ACMD
Advisory Council on the Misuse of Drugs

Reducing Opioid-Related Deaths in the UK

December 2016
Rt Hon. Amber Rudd, MP
2 Marsham Street
London
SW1P 4DF

Dear Home Secretary

In March 2016 the ACMD agreed to undertake a piece of work through its own volition to explore the recent increases in drug-related deaths in the UK.

The ACMD is of the view that death is the most serious harm related to drug use. In recent years, there have been substantial increases in the number of people dying in the UK where illicit drugs are reported to be involved in their death. The largest increase has been in deaths related to the misuse of opioid substances; 2,677 opioid-related deaths were registered in the UK in 2015.

The ACMD therefore set up a dedicated working group to examine how to reduce drug-related deaths, with a focus on opioid-related deaths.

**Key findings**

Through our brief review of the potential causes of recent trends in opioid-related death, the ACMD can assert with a good degree of confidence that the ageing profile of heroin users with increasingly complex health needs (including long-term conditions and poly-substance use), social care needs and continuing multiple risk behaviours has contributed to recent increases in drug-related deaths.

Other possible causes of recent increases include greater availability of heroin at street level, deepening of socio-economic deprivation since the financial crisis of 2008, changes to drug treatment and commissioning practices, and lack of access to mainstream mental and physical health services for this ageing cohort.

We found that although the current definition and measurement of opioid-related deaths across the UK is consistent and useful, there are weaknesses in current data collection methods that mean the trends over time can be difficult to interpret.
Improving the processes of collecting information on opioid-related deaths would ensure that policy makers have better information to make better decisions to reduce deaths. The ACMD also recommends that governments fund independent research in order to provide a better understanding of the causes and drivers of trends in opioid-related deaths, as well as all other drug-related deaths.

The ACMD welcomes the considerable expansion in the use of OST (opioid substitute treatment) in the UK since the mid-1990s. The ACMD would like to re-iterate the evidence that being in OST protects heroin users from overdose, and increasing coverage of OST has had a substantial effect in limiting the increase in drug-related deaths that would otherwise have occurred. The most important recommendation in this report is that government ensures that investment in OST of optimal dosage and duration is, at least, maintained. Access to allied healthcare and other services to treat comorbid, chronic physical and mental health issues, and to promote recovery from problematic drug use will also be important in reducing premature deaths.

Yours sincerely

Les Iversen

Prof Alex Stevens

Annette Dale-Perera

ACMD Chair

Co Chairs – Drug-related Deaths WG

Cc Rt. Hon. Jeremy Hunt, MP, Secretary of State for Health
Sarah Newton MP, Minister for Safeguarding, Vulnerability and Countering Extremism
Nicola Blackwood MP, Parliamentary Under Secretary of State for Public Health
Reducing Opioid-related Deaths

A report of the Advisory Council on the Misuse of Drugs

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1 Introduction and summary of findings

1.1 The Advisory Council on the Misuse of Drugs (ACMD) has a statutory duty under the Misuse of Drugs Act 1971 to advise ministers on measures that may be taken to reduce the harms associated with illicit drugs.

1.2 Death is the most serious harm related to drug use. Since 2012, there have been substantial increases in the numbers of people dying in the UK where illicit drugs are reported to be involved in their death. Table 1 displays the numbers of deaths that have been registered as drug misuse deaths and as opioid-related deaths in the most recent year for which data is available in each country of the UK. It also shows the percentage change in deaths recorded as opioid-related between 2012 and 2015.

Table 1: Drug misuse and opioid-related deaths in the UK (by year of registration)

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>England</td>
<td>2,300</td>
<td>1,842</td>
<td>58%</td>
</tr>
<tr>
<td>Wales</td>
<td>168</td>
<td>141</td>
<td>23%</td>
</tr>
<tr>
<td>Scotland</td>
<td>706</td>
<td>606</td>
<td>21%</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>114</td>
<td>88</td>
<td>47%</td>
</tr>
</tbody>
</table>

Sources: Office for National Statistics, National Records of Scotland, Northern Ireland Statistics and Research Agency

* drug misuse deaths mentioning an opioid – not all opioid deaths

1.3 As shown in Table 1, a very large number of drug misuse deaths are related to opioids, and this number has grown substantially in recent years. Indeed, figures from the Office for National Statistics (ONS) for 2015 registrations suggest that opioid-related deaths now accounted for a larger number of fatalities than traffic accidents. People who use opioids are also highly vulnerable to other causes of death; 43% of deaths recorded among a large cohort of opioid users in England were due to fatal overdose, with the majority dying of other causes (Pierce, et al., 2015).

