A nasal spray of the drug naloxone is used to revive a man who has overdosed on heroin.

SPENCER PLATT/GETTY

HARM REDUCTION

Too little, too late

Strategies to make drug use safer can curb opioid-related deaths, but interventions aren't reaching everyone.

BY CASSANDRA WILLYARD

Haven Wheelock carries a dose of naloxone everywhere she goes. She calls it a "magical medication" with the power to bring people back from the brink of death.

Wheelock runs a syringe-exchange programme for Outside In, a non-profit organization that provides medical care and other services for low-income and homeless people in Portland, Oregon. She has administered the opioid-blocking medication 21 times. The drug has never failed, but that doesn't make using it any less terrifying.

A few months ago, a woman overdosed across the street from the syringe exchange. Wheelock grabbed her naloxone kit, jumped over a metal barrier and raced across a road to reach the woman. She was lying on a filthy piece of forgotten land next to the motorway, with her lips turning blue. Wheelock squirted naloxone into one nostril, "And then I breathed for her, for what felt like a decade," she says. It didn't work. Wheelock administered a second dose, this time by injection. By the time the ambulance arrived, the drug had worked its magic. The woman was awake and talking.

The opioid epidemic in North America has become a public-health emergency. Synthetic opioids have brought about a surge in deaths since they entered the illicit drug market. In 2017, opioid-related overdose killed more than 50,000 people in the United States and Canada. To curb the death toll, "We need a fire hose on full tilt," says Susan Sherman, an epidemiologist at Johns Hopkins University in Baltimore, Maryland. "And we're just not there yet."

Getting there will require drug-use prevention and the treatment of addiction — both long mainstays of the public-health response to substance abuse. But it will also require a massive scale-up in harm-reduction interventions, which are strategies that acknowledge that abstinence is not an option for everyone, and that aim to make drug use safer. "The goal is to keep people alive," says Brandon Marshall, an epidemiologist at Brown University School of Public Health in Providence, Rhode Island. "You can't enter treatment if you're dead."

Although many harm-reduction strategies are already being adopted and expanded in the United States and Canada, serious political, legal and logistical hurdles stand in the way. Illicit drugs are more potent and deadly than ever before, access to naloxone is spotty, and sites where people can use drugs under the supervision of medical staff are still illegal in the United States.

LAZARUS DRUG

Opioid drugs work by binding to opioid receptors in the brain. This coupling produces a rush of dopamine, but it can also cause a person's breathing to slow dramatically or even stop. Naloxone works by binding to and blocking opioid receptors in the central nervous system. Because the medication binds more strongly to such receptors than do opioids such as heroin and fentanyl, it displaces the drugs that depress breathing. Naloxone was approved to reverse overdoses in the 1970s, but for decades it was available only in ambulances and emergency departments.

These days, naloxone is much easier to obtain. Police, firefighters and other first responders commonly carry the medication. Community programmes distribute it to drug users and their families. In April 2018, the US surgeon-general, Jerome Adams, issued an advisory that emphasized the importance of naloxone and encouraged people who come into contact with individuals at risk of an overdose to carry the medication. "Knowing how to use naloxone and keeping it within reach can save a life," Adams wrote.

The drug, previously available only as a liquid that had to be injected, has also become easier to use. In 2014, the US Food and Drug Administration approved a naloxone auto-injector called Evzio that provides verbal and visual instructions on how to use the device. And in April this year, the agency authorized a nasal-spray version of the drug, known as Narcan, which is what Wheelock used initially to help revive the woman by the motorway. The cost barrier to broader naloxone use is considerable: the branded version sells for US$4,100. Generic versions are on the way. Kaléo, the pharmaceutical company in Richmond, Virginia, that makes Evzio, announced that a generic form, which comes in a kit containing two doses, would retail for $178.

For naloxone to have an effect on opioid-overdose outcomes, it must be available to those who need it. In the United States, laws that govern access to naloxone differ from state to state. Between 2013 and 2016, nine states, including California, passed laws that give pharmacists the authority to dispense naloxone to anyone without a prescription. Other states, however, allow pharmacists to sell naloxone only to people who meet certain criteria, such as those who are enrolled in an addiction-treatment programme.

Researchers from global policy think tank the RAND Corporation and William Patterson University in Wayne, New Jersey, examined how differences in such laws affect overdoses[1]. The team's analysis suggests that US states that permit pharmacists to distribute naloxone to anyone had the greatest decreases in overdose deaths. In those states, the number of such

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deaths fell by an average of 27% in the second year after the laws were enacted, with greater declines occurring in subsequent years. Laws that stop short of permitting pharmacists to dispense the drug to anyone had little effect on overdose deaths.

