



**PHARMACY
VISION
20/20**

CSHP SEMINAR 20 • OCTOBER 21-25
Disneyland
RESORT

THE OPIOIDS HIDING AMONG US AND HARM REDUCTION STRATEGIES TO REDUCE RISK OF DEATH

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DISCLOSURE

- No potential conflicts of interest

LEARNING OBJECTIVES

1. Identify current trends of substances being laced with fentanyl
2. Demonstrate how to use fentanyl test strips and how to obtain them
3. Discuss the importance of providing naloxone to all patients using various illicit substances
4. Describe treatment options for patients with a benzodiazepine use disorder, methamphetamine use disorder, or cocaine use disorder, to treat the underlying condition and reduce exposure to opioids

CURRENT TRENDS OF ILLICIT SUBSTANCES BEING LACED WITH FENTANYL

TEST QUESTION #1

An Emergency Department (ED) patient is altered with pinpoint pupils. A urine drug screen (UDS) is obtained (results in table). After 10 minutes, the patient becomes unresponsive. The patient is given 3 doses of naloxone and becomes alert. The patient reports having snorted cocaine but no opioids. Which of the following is the most likely explanation?

- Opiates cannot be found through UDS
- Fentanyl was present in the cocaine, but would not cause a positive result on an opiate immunoassay
- THC can cause false positives for opioids
- Heroin was present in the cocaine, but not enough time has passed since snorting for it to show up in a UDS

Amphetamines	Negative
Benzodiazepines	Negative
Cocaine	Positive
Marijuana	Positive
Opiates	Negative
PCP	Negative

SYNTHETIC OPIOID OVERDOSE TRENDS

- In 2018, > 31,000 deaths involving synthetic opioids (other than methadone) occurred in the US
- Synthetic opioid-involved death rates increased by 10% from 2017 to 2018 and accounted for 67% of opioid-involved deaths in 2018
- Reports indicate that increases in synthetic opioid-related deaths are due to increases in fentanyl-related overdose deaths, with the source of the fentanyl more likely being illicitly manufactured than pharmaceutical

1. Gladden RM, et al. *Morb Mortal Wkly Rep.* 2016.
2. O'Donnell JK, Gladden RM & Seth P . *Morb Mortal Wkly Rep.* 2017.
3. O'Donnell JK, et al. *Morb Mortal Wkly Rep.* 2017.

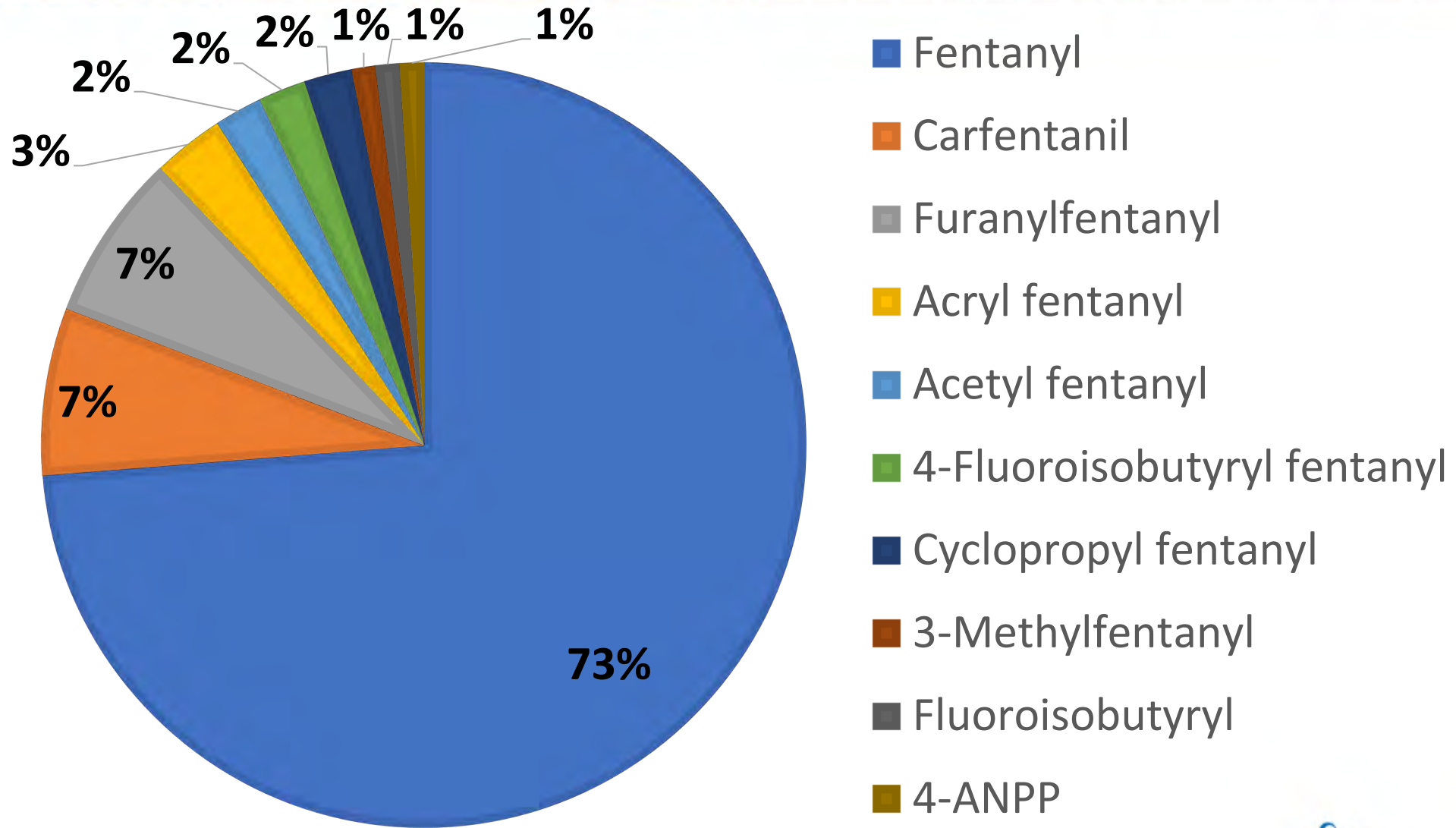
SYNTHETIC OPIOID OVERDOSE TRENDS, CONTINUED