1.4 In spring 2016, the ACMD decided to produce a report to advise ministers on how to reduce opioid-related deaths.

1.5 The report builds on the ACMD’s 2000 report on Reducing Drug-Related Deaths. It also builds on work carried out by public health agencies in the four countries of the UK, including by the Scottish Government, Public Health Wales, Public Health England, the

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1 'Opioid drug’ is used in this report to refer to substances derived from the opium plant that has analgesic and euphoric effects, and also to synthetic substances which mimic these effects.

2 As noted in chapter 2, the year of registration of a death may not be the same year as that in which it occurred. The opioid-related death column in this table includes deaths defined as drug misuse deaths (see section 2.3) where an opioid was recorded as being involved. The percentage rise recorded in Northern Ireland is affected by the inclusion of tramadol-related deaths as drug misuse deaths after 2012.
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Local Government Association and the Scottish National Forum on Drug Related Deaths, as well as the Scottish Drug Forum.

1.6 The ACMD is not a research institute and does not carry out original research. Instead, this report is based on analysis of published research, on research undertaken by members of the above-mentioned working group and consultation with stakeholders in the field. It makes important recommendations for filling large gaps in the existing evidence base on opioid-related deaths.

1.7 The report is split into four substantive chapters:

- Definitions and data on opioid-related deaths.
- Patterns and trends in opioid-related deaths.
- Causes and drivers of recent trends in opioid-related deaths.
- Policy and treatment responses to prevent opioid-related deaths.

1.8 The main conclusions of the report are as follows.

1.8.1 That the UK has high-quality systems for the recording of opioid-related deaths, but that more could be done to improve national information, especially on toxicology and prescribing, as well as on the contribution of opioid use to levels of mortality from other causes.

1.8.1 That a probable cause of the recent increases in drug-related deaths (DRDs) is the existence of a prematurely ageing cohort of people who have been using heroin since the 1980s and 1990s.

1.8.2 The vulnerability of these and other people who use heroin is likely to have been reduced by a reduction in the availability of heroin at street level that occurred in the UK in 2010 to 2012. Recent increases may represent a return to the underlying, increasing trend as heroin availability subsequently increased.

1.8.3 Other contributory causes of recent increases in deaths include multiple health risks (including poly-substance use and chronic use of alcohol and tobacco) among an ageing cohort of heroin or opioid users, deepening of socio-economic deprivation since the financial crisis of 2008, and changes to drug treatment and commissioning practices.

1.8.4 There are a number of evidence-based approaches that can be used to reduce the risk of death among people who use opioids. The strongest evidence supports the provision of opioid substitution treatment (OST) of optimal quality, dosage and duration.

1.8.5 Other substance misuse treatment options could be further developed in order to reduce the risk of death including broader provision of naloxone, heroin-assisted treatment for those for whom other forms of OST are not effective, medically-supervised drug consumption clinics, treatment for alcohol problems, and assertive outreach to engage heroin users who are not in treatment into OST (especially for those who are homeless and/or have mental health problems).
1.8.6 Improve access for heroin users to treatment for mental health problems, smoking cessation and tobacco harm reduction, HIV / hepatitis B / hepatitis C prevention and treatment, physical healthcare treatment for long-term conditions such as coronary and pulmonary heart disease, and other services (such as housing and employment services) which support wider recovery outcomes could reduce vulnerability to DRDs.

1.8.7 The report makes a number of recommendations for the reduction of opioid-related deaths; most importantly that investment in evidence-based OST be maintained. It is estimated that OST was preventing approximately 880 deaths per year in England in 2008 to 2011 (White et al., 2015). Without the expansion of OST that occurred in the 2000s, it is likely that opioid-related deaths would be even higher than they currently are. These services are currently under threat from reductions in local and national funding, especially in England.

1.8.8 The age profile of opioid-related deaths (discussed in chapter 3) suggests that relatively few young people are initiating problematic opioid use. Numbers of opioid-related deaths among people under 30 have fallen substantially since the early 2000s. This suggests that the UK is likely to see a long-term reduction in opioid-related deaths, as long as there is no new wave of initiation into problematic opioid use (e.g. larger increases in the misuse of heroin, fentanyl and/or oxycodone), as was seen with heroin in the 1980s and 1990s.

1.8.9 However, in the short to medium term, we are likely to see an increasing number of deaths among a shrinking population of prematurely ageing, increasingly vulnerable heroin or opioid users. Deaths among this cohort have been reduced and limited by previous government interventions, including those implemented after the ACMD’s report in 2000. ACMD calls on the government to renew and extend efforts to prevent these deaths.
2 Definition and data on opioid-related deaths

2.1 National statistics on deaths related to drug poisoning in the UK are monitored using figures provided by ONS, National Records of Scotland (NRS) and the Northern Ireland Statistics and Research Agency (NISRA). An understanding of how opioid-related deaths are defined and measured is essential in order to accurately interpret the annual figures and trends over time, and how they can be influenced by a number of factors.

