

Spotlight on Health

Drug Combinations and Their Risks

Opioid medications provide powerful pain relief that benefits many patients, including those with acute and chronic pain. For many patients, such as those with chronic pain due to cancer and those receiving palliative care, opioids are important for improving quality of life. However, for most patients, the benefits of long-term opioid use for pain management are less clear.¹ In addition, overprescription of these drugs may have contributed to the current public health emergency.²

The pervasive use and abuse of opioids, also known as the opioid epidemic, is on the rise. In the United States, this epidemic led to over 33,000 deaths from opioid overdose in 2015, nearly 5,000 more than in 2014.³ This increase is consistent with a disturbing trend: opioid-related overdose deaths have nearly tripled since 1999.³ One factor contributing to opioid-related deaths is dangerous drug combinations, including prescription and illegal drugs. In this newsletter, we will describe evidence of widespread concurrent use and misuse of opioids with other drugs and discuss steps that can be taken that may help reduce the number of overdose deaths.

Dangerous Drug Combinations

When taken in combination with opioids, benzodiazepines have additive and synergistic effects that can depress respiration. A recent study showed that many deaths caused by prescription opioids involved concurrent use of benzodiazepines (**Table**).⁴ Overdose deaths caused by this combination increased 1.7-fold since 2002-2003. Combinations of prescription opioids with heroin and alcohol also markedly increased, whereas combinations with antidepressants and cocaine stayed about the same (**Table**).⁴

Table. Prescription Opioid Drug-related Deaths 2014-2015 (n=41,491)⁴

Death in Combination With:	% of Total	Fold-increase Relative to 2002-2003
Benzodiazepines	28	1.7
Heroin	15	3.3
Alcohol	14	1.6
Antidepressants	13	1.0
Cocaine	10	0.8

State prescription drug monitoring programs (PDMPs⁵) suggest a much lower level of concurrent use than found in death records. PDMPs are electronic databases of patient prescriptions. Based on prescribing data alone, about 10% of patients concurrently fill both opioid and benzodiazepine prescriptions.⁶ Urine drug testing helps explain the disparity between death records and prescribing data.



Fentanyl and Heroin: A Deadly Drug Combination

Deaths related to synthetic opioids, such as fentanyl, tramadol, propoxyphene, and meperidine (but not methadone) (SO-M), were recently studied as a smaller group of all prescription opioid-related deaths.⁴ In this group, from 2002-2003 to 2014-2015:

- Overdose-related deaths increased 5.6-fold.
- Total heroin-related deaths increased 21-fold (to 25% of SO-M deaths).
- The largest increases in deaths were among those 18 to 34 years of age, males, and African-Americans.

Fentanyl-mixed heroin⁸ likely contributed to most deaths. Fentanyl is 50 to 100 times stronger than morphine and is often added to heroin without the user's knowledge, leading to death by overdose. A Quest Diagnostics study found that 19% of urine specimens that tested positive for heroin also tested positive for fentanyl,⁹ which is comparable to the 25% of deaths involving heroin with SO-M.⁴

A recent study examined more than 230,000 urine specimens collected from more than 144,000 patients in 2015.⁷ About 11% of urine drug tests results were positive for prescribed opioids and prescribed benzodiazepines.⁷ However, about 60,000 specimens (26%) contained both opioids and benzodiazepines, and about two-thirds of these showed evidence of 1 or more *nonprescribed* benzodiazepine or opioid. Death records indicate a similar level (28%) of concurrent opioid-benzodiazepine use among those who died of an overdose (**Table**).⁴

These results suggest that urine drug testing provides a more complete picture of patient drug use compared to other measures that rely on databases of prescribed drugs alone. Consequently, CDC guidelines recommend using both approaches to improve patient safety.¹

Responsible Prescribing and Testing

CDC guidelines state that physicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible, although concurrent use of these drug types may be appropriate in some situations (eg, use of opioids to manage pain in patients taking long-term, stable, low-dose benzodiazepine medication).¹

CDC guidelines also state that physicians should use urine drug testing before starting opioid drug therapy; furthermore, they should consider annual follow-up testing for other prescribed and nonprescribed medications, as well as illicit drugs.¹ The urine test results support this recommendation. For the specimens that tested positive for prescribed opioids, 19% tested positive for a nonprescribed benzodiazepine.⁷ Although not currently mentioned in CDC guidelines, testing for opioids before starting benzodiazepines might be considered as well.⁷ Urine test results showed that 15% of specimens that tested positive for a prescribed benzodiazepine also tested positive for a nonprescribed opioid.

Once a baseline for drug use is established and treatment decisions are made, ongoing drug testing can help monitor a patient for adherence to the medication regimen. Patients may be taking nonprescribed drugs or not taking their medications at all.

How the Laboratory Can Help

Quest Diagnostics offers urine drug tests for prescription and illicit opioids and other drugs that can affect pain management strategies (see [Prescription Drug Monitoring: Available tests questdiagnostics.com/home/physicians/testing-services/by-test-name/prescription-drug-monitoring/available-tests.html](http://questdiagnostics.com/home/physicians/testing-services/by-test-name/prescription-drug-monitoring/available-tests.html)). These test options include presumptive immunoassay screens that can detect many drug classes but do not determine which drug the patient is taking. Therefore, Quest also offers definitive liquid chromatography-tandem mass spectrometry assays to confirm presumptive immunoassay results and identify specific drugs and their metabolites.

Quest Diagnostics' medMATCH® reports match assay results to prescription information and provide a patient-specific interpretation.

References

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