

Quest Diagnostics Health Trends[™] Prescription Drug Monitoring Report 2017

Prescription Drug Misuse in America

Diagnostic Insights into the Growing Drug Epidemic

"According to the Centers for Disease Control and Prevention (CDC), the most recent data estimates that 142 Americans die every day from a drug overdose."¹

Draft interim report of the White House Commission on Combating Drug Addiction and the Opioid Crisis

August 2017

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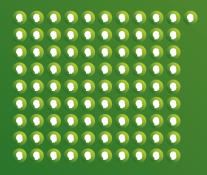
Executive Summary

The growth in opioid abuse has been called an epidemic, and for good reason: Between 2014 and 2015, overdose drug deaths in the United States increased by 11%, from 47,055 to 52,404, primarily driven by heroin and synthetic opioids other than methadone (such as fentanyl).² In the same period, overdose deaths from heroin rose 20%, from 10,574 to 12,989, and deaths from synthetic opioids other than methadone rose a staggering 72%, from 5,544 to 9,580.³

Yet, treatment of pain, especially chronic pain, is a major challenge for medical professionals, and opioids can provide significant relief for some patients. Moreover, opioids are not the only prescription drugs that may be misused. Ensuring proper use is also clinically challenging for anti-anxiety medications and drug treatments for attention deficit disorder. for instance.

A prescription drug monitoring program involving analysis of laboratory data can play a significant role in maximizing the benefit and minimizing the risk of harm to the patient and to the community. In the sixth edition of the Quest Diagnostics Health Trends[™] Prescription Drug Monitoring Report: Prescription Drug Misuse in America, we present an analysis of prescription drug use and misuse rates in the United States based on 3.4 million de-identified PDM test results performed between 2011 and 2016.

91 Americans die every day from an opioid overdose.⁴



Opioids (including prescription opioids and heroin) killed more than 33,000 people in 2015, more than any vear on record.

Nearly half of all opioid overdose deaths involve a prescription opioid.

20.5 million Americans (12 years and older) have a substance use disorder; 2 million involve prescription pain relievers and nearly 600,000 involve heroin (2015).⁵

Among the findings:

- · Most patient specimens tested showed signs of prescription drug misuse. The rate of inconsistency — a measure of inappropriate drug use that may indicate the patient is misusing one or more drugs — was 52% in 2016. While these findings compare favorably to our inaugural report of 2011, which found 63% of specimens tested were inconsistent, a majority of specimens tested show signs of potential drug misuse. The finding is a stark reminder that despite government and provider campaigns launched in recent years to educate the public about the perils of prescription drug abuse, inappropriate and potentially dangerous misuse of drugs is still prevalent.
- Drug misuse rates were high among most age groups, both genders, and a variety of types of health plans. Even women and men of childbearing age showed troubling patterns of prescription and illicit drug misuse. However, adolescents (10-17 years of age) showed a striking improvement, with the inconsistency rate dropping from 70% to 29% between 2011 and 2016.
- Dangerous drug combinations are common. Among 33,000 specimens tested for opioids, benzodiazepines, and alcohol, more than 20% were positive for both opioids and benzodiazepines, more than 10% were positive for both alcohol and opioids, and 3% were positive for all three. Among all specimens positive for heroin, 19% were also positive for non-prescribed fentanyl. And 12% of all specimens positive for prescribed opioids were also positive for prescribed benzodiazepines, suggesting one or more healthcare providers had prescribed these drugs for the patient. While co-prescribing may be medically appropriate for a limited number of patients, these drug combinations greatly increase the risk for potentially lethal respiratory depression.

In 2016, the CDC issued guidelines for the use of opioids by primary care healthcare providers in the management of adults with chronic pain.^{6,7} These guidelines include using non-opioid therapies where possible and patient education and goal-setting, including a plan for cessation of therapy. They also include use of urine drug testing before starting opioid therapy and consideratio of urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

As the world leader in diagnostic information services, Quest Diagnostics is well positioned to provide insights from diagnostic testing into health issues affecting



S	millions of Americans. Quest Diagnostics Health Trends
nt	reports are based on analysis of our national database of
	40 billion de-identified test results. The goal of the present
	Quest Diagnostics Health Trends report is to provide
	insights that help healthcare providers, health plans,
g	government officials, families, and patients at risk
n	understand the scope and nature of the prescription
	drug epidemic based on a nationally representative
	analysis of objective laboratory test data. Well informed
	clinical and public policy decisions may foster measures
	that reduce prescription drug misuse and abuse and
	empower better health for each patient and society
3	as a whole.