2.2 This chapter explores how opioid-related deaths are defined and measured across the countries of the UK. Consideration is given to comparability both over time and between specific countries within the UK and internationally. Where possible, potential improvements to the current definition are recommended and areas requiring further research are highlighted.

2.3 The definition and measurement of opioid-related deaths in the UK

2.3.1 Opioid-related deaths in the UK are currently defined as a subset of the headline indicator for drug misuse deaths that has been adopted across the UK since 2001 with a baseline year for measurement of 1999.

2.3.2 The definition of a drug misuse death is:

(a) deaths where the underlying cause is drug abuse or drug dependence (defined as an underlying cause of mental and behavioural disorder due to psychoactive substance use excluding alcohol, tobacco and volatile solvents); and
(b) deaths where the underlying cause is drug poisoning and where a substance controlled under the Misuse of Drugs Act 1971 was mentioned on the death certificate (ONS, 2002; Christophersen et al., 1998).

2.3.3 The indicator takes into account the need for international monitoring by the European Monitoring Centre for Drugs and Drug Addiction and is based on the information collected at death registration. Although there are minor differences in definitions used in different countries of the UK, opioid-related deaths are generally defined as drug misuse deaths where an opioid has been mentioned on the death certificate.

2.3.4 Specific rules are adopted for dealing with compound analgesics which contain relatively small quantities of drugs listed under the Misuse of Drugs Act, the major ones being dextropropoxyphene, dihydrocodeine and codeine. Where only these drugs are mentioned on a death record, it would not be counted as a drug misuse death if they are part of a compound analgesic (such as co-proxamol, co-dydramol or co-codamol) or cold remedy. Dextropropoxyphene is rarely, if ever, available other than as part of a paracetamol compound and so is excluded on all occasions, whether or not paracetamol or a compound analgesic was mentioned. However,

\[3\text{ In Northern Ireland, this definition is subtly different. There, drug misuse deaths are defined as: where the underlying cause is drug poisoning, drug abuse or drug dependence and where any of the substances controlled under the Misuse of Drugs Act (1971) are involved.}\]
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codeine or dihydrocodeine mentioned alone will be included as drug misuse deaths as they are routinely available and known to be abused in this form.

2.3.5 This headline indicator for drug misuse deaths was developed by a technical working group of experts from across government, the devolved administrations, coroners, toxicologists and drugs agencies as part of the government’s action plan, to reduce the number of these deaths (Department of Health, 2001).

2.3.6 Methods for measuring opioid-related deaths are comparable across England, Wales and Northern Ireland as the systems of death certification and registration are the same, requiring all deaths related to drug poisoning to be referred to a coroner for investigation. The information on the specific substances involved in the death is derived from all the information provided on the coroner’s death certificate.

2.3.7 In Scotland, the system of registration differs and requires DRDs to be investigated by a procurator fiscal (NRS: Sources of Information for Coding the Causes of Death). Scottish DRDs are identified using details from the death registration in addition to information from a specially-designed questionnaire, which is completed by forensic pathologists and lists the drugs and solvents that were found.

2.3.8 NRS requests this information for all deaths involving drugs or persons known, or suspected, to be drug-dependent. The form asks about the drugs or solvents “implicated in, or which potentially contributed to, the cause of death” and about “any other[s] which were present, but which were not considered to have had any direct contribution to this death”. Standard reporting for deaths involving opioids is based on opioids “implicated in, or which potentially contributed to, the cause of death”. So the Scottish figures for opioid deaths do not include (relatively few) drug misuse deaths for which the only reported opioids were present but not considered to have had any direct contribution to the death. They include (relatively few) deaths which are counted as “drug misuse” because of the presence of another controlled substance (e.g. diazepam) and for which the only opioid which was implicated in, or which potentially contributed to, the cause of death was a compound analgesic (see paragraph 2.2.4).

2.3.9 Deaths coded to opiate abuse which resulted from the injection of contaminated heroin are included for England, Wales and Northern Ireland. This differs from the approach taken in Scotland, where these deaths have been excluded. This is because the NRS is able to identify deaths which occurred as a result of the use of contaminated heroin, whereas in England, Wales and Northern Ireland these deaths cannot be readily identified.

2.3.10 In common with most other mortality statistics, figures for opioid-related deaths in the UK are presented for deaths registered in a particular calendar year. In England, Wales and Northern Ireland a death cannot be registered until the coroner’s inquest is completed, which can take many months or even years. This means that opioid-related deaths registered in a given year within these countries may have occurred in the years prior to the registration year and so are not directly comparable with figures from Scotland where the death registration system differs and almost all deaths are registered in the year they occurred (ONS, 2015; NRS, 2015).
2.3.11 Delays in receiving information on opioid-related deaths may hinder the effectiveness and timeliness of local responses to such deaths. In Wales and Scotland, the separate, national system for prompt investigation and reporting of all deaths which are suspected to be related to drugs (Welsh Government, 2014; ISD Scotland, 2016a). These systems capture information additional to that which is collected for the national recording of drug-related death statistics; information which is useful to clinicians and policy makers in developing practice and policy. Some areas in England and Northern Ireland have systems in place for prompt investigations of DRDs, but these are not universal and do not report to a central database.

