GUIDANCE ON HANDLING THE INCREASING PREVALENCE of Drugs Adulterated or Laced with Fentanyl
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Statement of the Problem

Fentanyl and its analogs are currently the primary drivers of deaths in the opioid overdose crisis and responsible for the third wave of the opioid epidemic (1). Fentanyl can be used knowingly or unknowingly. It has become ubiquitous in the illicit drug supply across the United States, often added to or sometimes replacing other drugs, including opioids such as heroin and non-opioids such as methamphetamine. Fentanyl has also been found pressed into counterfeit pills to be sold to people who may believe that they are buying authentic prescription medications (e.g., oxycodone or Xanax) and even sprinkled onto marijuana. The effect of fentanyl and its analogs is 50 (or more) times stronger than the effect of heroin (2). The unintended use of fentanyl, especially by people who have not built up a tolerance for opioids, has led to a spike in drug overdose deaths across the country. The potency of fentanyl is such that even experienced users with opioid use disorder (OUD) and tolerance can easily miscalculate dosage and experience a fatal overdose. Overdose by fentanyl can occur by ingestion, inhalation or injection. Overdose by fentanyl cannot occur by exposure through skin (3).

The high potency of fentanyl may require multiple doses of naloxone to reverse a fentanyl-involved overdose. Due to fentanyl and its analogs’ tendencies to produce profound rigidity in the diaphragm, chest wall and upper airway within a narrow dosing range (wooden chest syndrome), routine administration of naloxone may not be successful in reversing respiratory depression without airway management. Buprenorphine induction can be more difficult in the case of fentanyl use, but microdosing can be a good option for starting when fentanyl is the main drug of use.

Black, Hispanic and Native people with OUD may be disproportionately affected (4). Potential contributors during the pandemic include treatment center closures, closure of harm reduction programs and decreased access to naloxone, physical isolation preventing bystander rescue, mental health stressors, financial instability and changes to drug supply networks.

In this paper we offer principles and recommendations for remediating the impacts of the rising rates of drugs adulterated or laced with fentanyl.
We endorse four principles to address the escalating fentanyl crisis embedded in the ongoing opioid epidemic:

1. **Pursue an incremental approach to behavior change (harm reduction).**
2. **Emphasize engagement for persons who use drugs, as a first step.**
3. **Use integrated care to initiate engagement and treatment.**
4. **Be vigilant for fentanyl as the rule rather than the exception.**

**Principles for Remediating the Impacts of Fentanyl**

1. **An incremental approach to behavior change, often called harm reduction, is the essential and primary principle that should be applied when implementing efforts to address the consequential impacts of fentanyl exposure and use.** Centered on “meeting people where they are, but not leaving them there,” the goal of harm reduction is not abstinence, but reducing risks involved with drug use and improving the health of people who use drugs. No one achieves recovery after dying of an overdose. Most patients seeking help for substance misuse aren’t initially trying to achieve abstinence. According to the Stages of Change theory, approximately only 20–30% are in the active stage of actually making a change, yet many substance use disorder (SUD) programs are designed for that group. We risk losing the opportunity to significantly improve the health and function of the other 70%. Meeting people where they are, delivering motivational enhancement and setting goals for incremental change and gradual engagement rather than solely for abstinence makes sense. Recovery is almost always an incremental process; safer use and reductions in use are interim steps to be valued. Persons should not be denied ongoing SUD treatment when reducing their use but not achieving complete abstinence. The recommendations following this section offer a range of specific, effective harm reduction interventions.

2. **The second principle is that engagement always precedes treatment.** Programs should strive to offer whatever information or services a person with substance use challenges is open to receiving and encourage them to come back for a follow-up visit.

3. **Integrated care is the third principle.** Many people who use drugs may be seen in primary care before SUD specialty treatment. Even if they are identified as having a substance use challenge and open to a referral, there are not enough SUD treatment programs available to treat all persons in need. We need to move upstream in the cascade of care for engagement and initiation of treatment. The inequity of access to health care in the United States results in many communities not having access to SUD treatment at all. The most effective intervention to treat OUD is induction onto one of the FDA-approved medications for OUD, which include methadone, buprenorphine and extended-release injectable naltrexone. Medical settings (e.g., internal medicine, family medicine, pediatric, psychiatric and obstetric), whether inpatient, outpatient or emergency, provide an opportunity to screen and intervene, with peer support specialists and recovery coaches maintaining engagement and transitions between treatment settings.

4. **Vigilance for the common problem of fentanyl-adulterated illicit drugs is the fourth principle.** Clinicians, program staff and the people they serve should all assume that street drugs are contaminated with fentanyl until proven otherwise and that any overdose involves fentanyl until proven otherwise.
Testing for Fentanyl

Fentanyl test strips (FTS) use the same technology as an at-home pregnancy test and were originally developed to detect the presence of fentanyl in urine. FTS are now often used to detect the presence of fentanyl in drug samples diluted in water prior to consumption. The majority of FTS on the market cost $1 per strip and are 96-100% accurate in detecting the presence of fentanyl (5,6,7). The strips can detect at least 10 fentanyl analogs. FTS have been distributed mainly by harm reduction organizations, such as syringe services programs, or through a distributor’s website, but in some states they can be sold at any convenience store or bodega or dollar store. They are inexpensive, simple to use and can be carried in a wallet or purse. The single-use strips work like other over-the-counter testing products: the user dips the strip into water containing a small amount of well-mixed drug residue and waits a few minutes for the result. The appearance of a single line signifies the presence of fentanyl or fentanyl analogs, such as acetyl fentanyl, and two red lines signifies its absence. FTS do not measure the quantity or potency of fentanyl or fentanyl analogs present in a drug sample. A negative FTS result does not mean that the sample is completely safe to consume; the sample may contain a fentanyl analog not detected by the FTS or it may contain other non-fentanyl adulterants of concern.

