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NEW PSYCHOACTIVE SUBSTANCES: DRIVING GREATER COMPLEXITY INTO THE DRUG PROBLEM

New psychoactive substances both disrupt and support how the illicit drug market functions, driving greater complexity into the drug problem. Whichever regulatory approaches are pursued, early-warning systems should play a central role in protecting public health by detecting and prioritizing signals of harms and communicating this risk effectively.

The world is becoming increasingly complex. Part of the fallout from this is a steady stream of new risks that emerge and that can threaten public health. Some are familiar, others are novel. Spurred by globalization, the (re)emergence and spread of infectious diseases and the growth of the market in unlicensed and fake medicines are just two examples of policy areas that have required extensive changes to their regulatory systems—both at the level of legislation and implementation—to manage such risks more effectively (e.g. [1,2]). Further changes may be required in the future as new risks emerge. The field of drugs has not been immune to these global changes either [3]. As Reuter & Pardo note [4], one particular challenge are new psychoactive substances—a textbook, if not a little unorthodox, example of what can happen when entrepreneurs exploit globalization and technology.

Attempts to outwit drug laws by producing drugs that are not controlled are not new. In the 1920s pharma produced vast quantities of the morphine esters benzylmorphine and acetylpropionylmorphine to sell on the illicit opioid market [5]; in the 1960s, following the discovery and synthesis of tetrahydrocannabinol (THC), raids on clandestine laboratories found the ingredients and recipes to make 'synthetic marijuana' [6]; while in the late 1970s the fentanil α -methylfentanyl was being sold as heroin or 'synthetic heroin' [7]. What is new is the size, reach and complexity of the contemporary market in new substances. The explosive growth in their availability is not driven by clandestine laboratories, but by legitimate chemical and pharmaceutical companies in China [8,9]. These companies churn out vast quantities of legal replacements to controlled drugs—cannabinoids, stimulants, opioids, benzodiazepines—and ship them cheaply and quickly to Europe and elsewhere. From here they end up as 'legal highs', 'research chemicals' or 'food supplements' which are sold openly in the high street and online. They are also sold on the illicit drug market, either under their own name or passed off as illicit drugs such as ecstasy, heroin or cocaine. Of increasing concern is the number of counterfeit medicines being seized containing new substances, the most common fakes being tablets sold as diazepam and alprazolam.

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) monitors almost 600 new substances through the European Union (EU) Early Warning System—the vast majority detected in the last 5 years or so. Of course, many of these will not be a hit with users (how many of the drugs controlled under the UN Conventions are?); but this is not the point for the mass market. Given how fashions and societies change, it is true that we do not know what the fate will be for many substances [remember that Quaaludes, not MDMA were the original disco biscuits]; but it is also fair to say that suppliers are not looking for the next cannabis, MDMA, heroin or diazepam; they simply make substances

that can mimic their effects and that can be produced, transported and sold freely. In reality, most new substances are disposable, as manufacturers have replacement substances ready for sale even before a substance is controlled; the recipes for many thousands more are in the scientific and patent literature ripe for the picking, making the 116 controlled by China last year a drop in the ocean. Developing an effective regulatory system to limit the manufacture of new substances would appear to be a major challenge.

Many of the current epidemiological indicators are poorly suited or configured to monitor new substances. This reflects the complexity and highly dynamic nature of the market, including the fact that many users do not actually know what substance they are using. These limitations make quantifying the size of the public health threat difficult. None the less, signals from the EU Early Warning System and other sources suggests serious cause for concern. The market continues to grow. Consumers are no longer limited to psychonauts and clubbers, but include the vulnerable and marginalized, such as problem drug users and prisoners; they also include people who use new substances to self-medicate, as well as to enhance the body and mind [3]. There is strong evidence that some new substances are causing serious harms. These include serious non-fatal as well as fatal poisonings [10–14]. One striking development are outbreaks of mass poisonings caused by ‘legal highs’ containing synthetic cannabinoids. In 2014 in Russia, products containing MDMB-FUBINACA were linked to more than 600 poisonings, including 15 deaths over 2 weeks [10]. More than 700 suspected poisonings, including nine deaths with a possible link to ADB-FUBINACA, were reported in Mississippi, USA during 1 month in 2015 [11]. While outbreaks have been rare in Europe, during 2015 more than 200 people were hospitalized over a few days in Poland after smoking a product called ‘Mocarz’. The cause of these mass poisonings are due to the high potency of synthetic cannabinoids, that producers guess how much substance to use, and poor manufacturing processes leading to uneven distribution of the substance in the product—manufacturing flaws that are a recipe for disaster. A similar problem exists for the fentanils. Changes in the patterns of drug injection are also being driven by new substances [15–18]; the fallout from this includes HIV and hepatitis C, as well as bacterial infections which have sometimes manifested as outbreaks.