2.3.12 It is also important to share information between services on non-fatal overdoses, as these indicate individuals at increased risk of fatal overdose. Protocols for information sharing have been developed; for example, between ambulance and other services in some areas of Scotland (Scottish Drug Forum, 2016) and in Brighton and Hove (response to ACMD, August 2016). As a result of its joint inquiry with the Local Government Association, Public Health England has recently recommended greater information sharing on both fatal and non-fatal overdoses (Public Health England, 2016a).

2.3.13 Despite the noted differences, the measurements of opioid-related deaths in the UK are based on high-quality death certification systems that all use common International Classification of Disease coding. The definitions are based on an agreed headline indicator of drug misuse deaths for the UK. These systems ensure that there is broad comparability and consistency in the reporting of opioid-related deaths across the UK.

2.4 Improving the definition and measurement of opioid-related deaths in the UK

2.4.1 The agreed definitions and standards for the measurement of opioid-related deaths provide a useful indicator that can be used both nationally and internationally. However, as the indicator is based on the information collected at death registration, there are known issues with quality and comparability over time and improvements could be made.

2.4.2 The primary function of the coroner or procurator fiscal is to establish the circumstances and cause of death and to investigate the possibility of any criminal involvement. Collecting statistical data and informing local service provision are secondary concerns. If a post-mortem is carried out it may, but does not necessarily, include a toxicological examination.

2.4.3 Where a toxicological examination is carried out, there is still no guarantee that all substances present in the deceased’s body will be identified; only those drugs which are tested for will be detected. Technical advances may enable the detection of small quantities of substances that could not have been found in the post-mortems that were performed several years ago; the range of opioids (and other substances) for which tests are conducted may change. Where several substances are detected, the post-mortem may not be sufficiently detailed to detect which one was primarily responsible for the death. Even if a detailed post-mortem and toxicology
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examinations are conducted, it may still be difficult to ascribe death to specific substances.

2.4.4 These circumstances pose specific issues with the data on opioid-related deaths. Only a general description was recorded on the coroner’s death certificate (such as ‘drug overdose’ or ‘multiple drug toxicity’) for 12.5% of drug poisoning deaths registered in England in 2015 and for 6% of drug poisoning deaths in Northern Ireland in 2014 (ONS, 2016; NISRA, 2015). It is likely that some of these deaths will involve opioids.

2.4.5 An increasing proportion of DRDs reported involve more than one substance, often in combination with alcohol (ONS, 2015; NISRA, 2015; NRS, 2016). However, as there are no standardised collections across the UK of what toxicological assessments have been carried out, it is currently impossible to tell whether this reported increase in deaths involving multiple substances is due to a genuine increase in multiple drug use or an increase in the amount of substances being tested for or being identified under toxicological examination.

2.4.6 It is possible that an individual had a complex pattern of drug use including addiction to, or regular use of, several substances or switching between substances. Similarly, an individual may have problems with a particular opioid, for example heroin, but die from an overdose of a different opioid drug such as methadone. The detail on all the substances involved in this type of death is not likely to be present in information solely based on death registrations.

2.4.7 Many drugs of abuse may also be prescribed for medicinal use and, conversely, many medicinal drugs are taken for recreational or other use. This is a particular issue for opioids as generally no information is received during the death registration process on whether an opioid implicated in a death was prescribed, bought over the counter (OTC) or illegally obtained.

2.4.8 The National Programme on Substance Abuse Deaths, St George’s, University of London, aims to address some of these identified issues with data collection, specifically requesting more detailed information from coroners on the circumstances surrounding the death and the inquest proceedings. Information is submitted to the programme on a voluntary basis, therefore the geographical coverage across the UK is not complete and the figures are not consistent with those produced by the national systems. More could be done to improve links with the national statistics.

2.5 Recording deaths where other issues are involved

2.5.1 Monitoring DRDs based on deaths with an underlying cause of drug poisoning ensures consistency and comparability internationally as the conditions on the death certificate as coded using the World Health Organization's (WHO) International Classification of Diseases, Tenth Revision (ICD-10) and the underlying cause is selected from those conditions according to internally agreed rules (WHO, 2016).