- As of January 2020, 49 states had encountered fentanyl-containing counterfeit pills
 - Hawaii was the only state without confirmed cases of fentanyl-containing counterfeit pills
- Colorings, markings, and shape of counterfeit pills were consistent with authentic prescription medications
- Theorized that fentanyl analogs, such as acetyl fentanyl, furanylfentanyl, and carfentanil, are also being illicitly distributed

3. O'Donnell JK, et al. *Morb Mortal Wkly Rep.* 2017.

4. The Partnership for Safe Medicines. www.safemedicines.org

Nationwide Reports of Fentanyl, Synthetic Opioids, and Precursor Chemicals, 2017



5. Drug Enforcement Administration. www.dea.gov.

FENTANYL

Synthetic Opioid

- 50 x more potent than heroin
- 100 x more potent than morphine



Figure: Lethal doses of heroin (30 mg) and fentanyl (3 mg)

Prescription opioid, but is also illicitly manufactured

Often pressed into counterfeit pills or mixed with heroin or cocaine (with or without the user's knowledge)

6. Centers for Disease Control and Prevention. www.cdc.gov

7. Foundation for a Drug Free World. www.drugfreeworld.org

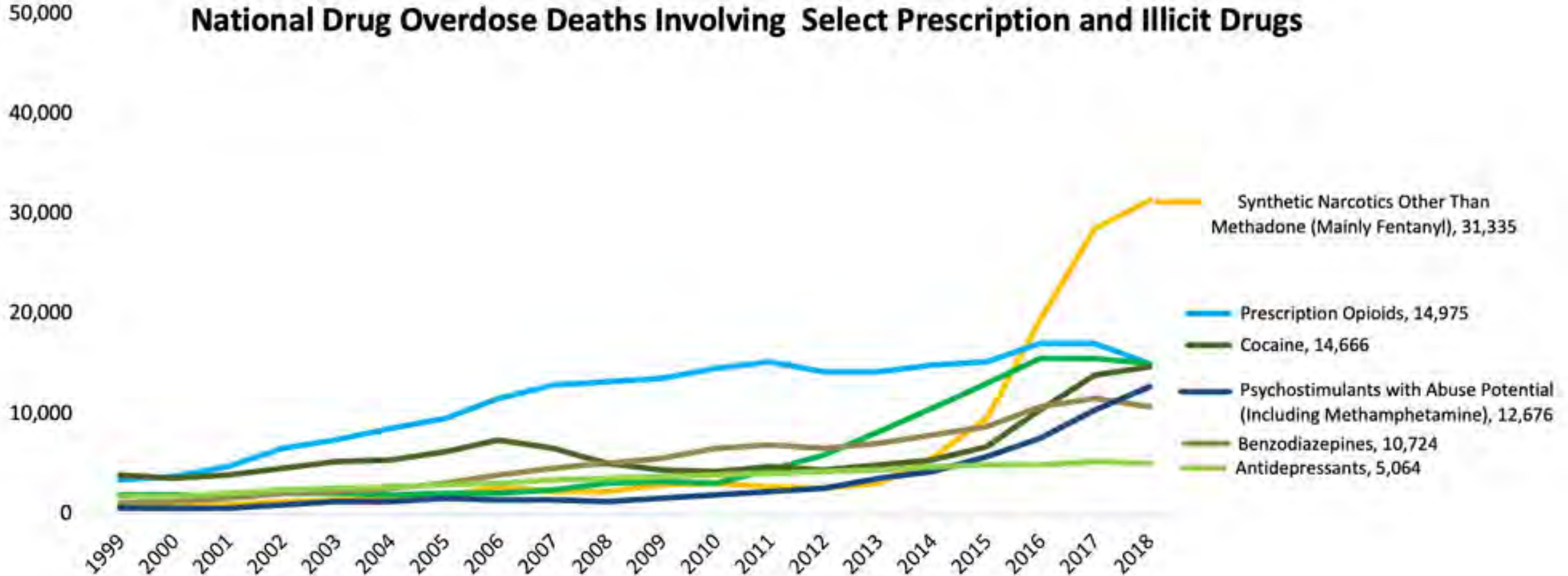
DEA ISSUES WARNING OVER COUNTERFEIT PRESCRIPTION PILLS FROM MEXICO

Report from November 4, 2019

Sampling of tablets seized
nationwide between January -
March 2019 found that 27%
contained potentially lethal
doses of fentanyl

