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Perspective

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Addressing the Fentanyl Threat to Public Health

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Fentanyl, a powerful synthetic opioid, poses an increasing public health threat. Low production costs encourage suppliers to "cut" heroin with the drug, particularly white powder heroin sold in the eastern United States.[1] Fentanyl also appears as a prevalent active ingredient in counterfeit OxyContin (oxycodone) tablets. The result is that fentanyl plays a major role in rising mortality due to heroin or opioid overdose. It poses a serious overdose risk because it can rapidly suppress respiration and cause death more quickly than do other opioids.

From 2012 through 2014, the number of reported deaths involving fentanyl more than doubled, from 2628 to 5544. We estimate that 41% of the roughly 7100 heroin-related deaths during this period involved fentanyl.[2] The graph illustrates this calculation, placing heroin and fentanyl at the center of continued growth in opioid-related mortality.

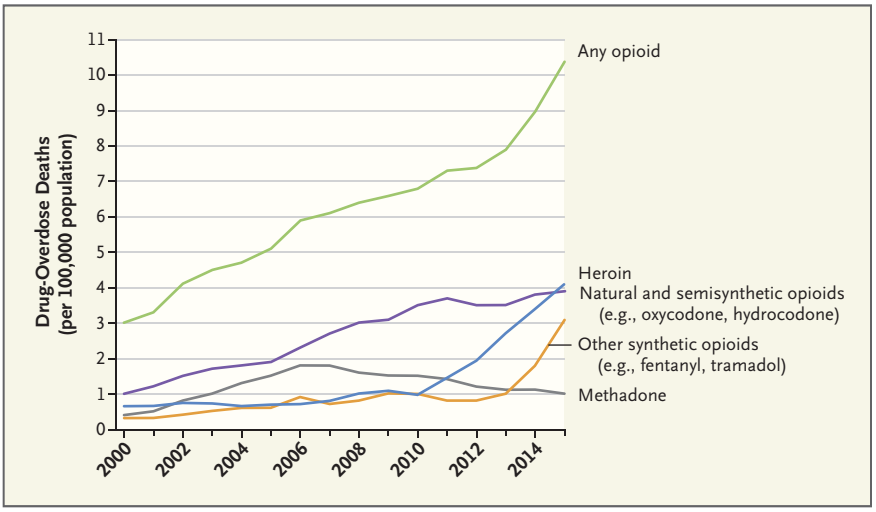
Governments are struggling to determine how best to deploy the tools at their disposal to address widespread fentanyl-related deaths. We believe there is merit to a harm-reduction approach involving increased transparency for users and public health and public safety organizations, harm-reduction policing, expanded naloxone use, and targeted treatment.

Many people who die from fentanyl overdose appear to have been unaware that they were using the drug.[3] In addition to being mixed with heroin, fentanyl is sometimes sold as methylenedioxymethamphetamine (MDMA), or ecstasy. Recent analysis in Canada showed that fentanyl was present in 89% of seized counterfeit OxyContin tablets. In the United States, recent fatalities have also been attributed to fentanyl in counterfeit Xanax (alprazolam), Norco (acetaminophen–hydrocodone), and other medications.

Rising fentanyl use reflects the drug's potency and low production costs. Even with declining prices, heroin costs about $65,000 per kilogram wholesale, whereas illicit fentanyl is available at roughly $3,500 per kilogram. Drug dealers thus face strong incentives to mix fentanyl with heroin and other street drugs. The drug appears to significantly reduce market prices of illicit opioids (and some other substances), while dramatically increasing risk.

Producing precise fentanyl doses also requires specialized equipment and knowledge. Street-drug suppliers who are unwilling or unable to provide precise dosing create especially acute overdose risks.

It's useful to distinguish "use reduction" and "harm reduction"



Drug-Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000–2014.
Data are from the Centers for Disease Control and Prevention.

as goals policymakers might adopt to minimize the social harms of fentanyl use. Simple use reduction aims to decrease the volume of illicit-drug consumption, whereas harm reduction seeks to reduce the harmful consequences associated with such use, even if policy measures don't reduce overall use.

In this case, a harm-reduction approach focuses on the fact that many drug users who die from fentanyl overdose don't know that they're ingesting it. Harm reduction therefore involves channeling use of heroin, OxyContin, and other products toward the least risky formulations. We believe that means using policy tools to make illicit markets more transparent, strengthen incentives for drug suppliers to avoid introducing fentanyl into their products, and increase the likelihood that overdoses can be reversed.

