

Institution: The University of Manchester		
Unit of Assessment: 2 (Public Health, Health Services and Primary Care)		
Title of case study: Stimulating debate, changing practice and influencing policy in tackling drug-related deaths in the UK, Europe and USA		
Period when the underpinning research was undertaken: February 2011 - January 2018		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Tim Millar	Professor of Substance Use and Addictions Reader Senior Research Fellow	2018 - present 2016 - 2018 2009 - 2016
Matthias Pierce	Research Fellow Research Associate	2016 - present 2011 - 2016
Graham Dunn	Professor of Biomedical Statistics	2004 - 2019
Andrew Jones	Senior Lecturer in Healthcare Sciences Senior Research Fellow Research Fellow	2018 - present 2016 - 2018 2004 - 2016
Period when the claimed impact occurred: September 2015 - April 2020		
Is this case study continued from a case study submitted in 2014? N		
1. Summary of the impact		
<p>Deaths due to drug misuse are an increasingly common cause of premature mortality. University of Manchester (UoM) researchers carried out the largest studies of drug-related mortality ever conducted internationally, based on a national cohort of persons treated for drug misuse and with criminal justice system involvement. We highlighted the protective effect of opioid substitution treatment. Our findings have enhanced understanding of the drivers of drug-related mortality for practitioners, policymakers, governments and the public, and guided clinical responses and national policies. We have stimulated debate on the key role of opioid substitution treatment in reducing fatal overdose, contributing to national policy and to changes in practice, affirming the importance of harm reduction to reduce risk.</p>		
2. Underpinning research		
Context		
<p>Fatal overdose involving illicit drugs is a major public health problem and there has been an alarming increase in the frequency of these tragic events in England and Wales, where approximately 80% involve opioids. North America is experiencing a fatal opioid overdose 'epidemic'.</p> <p>The UK's sharp rise in fatal overdose rates coincided with a radical shift in the emphasis of government policy. Previously, opioid misuse treatment focussed on harm reduction, with opioid substitution treatment (OST) the mainstay of care. From 2010 this emphasis shifted: the newly elected Government's drug strategy 'Reducing Demand, Restricting Supply, Building Recovery: Supporting People to Live a Drug Free Life' stated: "... <i>instead of focusing primarily on reducing the harms ... [our approach will support] ... recovery as an achievable way out of dependency.</i>"</p> <p>Coinciding with substantial funding cuts and new performance indicators based on the number of patients discharged (abstinent) from treatment, this shift shaped an environment that encouraged patients to cease OST / reduce their dose to pursue abstinent recovery. Ministers went so far as to propose arbitrarily time-limiting the permissible duration of OST. In the USA, OST has long been hard to access and of variable quality, driven by: a) views of addiction as a 'moral failing'; b) an established treatment ideology that favours non-prescribing alternatives. Thus, "<i>there is substantial evidence that [substitution treatment] - which has faced ideological resistance on and off for decades - reduce the mortality rate among people addicted to opioids by half</i>" (New York Times, 29/12/2018 - citing [2]); "... <i>use of... [OST medications] ... remains surrounded by misconceptions and prejudices that have hindered their delivery</i>" (Office of the Surgeon General, 2018). Recent work suggests that only 10% of patients in the USA can access OST (Wakeman et al, 2020). Federal</p>		

regulations in particular have been an obstacle to accessing OST.

Key research findings relevant to the impact

Understanding of opioid-related mortality has been hampered by underpowered research. Our research team addressed this deficiency by assembling the largest illicit opioid user cohort internationally to date (entire treatment population and all users known to the criminal justice system in England), linked to Office for National Statistics mortality registrations (n=198,247; 541,891 person-years of observation; n=3,974 deaths). Our investigation was:

- the largest study of treatment and fatal overdose ever undertaken, with abundant statistical power
- the first to investigate age-related increase in fatal overdose risk beyond age 45 (*highly pertinent as the 'Trainspotting' generation of heroin users enters middle age*)
- the first to calculate age-specific trends in excess mortality risk

We demonstrated that fatal overdose risk:

- doubles with increasing age (risk at age 45-64 >2 times that at 18-24 years) [1], [2]
- is halved during OST, compared to non-treatment periods [2]
- is not reduced during non-OST treatments [2]
- quadruples at discharge from OST, even for ostensibly 'abstinent' patients [2]

We also found that: disease, suicide or homicide account for >50% of premature mortality (death <65 years) in opioid users [1]; prescribing of methadone (vs. buprenorphine) may be contraindicated in older patients [3]; treatment risk mitigation was most pronounced for those with the greatest behavioural/demographic risk, [2] but weaker for criminal justice-involved patients [2], [4]; until 2010, treatment had saved up to 1,000 lives per annum in England [5].