About this report

The sixth edition of the Quest Diagnostics Health Trends™ Prescription Drug Monitoring Report: Prescription Drug Misuse in America examines patterns and trends in prescription drug use and misuse based on an analysis of 3.4 million de-identified results of laboratory tests performed by Quest Diagnostics between 2011 and 2016. Quest Diagnostics provides laboratory testing services that help healthcare providers identify appropriate and inappropriate use of several widely prescribed, but abuse-prone drugs, including opioids and other pain medications. The services also help healthcare providers identify use of illicit drugs, including marijuana (which remains a Drug Enforcement Agency Schedule I drug), cocaine, and heroin.

Laboratory test results provide objective information that can assist healthcare providers with assessing patients' use of prescribed medications, other controlled prescription medications, and illicit drugs. Quest Diagnostics provides a comprehensive range of prescription drug monitoring laboratory services to aid clinical assessment using tandem mass spectrometry and other state-of-the-art laboratory technologies. The present analysis includes test results from patients in all 50 states and the District of Columbia, and from a range of practice settings. Test results from drug rehabilitation clinics and addiction specialists were excluded from the analysis, given the higher rates of testing and potentially higher rates of inconsistency in populations served in these clinical segments; thus, drug misuse rates are likely even higher than those reported here.

A healthcare provider will order testing and, on the test form, indicate the drug or drugs prescribed for the patient as well as the drug test panel to be performed. Quest Diagnostics categorizes test results as "consistent" or "inconsistent" based on the presence of drug metabolites identified through laboratory testing and their alignment with the information provided by the healthcare provider on the test order.

A consistent result indicates that the prescribed drug or drugs found match those the healthcare provider indicated were prescribed for the patient on the test order. An inconsistent test result indicates a mismatch between prescribed and detected medications/drugs

Because drug rehabilitation clinics and addiction specialists were excluded from the analysis, the complete figures for drug misuse are likely even higher than those determined by our analysis.

An inconsistent result occurs when:

- Additional drugs are found: all prescribed drugs are detected, but at least one other drug, nonprescribed or illicit, is also detected.
- Different drugs are found: none of the prescribed drugs are detected, but at least one other drug, non-prescribed or illicit, is detected.
- No drugs are found: none of the drugs prescribed for the patient are detected and neither are any non-prescribed or illicit drugs.

A non-prescribed drug refers to a drug that is a prescription medication but which was not prescribed for the patient as indicated by the healthcare provider on the test order.



Inconsistent results can reflect potential problems for the patient and the healthcare system. Combining a prescribed drug with non-prescribed or illicit drugs can lead to dangerous drug combinations, and suggests the possibility that the patient is using a drug or drugs without the benefit of oversight from a healthcare provider. Not taking a prescribed drug may contribute to healthcare waste and failed treatment, and the potential for unintentional or criminal diversion.

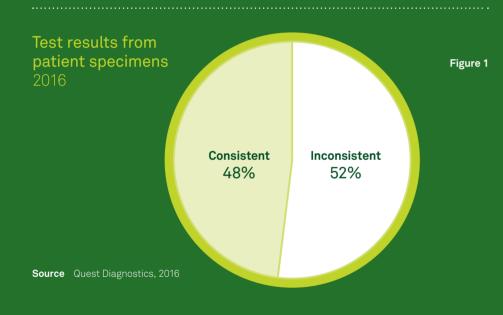
Test results were analyzed by gender, age, and type of health plan (Medicare, Medicaid, or private) as well as geography, and by drug type and combination, to provide a full picture of the populations in which drug misuse is most prevalent.

New to this year's Report are findings from analysis of test results of various potentially deadly drug combinations. These include patients who were found to have combined fentanyl and heroin, as well as those who combined opioids, benzodiazepines, and/or alcohol.



More than half of patient specimens showed signs of prescription drug misuse

22% of all specimens tested used non-prescribed or illicit drugs in addition to their prescribed drugs, reflecting the potential for dangerous drug combinations.



