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COMMENTARY

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Commentary on Copeland *et al.*: Does xylazine in the United Kingdom foreshadow a European synthetic polysubstance drug crisis?

A Taliban opium ban threatens Europe's heroin supply. The discovery of xylazine in counterfeit pills and vaporisers in the UK—mixed with fentanyls, nitazenes and designer benzodiazepines—potentially foreshadows a polysubstance, synthetic drug crisis. Despite great uncertainty, renewed efforts are needed to track synthetics and provide safer options.

A ban announced by the Taliban in 2022 resulted in a ~95% decrease in the cultivation of poppy plants in Afghanistan by 2023 [1]. Because Afghanistan serves as the primary supplier of heroin to Europe, there is considerable concern that—as stockpiled supplies dwindle over the coming years—widespread replacement by powerful synthetic opioids may occur. In a worst case scenario, this could trigger an overdose crisis similar to that seen in North America over the past decade [2, 3].

Lessons from other heroin supply disruptions, including a prior Taliban opium ban in 2000 to 2001, indicate that displaced demand for heroin often shifts to other substances [4]. In a best-case scenario, demand for heroin would be replaced by expanded uptake of treatments like buprenorphine, methadone, diacetylmorphine maintenance programs or other medical safer supply regimens. Illicit markets can also occasionally spontaneously shift toward safer products, such as the uptake of diverted buprenorphine in Finland during the 2000 to 2001 heroin shortage [4]. It is also plausible that demand would switch drug classes, leading to a greater use of illicit stimulants or diverted benzodiazepines, which can cause considerable morbidity, but are less likely than opioids to result in fatal overdose. However, there is substantial precedent for consumption to switch to synthetic opioids, such as fentanyls or nitazenes, which has occurred broadly in North America, and in more limited instances in Europe [3, 4].

Copeland *et al.* [5] provide novel evidence of the sophistication of synthetic drug markets in the United Kingdom. They find that xylazine—a veterinary tranquilizer that has increasingly been used to augment the fentanyl supply in the United States [6, 7]—is broadly present in the United Kingdom. They report cases of xylazine found in counterfeit pills ostensibly sold as various prescription medications, and in vaporizers 'vapes' ostensibly containing Δ-9-tetrahydrocannabinol. Among overdose deaths, xylazine was present alongside a dizzying array of synthetic substances, including fentanyls, nitazenes and designer benzodiazepines. The detection of powerful polysubstance formulations, in counterfeit products, mirrors current trends in North America, albeit at a smaller scale.

Their findings add to an emerging body of evidence about rising synthetic polysubstance use in Europe. In addition to the United Kingdom, xylazine is also spreading in Estonia [5, 8]. Dozens of novel synthetic opioids have been detected sporadically in European markets over the past decade [9]. Yet more recently, several have risen sharply in prevalence among overdose deaths. Nitazenes have driven increased numbers of deaths in Estonia, Latvia and the United Kingdom [2, 10, 11] and they have also been reported recently in France [12] and Ireland [13]. Novel synthetic 'designer' benzodiazepines have also been rising in prevalence across European nations [14], in particular etizolam, which is now implicated in two-thirds of overdoses in Scotland [15]. When taken together, these examples may represent early evidence of a broader shift toward synthetic drugs replacing agricultural products (like heroin) in Europe.

An additional concerning aspect of the findings presented by Copeland *et al.* [5] is that xylazine was packaged in counterfeit pills and vaporizers. In North America, counterfeit pills have broadened the populations affected by the rising overdose crisis, including adolescents [16]. Diverted prescription opioids are already involved in a growing fraction of all overdose deaths in several European nations [2, 17]. The packaging of synthetic drugs in counterfeit products may increase the likelihood of widespread uptake, given the decreased barriers to initiation with pills and vaporizers compared to powder drug formulations.

Although it remains impossible to accurately predict if synthetic opioids will expand exponentially in Europe, there is ample room for concern. In response, improved surveillance is needed to understand the scope of synthetic drug use [18]. Ensuring comprehensive testing for novel synthetic substances in overdose toxicology is valuable;

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however these data typically suffer from long reporting delays. Comprehensive testing through wastewater surveillance represents an underutilized, but timely approach to understand population-level dynamics [18]. Drug checking services in harm reduction spaces can offer similar insights and empower the consumers of synthetic drugs to shift their demand toward safer products.

Should heroin supplies plummet across Europe, the best-case scenario would be their replacement by medically administered products such as buprenorphine, methadone and other safer supply initiatives. Inspiration can be drawn from the Norwegian experience during the previous Taliban opium ban. The country significantly expanded access to methadone, and the engagement of people who use drugs in social and health services, and subsequently saw large decreases in overdose mortality [4]. Similarly, the widespread barriers to accessing social and health services in North America are broadly thought to be driving the overdose crisis there. Better access to these services in Europe is believed to have been a key protective factor [19]. Therefore, the current potential crisis in Europe may represent a valuable opportunity to invest in renewed addiction treatment and social services to prevent demand for synthetic opioids from taking hold.

KEYWORDS

counterfeit, drug checking, Europe, opium ban, overdose, polysubstance, safer supply, xylazine

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