In policy terms, the key implications of the underpinning research are:

- Ageing of the UK's heroin users is a substantial contributor to increasing fatal overdose incidence. Most of these people started using heroin in the 1980s /early 1990s as young adults; they are now entering middle age, prematurely frail, and with deteriorating health. Without intervention to reduce their risk, rates of fatal overdose will continue to increase.
- The shift away from harm reduction/OST and the emphasis on discharging patients will have placed opioid users at much greater risk, exacerbating their already increasing age-related risk. Without renewed investment in prioritising harm reduction through OST, fatal overdose rates will increase to an even higher level.
- Poor accessibility of OST, hitherto available to only a very small minority of patients, exacerbates the USA's fatal overdose 'epidemic'. Improved accessibility, requiring a change in policymakers' and the public's views of OST, as well as regulatory change, would lead to a marked risk reduction nationally.

3. References to the research

1. **Pierce, M.**, Bird, S.M., Hickman M., **Millar, T.** National record linkage study of mortality for a large cohort of opioid users ascertained by drug treatment or criminal justice sources in England, 2005–2009. *Drug and Alcohol Dependence* 2015; 146: 17-23. doi:[10.1016/j.drugalcdep.2014.09.782](https://doi.org/10.1016/j.drugalcdep.2014.09.782) (52 citations, Web of Science (WoS), 12 January 2021).
2. **Pierce, M.**, Bird, SM., Hickman, M., Marsden, J., **Dunn, G.**, **Jones, A.**, **Millar, T.** Impact of treatment for opioid dependence on fatal drug-related poisoning: a national cohort study in England. *Addiction* 2016; 11(2): 298-308. doi:[10.1111/add.13193](https://doi.org/10.1111/add.13193) (67 citations, WoS, 12 January 2021); (Altmetric 943 - high attention score vs. outputs of the same age: 99th percentile).
3. **Pierce, M.**, **Millar, T.**, Robertson, J.R., Bird, S.M. Ageing opioid users' increased risk of methadone-specific death in the UK. *International Journal of Drug Policy* 2018; 55:121-127. doi:[10.1016/j.drugpo.2018.02.005](https://doi.org/10.1016/j.drugpo.2018.02.005) [10.1111/add.13193](https://doi.org/10.1111/add.13193) (7 citations, WoS, 12 January 2021).
4. **Pierce, M.**, Bird, S.M., Hickman, M., Marsden, J., **Dunn, G.**, Seddon, T., **Millar, T.** Effect of initiating drug treatment on the risk of drug-related poisoning death and

acquisitive crime among offending heroin users. *International Journal of Drug Policy* 2018; 51: 42-51. doi:[10.1016/j.drugpo.2017.09.017](https://doi.org/10.1016/j.drugpo.2017.09.017) (3 citations, WoS, 12 January 2021).

5. White, M., Burton, R., Darke, S., Eastwood, B., Knight, J., **Millar, T.**, Musto, V., Marsden, J. Fatal opioid poisoning: a counterfactual model to estimate the preventive effect of treatment for opioid use disorder in England. *Addiction* 2015; 110(8): 1321-9. doi:[10.1111/add.12971](https://doi.org/10.1111/add.12971) (13 citations, WoS, 12 January 2021).

4. Details of the impact

Context

Because drug misuse is a highly politicised policy area, government strategies tend to be ideologically driven. Therefore, generating impact requires a complex process of stimulating debate to nudge the direction of policy, whilst driving optimal clinical practice through evidence-based guidelines and recommendations. In the UK, this process operates via agencies such as Public Health England (supporting local treatment commissioning), the Advisory Council on the Misuse of Drugs (the Government's statutory, independent advisory body) and clinical and practitioner guidelines.

Pathways to Impact

Our research group brought its findings to the attention of key stakeholders, including policymakers and providers of clinical services. Millar (PI) was invited to join the national expert groups considering drug-related mortality:

- Advisory Council on the Misuse of Drugs: working group on opioid related deaths (2016)
- Public Health England: Drug-related Deaths Inquiry (2016)
- Collective Voice / NHS National Substance Misuse Provider Alliance: expert group on drug-related mortality representing all treatment providers in England (2017)

By invitation, we presented evidence to:

- House of Commons Health and Social Care Select Committee Review of Drug Policy (2019) (parliamentary committee overseeing the Department of Health and Social Care)
- NHS Substance Misuse Provider Alliance Drug-related Deaths Conference (2017)
- Scottish Government / Partnership for Action on Drugs in Scotland Expert Meeting on Drug Deaths (2017)
- Three sessions of the European Monitoring Centre on Drugs and Drug Addiction (EMCDDA, the European illicit drugs agency) Expert Meeting on Drug-related Deaths (2013, 2017, 2017). Additionally, EMCDDA commissioned Millar to undertake an assessment of drug-related deaths in Europe (2016).