2.5.2 There will, however, be certain types of opioid-related deaths that are not captured using this approach, either because the opioid use is not selected as the underlying
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cause or because opioid use may not be known by the certifier. Where it is known that opioid use was indirectly involved in a death this may sometimes be omitted from the death certificate for the sake of the relatives who may be concerned about the stigma attached to drug abuse (Christophersen et al., 1998). Deaths that arise from chronic conditions and infections where opioid use or injecting has contributed, may not be recorded as an opioid-related death. Only 38 drug misuse deaths registered in England and Wales in 2015 where an opioid was mentioned were not recorded as being an accidental poisoning (1,665 deaths), a suicide (284), or an assault by drugs (3).4

2.5.3 The ageing profile of opioid users is a known phenomenon (Gossop, 2008; Gfroerer et al., 2003). Older opioid users commonly present with a range of multiple morbidities (Clausen et al., 2009; Hser et al., 2004). Deaths involving blood-borne viruses and infections acquired by injecting opioids, such as HIV/AIDS, hepatitis, clostridium novyi, anthrax, septicemia and necrotising fasciitis, are likely to be underestimated (Berger et al., 2014; Hanczaruk et al., 2014; Kimura et al., 2004; Mathers et al., 2013; McGuigan et al., 2002; Powell et al., 2011). Globally, it has been estimated that injecting drug use (largely of heroin) contributes substantially to the health burden, including deaths, associated with HIV, hepatitis C and hepatitis B (Degenhardt et al., 2016). Furthermore, the risk of fatal overdose increases substantially with age (Pierce et al., 2015). The age-related increase in DRD-risk is particularly marked for methadone-specific DRDs (i.e. methadone but neither heroin/morphine nor buprenorphine implicated in the death) (Gao et al., 2016). Moreover there is evidence of an interaction between older age and hepatitis C infection in elevating DRD-risk (Merrall et al., 2012). A number of international cohort studies of treated drug users have found that the problematic use of illicit drugs is associated with an increase of excess mortality (Bird, 2010; Crump et al., 2013; Degenhardt et al., 2011; Merrall et al., 2012). Within England, mortality in opioid users is elevated for a number of causes which would not be included under the current definition: infections, respiratory, circulatory and liver diseases as well as suicides and homicides not directly related to drug poisoning (Pierce et al., 2015).

2.5.4 Drug use is also associated with higher risk of road traffic and other accidents, such as falls from heights and drowning where the perception or assessment of risk is impaired and reaction times slowed (Clausen et al., 2009; Degenhardt et al., 2011). In 2014, at least 3% of all fatal road traffic accidents in Great Britain noted that the driver or rider being impaired by drugs was a contributory factor (Department for Transport, 2015). These cases will also not be included in the standard definition as road traffic accident would be recorded as the underlying cause.

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4 Even some of these 38 deaths that were recorded under ‘mental and behaviour disorders due to drug use’ may have been poisonings, as the coroners’ reports of them included phrases such as ‘respiratory depression’ and ‘hypoxic brain injury’, both sequelae of opioid overdose.
2.6 Linking information on deaths to other data

2.6.1 A number of recent studies demonstrate the feasibility and utility of linking treatment and mortality data to improve our understanding of deaths related to drug use, including both fatal overdose and deaths due to other causes (White et al., 2015; Pierce et al., 2015; Pierce et al., 2016).

2.6.2 Data collected by the National Programme on Substance Abuse Deaths at St Georges University of London suggest that for many people whose death was related to methadone, there was no record that they had been prescribed. However, information on prescriptions is not systematically reported by coroners (Claridge & Goodair 2015).

2.6.3 At a local level, in Scotland and Wales there are initiatives for local partner reporting and investigation of DRDs which provide invaluable data, analysis and local intelligence. In England, with changes in commissioning and the move to local health and well-being boards, standardised national reporting of local systems is problematic. Many of the mandatory reporting structures for serious incidents and DRDs are located in local health rather than local authority commissioning structures. While most substance misuse providers have systems for investigating serious incidents and deaths, there are no standard reporting requirements or mechanisms for collecting data from these reports at regional or national levels.

2.7 Conclusions

2.7.1 Collecting accurate information and data on DRDs is critical to understand trends in premature deaths among opioid users. Understanding trends in who is dying of drug poisoning and why is critical to informing strategies to reduce these deaths at national and local levels. There is a particular need to provide better and more comparable information from toxicological tests carried out on the deceased, and to record whether people who die from an opioid-related death are in receipt of a medical prescription for an opioid.

2.7.2 The current definition and measurement of opioid-related deaths across the UK is consistent and useful. However, it has been noted that there are several weaknesses in the current collection methods that mean the trends over time can be difficult to interpret. Improving the processes for defining and measuring opioid-related deaths would ensure that policy makers have better information to make better decisions to reduce deaths. This could be achieved by greater standardisation of coroners' reporting of drug-related deaths.