An inconsistent result occurs when:

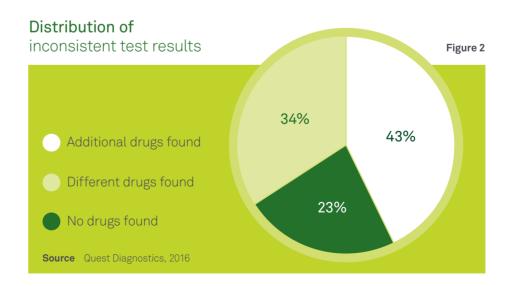
- Additional drugs are found: all prescribed drugs were detected, but at least one other drug, non-prescribed or illicit, was also detected.
- Different drugs are found: prescribed drug(s) was not detected, but at least one other drug, non-prescribed or illicit, was detected.
- No drugs are found: at least one prescribed drug was not detected; non-prescribed or illicit drug(s) were also not detected.

In 2016, 52% of patient test results were inconsistent, suggesting more than half of patients misused their prescription drugs, putting their health at risk. Of these inconsistent results, 43% were due to drugs in addition to the drug(s) prescribed, indicating that many patients exposed themselves to potentially dangerous drug combinations.

While high, the misuse rate in 2016 is an improvement from the rate observed in 2011, when 63% of specimens tested showed signed of inconsistency.

Among the 52% of specimens found with inconsistent results:

- 43% of patient specimens with inconsistent test results (22% of all specimens tested) were positive for non-prescribed or illicit drugs in addition to their prescribed drugs.
- 23% of patient specimens with inconsistent test results (12% of all specimens tested) did not show the drugs they had been prescribed, or any other tested drug.
- 34% of patient specimens with inconsistent test results (18% of all specimens tested) did not show the drugs they had been prescribed, but were positive for other illicit or non-prescribed drugs.





Why would a prescribed drug not be found?

- Patients may not take their prescribed drugs due to concerns over side effects, or because their pain has subsided.
- Some patients may not take their prescribed drugs because they cannot afford them.
- · Some patients sell or give their drugs to others not authorized to use them.
- A small number of patients may be rapid metabolizers of the prescribed drug and the drug or metabolite is undetectable at the time of testing.

Health Trends[™] 2017 Finding #2

The level of prescription drug misuse appears to be falling

The trend in drug misuse 2011-2016

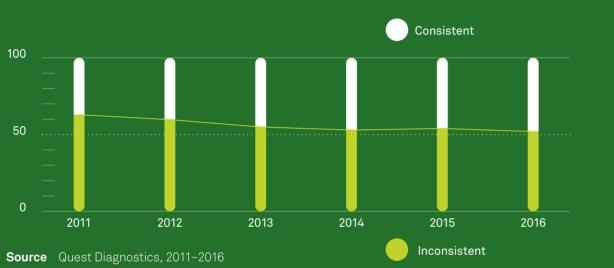


Figure 3

63% 52% 2016 2011 Inconsistency rate Inconsistency rate The 11% decline in the inconsistency rate from 2011 to 2016 is potentially due to better information, less misuse, and better compliance

Although the inconsistency rate remains high, it has declined steadily since 2011, from 63% in 2011 to 52% in 2016. This represents an absolute decrease of 11% over five years.

The decline since 2011 in inconsistent test results is likely due to a combination of factors:

- More accurate information provided about the drugs the patient has been prescribed, leading to a better match between what is expected and what is detected
- · Less misuse of additional drugs other than those prescribed.

Declines in misuse and improvements in compliance, as suggested by the trend in test results, are themselves likely due to a combination of factors, including improved patient and healthcare provider education about the risks of opioids and drug combinations; use of available tools by healthcare providers, including prescription drug monitoring programs; increased public awareness of the opioid epidemic; and FDA-sponsored Risk Evaluation and Mitigation Strategies (REMS) programs.



 Better compliance with prescriptions.

Decrease in inconsistency rate 2011-2016 Health Trends[™] 201 Finding #3

Dangerous drug combinations are common

19% of specimens positive for heroin were also positive for non-prescribed fentanyl, a potentially deadly combination because it may depress respiration.

Heroin & non-prescribed fentanyl-positive

Heroin-positive

Heroin and fentanyl: A lethal combination

Fentanyl is a synthetic opioid that is 50 to 100 times more potent than morphine. It is a schedule II prescription drug with legitimate medical uses, but is also a drug of abuse. Fentanyl is often mixed with heroin, with or without the user's knowledge, to increase drug effects.