Our group also influenced wider public debate and advocacy in the USA. Millar worked with a UK drug policy charity (DrugScope) that published a lay, social media summary of our findings (blog received four times as many views, n=1,700, in a fortnight than the annual average). Social media exposure attracted attention from US-based advocates and media outlets lobbying for more accessible OST provision in the USA (where health systems hamper research of this type). They broadcasted findings regarding OST's protective effect within their work to shift public opinion and Federal Government policy. Impact in this public arena is clearly evident from the work's Altmetric score of 943 (measures attention, influence and impact) of 22 May 2020, which ranks [2] in the 99th percentile for journal outputs of similar age / ever tracked. Altmetric lists: cites in 217 news stories from 99 outlets, including prominent coverage in the UK (*Guardian*) and US (*New York Times* and *Washington Post*) national media; 175 tweets from 118 users, (reaching an upper bound of 404,260 followers), 34% from the USA and additionally the UK, Canada, Australia, Spain, Ireland, New Zealand, Bosnia & Herzegovina, and Indonesia; 65% of all tweets by members of the public (indicative of impact on public opinion); 11 posts from 8 blogs.

Reach and significance of the impact

The research identified specific groups within this clinical population that are at elevated risk. This improved awareness of the underlying demographic driver of increasing fatal overdoses

in the UK, whilst enabling treatment services to identify patients at highest risk. Most importantly, it reaffirmed the importance of OST as a harm reduction intervention that will attenuate increasing fatal overdose rates, as reflected in advice from the Advisory Council on the Misuse of Drugs and from the House of Commons Health and Social Care Select Committee, and also in legislative changes in the USA designed to enhance OST's availability.

a. Impact on guidance and recommendations: There is abundant evidence of our group's impact in informing policy recommendations and clinical guidance. Between first publication (in 2015) and 2019, key findings were reported in:

- House of Commons Drug Policy Parliamentary Debate, 2017 [A]
- House of Commons Health and Social Care Committee Report on Drug Policy, 2019 [B]
- UK Clinical Guidelines [C]
- Clinical guidance (to all treatment providers) on reducing overdose [D]
- Four reports, including [E, F, G], from the Advisory Council on the Misuse of Drugs
- Two reports by Public Health England, including [H]
- Scottish Government investigation of drug-related death among women
- EMCDDA assessment of drug deaths [I]
- Canadian Clinical Practice Guidance [J]

b. Impact on practice: Our research has had a direct influence on UK clinical practice. The UK's largest treatment provider (with approximately 35,000 opioid-dependent patients), with our input, developed risk assessment processes [K] used to assess all service users and that are informed directly by [1] and [2]. Additionally, national best practice guidelines on risk assessment ([D], page 6), formulated by representatives of all treatment providers in England, cite the risk factors identified by the group, recommending that these should "... *inform the risk management plan for an individual ...*". During 2018/19 these providers treated 139,845 of the (approximately) 260,000 people in England who use illicit opioids. During the Covid-19 emergency, the Advisory Council on the Misuse of Drugs (ACMD) cited our work when approving changes to the controlled drugs prescribing regulations, noting that it provides "*high quality evidence*" that opioid users are "*at an already significantly elevated risk of mortality from the underlying health conditions that commonly cause complications in those who contract Covid-19*" (ACMD advice on proposed legislative changes to enable supply of controlled drugs during a pandemic: letter to the Home Secretary, 7 April 2020, pages 10 and 12). The Council advised that altering the regulations to permit less frequent attendance at pharmacies would help opioid users to maintain social distancing, benefitting up to 140,000 patients in England and approximately 30,000 in Scotland and Wales. In addition, the EMCDDA recommended that EU member states should "*investigate the scope of assessing rates of drug-related death among known cohorts of problem opioid users*" [I], based on our group's methodology.

c. Impact on policy: Our research has influenced a shift in policy as regards harm reduction. As stated above, because drug misuse is a highly politicised policy arena, shifts in the direction of policy seldom occur in response to (or are attributed to) findings from a single study. However, our group's work has made a significant contribution (evident from the number and range of citations [A-J]) to a body of evidence that has shifted the policy discourse to recognise the pressing need to again embrace harm reduction. As a result:

- Public / policy awareness of OST's key role in reducing fatal overdose rates has been enhanced (proposals to time-limit OST were dropped).
- In the UK, both the House of Commons Health and Social Care Select Committee [B] and the Advisory Council on the Misuse of Drugs [F] (both cited our group's work) recommended renewed investment in drug treatment / OST and a renewed focus on harm reduction to attenuate fatal overdose risk among the approximately 340,000 illicit opioid users in England, Scotland and Wales.
- In the USA, the Federal Government yielded to pressure from the media and advocacy groups and passed legislation (Support for Patients and Communities Act, 2018)

designed to address the opioid overdose epidemic. This lifted restrictions on prescribing OST in addiction treatment to the benefit of the approximately 2,000,000 individuals in the USA who have been diagnosed with an opioid misuse disorder.

5. Sources to corroborate the impact

- A. The Hansard record of the House of Commons Drug Policy Debate, 18 July 2017, page 80 “...research from the University of Manchester shows that those who leave treatment drug-free are just as likely to die of an overdose...”: *Evidences impact in shifting policy discourse.*
- B. House of Commons Health and Social Care Committee (2019) ‘Drugs Policy: First Report of Session 2019–20’ London: House of Commons evidence on page 6, para 3. *Highlights findings regarding the extent of ill health and its contribution to excess mortality.*
- C. Clinical Guidelines on Drug Misuse and Dependence Update 2017 Independent Expert Working Group (2017) ‘*Drug misuse & dependence: UK guidelines on clinical management*’ Dept of Health, London, page 13. *Cites UoM findings regarding excess mortality risk.*
- D. Collective Voice and the NHS Substance Misuse Provider Alliance (2017) ‘*Improving Clinical Responses to Drug-Related Deaths: A summary of best practice and innovations from drug treatment providers*’ London, Collective Voice and the NHS Substance Misuse Provider Alliance – evidence cited on pages 8, 9. *clinical services. Highlights UoM research findings pertinent to assessing patients’ fatal overdose risk.*
- E. Advisory Council on the Misuse of Drugs (2015) ‘*How can opioid substitution therapy (and drug treatment and recovery systems) be optimised to maximise recovery outcomes for service users?*’ London, Home Office - pages 13 and 19. *Cites UoM findings to highlight hazard of neglecting OST and regarding the poor physical health of older opioid users.*
- F. Advisory Council on the Misuse of Drugs (2016) ‘*Reducing opioid-related deaths in the UK*’, London, Home Office, pages 3, 10, 11, 16, 17, 23, 26, 31, 32. *Highlights UoM findings regarding age-related increase in fatal overdose risk / interaction with multiple physical comorbidities, importance of maintaining OST investment to reduce risk, danger of encouraging patients to cease OST prematurely.*
- G. Advisory Council on the Misuse of Drugs (2019) ‘*Ageing cohort of drug users*’ London, Home Office, pages 13, 14, 15, 37. *Highlights UoM findings regarding age-related increase in fatal overdose risk and interaction with methadone-specific risk, and age increases in excess mortality for a range of specific causes.*
- H. Public Health England (2016) ‘*Understanding and preventing drug-related deaths: The report of a national expert working group to investigate drug-related deaths in England*’ London, Public Health England, pages 14, 15, 31, 32. *Highlights UoM findings regarding the major contribution of ageing heroin user cohort to the rise in fatal overdoses, risk of treatment transitions, potential contribution of poor recovery-oriented practice, and importance of OST in mitigating risk.*
- I. EMCDDA DRD 2016 Project Steering Group (2017) ‘*EMCDDA assessment of drug-induced death data and contextual information in selected countries*’ EMCDDA, Lisbon, pages 14, 22, 24, 25, 28, 32. *Recommends UoM’s method to EU Member States for investigating drug-related mortality.*
- J. Bruneau, J. et al., on behalf of the CIHR Canadian Research Initiative in Substance Misuse (2018) ‘*Management of opioid use disorders: a national clinical practice guideline*’ Canadian Medical Association Journal, March 5;190:E247-57. doi:[10.1503/cmaj.170958](https://doi.org/10.1503/cmaj.170958) - pages 253/4 and 255 (conclusion).
- K. Letter from Head of Research, Change Grow Live (dated 21 September 2020), *stating the contribution of UoM research to processes for assessing the risk of fatal overdose among an active caseload of 35,000 opioid-dependent patients and impact on clinical practice.*