Even where the law allows access to naloxone, however, there are still barriers to overcome. The stigma that surrounds drug use can be intense. Some drug users might feel unable to walk into their local pharmacy — where friends and neighbours shop — to purchase naloxone. And even when they do, there is no guarantee that they will find what they came for. In a 2017 study, researchers found that only around one-quarter of the pharmacies in Canada that they contacted had the drug in stock[2]. And although California's laws allow pharmacists to provide naloxone without a physician's prescription, a 2018 'secret shopper' study of more than 1,000 pharmacies found that just 23% were willing or able to do so[3].

For those who cannot or will not get naloxone from a pharmacy, Jamie Favaro offers an alternative: delivery by post. In 2017, the social worker and harm-reduction advocate launched NEXT Distro. The project enables people to request drug-use supplies online, which are then delivered to their home. The kits include everything that would be available at a syringe exchange, including naloxone, syringes, alcohol pads and bandages. Because such kits fall into a legal grey area — syringes combined with drug-related educational material could be considered to be drug paraphernalia — the project is authorized to operate only in New York state, which granted NEXT a waiver to operate as a syringe exchange. A related project, Next Naloxone, ships the overdose antidote to drug users and their friends and family members. Supplies from both projects are free, thanks to the support of foundations and private donations. "This project is really about economic and social justice," Favaro says.

A client at the supervised injection site Insite in Vancouver, Canada, collects her kit.

LEFT: LAURENT VU THE/AFP/GETTY; RIGHT: SALWAN GEORGES/*THE WASHINGTON POST* VIA GETTY

BEHIND BARS

One group of people at high risk of overdose are those recently released from prison. Opioids can be hard to come by in jails. By the time that inmates are released, "Their tolerance for the opioid is no longer there," says Alex Kral, an epidemiologist who studies criminal justice and substance use at RTI International, an independent research institute in San Francisco, California. Yet they might still use the same amounts that they did before they were incarcerated. A 2007 study showed that inmates in Washington state were 129 times more likely to overdose in the 2 weeks after their release than were people who had not been in prison[4]. Former inmates' risk of death — the leading cause of which was drug overdose — was 13 times higher.

To combat such deaths, some US states, including New York, have begun to offer naloxone to inmates on release. According to the US Bureau of Justice Statistics, more than half of people in state prisons and local jails have a drug dependency or abuse drugs, so providing naloxone makes sense, says Kimberly Sue, medical director of the Harm Reduction Coalition, an advocacy group in New York City. "We should be lowering barriers," she says.

Rhode Island provides naloxone to inmates on release, but also offers a comprehensive opioid-addiction treatment programme. Launched in 2016, the scheme enables former inmates with a history of dependency to obtain one of three medications: methadone, buprenorphine or naltrexone. Traci Green, an epidemiologist at Brown University, and her colleagues compared the number of post-incarceration overdose deaths during the six months before the programme began with the same period one year later[5]. They found a 61% decrease in such deaths. That decrease contributed to a 12% reduction in overdose deaths in Rhode Island. "The correctional system is one that is deserving, worthwhile, and critical to addressing our current opioid crisis," Green says. "It's actually going to be the way that we make a faster exit out of this horrible situation that we're in."

POISONED SUPPLY

Illicit drugs have become so deadly mainly because they are now being diluted with fentanyl. This powerful painkiller has been administered to patients during surgery since the 1960s, and is still commonly prescribed for post-operative and chronic pain. But in the past decade, fentanyl and other synthetic opioids have made their way into the illegal-drug supply. These drugs are cheaper than heroin and more potent, so some suppliers began to add them to heroin to maximize profit.

Fentanyl's potency makes it particularly deadly. "Overdose is immediate," Kral says. "You have a very small window to resuscitate someone." Research by the US Centers for Disease Control and Prevention shows that the number of opioid deaths involving fentanyl roughly doubled each year from 2013 to 2016. "What we're dealing with right now is a toxic drug supply. People are being poisoned," says Thomas Kerr, director of research at the British Columbia Centre on Substance Use in Vancouver, Canada.

Technologies that enable drug users to test for fentanyl could help. The simplest, cheapest detection device is a test strip containing antibodies that bind to fentanyl. People can use the strips to detect fentanyl in their urine, but they can also test the drugs that they plan to take by mixing a little of it with water and dipping the end of a strip in the solution. The presence of fentanyl will yield a positive result. But how useful these test strips are is unclear. In some cities, contamination with fentanyl is becoming the norm. At a supervised consumption site in Vancouver called Insite, for example, 84% of heroin samples that were tested between July 2016 and June 2017 contained fentanyl[6]. "Dealers are flooding the market with it," says Geoff Bardwell, who studies harm-reduction interventions at the British Columbia Centre on Substance Use. In places such as Vancouver, where fentanyl is so common, a positive result isn't particularly meaningful. What's more, people might not be willing to use the strips. When Insite offered its visitors fentanyl test strips, for instance, only about 1% accepted, and most tested their drugs after they had already used them.

