



HHS Public Access

Author manuscript

Addiction. Author manuscript; available in PMC 2023 March 08.

Published in final edited form as:

Addiction. 2019 May ; 114(5): 785–786. doi:10.1111/add.14587.

Fentanyl: the many challenges ahead

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We welcome the insights, comments and recommendations of all the respondents to our earlier published report [1–4]. We agree fully with Dr Wakeman’s assessment that further crackdowns on the fentanyl supply would likely have disastrous effects on opioid users, favouring the more potent, more concealable analogues. The current system of global prohibition, rather than offering strategies to resolve the current fentanyl problem, it is likely its cause and it is time to consider alternative remedies. In Portugal, drug possession and acquisition have become civil rather than criminal offences and an evidence-based drug strategy has been introduced to prevent drug use, expand treatment for dependence and dissuade others from continued use. This has shown encouraging results and deserves further study as a possible paradigm [5, 6].

Dr Bisaga makes many excellent points about the challenges fentanyl presents to existing opioid treatment modalities and the need for more empirical data for their revision. Buprenorphine induction is known to precipitate withdrawal among persons who are opioid dependent but the protracted withdrawal from short-acting fentanyl use reported by Dr Bisaga is puzzling. Research among active heroin injectors has found that, while some experience suspected fentanyl as having a short duration of effect, others report it lasting for many hours, even in cases of high opioid tolerance [7]. Further studies of illicitly manufactured fentanyls’ pharmacodynamics, including analogs, mixtures, adulterants and contaminants, are needed to understand this apparent contradiction. A modified Zurich or Bernese method, utilizing microdoses of buprenorphine while tapering full agonist opioids [8], looks promising. Research on full agonist substitution therapies, eg using hydromorphone, as well as ones with a longer pedigree, such as heroin maintenance therapy, should also be pursued [9].

We strongly concur with Mounteney and colleagues that surveillance along with international data sharing are essential for perceiving the commonalities and differences in the global fentanyl epidemic [10]. In dividing these into macro regions, however, we would take issue with the North American/European split. It is certainly the case that Europe

Conflict of interest declaration: None

and the United States differ in their health care arrangements, treatment services and opioid supplies but Canada also presents some contrasts with the US. Like the US, Canada's opioid pill prescribing has outstripped the rest of the world but it has different heroin sources and a system of universal healthcare, although less comprehensive than in some European countries. Canada also has progressive harm reduction and treatment policies including over 25 supervised consumption sites and government approved prescription of heroin for the treatment of opioid use disorder.

We agree that diverted pharmaceutical fentanyl presents a different case to fentanyls that are illicitly manufactured. Pharmaceutical fentanyl, often in the form of patches, is easily identifiable so users' demand can play an active role in the market. However, the replacement of heroin by illicitly manufactured fentanyl in its disguised form, regardless of whether heroin's demand is high in the US or low in Europe, is a further piece of evidence that the switch to illicitly produced synthetics is driven by supply factors and not by demand.

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