Among specimens positive for heroin, 19% were also positive for non-prescribed fentanyl. This drug combination is especially dangerous due to the high potency of fentanyl, meaning even a very small quantity has a very powerful effect on depressing respiration.

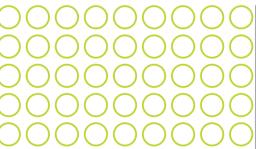
More than 20% of patient specimens tested positive for both benzodiazepines and opioids, and 10% for alcohol and opioids

>20% >10% Positive for Positive benzodiazepines for alcohol metabolites and opioids and opioids >3% Positive for all three groups

Among the 33,833 specimens tested for opioids, benzodiazepines, and alcohol, more than 20% were positive for both opioids and benzodiazepines, more than 10% were positive for both alcohol and opioids, and 3% were positive for all three. These combinations greatly increase the risk for respiratory depression, and should be avoided. More detail on these results appear later in the Report.



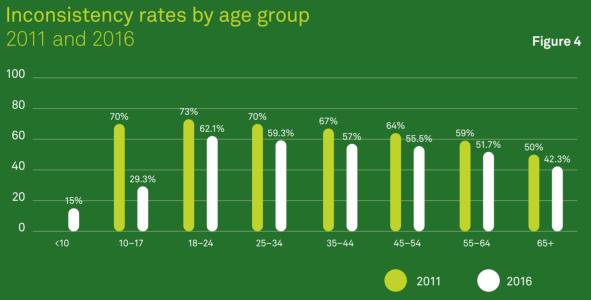
- The fentanyl-heroin overlap is discussed in more detail later in this Report.
- Quest Diagnostics testing services identify fentanyl and the metabolite 'norfentanyl', but not synthetic analogs similar to fentanyl that are sometimes referred to, mistakenly, as fentanyl in lay media coverage of the prescription drug epidemic. Analysis of these drugs, which include carfentayl, furanylfentanyl, and acetylfentanyl, are not included in our study.



Patient specimens testing negative for all three groups Finding #4

Misuse is high across multiple patient categories

Between 2011 and 2016. inconsistency rates improved for all age groups



Source Quest Diagnostics, 2011–2016

Prescription drug misuse is not confined to one sector of the healthcare field. Patients in most age groups, from all payer types, and of both sexes had high rates of inconsistency in test results between what was prescribed and what was found.

Misuse was lowest among the very young and the elderly

Inconsistency rates for 2016 were lowest among the very young and the elderly. Specimens from patients 18 to 44 years of age had a higher rate of inconsistency than the overall tested population at 58% versus 52% among all patients. Specimens of patients 65 years of age or older experienced inconsistency rates of 42%.

Inconsistency rates improved for all age range groups between 2011 and 2016. Tests of children younger than 10 years of age showed a decline in the inconsistency rate from 31% in 2011 to 15% in 2016, an absolute decrease of 16% and a relative decrease of 52%. While outside the scope of our analysis, we theorize that the improved rates for the youngest patients may reflect responsible actions by parents or guardians.

The largest improvement between 2011 and 2016 was seen in the 10 to 17 years age group, decreasing from 70% to 29%, an absolute decrease of 41%, and a relative decrease of 59%.





Table 1Top 3 Drug Misuse Classes by Age Group, 2016

Age group (years)	First	Second	Third
<10	Amphetamines	Methylphenidate	Opiates
10 to 17	Amphetamines	Methylphenidate	Marijuana
18 to 24	Marijuana	Benzodiazepines	Amphetamines
25 to 64	Benzodiazepines	Opiates	Marijuana
>64	Benzodiazepines	Opiates	Oxycodone

The drugs most likely to be misused change with age

This Report examined the drug groups associated with the highest number of inconsistencies for various age groups. (Table 1).

Among the youngest patients, under 10 years of age, the most common drug class found in inconsistent test results was amphetamines, followed by methylphenidate and opiates. Both amphetamines and methylphenidate are stimulants, and are frequently prescribed to treat children with attention-deficit hyperactivity disorder (ADHD). Opiates are prescribed as pain relievers.