On the transparency front, law enforcement and the health care delivery system provide the two major institutional levers to address this public health threat. Both sectors offer opportunities for surveillance and development of an early-warning system about fentanyl's presence in various drug products. Improved epidemiologic surveillance systems such as the precariously funded Arrestee Drug Abuse Monitoring program are critical. Laboratory-informed epidemiologic surveillance tools that reach hidden or vulnerable populations typically missed by household surveys are also essential. Data from such systems can form the platform for an early-warning system like those recently adopted in Europe.

Harm-reduction technologies may also help redirect user demand away from products containing fentanyl, though their effectiveness is unproven. Pill-testing technology could be provided to clubs, festivals, police officers, and safe injection sites to detect the presence of fentanyl. Several European countries are using such approaches for detecting other additions to street drugs. These efforts, while promising, have yet to be carefully evaluated. For example, the track record of distribution of MDMA pill-testing kits is mixed. The promise is that by testing and helping to shift demand away from fentanyl-laden products, we can create incentives for drug sellers to undertake measures to prevent fentanyl from entering their products.

Within the policing arena, traditional drug-enforcement approaches emphasize use reduction. Given the dangers of a substance such as fentanyl, use reduction can indeed benefit public health by deterring distribution, sale, and use. Cracking down on illegal laboratories and other links in the supply chain would probably help disrupt the fentanyl market.

Over time, however, use reduction has often provided too little incentive for illegal-market participants to reduce public health risks.[4] Indeed, law-enforcement policies can aggravate public health harms. For example, intensive policing interventions — particularly those targeting buyers caught with syringes — increase needle sharing, raising the risk of HIV transmission.

In light of such experiences, some police departments and prosecutors have sought to align their efforts more closely with public health objectives. Thus, the aim is not to entirely suppress illicit-drug sales, but rather to channel the market in less harmful directions. Harm-reduction policing seeks to place the burden of reducing unintentional fentanyl consumption on the individuals and organizations than can most effectively reduce that risk. It may prove most effective to assign liability (through enhanced penalties or increased enforcement attention) to individuals and organizations (e.g., gangs) that supply illicit drugs containing

fentanyl. Right now, severe penalties are sometimes applied to dealers implicated in fatal overdoses. A more measured response would impose harsher penalties on distributors and sellers found to have sold drugs containing fentanyl, even if these drugs did not cause immediate harm.

Health care delivery has an equally key role in reducing the likelihood of death when overdose occurs and in preventing overdose through opioid-use disorder treatment. Naloxone is effective in preventing death due to overdose when administered in a timely fashion at the right dose. Naloxone can reverse fentanyl overdoses, but it appears to require more rapid administration (and perhaps escalation to additional doses) than is needed for heroin or other opioids.[5]

These facts have three implications: naloxone kits will need to meet higher dosage requirements when fentanyl is present; user-friendly formulations (intranasal and auto-injector) should be rapidly available at the site of a fentanyl overdose, which means equipping first responders with appropriate kits; and naloxone should be made available to users. That could be accomplished by provision of take-home naloxone, which would require altering pharmacy regulations in many states. It would also mean encouraging users not to use alone and teaching them how to respond if they encounter a likely fentanyl overdose. Timely availability of naloxone could also be provided by creating so-called safe bases for taking drugs — an approach that's been used with some success in Canada and Europe.

An audio interview with Dr. Frank is available at NEJM.org

Expanded access to evidence-based substance use disorder treatment — particularly medication-assisted therapy — would also help. The Affordable Care Act (ACA) includes provisions expanding access both within the specialty addiction sector and within general medical care. Although the ACA's future is uncertain, we are heartened by strong bipartisan support for its provisions on coverage for mental and substance use disorders and for other initiatives to expand access to treatment (in the 21st Century Cures Act).

Health care providers should recognize that treatment itself can pose overdose risks by reducing tolerance in drug users who continue to use at some level. Similar threats arise from periods of enforced or encouraged abstinence — hence the high overdose incidence among people just released from jails, prisons, or other secure settings, who would benefit from receiving naloxone and appropriate harm-reduction services.

Fentanyl's low production costs and high death toll pose a distinctive challenge that requires a concerted response. We believe a full package of prevention, treatment, and harm-reduction interventions is the best bet for reducing a frightening public health threat and saving lives.

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Disclosure forms provided by the authors are available at NEJM.org.

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