The legality of drug-checking supplies, such as FTS, still varies state to state. While some states still categorize FTS as illegal drug paraphernalia, other states — including New Mexico, Colorado, Rhode Island, Maryland and Arizona — no longer consider FTS to be illegal. FTS can now be purchased using federal dollars (8).

Several studies have investigated the impact of FTS. In one study, 85% of persons using illicit drugs desired to know about the presence of fentanyl before using drugs and reported positive behavior changes, including:

• Using a smaller dose.
• Snorting instead of injecting (10%).
• Pushing the plunger more slowly while the needle is still in the vein to gradually assess the effect of the drug.
• Having naloxone nearby. Using the drug with someone else around.
• Choosing not to use the drug at all.

Although more evidence is needed to confirm the impact of field FTS on behavior change, the indication that empowering people with information may help reduce harm is promising. There is no evidence that it has a permissive effect on promoting drug use.
TESTING USING MASS SPECTROMETERS OR REAGENT TESTING

FTS detect fentanyl and at least 10 fentanyl analogs. But with the increased enforcement efforts to combat the proliferation of nonpharmaceutical fentanyl analogs, illicit drug distribution networks have looked beyond those analogs detected by FTS to other emerging and less-regulated euphoric novel synthetic opioids as well as non-opioids which act synergistically with opioids. Any illicit drug sample could be adulterated with any number of adulterants, and the number of potential adulterants increases with every passing month. Recent availability of automated mass spectrometers allows identification of many adulterants, including fentanyl; however, they are expensive, require training to use and are not certified for use in clinics. They do not determine the concentration or amount of fentanyl or other adulterant in a sample. They are useful for public health and forensic monitoring in community populations.

DRUG SCREENING FOR FENTANYL

Current options for testing patients for fentanyl require formal laboratory handling. Standard urine drug screens do not include fentanyl, which must be ordered separately. Drug screening using oral swabs including fentanyl is available in the standard screening panels, and this form of testing may be more acceptable to many patients. Lack of a point-of-service fentanyl test that does not require sending out to a certified laboratory (Clinical Laboratory Improvement Amendments [CLIA] waived test) is a major obstacle to implementing rapid evaluation for fentanyl more widely.

Even in the absence of testing, the escalating prevalence of fentanyl in the drug supply (30-70+% of the opioid supply depending on the region, and unknown but increasing rates in other drugs) means that health care providers and drug users should think of fentanyl as the rule rather than the exception.
Recommendations for Remediating the Impacts of Fentanyl

1. All health care providers should periodically screen patients for use of illicit substances using validated screening survey instruments.

2. All health care providers should promote and increase access to harm reduction services and supports. People who use drugs should be:
   - Advised to assume that any illicit drug contains fentanyl until proven otherwise.
   - Provided with naloxone and educated on how to administer it.
   - Provided with FTS wherever possible and encouraged to use them regularly where available.
   - Advised to test an illicit drug that they have not used before.
   - Advised to take an initial highly diluted microdose of an illicit drug that they have not used before on the assumption that it contains fentanyl and could cause overdose.

3. Laboratory companies and health care systems should include fentanyl on all comprehensive drug screen panels.

4. The Centers for Medicare and Medicaid Services (CMS) should prioritize approving one or more point-of-service tests for the presence of fentanyl in blood, urine or saliva that does not require sending the sample to a certified laboratory (CLIA waived tests).

5. All states should make FTS legal for over-the-counter sales.

6. Hospitals should seize more opportunities to initiate medications for OUD (MOUD) and induct people on FDA-approved MOUD when they present for help. This includes during emergency room visits and prior to hospital discharge following an overdose. Interns, residents and fellows in ER medicine, internal medicine, psychiatry, obstetric and pediatrics receive inadequate education and are unprepared to identify and intervene in a meaningful and collaborative fashion that would have a real impact on outcomes.

7. Communities should better integrate urgent management in emergency departments and hospitals following overdose with continuing services in substance use treatment programs.

8. Local, state and federal law enforcement agencies should decriminalize substance use.

9. Communities should implement better integration of health care and SUD treatment and services with criminal justice stakeholders (10).

   - Increase access to deflection and pre-arrest diversion programs that encourage treatment in lieu of incarceration.
   - Increase access to evidence-based treatment for OUD and other SUDs in jails and prisons, including follow-up and linkages to community-based care and treatment. The highest risk of overdose is in the weeks following incarceration; all persons leaving incarceration should be advised of their increased overdose risk and provided with naloxone, FTS and linkage to care in the community.

10. Health care organizations, including primary care clinics, should give performance feedback to individual clinicians and programs on their rates initiating induction of MOUD medication-assisted treatment (MAT) and referral to OUD treatment.

11. Federal law and CMS regulation should include safe harbor provisions related to using Contingency Management for SUDs. Contingency Management is an evidence-based and highly effective treatment strategy for SUDs (11).
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References