Among patients ages 10 to 17, amphetamines and methylphenidate again dominate inconsistent findings, followed by marijuana. As noted above, inconsistency in this group has declined dramatically in recent years, from approximately 70% in 2011 to 44% in 2015 and 29% in 2016.

Among patients ages 18 to 24 years, marijuana was the most common drug found in inconsistent tests, followed by benzodiazepines and amphetamines.

Among patients ages 25 and above, benzodiazepines were the most common inconsistent result, followed by opiates. Marijuana was the third-most common finding in those up to age 64, replaced by oxycodone among those 65 and older.

Health Trends[™] 2017 **Finding #4**

Benzodiazepines are prescribed as anxiolytic and sedative drugs. These results highlight a troubling pattern of benzodiazepines and opioid misuse. The misuse of opioids is especially troubling due to risk of harm or potentially fatal overdose that is associated with concurrent use of benzodiazepine drugs and other central nervous system depressants.

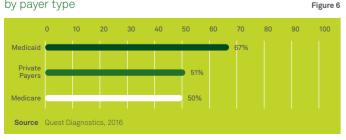
The primary problem with the chronic use of benzodiazepines is the development of tolerance and dependence. This compounds the challenges of prescribing and using opioids and other pain relievers. Clinicians have difficulty counseling patients who claim to require both classes of drugs, and more education is needed to address benzodiazepine prescription and use as part of our national epidemic of drug use and misuse.

Between 2009 and mid-2015, benzodiazepine prescriptions were steady at more than 80 million prescriptions per year. In the period from August 2014 to July 2015, 19% of the prescriptions were for adults ages 20 to 39, 41% for ages 40 to 59 and 38% for age 60 and over. More than two-thirds of benzodiazepine prescriptions were written for female patients.⁹

High misuse rates regardless of payer type

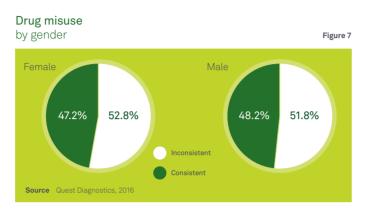
As was seen in previous Reports, test results from patients insured by Medicaid had the highest inconsistency rates of the three major payer groups. This higher rate may reflect increased testing frequency, patient medical conditions, or differences in patient characteristics. The differences in inconsistent test result rates between patients insured by private payers and Medicare were small.

Inconsistency rate by payer type



Drug misuse is common in both men and women

The inconsistency rates were virtually identical for men and women (52.8% vs. 51.8%) in 2016.



Reproductive age and drug use

Drug use and misuse carries special risks for those of reproductive age (here defined as ages 15 to 45), and therefore requires special caution. In males, both opioids and marijuana lower luteinizing hormone (LH) testosterone, interfering with spermatogenesis and decreasing fertility.¹² In females, opioid exposure during pregnancy increases the risk for birth defects such as neural tube defects, gastroschisis (affecting gut development), and congenital heart defects, as well as neonatal abstinence syndrome, a form of drug withdrawal.^{13,14,15}

Birth defects often result from exposures during the first few weeks of pregnancy, which is a critical period for organ formation. Benzodiazepines have been demonstrated to cause harm to the developing fetus.¹⁶ Their use shortly before the delivery may result in the floppy infant syndrome, with the newborns suffering from hypotonia, lethargy, and breathing and feeding difficulties. Chronic exposure to benzodiazepines in utero has been associated with neonatal withdrawal syndrome. Counseling and monitoring women of reproductive age is important for these reasons. Using the lowest effective dose for the shortest period of time minimizes the risks to the fetus.¹⁷ Among specimens tested from men and women of reproductive age, the rate of inconsistency (58%) was higher than the overall tested population (52%). In addition to an analysis of testing data, we also examined drugs prescribed as indicated by the physician on the test order form for patients.

As shown in Table 2, opiates were the most common drug class prescribed. Benzodiazepines and oxycodone took up the second and third places, but differed in their rank for men and women, with benzodiazepines more common in women and oxycodone more common in men.

Women Age 15– Opiates Benzodiazepine

Oxycodone

Table 3 shows comparable figures for non-prescribed drug classes. Marijuana, benzodiazepines, and opiates were the three highest classes, and fell in the same order for both men and women. Men were more likely to use marijuana, and women were more likely to use benzodiazepines.

