treatment specialists and public health officials. And the large differences we found between states in the completeness of opioid-related overdose mortality reporting makes it more difficult to identify geographic regions most at risk."

The most common drugs involved in prescription opioid overdose deaths include⁷ methadone, oxycodone (such as OxyContin®) and hydrocodone (such as Vicodin®). Extremely potent synthetic opioids like fentanyl are also being abused by a rising number of people. Now, researchers warn a particularly powerful combination of commonly prescribed drugs significantly raises your risk of death.

Benzodiazepine Overdoses Are Also Rising

While opioids make the most frequent headlines, another class of drugs — benzodiazepines⁸ or "benzos," widely prescribed for anxiety and insomnia — also claims its share of lives. Prescriptions for these drugs, which include Valium, Ativan, Klonopin and Xanax, tripled from 1996 to 2013, but this doesn't fully account for the uptick in overdoses, which quadrupled during that time.⁹

As for why the rate of overdose deaths rose faster than the rate of prescriptions, Dr. Chinazo Cunningham, one of the study's authors, told STAT News,¹⁰ "Our guess is that people are using these prescriptions in a riskier way." The number of pills prescribed to each adult increased over the study period, for instance, which suggests Americans may be taking higher doses or taking the drugs for longer periods, both of which increase the risk of overdose.

Combining the drugs – which act as sedatives – with alcohol is also risky, as is using the drugs along with opioids. Prescription records also show the use of benzos has risen alongside the use of opioids, and that the sedatives are often used alongside the painkillers to enhance the high.¹¹

According to Dr. David Juurlink, head of clinical pharmacology and toxicology at Sunnybrook Health Sciences Center in Toronto,¹² "Prescribing opioids and benzodiazepines together is like putting gasoline on a fire," adding that "Benzodiazepines are grossly overprescribed ... and many people don't necessarily benefit from them."

Estimates suggest more than 4 in 10 seniors use benzos for anxiety or insomnia, even though their long-term effectiveness and safety remain unproven, and their use has been linked to a higher risk of Alzheimer's disease.¹³

Older adults who used benzodiazepines for three months or more had a 51% greater risk of Alzheimer's disease than those who did not, and the risk increased the longer the drugs were used. According to the authors, "The stronger association observed for long term exposures reinforces the suspicion of a possible direct association ..."

Opioid-Benzodiazepine Combination Raises Risk of Death 5-Fold

A number of studies have already highlighted the deadly risk you take when combining opioids with benzos. Most recently, research^{14,15} published in JAMA looked at how the risk of overdose changes when you combine the two drugs for a number of days in a row.

As it turns out, during the first 90 days of concurrent use, your risk of a deadly overdose rises fivefold, compared to taking an opioid alone. Between days 91 and 180, the risk remains nearly doubled, after which the risk tapers off, becoming roughly equal to taking an opioid alone. According to the authors:

"Policy interventions should focus on preventing concurrent opioid and benzodiazepine use in the first place instead of reducing the length of concurrent use. Patients using both medications should be closely monitored, particularly during the first days of concurrent use."

The study also found that the greater number of clinicians were involved in a patient's care, the greater the risk of overdose — a finding that highlights the lack of communication between doctors prescribing medication to the same patient, and the clear danger thereof. As noted by senior study author Yuting Zhang, Ph.D., of the University of Pittsburgh Graduate School of Public Health, "These findings demonstrate that fragmented care plays a role in the inappropriate use of opioids."

Other Studies Confirm Extreme Risk of Opioid-Benzo Mix

Other studies have come to similar conclusions. A 2013 study found the combination of opioids and benzos was the most common drug combination in cases where an overdose death involved two or more drugs.¹⁶ According to the National Institute of Drug Abuse, more than 30% of opioid overdoses involve concurrent use of benzos.¹⁷

Remarkably, another 2013 study¹⁸ discovered "substantial co-use" of opioids and benzos among pregnant women that led to death, which is doubly tragic. As reported in a third study that year, which stressed the importance of urine drug testing whenever patients are prescribed an opioid, to ensure their safety:¹⁹

"[C]oadministration of [opioids and benzodiazepines] produces a defined increase in rates of adverse events, overdose and death, warranting close monitoring and consideration when treating patients with pain. To improve patient outcomes, ongoing screening for aberrant behavior, monitoring of

treatment compliance, documentation of medical necessity, and the adjustment of treatment to clinical changes are essential."

A study²⁰ published in 2017 found the ratio of patients, aged 18 to 64, who used opioids and benzos concurrently rose from 9% in 2001 to 17% in 2013, a relative increase of 80%. Not surprisingly, concurrent use of opioids and benzos for at least one day doubled the odds of an opioid overdose compared to taking just opioids.

Why Opioid-Benzo Combination Is so Deadly

In 2014, Ohio ended up using an opioid/benzo mix in a death row execution when the conventionally used drugs were unobtainable.²¹ That just goes to show this drug combination has an assured lethality at the "right" dosage. The reason these two drugs are so hazardous in combination is because both are potent central nervous system (CNS) depressants.