But other locales have had more success. Marshall and his colleagues recruited 93 young adults from Rhode Island who use drugs, and gave them 10 strips each to test either their

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A drug thought to be the potent opioid fentanyl is tested in a lab.

drugs or their urine for fentanyl[7]. One month later, 77% reported using at least one test strip. Half got a positive result for fentanyl contamination. Of those people, half reported that they then altered their behaviour by taking a smaller dose at first, keeping naloxone nearby, using drugs when other people were present, or even, in a few cases, discarding the drug.

More-sophisticated devices can provide information about the amount of fentanyl and other potential contaminants in drugs, but they also come with downsides: the machines are expensive to buy and run, and people who use drugs have to hand over some of their supply (or used paraphernalia) to a technician to be tested at a syringe exchange or other facility. Because of the stigma that surrounds drug use and the fear of arrest, some people might not be willing to do so. The participants in Marshall's study, for example, "really liked the fact that they could take the test strip home and use it in a private environment", he says.

SAFE ROOM

In Canada and Australia, people who use drugs have an option for taking them that is not available in the United States: facilities that allow people to bring in and use drugs in a clean environment under the supervision of trained staff who are equipped with naloxone. "When it comes to opioid overdose, one of the best tools we have is supervised drug-consumption rooms," Kerr says. "There have been millions of injections performed in supervised consumption facilities throughout the world — there's never been a fatality."

Despite strong evidence that these sites, which include Insight in Vancouver, save lives, only one such site exists in the United States — and it is unsanctioned. The site, which launched in 2014, operates in an undisclosed location to stay hidden from law enforcement. The facility provides six injection booths, clean needles, supervision by staff members or volunteers and naloxone in case of overdose. According to data presented in April at the 26th Harm Reduction International Conference in Porto, Portugal, about 540 people have performed more than 9,000 injections at the site since it opened. Owing mainly to fentanyl contamination, the overdose rate has increased dramatically during that time — from 1 per 1,000 injections in 2015 to 6 per 1,000 in 2019 — yet none of the 26 people who overdosed at the facility died.

Many US cities have proposed opening safe injection sites, but Philadelphia in Pennsylvania might be first to act. Safehouse, a non-profit organization that launched in the city in 2018, hopes to open a safe consumption site. But in February, the federal government sued Safehouse and claimed that creating such a facility would violate the US Controlled Substances Act. The law contains a section that prohibits people from opening or running places where illegal drugs are knowingly used. Safehouse, which filed a countersuit in April, claimed that the law does not apply to a non-profit organization that is providing a "good faith, public-health approach to overdose-prevention services, including a supervised consumption room". The legal battle has yet to be resolved, but advocates hope that a win for Safehouse would set a precedent for bringing similar facilities to other cities.

Sue finds the resistance to supervised injection sites in the United States frustrating. "I get very angry because I have the same conversation, over and over again," she says. No one in the harm-reduction community, she contends, views safe consumption sites as a panacea for the opioid crisis. "It's a very specific intervention to solve a very specific problem," she says. "We need to keep people safe from dying."

Supervised injection sites are particularly controversial, but all harm-reduction strategies have received push-back at one time or another. In the United States, "We really do feel like substance use and addiction is a choice and it's a moral failing," Sue says. To some people, harm-reduction efforts look like an endorsement of drug use. But advocates say that they form a crucial piece of an effective public-health response to a complex problem. The strategies not only save lives, but also help to connect people who use drugs with health-care services, including referrals to treatment programmes. "So much is just focused on prevention, treatment and interdiction," Sherman says. Harm reduction often gets dismissed as being too radical.

Even some senior government officials struggle to accept the value of harm reduction. In a 2018 blog post about fentanyl test strips, Elinore McCance-Katz, assistant secretary for mental health and substance use at the US Substance Abuse and Mental Health Services Administration in Rockville, Maryland, seemed to argue against the use of harm-reduction strategies when she wrote: "There is known, life-saving, evidence-based, medication-assisted treatment available to individuals who have these conditions. Let's not write off their access to that; let's not determine in advance that they won't seek help, and let's not rationalize putting tools in place to help them continue their lifestyle more 'safely'." McCance-Katz declined to provide additional comment.

Those sentiments are difficult to hear for people such as Wheelock. "We know what works, and we can't bring it up to scale," she says. The result is heartbreak. Wheelock went through a two-month period in which she lost one friend or acquaintance weekly. She saves as many people as she can, but each rescue takes an emotional toll.

After she revived the woman by the road, Wheelock made her way back across the road and lit a cigarette. She is known for being calm — even bossy — in a crisis. "Then, as soon as everything is taken care of, I cry," she says. "Every time." ■

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