Women Age 15 – Marijuana Benzodiazepine Opiates

Table 3

Among young children, the most common nonprescribed drugs found were methylphenidate and amphetamines Among younger adults, the most commonly detected drug was marijuana, while for older adults, it was benzodiazepines



Table 2Top 3 Prescribed Drug Classes, Men and Women Age 15–45

	Drugs pres	cribed	
-45	%	Men Age 15–45	%
	43.2	Opiates	35.8
es	28.1	Oxycodone	25.6
	24.5	Benzodiazepines	19.8

Top 3 Non-Prescribed Drug Classes, Men and Women Age 15–45

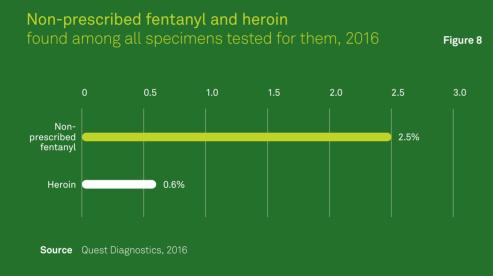
	Drugs found NOT	prescribed	
-45	%	Men Age 15–45	%
	14.3	Marijuana	21.1
es	14.3	Benzodiazepines	10.9
	8.1	Opiates	8.6
• • • • • •	••••••••••••••••••	••••••••••••••••••••••••	•••••

Men were more likely to use marijuana, and women were more likely to use non-prescribed benzodiazepines

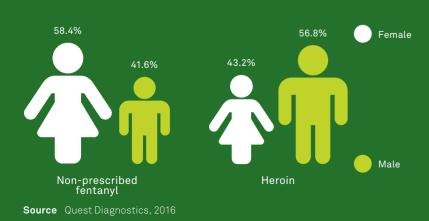
Health Trends[™] 2017 Finding #5

Further details on drug combinations

Of specimens tested for alcohol, benzodiazepines, and opioids, 3% were positive for all three a highly dangerous combination



Non-prescribed fentanyl and heroin positivity rates





Drug mixing can be dangerous and is a contributor to the ongoing epidemic of drug overdose deaths. Many users who don't have prescriptions for multiple drugs, and who have not received education about the dangers of combining medications, are unaware of those dangers.7

Heroin and fentanyl

Following a four-fold sales increase between 1999 and 2010, prescription pain reliever medication sales dropped for 2013, 2014, and 2015.9 Despite the decline in prescription drug sales, annual drug deaths have continued to increase. There are two major driversaccess to drugs and use of high-risk drugs and medications. Access to drugs comes from prescriptions written for pain reliever medications as well as illicitly manufactured drugs like heroin and fentanyl. Illicitly manufactured fentanyl is often substituted for or mixed with heroin, without the drug user's knowledge.

Results of our analysis suggest that a small, but not insignificant, percentage of patients used nonprescribed fentanyl and/or heroin.

Results from patients who tested positive for non-prescribed fentanyl and heroin showed (see Figures and Table 4):

Of the 50,192 specimens tested for fentanyl, over 12% were positive.

- 2.5% of these tested specimens were positive for non-prescribed fentanyl.
- 42% of these specimens were from male patients.
- 37% of non-prescribed fentanyl specimens were from patients younger than age 45.
- For non-prescribed fentanylpositive specimens:
- · Benzodiazepines were the most common non-prescribed drug (27%), followed by opiates (23%).
- 7% were positive for heroin.



Heroin positive	%	Non-prescribed fentanyl positive	%
Marijuana	28.3%	Benzodiazepines	27.1%
Benzodiazepines	19.4	Opiates	22.8
Fentanyl	18.7	Marijuana	18.0
Cocaine	18.5	Cocaine	11.2
Amphetamines	14.6	Oxycodone	7.2
Alcohol	7.8	Heroin	6.8

Of the 74,050 specimens tested for heroin, 0.6% were positive.

- 57% of heroin-positive tests results were from male patients.
- 57% of heroin-positive test results were from patients younger than 45 years old.
- Marijuana was the most common non-prescribed drug in heroin-positive specimens (28%), followed by benzodiazepines (19%) and non-prescribed fentanyl.

Fentanyl and heroin maps

Analysis of heroin and nonprescribed fentanyl positivity by state reveals some of the complexity of the relationship between these two drugs. Note that in two of the states with the highest levels of heroin positivity, West Virginia and Virginia, healthcare providers did not order enough fentanyl tests to be included in the analysis.