2.7.3 In particular, it is currently impossible to assess whether the increase in deaths involving poly-drug use (including opioids) observed in the data is evidence of an increasing trend of use or better identification and recording. Better measurement of deaths involving multiple substances, particularly where opioids are involved, would provide a better understanding of the complex treatment needs of users and potentially allow multiple substance use to be highlighted in harm reduction campaigns.
2.7.4 The opioid-misusing population in the UK is ageing and known to have multiple and complex health problems (Royal College of Psychiatrists, 2011). The current definition does not capture the wider burden of opioid use on a range of infections and chronic diseases. Estimating the wider burden of opioid use, particularly the potential contribution to chronic conditions, would enable better and more targeted service planning. In order to do this, better systems are needed for defining and capturing data on all premature deaths among opioid users with particular consideration given to chronic ill health and all external causes in addition to poisoning.

2.7.5 Some areas of the UK have systems in place to deliver prompt, multi-agency investigations of deaths that are suspected to be drug-related. In Wales, this feeds into a national database. Such prompt investigation and reporting can improve the local and national responses to opioid-related deaths.

2.7.6 The ACMD recommends improving the current processes by creating data standards for local reporting that feed into national systems. This may include coroners reporting, toxicological assessments to understand poly-substance use, local partnership investigations and information sharing on DRDs and non-fatal overdoses, strengthening links between national datasets including death registrations, and national treatment monitoring systems.
3 Patterns and trends in opioid-related deaths

3.1. Trends in the number of deaths involving opioids

3.1.1 Figure 1 shows the trend in the number of deaths involving opioids in England, Scotland, Wales and Northern Ireland by the year in which deaths occurred, rather than the year in which they were registered. Although the annual number of deaths fluctuated somewhat, none of the jurisdictions exhibited a sustained increase in opioid-related deaths over the last five years of the period shown. England, Scotland and Wales exhibited a diminished number of deaths during 2010, the period of reduced availability of heroin at street level. The number of deaths in Northern Ireland is small, but exhibited a similar pattern at that time. However, in Scotland the annual number of deaths returned rapidly to around the levels seen in 2008 and 2009 and, despite a modest decline in 2012 and 2013, increased again markedly (not shown) in 2014 with registration data for 2015 suggesting a further increase. In England, the annual number of deaths remained at a lower level for several years, before returning to the previous levels in 2013. In Wales the annual number of deaths remained at a much reduced level following the 2010 ‘dip’.

3.1.2 These figures were received prior to the publication of the most recent statistics for DRDs in England & Wales and Scotland, which show a substantial increase in DRDs registered during 2015 for all three countries. These suggest that the trend in opioid-related deaths has regained its pre-2010 trajectory.

Figure 1: Trend in the number of opioid-related deaths by year of death: England, Scotland, Wales, Northern Ireland: 1993 to 2013

![Graph showing the trend in the number of opioid-related deaths by year of death for England, Scotland, Wales, and Northern Ireland from 1993 to 2013](image)

3.1.3 In England there were substantial year-on-year increases in the number of opioid-related deaths during the 1990s, likely to have been driven by an increasing number of people using heroin. This sustained increase peaked in 2000 (1437 deaths), with a clear decline in each of the subsequent three years. The annual number of deaths increased again from 2004 and by 2007 (1490 deaths) slightly exceeded the peak observed at the start of the decade.
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3.1.4 The available time series for Scotland is shorter. Although the general pattern between 2000 and 2010 was similar to that for England, by 2009 the annual number of deaths (509) in Scotland was much greater than at the start of the decade (258).

3.1.5 The number of deaths in Wales is smaller and, notwithstanding a slight ‘dip’ in 2003 (as also observed in England and Scotland), exhibits gradual year-on-year increases throughout the time series, doubling between 2000 and 2009 (from 73 to 150 deaths), until the period of reduced availability of heroin.

3.1.6 The number of deaths in Northern Ireland during 2013 (58) was almost three times that observed in 2000 (21).

3.1.7 Figure 2 shows the number of deaths in England and Wales involving opioids each year according to decade of birth (those born prior to the 1950s or after the 1980s account for a very small number of deaths and are not included here). The figures shown here are a three-year moving mean, to smooth short-term fluctuations in the figures. It is important to consider that onset of illicit opioid use typically occurs between the latter teens and mid-twenties. Members of the 1980s birth cohort first started to appear in the DRD data during the late 1990s and their numbers built gradually over the subsequent decade. While the latter group contributed to an increasing trend between 2005 and 2009, their numbers plateaued thereafter. Consistently, the vast majority of deaths have occurred among those born during the 1960s and 1970s, which are the birth cohorts which reached typical age of onset during the heroin ‘epidemic’ which started in the early 1980s and which is thought to have subsided during the mid- to late-1990s.

Figure 2: Decade of birth for opioid related drug misuse deaths by year: number of deaths (3 year moving mean): England and Wales

3.1.8 Data for Scotland are available for a shorter time series (2000-2014), so cannot be incorporated in Figure 2, but show a similar trend for that period.

