Facing fentanyl: should the USA consider trialling prescription heroin?

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In 2016 in the USA, 19 547 fatal overdoses (about a third of all fatal overdoses) were attributed to synthetic opioids, primarily fentanyls.[1] Fentanyl, almost always sold as or mixed with illicitly sourced opioids, sharply increases risk of overdose. Its potency (roughly 50 times that of heroin) makes accurate dosing and titration difficult. The duration of desired effects is shorter than that of other abused opioids, necessitating more frequent dosing. Each of these factors increases risk of overdose and the social damage caused by non-prescription opioid use. Additional interventions that take account of the increasing lethality of street drugs are needed.

Price, concealability, and accessibility make fentanyls attractive for drug dealers. In some North American street opioid markets, fentanyls have become ubiquitous. Insite, Vancouver's drug consumption outreach service, tested 173 samples in July, 2016, and found that more than 90% of the drugs they tested that were reported to be heroin or mixtures containing heroin also contained fentanyls.[2] According to the European Monitoring Center on Drugs and Drug Addiction, fentanyl has become the most commonly used opioid among injecting drug users in Estonia.[3]

Data from death certificates in the USA show that synthetic opioids (which are primarily fentanyls) account for the increases in deaths from heroin and prescription opioids since 2014 (figure).[4] More surprisingly, synthetic opioids also appear to account for the increase in deaths from cocaine.

Policies have failed to reverse, or even slow, the sharp rise in opioid overdose deaths in the USA. Apart from recommending increased interdiction of synthetic opioids and the development of higher-affinity longer-acting antagonists, the US Government has not developed policy interventions specifically targeted at fentanyls.[5] Persuading opioid users to avoid street markets takes on a new urgency. Expansion of opioid substitution therapy and naloxone is imperative. Yet, methadone and buprenorphine are unappealing to many dependent users and some methadone patients continue illicit drug use.[6] As fentanyl permeates illicit markets, heroin-assisted therapy (HAT), a treatment modality that is offered in Europe and the UK but dismissed in the USA, deserves serious consideration.

Under HAT, dependent heroin users in whom other treatments have failed are given pharmaceutically manufactured heroin several times per day in clinics. With clinical advice, patients find an appropriate dose, typically stabilising within 3 months at about 500 mg per day.[7] The UK of course has a long tradition of permitting heroin prescription by individual physicians, but few patients are maintained on heroin, principally because of cost.

A randomised controlled trial in the UK found that 31 (72%) of 43 patients receiving supervised injectable heroin had reduced consumption of illicit heroin compared with 11 (26%) of 42 patients receiving oral methadone, and 38 (88%) of 43 patients receiving injectable heroin remained in the study at 26 weeks compared with 29 (69%) of 42 receiving oral methadone.[8] Similar studies from Switzerland and Germany have shown that HAT decreases the use of illicit substances and increases patient retention.[9,10] No study has not found a substantial improvement in major outcomes with use of heroin versus methadone. Unlike other harm reduction policies proposed, such as take-home naloxone, HAT reduces the risk of overdose by rapidly removing users from street markets.

Though successful at the individual level, HAT does have low participation rates (about 10% of chronic heroin

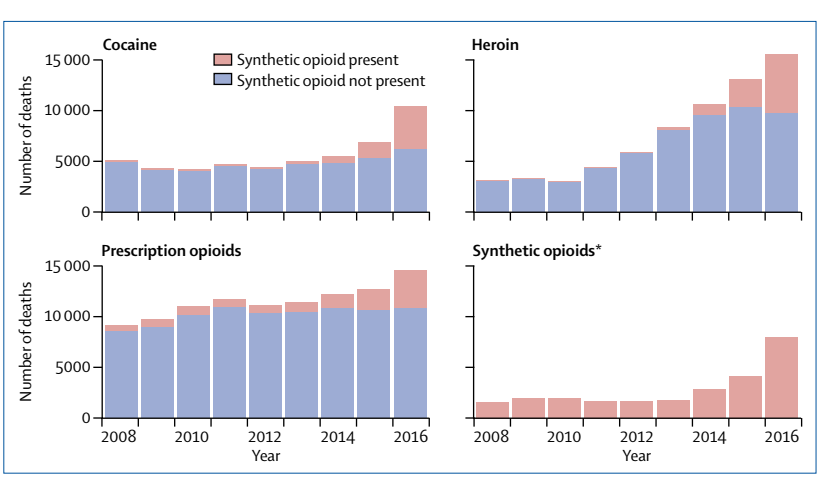

Figure: **US drug overdose deaths**
Data are deidentified public use multiple cause of death certificate files produced by the National Center for Health Statistics, years 2008–16.[4] *Excludes cocaine, heroin, prescription opioids, and psychostimulant deaths.

users in Switzerland[11]), limiting the public benefits that would warrant the cost and debate over such treatment.[12] However, the extent of adoption required to produce a desired population-level effect in the USA is unknown. But the increased lethality of today's street opioids (ie, higher chance that a use will result in fatality) in the USA versus 5 years ago might motivate participation, especially in fentanyl-saturated markets. HAT might be an effective treatment option for only a modest share of regular heroin users. However, shifting even 10% of dependent heroin users from a market awash with fentanyl might be cost-effective by reducing overdoses, criminal activity, repeated emergency service calls, emergency department episodes, and the social contagion of drug use.

Piloting HAT in the USA, let alone its adoption as a routine treatment, faces many complications. Heroin's Schedule I classification creates legal barriers for an experiment, and the political obstacles are even more daunting. Some will balk at the adoption of a programme involving the distribution of the opioid with the greatest associated historic harm and insist that this problem can only be solved by expanding already available treatments. Beyond this, practical issues exist, such as safeguarding heroin in high-crime environments and making it accessible to a population that is more dispersed than in cities such as Zurich and Amsterdam.

Yet it would be irresponsible to ignore the accumulating research base that shows that HAT can be an effective intervention. Denmark adopted HAT in 2010 without any clinical trial, given the strength of the available evidence. HAT does not solve the opioid problem. Nevertheless, if done properly and in conjunction with existing treatment options, it can make a life-saving contribution. The barriers facing HAT in terms of political opposition and practical implementation are hardly more daunting than those that faced needle exchange programmes in the USA during the mid-1980s.

A trial could involve a small number of sites, selected for the variety of challenges. For example, one site might be urban with high numbers of heroin overdoses, good social and treatment services, and adequate public transportation (ie, one with great need and a promising environment for HAT). Other jurisdictions might be chosen in which some of the facilitating factors are absent. HAT might well be an intervention that should be implemented only in communities with specific characteristics.

Resources and attention should continue to expand access to opioid substitution treatment and naloxone. But evidence from programmes in the UK, continental Europe, and Canada, coupled with the increasing urgency to get users out of street markets, strengthens the case for more targeted harm-reduction policies. HAT is not an alternative to other policies that aim to reduce the demand for and supply of illicit opioids, such as drug education prevention and law enforcement. In the context of a true public health emergency, previously unpalatable interventions need serious and prompt consideration.

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