Results showed:

- Some states had very similar rates of heroin and non-prescribed fentanyl use, including Georgia and Tennessee, which had among the lowest positivity levels for both drugs.
- In many states, fentanyl may be replacing heroin. In Mississippi and Oklahoma, for example, there were very low levels of heroin positivity but very high levels of non-prescribed fentanyl positivity.
- Three highly populated states, California, Florida, and New York, had similar rates of non-prescribed fentanyl positivity (all between 2% and 3%), but divergent rates of heroin positivity, with less than 0.5% in California and Florida, but over 8% in New York.

Heroin positivity rates Continental USA, 2016



Non-prescribed fentanyl positivity rates Continental USA, 2016



For a graphic-rich depiction of our test results by state, please visit QuestDiagnostics.com/HealthTrends

Alcohol, benzodiazepines, and opioids

Patients using opioids along with benzodiazepines and/or alcohol have increased risk for fatal/ nonfatal overdose. The combination presents a challenge to healthcare providers who manage chronic pain.^{6,10} The data presented in this Health Trends Report indicate that these interactions are occurring with alarming frequency.

All of these drug interactions can be very dangerous due to the cumulative respiratory depression effects. Combining all three drug classes magnifies the dangers.

In the Quest Diagnostics Drug Testing Index,[™] benzodiazepines were the fourth most commonly identified drug class (trailing only marijuana, amphetamines, and oxycodone).¹¹ Benzodiazepine drug use detection was approximately 30% as common as marijuana. The Quest Diagnostics Drug Testing Index examines illicit drug use by America's workforce based on an analysis of de-identified results of more than 10 million laboratorybased tests performed annually, by Quest Diagnostics for U.S. employers. and opioids:

- over 20% were positive for both opioids and benzodiazepines.
- over 10% were positive for both alcohol and opioids.
- 3% were positive for all three drug classes.





There were 6,844 test results

benzodiazepines and opioids:

40% had prescriptions for

16% demonstrated non-

prescribed use of both

both drug classes.

drug classes.

demonstrating concurrent use of

Among the 33,833 specimens tested for alcohol, benzodiazepines,

Alcohol-benzodiazepines-opioids Tested population overlap

Figure 12

- Benzodiazepine positive
 - Alcohol metabolite exposure positive
- **Source** Quest Diagnostics, 2016



Research methodology

Study objectives

The objectives of our study were to assess and identify the scope of prescription drug misuse in America, and identify patterns of misuse over time in a large nationwide population.

We assessed:

- Inconsistency rate by age, drug group, gender, health plan payer group (Medicaid, Private Payer, and Medicare), and geography (HHS Regions).
- The patterns of inconsistency, including:
 - The use of different drug groups (illicit or controlled) other than those prescribed
 - The use of additional, non-prescribed (illicit or controlled) medications
- The failure to use or detect prescribed drugs
- The positivity rates of heroin and non-prescribed fentanyl drug testing by age, gender and state
- The rates of opioid, alcohol, and benzodiazepine polypharmacy use

Testing methodology

The objectives of this study were to assess the scope and demographic drivers of prescription drug misuse in America. As with our earlier Reports, we examined the association of age, gender, payer type, and geography on inconsistency rates. All patients were tested using our proprietary prescription drug monitoring service and medMATCH® reporting methodology for tests of commonly prescribed and abused drugs, including pain medications, central nervous system medications, and amphetamines, as well as certain illicit drugs such as marijuana and cocaine. Effective February 2015, the number of drugs included in our analysis increased from 26 to 44 as we supplemented testing data of profile-based drug panels with individual drug tests.

Our medMATCH reports indicate whether the prescribed drug(s), as specified by the ordering provider, or other drugs are detected in a specimen. Drug testing includes presumptive immunoassay screens as well as definitive mass spectrometry quantitative analyses and confirmations of presumptive positive results. Mass spectrometry is the most sensitive and specific drug testing method. The mass spectrometry definitive methods of analysis included liquid chromatography-tandem mass spectrometry (LC-MS / MS) performed in our clinical laboratories.

Quest Diagnostics Health Trends studies are performed in compliance with applicable privacy regulations and the company's strict privacy policies, and are deemed exempt by the Western Institutional Review Board.