3.1.9 The number of deaths in Northern Ireland is small and analysis by subgroups is subject to considerable annual fluctuation, but it is perhaps notable that a larger
proportion (30% to 40% in some years) of deceased persons is from the 1980s birth cohort than in the other jurisdictions.

3.1.10 Figure 3 shows the three-year moving mean for the number of opioid-related deaths that occurred each year in England and Wales, by age at death. The early part of the trend shows increasing numbers of deaths among all age groups, most markedly among those under the age of 30 years and aged 30 to 39 years. This is likely to reflect increasing prevalence of opioid use in those groups, who initiated opioid use during the early 1980s (the initial phase of the heroin 'epidemic') and because significant numbers of young people initiated opioid use during the 1990s (the latter phase of the heroin 'epidemic'). From around 2001 the pattern started to shift:

- The number of deaths fell very sharply among the under 30s.
- It plateaued among those in their 30s.
- Following a brief hiatus, it increased among those in their 40s.

It is plausible that, at this stage:

- the number of users under 30 years declined as people who use heroin aged out of their 20s, at a time when fewer young people were initiating opioid use;
- the number of users in their 30s was fairly static, because those users moving from their 30s to their 40s were replaced by those moving from their 20s to their 30s;
- the number of users in their 40s increased as the early initiates of the 1980s reached the end of their 30s.

The number of deaths among younger users continued to decline, reasonably consistently, for the remainder of the time series, albeit with a brief plateau from 2006 to 2009. Towards the end of the time series, the number of deaths among those in their 30s started to decline, which may reflect a population that was entering its 40s with reduced 'replacement' from younger age groups. The number of deaths among those in their 40s increased each year, overtaking deaths among the younger two age groups. At the same time, there was a discernible increase in the gradient of the trend line for those aged 50 to 59 years and a slightly later, more modest, increase for those aged over 60 years.
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Figure 3: Age at opioid-related death by year: number of deaths (3-year moving mean): England and Wales

3.1.11 Figures for Scotland show a similar overall pattern with respect to ageing, but the trend is delayed by around a decade compared to England and Wales. Figures for Northern Ireland are too small to allow meaningful comparison by age group.

3.1.12 It is important to consider that all of these changes occurred against the backdrop of changes in the context of opioid use which, themselves, are likely to have had an impact on the trend in DRDs. The early 2000s saw a considerable expansion in the treatment system (OST being protective against fatal overdose) (Pierce, et al., 2016).

3.1.13 The increase in the number of deaths among older users is particularly striking, given that we would expect the size of the opioid-using cohort to dwindle over time, and with age, due to exit from the using population via death or abstinence. However, there is strong evidence that the risk of fatal overdose among opioid users increases substantially with age (Pierce, et al., 2015; Pierce, et al., 2016; Merrall, et al., 2012). The risk among those over the age of 45 is approximately double that for those under the age of 25 years. Thus, it is likely that we are observing an increasing rate of opioid-related death among a dwindling population of users who are ageing.

3.1.14 Figure 4 shows the mean age at death for males and females (England and Wales). The mean age at death is consistently higher for women than for men, as in the general population. This is likely to reflect that female opioid users have a very much lower risk of fatal overdose than males at younger age, but that this risk atrophies with age (Pierce, 2015).
Figure 4: Mean age (years) of opioid-related deaths by year by gender: England and Wales

3.1.15 Figure 5 shows the (three-year moving mean) number of opioid-related deaths of men and women (England and Wales). Most deaths occurred among males, but women have tended to account for an increasing proportion of deaths in recent years and the number of female deaths increased consistently across the time series, in contrast to the variability in the number of deaths among males. Again, these observations may reflect partially the lesser risk that women experience at younger age (Pierce, 2015) combined with their faster acceleration in risk with age, bearing in mind that, for both genders, the opioid-using population has aged over the course of the time series.

Figure 5: Number of opioid-related deaths by year by gender (3-year moving mean): England and Wales
3.2 Trends in the type of opioid(s) involved in opioid-related deaths

3.2.1 Figure 6 shows the trend in the type of opioid involved in opioid-related deaths in England and Wales.

![Figure 6: Trends in the type of opioid(s) involved in opioid-related deaths: 1993 to 2013: England and Wales](image)

3.2.2 It is important to note that there may be variations in the extent of toxicology screening over time and that trends in the drugs detected in toxicology may be influenced by this variation. Notwithstanding this, most opioid-related deaths involve heroin/morphine and thus the trend for these largely mirrors the overall trend for opioids. There has been a marked and consistent year-on-year increase in the number of deaths found to involve tramadol and also in deaths found to involve codeine (excluding compound formulations). The most recent data (for 2015 registrations of deaths) shows a subsequent decline in deaths related to tramadol, which may reflect its control under schedule 3 of the Misuse of Drugs Act in 2014, following the ACMD’s advice on this in 2013 (ACMD, 2013a).