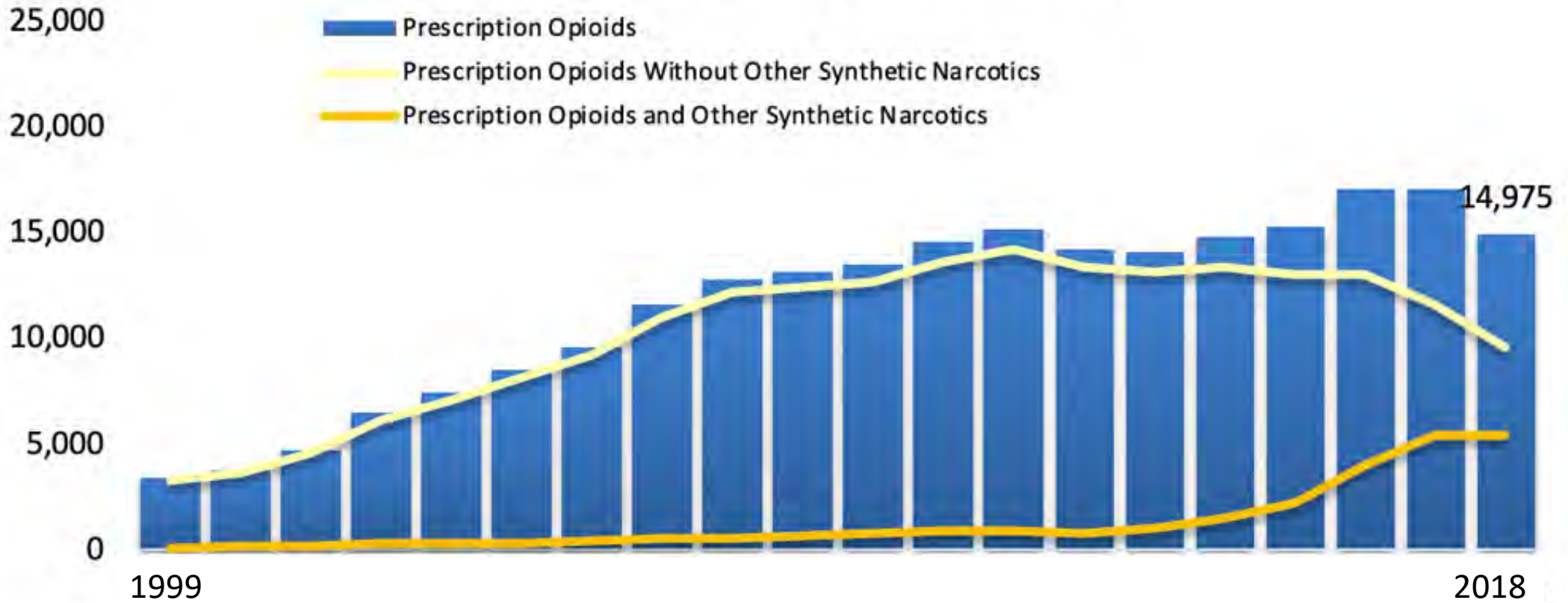


8. Drug Enforcement Administration. www.dea.gov.



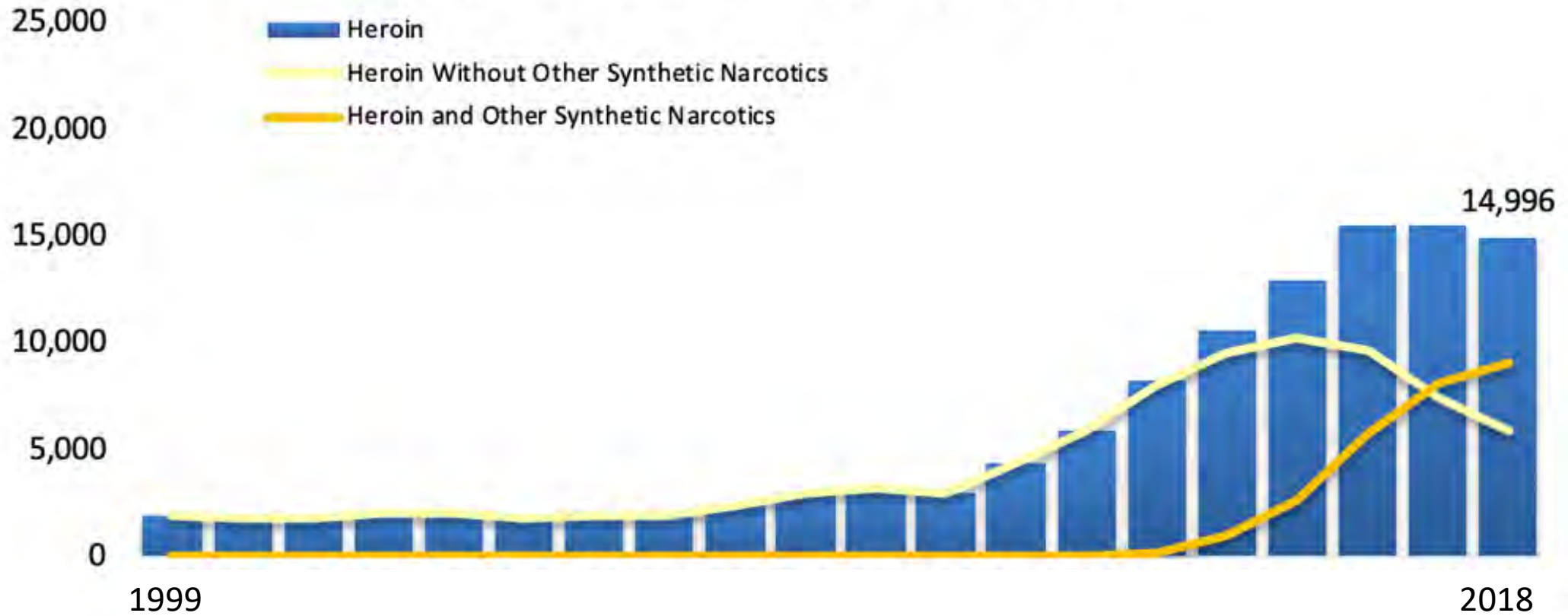
9. Centers for Disease Control and Prevention, National Center for Health Statistics. www.drugabuse.gov.

National Drug Overdose Deaths Involving Prescription Opioids, Number Among All Ages, 1999-2018



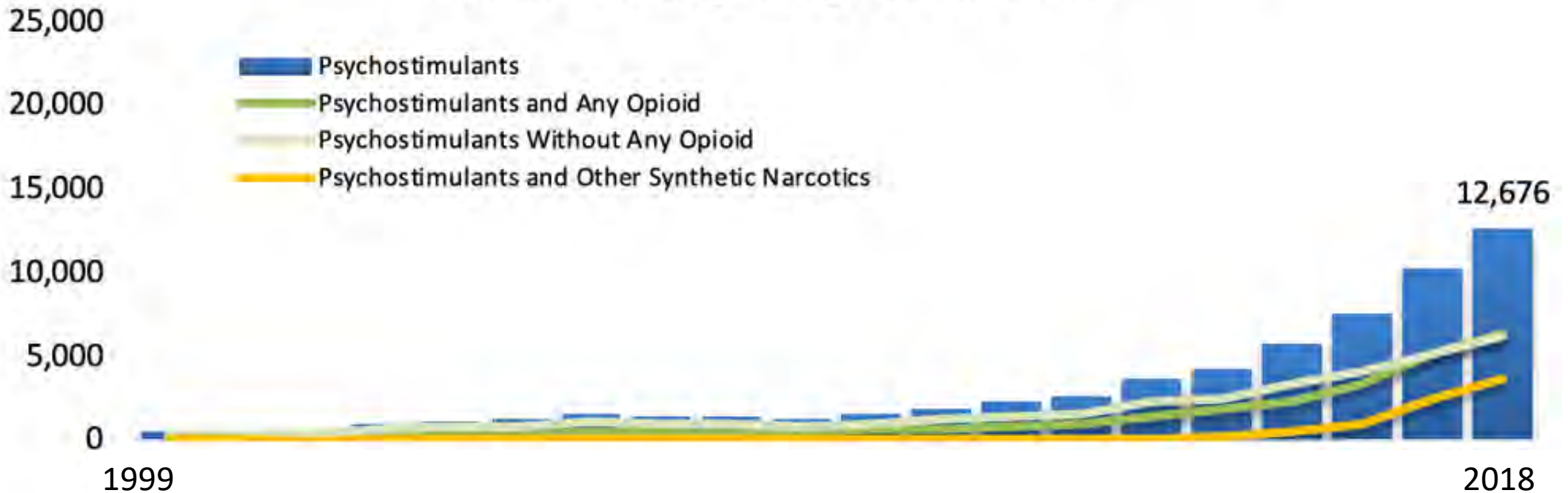
9. Centers for Disease Control and Prevention, National Center for Health Statistics. www.drugabuse.gov.