Your CNS, which includes your brain and spinal cord, coordinates and regulates the activity of automatic functions such as breathing. Respiratory depression, meaning slow and erratic breathing, can occur on both drugs, which leads to a buildup of carbon dioxide. In a sufficiently large dose, breathing can cease altogether, leading to death.

Like opioids, benzodiazepines are not intended for long-term use, yet many chronic pain patients end up staying on them for years, and may even take them with opioids for long periods of time. As noted by Dr. Len Paulozzi, medical epidemiologist at the Centers for Disease Control and Prevention, benzos "are prominent fellow travelers with opioids. The problem is, people get on them and they stay on them ..."

Opioids Account for Three-Quarters of Drug Deaths Worldwide

In related news, the 2018 World Drug Report²² reveals pharmaceutically produced opioids now account for more than three-quarters of all drug overdose deaths worldwide. Fentanyl abuse is rising in the U.S., while Africa and Asia are struggling with rising overdose deaths from Tramadol. While doctors are still a primary source of

opioids, illegal drug traffickers have started cashing in on the opioid abuse trend, manufacturing and selling them illegally.

According to Yury Fedotov, executive director of the United Nations Office on Drugs and Crime, "We are facing a potential supply-driven expansion of drug markets, with production of opium and manufacture of cocaine at the highest levels ever recorded." Between 2016 and 2017 alone, the global opium production rose by 65%.

In a June 26 address to observe International Day Against Drug Abuse and Illicit Trafficking, United Nations secretary-general António Guterres said,²³ "I urge countries to advance prevention, treatment, rehabilitation and reintegration services; ensure access to controlled medicines while preventing diversion and abuse; promote alternatives to illicit drug cultivation; and stop trafficking and organized crime."

Opioid Makers Shrink Payments to Doctors

One of the factors suspected of contributing to the burgeoning opioid epidemic is kickbacks to the doctors who prescribe them. According to a 2017 study,²⁴ more than 68,000 physicians received drug company payments totaling more than \$46 million between August 2013 and December 2015. This means 1 in 12 U.S. physicians collected kickbacks from drug companies producing prescription opioids.

The top 1% of physicians received nearly 83% of the payments, and fentanyl prescriptions was associated with the highest payments. Many of the states struggling with the highest rates of overdose deaths, such as Indiana, Ohio and New Jersey, were also those showing the most opioid-related payments to physicians, clearly demonstrating a direct link between doctors' kickbacks and patient addiction rates and deaths.

Increasing pressure on drug companies — in large part brought to bear by lawsuits over deceptive marketing and charges being filed against executives and sales reps for their role in manufacturing demand — now appears to be paying off. According to a recent

ProPublica analysis,²⁵ drug company payments to doctors related to opioids decreased 33% between 2015 and 2016, from \$23.7 million to \$15.8 million.

The most significant decrease was related to Subsys, a fentanyl spray made by Insys. The company's founder, John Kapoor, was arrested in October 2017, charged with bribing doctors to overprescribe the drug. Other Insys executives and sales reps were arrested on conspiracy and racketeering charges.²⁶ In 2015, the company doled out more than \$6 million in Subsys-related payments. In 2016, that amount shrunk to less than \$2.4 million.

Purdue Pharma, heavily criticized for its deceptive marketing of OxyContin, no longer pays doctors to speak about the drug, and laid off its last opioid sales reps in June 2018.²⁷

While the cutbacks in payments are a step in the right direction, research shows it doesn't take huge sums of money to influence a doctor's prescribing habits. A single free meal received in relation to marketing of an opioid has been shown to result in a greater number of prescriptions for the drug in the following year.^{28,29}

Addiction Is a Very Real Problem With Benzodiazepines

Getting back to the issue of benzodiazepines, it's important to realize these drugs are every bit as addictive and dangerous as opioids, and when taken together, the risk of death is magnified fivefold. Benzos exert a calming effect by boosting the action of the neurotransmitter gamma-aminobutyric acid (GABA), which in turn activates the gratification hormone, dopamine, in your brain.

Side effects include memory loss, hip fractures, impaired thinking and dizziness. Ironically, symptoms of withdrawal include extreme anxiety – in many cases worse than the original symptoms that justified the treatment in the first place. Other side effects of withdrawal include hallucinations, depersonalization and derealization, formication (skin crawling) and sensory hypersensitivity, perceptual distortions, convulsions, and psychosis.

There are far safer ways to address anxiety and insomnia, starting with exercise, optimizing your gut microbiome and omega-3 level. The Emotional Freedom Techniques (EFT) is another effective tool that can help reprogram your body's reactions to the unavoidable stressors of everyday life. This includes both real and imagined stressors, both of which can be significant sources of anxiety. It can also help reduce pain.

In the following video, EFT therapist Julie Schiffman discusses EFT for stress and anxiety relief. Please keep in mind that while anyone can learn to do EFT at home, for serious issues like persistent or severe anxiety you should consult with an EFT professional to get the relief you need. Pain can also be safely addressed without opioids.

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