Writing on the topic in 1975, Alexander Shulgin noted that: ‘the variety of drugs currently involved in the drug abuse problem is very extensive. As these materials become better defined and their use better controlled, they will be replaced with substitute compounds, which will provide society with new, unknown, and unmanageable substances’ [19]. Are contemporary new psychoactive substances the epitome of Shulgin’s predictions? Faced with

this scenario, it certainly gives pause for thought on the choices of regulatory approach.

Whichever approaches are pursued, it is likely that over time they will need to be changed to respond to this dynamic market and increasingly innovative attempts to circumvent regulation. In addition, early-warning systems will need to be strengthened so they continue to play a central role in protecting public health by detecting and prioritizing signals of harm and communicating this risk effectively.

Declaration of interests

None.

Keywords Early-warning systems, counterfeit medicines, fentanils, globalization, mass poisonings, new psychoactive substances, synthetic cannabinoids.

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A CHORUS OF PESSIMISM SURROUNDING THE NEW PSYCHOACTIVE SUBSTANCES PROBLEM

States are troubled by the challenges posed by new psychoactive substances (NP). A growing chorus of scholars are critical of blanket bans, such as the one adopted recently by the United Kingdom. Little is known about the consequences of the ban; good evaluations of the experiences of Ireland, Australia and the United Kingdom are needed urgently.

We welcome the insightful comments to our paper [1] questioning the effectiveness of the UK ban on new psychoactive substances. Each author's comments highlight the difficulties facing countries attempting to regulate the

rapidly evolving market of non-controlled psychoactives. Perhaps more troubling, the chorus of regulatory challenges from other times and places reaffirms our underlying pessimism about the solubility of the new psychoactive substances (NPS) problem; the available choices all leave much to be desired.

Any effort to create a legal regulatory system is almost certain to face challenges both in court and in the market. Much more is known today about neurology, the brain, chemistry, etc. than when states first controlled 'traditional' drugs 50 or 100 years ago; this advantages the producers. Control is complicated further by the fact that, as Evans-Brown & Sedefov [2] point out, globalization makes supply of such drugs easier than before. Given these challenges, more states are seriously considering blanket bans as one solution; our paper failed to note that Australia imposed such a ban in 2015 [3].

However, the commenters share our apprehension about this approach. Krajewski underscores the lack of evidence of harm and the almost reactionary response of the state to ban mind-altering substances [4]. A sweeping application of the precautionary principle precludes data collection and assessment, as Uchtenhagen reiterates [5]. More troublesome is that a blanket ban ignores the full scope of the problem, namely the drivers behind demand for these substances. Uchtenhagen alludes to the fact that benefits are absent in the discussion of regulation of NPS [5]. Such benefits include medical, but he also touches upon the spiritual/recreational benefits of use of certain drugs; these are rarely part of the drug policy debate [6].

In order to frame the NPS problem properly we argue that states ought to consider the weight of benefits [7]. Wilkins & Rychert aptly detail the most recent developments of New Zealand's Psychoactive Substances Act [8]. For all the law's shortcomings, it was innovative in recognizing pleasure as a benefit. However, implementation has stalled and now the law functions as a blanket ban. Given that New Zealand's law punishes personal possession, authors note that it may be even harsher than the UK law.

Will a blanket ban succeed in displacing drug use away from NPS towards the traditional substances that they mimic? Krajewski's hesitation to endorse our argument is reasonable, and we believe that this probably will depend upon the class of drug, in addition to the nature of its supply chain. Some NPS may offer entirely new drug experiences, gaining some modest market share. For some users, principally those not subject to drug testing, natural cannabis may emerge as a less harmful and more attractive alternative to cannabimimetics currently on offer. However, Evans-Brown & Sedefov echo Krajewski's point that some substances, particularly uncontrolled opioids, may become 'increasingly intertwined'