National Drug Overdose Deaths Involving Heroin Number Among All Ages, 1999-2018



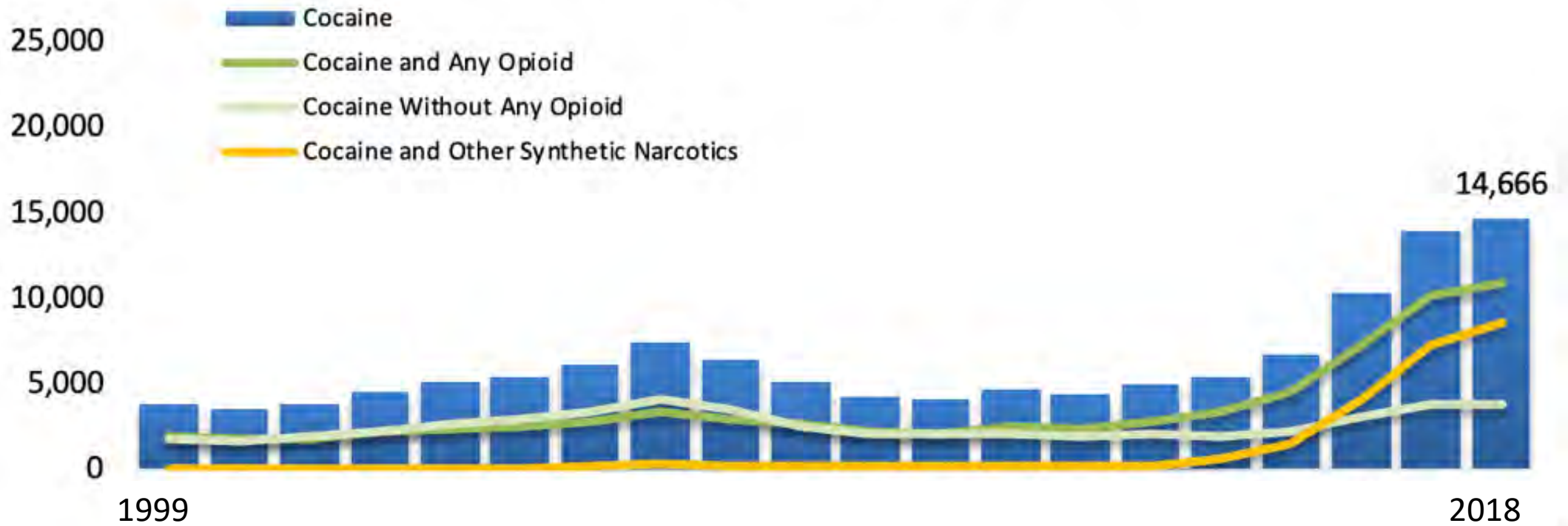
9. Centers for Disease Control and Prevention, National Center for Health Statistics. www.drugabuse.gov.

National Drug Overdose Deaths Involving Psychostimulants With Abuse Potential (Mainly Methamphetamine), by Opioid Involvement Number Among All Ages, 1999-2018



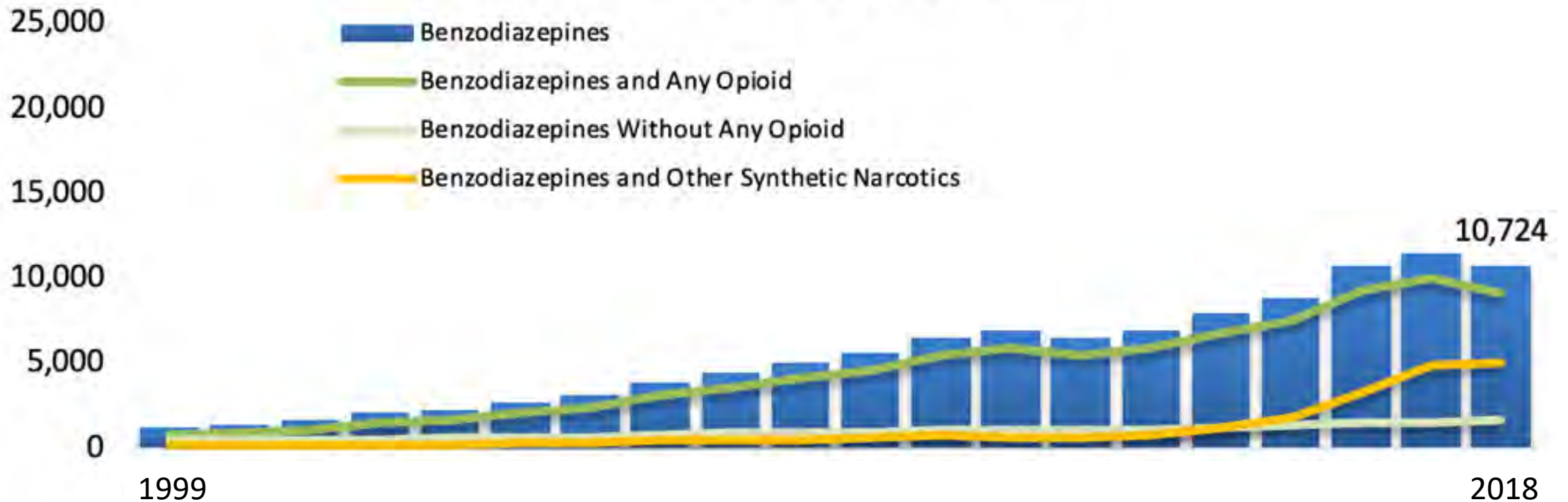
9. Centers for Disease Control and Prevention, National Center for Health Statistics. www.drugabuse.gov.