CDC Guidelines for Prescribing Opioids for Chronic Pain, United States

The 2016 Centers for Disease Control guideline provides recommendations for primary care healthcare providers in the management of patients 18 years and older with chronic pain. Chronic pain is defined as lasting longer than three months or past the time of normal tissue healing. The guidelines exclude chronic pain associated with cancer, palliative care, and end-of-life care.

Guidelines recommendations include:

- Use non-opioid therapies when possible.
- Start low and go slow when opioid pharmacotherapy is indicated.
- Discuss the treatment plan with the patient, including goals and how therapy will be discontinued if the risks outweigh the benefits.

The CDC also recommends that healthcare providers review state PDM data where available, and perform drug tests on their patients prior to starting (baseline) and periodically during opioid drug therapy, as "urine drug tests can provide information about drug use that is not reported by the patient."

The guidelines and further information on them are available online:

JAMA publication of CDC Guideline⁶

http://jama.jamanetwork.com/article.aspx?articleid=2503508

CDC MMWR Guideline⁷

http://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm

CDC Fact sheet¹⁸

http://www.cdc.gov/drugoverdose/pdf/guidelines_factsheetproviders-a.pdf

CDC Checklist¹⁹

http://www.cdc.gov/drugoverdose/pdf/pdo_checklist-a.pdf

Strengths and limitations

Our study's strengths include its size, geographic scope multiple years of test results, and its use of validated testing by the highly reliable mass spectrometry method Its limitations include the geographic disparities (nearly 77% of testing came from 12 states representing nearly half of the US population) and the inability to validate or contextualize test results with medical records. Like an laboratory test, a clinical determination of drug misuse requires consideration of several factors, including test results, patient history, and symptoms, made in the context of a complete medical assessment.

Laboratory testing does not identify addiction or impairment due to drug use. Patient variations, includir hydration state, time since last drug use, and genetic differences in drug metabolism, as well as methodolog limitations, can contribute to a failure to detect drugs in a small minority of specimens. An inconsistent result may also be due to incomplete prescribing information provided by the healthcare provider.

Quest Diagnostics Health Trends Reports

As the leading diagnostic information services provider Quest Diagnostics maintains the largest private clinical laboratory database in the United States. Consisting of 40 billion data points from de-identified patient testing the database provides laboratory information on the vast majority of conditions and diseases affecting Americans. Quest Diagnostics Health Trends reports are designed to identify and track disease and wellness benchmarks to inform patients, healthcare professionals, and policymakers about the current status of the nation's health.



e,	Moreover, it is possible that in some cases, patients in our study were referred to testing because their
d.	healthcare providers suspected a high probability of
у	misuse, while the index of suspicion was lower for others
Ý	who were not tested. In addition, some healthcare
r	providers may have neglected to indicate all prescribed
ıy	drugs a patient was taking when submitting the test
ł	request. These dynamics may have changed over time.
t	
	Our analysis assessed patterns of prescription drug
	misuse for the population served by healthcare
	providers ordering testing from Quest. Quest provides
	testing services to approximately half of all healthcare
ng	providers and hospitals in the United States. Quest does not serve all healthcare providers and these insights
у	may not accurately be reflective of the entire population.
n	Again, dynamics in our client base may have changed over time and inclusion criteria (testing performed by Quest) may have affected our observations.

r,	Quest Diagnostics Health Trends reports include
al	analysis of our comprehensive prescription drug testing
f	services for healthcare providers and workforce drug
g,	testing for employers. The latter type of analysis is
	referred to as the Quest Diagnostics Drug Testing Index.™
	To access these Reports, visit QuestDiagnostics.com/
	HealthTrends and QuestDiagnostics.com/DTI
	For more information, visit

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Contributors

This Report was developed by a team of Quest Diagnostics medical, technical, and informatics experts including Leland McClure, PhD, Justin Niles, and Harvey W. Kaufman, MD.

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About Quest Diagnostics

Quest Diagnostics (NYSE:DGX) is the leading provider of diagnostic information services that patients and healthcare professionals need to make better healthcare decisions. Quest Diagnostics (NYSE: DGX) empowers people to take action to improve health outcomes. Derived from the world's largest database of clinical lab results, our diagnostic insights reveal new avenues to identify and treat disease, inspire healthy behaviors, and improve healthcare management.

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