

Project Details	
Project Code	MRC21NMHBr Hickman
Title	Assessing the contribution of novel illicit benzodiazepines to the increase in opioid overdose deaths
Research Theme	Neuroscience & Mental Health
Summary	There has recently been an increase in overdose deaths where both opioids and illicit benzodiazepines (BZDs) are present. We wish to establish first how heroin users view the advantages and dangers of taking these drugs and then to assess in laboratory studies the interactions between novel BZDs and opioids at the cellular and whole animal levels to determine the mechanisms by which they might interact to heighten the likelihood of overdose.
Description	<p>Heroin users are often polydrug users also taking one or more of alcohol, BZDs, crack cocaine, amphetamines and gabapentinoids along with heroin or while on opioid substitution treatment (OST) with methadone or buprenorphine. In recent years there has been an increase in opioid overdose deaths and in many of these a BZD is also present. Whilst BZD use by heroin users is well established the recent appearance of novel, potent illicit BZDs (alprazolam (Xanax), etizolam and flualprazolam) would appear to have increased the incidence of overdose deaths in which these drugs and an opioid are present. What we do not know at present is whether drug users are taking larger doses of these illicit BZDs that are more likely to contribute to overdose because they are cheap and readily available or whether these newer BZDs are in themselves more dangerous, especially when combined with opioids. To investigate the reasons behind and consequences of co-use of opioids and BZDs we will first interview heroin users to elicit their views on the effects and dangers of Xanax, etizolam and flualprazolam, and then go on to perform laboratory studies to determine the nature of and mechanisms underlying interactions between these two classes of drug. This project is a fairly unique example of reverse translational research in which the critical information that will direct the investigation is first obtained through discussion with drug users to determine how they see the advantages and disadvantages of co-use of BZDs and opioids. That information will inform the subsequent overdose death statistics and laboratory research. The objectives of this project are to determine (i) how opioid users perceive the dangers of taking both opioids and BZDs. (ii) whether opioid users perceive any differences between the effects of established medicinal BZDs (diazepam and temazepam) and novel, illicit BZDs (alprazolam, flualprazolam and etizolam). (iii) from post mortem case reports and government drug death statistical data whether novel BZDs are similarly associated with deaths involving heroin and opioid drugs used in OST or whether there is specific interaction with one type of opioid drug (e.g. heroin). (iv) whether BZDs affect opioid receptor function or signalling in neurones. (v) whether BZDs potentiate opioid depression of respiration and thus enhance the likelihood of opioid overdose and if so, by what cellular and molecular mechanisms (vi) whether BZDs also enhance the pleasurable (rewarding) effects of opioids, promoting combined use but potentially leading to a fatal interaction. This is a multidisciplinary research project that will provide the student with an</p>

	<p>unprecedented breadth of training and experience in epidemiological and qualitative research methods, as well as in laboratory research using in vitro brain slice electrophysiology and in vivo animal behavioural techniques. This may seem an overly demanding range of approaches that could overwhelm a student. However, the named supervisors have previously supervised a very successful PhD studentship which used a similar combination of approaches to examine gabapentinoid-opioid interactions and the published work from that studentship has had major implications for the prescribing of these drugs and has stimulated similar research in heroin-using populations in other countries. This project will provide the student with training in interdisciplinary research. In addition to publishing high quality research papers the student will have the opportunity to discuss the implications of their work with drug service users and drug workers (e.g. at meetings with the Bristol Drug Project, PostScript360 and PHE) as well as to present their data at international scientific meetings (e.g. Addictions, a biennial meeting of world addiction experts and the International Narcotics Research Conference) and to other interested bodies (e.g. Drug Science).</p>
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Supervisory Team

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