National Drug Overdose Deaths Involving Cocaine, by Opioid Involvement Number Among All Ages, 1999-2018



9. Centers for Disease Control and Prevention, National Center for Health Statistics. www.drugabuse.gov.

National Drug Overdose Deaths Involving Benzodiazepines, by Opioid Involvement Number Among All Ages, 1999-2018



9. Centers for Disease Control and Prevention, National Center for Health Statistics. www.drugabuse.gov.

FENTANYL IN MARIJUANA

October 21, 2019 - KUTV News Report in Salt Lake City, UT

“It looks like weed, but it's not: Law enforcement warn of fentanyl disguised as cannabis”

- Substance tested positive for fentanyl, heroin, tramadol, and traces of methamphetamine
- Previously, similar substances had been found in Ohio and Canada

10. Salt Lake City, KUTV. <https://kutv.com>.

Statistically significant changes in drug overdose death rates involving synthetic opioids by select states, United States, 2017 to 2018

California:

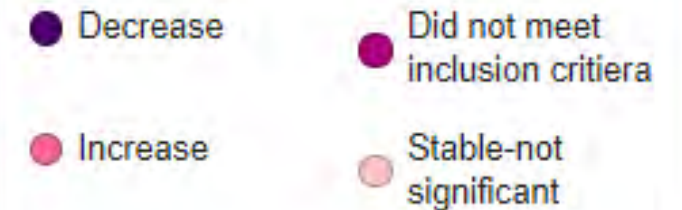
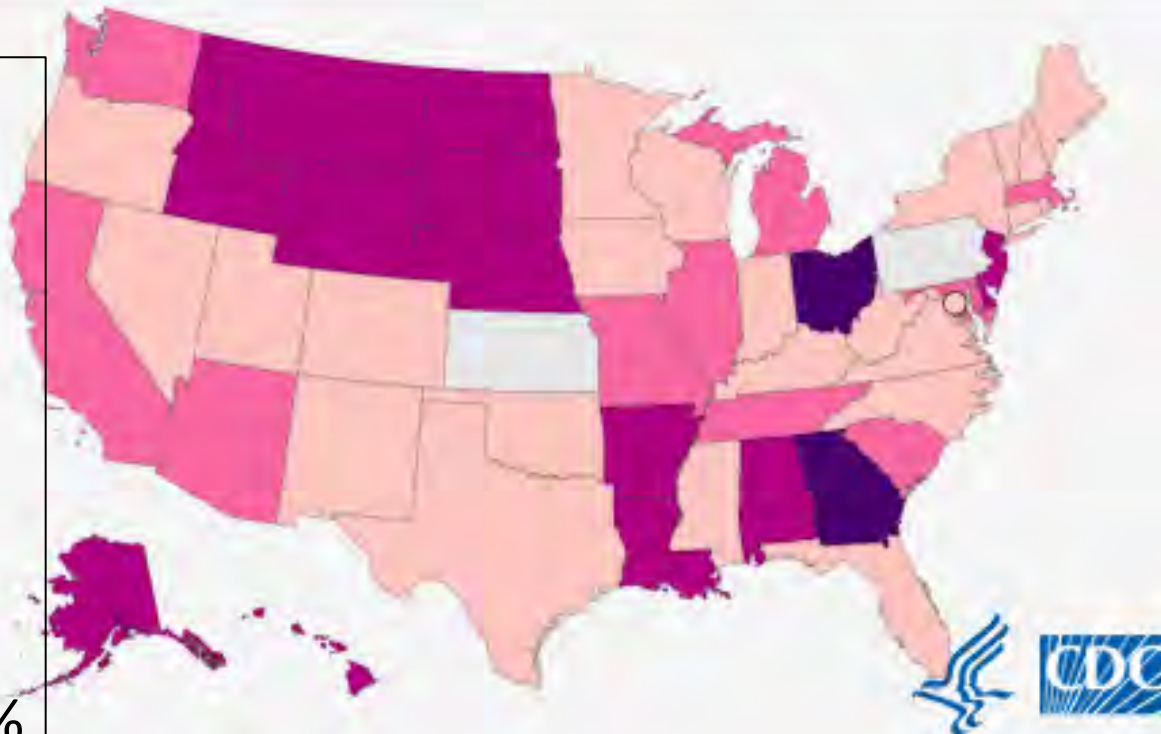
2017 Deaths: 536

2017 Rate: 1.3

2018 Deaths: 865

2018 Rate: 2.2

% Change from
2017 to 2018: 69.2%



11. Centers for Disease Control and Prevention/National Center for Health Statistics. wonder.cdc.gov.

FENTANYL TEST STRIPS

TEST QUESTION #2

Which of the following is true regarding fentanyl test strips?

- a. Each strip costs about \$10
- b. Fentanyl can only be identified in the urine after drug use
- c. One line appearing on the strip indicates that fentanyl is present
- d. They can only detect fentanyl, not fentanyl analogs

TEST QUESTION #3

Which of the following is true regarding the limited studies on use of rapid fentanyl test strips?

- a. Results are promising regarding the use of rapid fentanyl test strips by people who use drugs to modify behaviors to reduce harm
- b. Results have identified that people who use drugs with minimal training are not able to appropriately use the rapid fentanyl test strips
- c. Rapid fentanyl test strips were only able to detect fentanyl in samples of heroin or other opioids, but not other illicit substances
- d. Currently, all studies have been conducted outside the United States, so the results are not applicable to people who use drugs in the United States

DIFFERENCES IN METHODS USED TO DETECT FENTANYL

Urine Drug Screen (UDS)

- Only determines if fentanyl was present **after** illicit substance ingestion
- Synthetic opioids (including fentanyl) do not show up through UDS with point of care drug testing (POCT) or opiate immunoassays
- Separate immunoassay specific for fentanyl must be utilized to detect fentanyl

Rapid Fentanyl Test Strips

- Can tell the user if fentanyl is present in the illicit substance **before** ingesting so the user can implement measures to reduce opioid overdose risk
- Can be used to test unregulated drugs in pill or powder form (i.e. cocaine, methamphetamine, 3,4-methylenedioxy-methamphetamine [MDMA], ketamine, heroin and other opioids)

12. Milone MC. *J. Med. Toxicol.* 2012.

13. Harm Reduction Coalition. harmreduction.org.

RAPID FENTANYL TEST STRIPS

- Originally developed and manufactured by Canadian biotech company BTNX, Inc. (other brands also available now)
- Originally manufactured to test for fentanyl in urine, but found to also be useful in testing illicit substances for fentanyl before use
- Can also detect several fentanyl analogs: carfentanil, p-fluoro fentanyl, valeryl fentanyl, 3-methyl fentanil, sufentanil, butyryl fentanyl, acetyl fentanyl, furanylfentanyl, ocfentanil, remifentanil, norfentanyl
- No significant cross-reactivity to other opiates (i.e. morphine and heroin)
- Cost: ~\$1-2 per strip or FREE from Harm Reduction/Needle Exchange Programs

13. Harm Reduction Coalition. harmreduction.org.

14. Prevent Overdose Rhode Island. preventoverdoseri.org

RAPID FENTANYL TEST STRIPS - STEPS FOR USE

1. Mix with water

- If injecting: Prepare shot first, then add ten drops of water to cooker and stir well
- If snorting: Add ten drops of water into the empty baggie that drugs came in and mix well
- If using pills: Crush one pill in an empty baggie and then dump out the powder. Then add ten drops of water into the baggie and mix well

2. Dip fentanyl test strip into the water up to the wavy lines (not past solid blue line just above the wavy lines) and wait fifteen seconds, then take it out

3. After 1-2 minutes, count the number of red lines

13. Harm Reduction Coalition. harmreduction.org.

14. Prevent Overdose Rhode Island. preventoverdoseri.org

RAPID FENTANYL TEST STRIPS



Liquid pulled
into test area
through
capillary action

Test area
1 line = positive
2 lines = negative

Hold this end



13. Harm Reduction Coalition. harmreduction.org.
14. Prevent Overdose Rhode Island. preventoverdoseri.org
15. Matt Adams Foundation for Opioid Recovery. mattadamsfoundation.org.

FENTANYL TEST STRIP USE WITH METHAMPHETAMINE AND MDMA

- The molecular composition of methamphetamine and MDMA can produce a positive result if too high of a concentration of the drug is tested
- To obtain an accurate result, the sample should be diluted in ~ a half cup of water
 - If fentanyl is present, the half cup of water will result in a positive test
 - If no fentanyl is present, the dilution will give an accurate negative result
- Whole shards or pieces dissolved in only a cooker or small amount of water should not be tested

13. Harm Reduction Coalition. harmreduction.org.

FENTANYL TEST STRIP STUDIES - KARAMOUZIAN, 2018

Dates of Study, Location: July 2016-June 2017, Vancouver, Canada

Study Participants: Clients at a safe injection facility (SIF)

Study Objectives: Determine:

1. if client-supplied illicit substances tested positive for fentanyl using the rapid fentanyl test strips
2. what the client perceived the illicit substance to be prior to being checked
3. whether the client intended to dispose of the drug or reduce the dose if fentanyl was present
4. if an overdose occurred

16. Karamouzian et al. *Harm Reduction Journal*. 2018

FENTANYL TEST STRIP STUDIES - KARAMOUZIAN, 2018

Results: In response to study objectives:

- 1) 1121/1411 (79.4%) of all substances tested were positive for fentanyl
- 2) Majority of samples were client-reported heroin (84.1% positive for fentanyl)

3)

Fentanyl Presence	Dose reduction Yes; n (%)	Odds ratio (95% CI); P value	Drug disposal Yes; n (%)	Odds ratio (95% CI); P value
Positive	142 (36.32)	9.36 (4.25–20.65); 0.0001	50 (11.47)	1.60 (0.79–3.26); 0.186
Negative	7 (5.74)		10 (7.46)	

- 4) 120 overdoses; 94% tested post-consumption (OR=5.97; 95% CI 2.41–14.78)

16. Karamouzian et al. *Harm Reduction Journal*. 2018

FENTANYL TEST STRIP STUDIES – KRIEGER 2018 AND GOLDMAN 2019

Dates of Study, Location: May-September 2017, Rhode Island

Study Participants: Young adults (age 18–35years) with self-reported drug use in the past 30days, N = 93; Two-part study including the same participants

Study Objectives:

- Part 1: Through survey assessment, determine participants' socio-demographic and behavioral characteristics, overdose risk, suspected fentanyl exposure, and willingness to use take-home rapid test strips
- Part 2: Through completion of a quantitative and structured qualitative interview, determine participants' attitudes regarding fentanyl test strips after training on how to use them and 2-4 weeks with a take-home supply of 10 fentanyl test strips

17. Krieger, et al. *Harm Reduction Journal*. 2018

18. Goldman, et al. *Harm Reduction Journal*. 2019

FENTANYL TEST STRIP STUDIES – KRIEGER 2018 AND GOLDMAN 2019

Results Part 1:

- Mean age of 27 years (SD=4.8), 56% were male and 56% were white, followed by mixed race (30%) and black (14%)
- Over half (54%) reported regular non-medical use (defined as at least once a week) of prescription opioids while ~ one third reported heroin (37%) and cocaine use (37%)
- Almost half had injected drugs (48% ever in lifetime and 42% in last 6 months) and 37% reported previous overdose (OD)

17. Krieger, et al. *Harm Reduction Journal*. 2018

18. Goldman, et al. *Harm Reduction Journal*. 2019

FENTANYL TEST STRIP STUDIES – KRIEGER 2018 AND GOLDMAN 2019

Results Part 1, continued: (Stratified by history of overdose)

- 48% reported concern about overdosing, with those who had ever overdosed being significantly more likely to report concern ($p < 0.01$)
- 70% expressed concern about their drugs being contaminated with fentanyl; however, expressing concern was not significantly associated with participants having ever overdosed
- A greater number of individuals who had ever overdosed (68%) vs. those who had not (35%) reported confidence that they had used fentanyl-laced drugs ($p = 0.01$)
- 93% wanted to know if fentanyl was in their drugs before taking them (this was not significantly associated with overdose history)

17. Krieger, et al. *Harm Reduction Journal*. 2018

18. Goldman, et al. *Harm Reduction Journal*. 2019

FENTANYL TEST STRIP STUDIES – KRIEGER 2018 AND GOLDMAN 2019

Results Part 2:

- After training, 95% agreed or strongly agreed that they planned to use the provided rapid fentanyl take-home test strips and 99% reported that it would be easy to use the fentanyl testing strips
- After 2-4 weeks, 81 participants (87%) returned for follow-up
- 62 participants (77%) had used at least one FTS, and of those, a majority found them to be useful and straightforward to use
- About half of the participants from each group who received a positive test result reported altering the way they use drug (Table 2 provides more details)

17. Krieger, et al. *Harm Reduction Journal*. 2018

18. Goldman, et al. *Harm Reduction Journal*. 2019

FENTANYL TEST STRIP STUDIES – KRIEGER 2018 AND GOLDMAN 2019

Results Part 2, continued:

Table 2 Fentanyl rapid test strip use among young adults who use drugs in Rhode Island ($n = 81$)

Characteristic	N (%)
Participants who used at least one test strip	62 (76.5)
Of the participants who used at least one FTS ($n = 62$), participants reported ^a :	
Regular heroin use	23 (37.1)
Regular cocaine use	24 (38.7)
Non-medical prescription pill use	13 (21.0)
Lifetime injection drug use	29 (46.7)
Of the participants who used at least one FTS ($n = 62$), the number (proportion) who received at least one positive FTS	31 (50.0)

Table 2, continued

Characteristic	N (%)
Of the who received at least one positive FTS ($n = 31$), participants reported altering the way they used drugs ^a :	
Used less	14 (45.2)
Used with someone else around	12 (38.7)
Went slower	13 (41.9)
Did a tester	11 (35.5)
Threw them out	3 (9.7)
Sold them	3 (9.7)
Gave them away	2 (6.5)

^aThese categories are not mutually exclusive

17. Krieger, et al. *Harm Reduction Journal*. 2018

18. Goldman, et al. *Harm Reduction Journal*. 2019

FENTANYL TEST STRIP STUDIES – PEIPER, 2019

Dates of Study, Location: September-October 2017, Greensboro, North Carolina

Study Participants: 125 people who inject drugs (PWID) completed an online survey about their most recent FTS use

Study Objectives: Determine:

1. whether PWID engaged in any of the following changes in drug use behavior after using FTS: used less than usual, administered tester shot, pushed syringe plunger slower than usual, and snorted instead of injected
2. whether PWID felt that FTS use made them feel better able to protect themselves from overdose

19. Peiper, et al. *International Journal of Drug Policy*. 2019

FENTANYL TEST STRIP STUDIES – PEIPER, 2019

Results:

- 63% reported a positive FTS result and 81% reported using FTS prior to consuming their drugs
- For the outcomes, 43% reported a change in drug use behavior and 77% indicated increased perceived overdose safety by using FTS
 - PWID with a positive FTS test result had 5x the odds of reporting changes in drug use behavior compared to those with a negative result
 - PWID who used the FTS after drug consumption were 70% less likely to report behavioral changes at subsequent drug consumption compared to those who used it before consumption

19. Peiper, et al. *International Journal of Drug Policy*. 2019

FENTANYL TEST STRIP STUDIES – DOPE PROJECT PILOT

Dates of Study, Location: August 2017-January 2018, San Francisco, CA

Study Participants: People receiving services at one of five Syringe Access Collaboratives (SAC), 242 surveys were completed

Study Objectives: Fentanyl test strip monitoring survey published only on harmreduction.org website (specific objectives not reported)

Findings:

- Crystal meth/speed and black tar heroin made up the largest percentages of drugs tested (32.2% and 37.2%, respectively)
- A variety of heroin types that were not reported to be black tar made up 14.1% of drugs tested, while other drugs tested included crack cocaine, powdered cocaine, Xanax, ecstasy, unmarked pills, and meth/heroin mixes

20. Harm Reduction Coalition. harmreduction.org.

FENTANYL TEST STRIP STUDIES – DOPE PROJECT PILOT

Findings, continued:

- Participants reported an almost even split between testing their products before they used, or after (51.8% and 48.2%, respectively)
- Participants reported utilizing a number of harm reduction strategies (specific % not reported) to keep themselves safe after learning the results of the test
- 58.8% reported sharing the results of the test with their community regardless of whether the result was positive or negative
- 78% of speed/crystal meth samples and 67% of the crack cocaine samples tested positive for fentanyl
 - Of note, positive results were being reported back to program staff at higher rates than negative results

IMPORTANCE OF PROVIDING NALOXONE TO ALL PATIENTS USING ILLICIT SUBSTANCES

TEST QUESTION #4

Which of the following patients should be encouraged to obtain naloxone to prevent a possible drug overdose?

- a. Patient with a benzodiazepine use disorder
- b. Patient with a methamphetamine use disorder
- c. Patient with a cocaine use disorder
- d. Patient with an opioid use disorder
- e. All the above

NALOXONE FOR ALL PATIENTS USING ILLICIT SUBSTANCES

- Due to the increasing trends of fentanyl in many illicit substances, all patients with a substance use disorder (especially those obtaining illicit substances) should be offered naloxone to prevent an opioid-related overdose
- Naloxone will only reverse the opioid overdose if fentanyl or another opioid is present
- Naloxone will not cause harm to a person who may be unresponsive due to another reason

21. Boyer EW. *N Engl J Med*. 2012.

NALOXONE WITH FENTANYL

- “Naloxone-resistant fentanyl” – News articles have suggested fentanyl and its analogs cannot be reversed with naloxone
- Currently, there is no robust evidence supporting naloxone-resistant fentanyl
- Fentanyl is more potent and has a quicker onset of action so larger doses may be necessary and the window for overdose and rescue may be shorter than with other opioids

22. Health in Justice Action Lab: Changing the Narrative Initiative. www.changingthenarrative.news.

23. Canadian Centre on Substance Abuse. www.ccsa.ca.

TECH & SCIENCE

FENTANYL FOUND IN GEORGIA RESISTS LIFE-SAVING NALOXONE ANTIDOTE

Health

New Strain of Fentanyl Is Resistant to Our Only Overdose Antidote

NALOXONE FURNISHING BY PHARMACISTS

- CA law authorizes pharmacists to furnish naloxone according to a protocol adopted by the Board of Pharmacy (BOP) in CA Code of Regulations, title 16, [section 1746.3](#)
- Pharmacists must complete \geq one hour of an approved CE program specific to use of naloxone in all routes of administration in the protocol, or an equivalent curriculum-based training program completed in a board-recognized school
 - Free webinar available on CA BOP website meets protocol requirement:
 - <https://www.pharmacy.ca.gov/licensees/webinars/naloxone.shtml>
 - Pharmacists can earn one hour of CE credit for completing webinar
 - Video can be viewed at any time, no registration required

24. California Board of Pharmacy. www.pharmacy.ca.gov.

TREATMENT OPTIONS FOR BENZODIAZEPINE, METHAMPHETAMINE, AND COCAINE USE DISORDER

BENZODIAZEPINE TAPER

- Aim to complete taper over several weeks to months
 - Slower taper may be necessary for apprehensive patients, those on high doses of benzodiazepines, or those taking benzodiazepines for a long time
 - Taper > 6 months is not recommended due to the patient focusing too much on the taper process
- Taper by 10-25% every 1-2 weeks based on patient tolerability
 - Evidence supports halting at 50% of original dose for 1-2 months
- Patient should set goals prior to taper and be involved in the long-term plan
- Some patients may benefit from switching to a longer-acting benzodiazepine

25. National Center for PTSD. www.pbm.va.gov.

26. Fuller MA, Sajatovic M. 2009. Hudson, OH: Lexi-Comp Inc.

27. Tannenbaum C, et al. *Jama Intern Med*. 2014.

EQUIVALENT DOSES OF BENZODIAZEPINES

	Benzodiazepine	Elimination Half-life	Approximate Dosage Equivalent
Longer-Acting	Chlordiazepoxide	> 100 hours	10 mg
	Diazepam	> 100 hours	5 mg
	Flurazepam	> 100 hours	30 mg
Short/Intermediate-Acting	Alprazolam	5 – 25 hours	0.5 mg
	Clonazepam	20 – 50 hours	0.25 – 0.5 mg
	Lorazepam	10 – 20 hours	1 mg
	Temazepam	10 – 20 hours	10 – 20 mg
Short-Acting	Triazolam (Halcion®)	1.5 – 5 hours	0.25 mg

25. National Center for PTSD. www.pbm.va.gov.

TREATMENT OPTIONS FOR METHAMPHETAMINE USE DISORDER

- No established pharmacotherapeutic intervention
- Many medications studied including stimulants, antidepressants, modafinil, antipsychotics, anticonvulsants, naltrexone, n-acetylcysteine, and atomoxetine
 - Heterogeneity of subject use patterns (bingeing vs daily use) makes generalization of clinical trials difficult
 - Agents with ≥ 2 randomized clinical trials with limited positive outcomes include dextroamphetamine, methylphenidate, bupropion, mirtazapine, topiramate and naltrexone
 - Soares, et al. found mirtazapine and SR methylphenidate showed modest effects in improving abstinence with heavy users requiring longer treatment and higher doses

28. Gasper J & Puzantian T. cpnp.org.

29. Soares E & Pereira FC. *Expert Opin Pharmacother.* 2019.

TREATMENT OPTIONS FOR COCAINE USE DISORDER

- No established pharmacotherapeutic intervention
- Psychosocial interventions currently have the most evidence
- Several literature reviews have found that psychostimulants, modafinil, bupropion, topiramate, and disulfiram show the most promise
- Evidence is limited by heterogeneity of studies, small sample sizes, and inconsistent results

30. Buchholz, et al. *Curr Opin Psychiatry*. 2019.



TEST QUESTIONS

TEST QUESTION #1

An Emergency Department (ED) patient is altered with pinpoint pupils. A urine drug screen (UDS) is obtained (results in table). After 10 minutes, the patient becomes unresponsive. The patient is given 3 doses of naloxone and becomes alert. The patient reports having snorted cocaine but no opioids. Which of the following is the most likely explanation?

- Opiates cannot be found through UDS
- Fentanyl was present in the cocaine, but would not cause a positive result on an opiate immunoassay
- THC can cause false positives for opioids
- Heroin was present in the cocaine, but not enough time has passed since snorting for it to show up in a UDS

Amphetamines	Negative
Benzodiazepines	Negative
Cocaine	Positive
Marijuana	Positive
Opiates	Negative
PCP	Negative

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Which of the following is true regarding fentanyl test strips?

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- b. Fentanyl can only be identified in the urine after drug use
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TEST QUESTION #3

Which of the following is true regarding the limited studies on use of rapid fentanyl test strips?

- a. Results are promising regarding the use of rapid fentanyl test strips by people who use drugs to modify behaviors to reduce harm
- b. Results have identified that people who use drugs with minimal training are not able to appropriately use the rapid fentanyl test strips
- c. Rapid fentanyl test strips were only able to detect fentanyl in samples of heroin or other opioids, but not other illicit substances
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- a. Patient with a benzodiazepine use disorder
- b. Patient with a methamphetamine use disorder
- c. Patient with a cocaine use disorder
- d. Patient with an opioid use disorder
- e. **All the above**

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