3.2.3 The recent and increasing appearance of oxycodone and fentanyl, albeit in small numbers of deaths (51 and 33, respectively, in 2013), is striking. These substances have been associated with large increases in opioid-related deaths in North America (King et al., 2014). The scale of the increase in the UK is not as large, but should be cause for close monitoring of future trends.
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3.2.4 Figure 7 shows that heroin/morphine was the drug most commonly involved in the 1,609 deaths involving opioids in England and Wales during 2013 (51%). This proportion has varied during the last decade of the time series, from as little as 40% (2011) to as much as 65% (2004). Methadone was involved in around a quarter of deaths. The proportion of deaths involving tramadol increased very markedly up to 2013; during 2013 it was involved in 15% of deaths involving opioids. More than one substance was present in most opioid-related deaths.

Figure 7: Type of opioid involved in opioid-related drug misuse deaths: 2013: England and Wales

3.2.5 There has been a marked decline in the proportion of opioid-related deaths recorded as involving heroin/morphine alone; however, it is not known whether this reflects a trend to more extensive toxicological testing. In 2013, 68% of deaths in England and Wales involving heroin/morphine were recorded as also involving another substance (Figure 8). Alcohol (56%) was the substance most commonly recorded in deaths during 2013 involving heroin/morphine and other substances, followed by other opioids (including methadone), benzodiazepines, and methadone (Figure 9).

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5 Figure 7 may underestimate the proportions related to specific opioids, as some deaths are recorded as being related to an unspecified opioid.
3.2.6 There has also been a marked decline in the proportion of opioid-related deaths recorded as involving methadone alone; again, it is not known whether this reflects a trend to more extensive toxicological testing. In 2013, 76% of deaths in England and Wales involving methadone were recorded as also involving another substance (Figure 10). Alcohol has tended to be the substance most commonly recorded in deaths involving methadone and other substances (Figure 11), but this shows a very marked recent decline which corresponds to an increase in deaths also involving...
other opioids. Similarly, there has been a recent decrease in the number of methadone-related deaths for which benzodiazepines were also recorded.

**Figure 10: Proportion of deaths involving methadone alone or in combination with other substances: 2013, England and Wales**

![Pie chart showing proportions of methadone alone and with other substances.]

**Figure 11: Percentage of deaths involving methadone and other substances, by selected substance type involved: 2013, England and Wales**

![Bar chart showing percentages of deaths involving methadone and other substances.]

3.2.7 The majority (70%) of deaths in England and Wales involving tramadol are also recorded as involving another substance (Figure 12). During 2013: 36% of deaths involving tramadol and other substances were recorded as also involving alcohol; 32% antidepressants; 27% heroin; 21% benzodiazepines; and 14% methadone (Figure 13). The presence of antidepressants in almost one-third of deaths involving Tramadol may, perhaps, indicate deaths involving prescribed tramadol.
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Figure 12: Proportion of deaths involving tramadol alone or in combination with other substances: 2013 England and Wales

![Pie chart showing 30% tramadol alone and 70% with another substance(s).]

Figure 13: Percentage of deaths involving tramadol and other substances, by selected substance types: 2013, England and Wales

![Bar chart showing percentages of deaths involving tramadol and other substances: Alcohol (35%), Antidepressants (30%), Heroin/morphine (25%), Benzodiazepines (20%), Methadone (15%).]
4 Causes and drivers of trends in opioid-related deaths in the UK

4.1 Introduction

4.1.1 In order to reduce the numbers of opioid-related deaths in the UK in future, it is important to develop our understanding of the causes and drivers of change in these numbers in the past.

4.1.2 The previous section has shown that there have been substantial changes in opioid-related deaths in recent years. A number of potential causes of these changes have been suggested, and these will be considered here. They include:

- The ageing of the heroin-using population; this combines with their wide variety of risk behaviours and their increasingly complex health problems and substance use patterns.
- Changes in the availability and purity of heroin at street level.
- Socio-economic changes, including increasing deprivation and cuts to support services in deprived areas.
- Changes in the commissioning and provision of drug treatment.

4.1.3 It should be noted that research has not definitively established the causal contribution of each of these factors to changing trends in DRDs.

4.2 Ageing, risk and health behaviours

4.2.1 The previous chapter has shown the increasing age in the profile of opioid-related deaths of both men and women.

4.2.2 Research has shown that heroin users become more vulnerable to death from overdose as they age (Darke, 2016; Pierce et al., 2015; Merrall, Bird, & Hutchinson, 2012). As they age, they also become more vulnerable to a range of other health problems, including respiratory, cardiovascular, liver and communicable diseases. These vulnerabilities are exacerbated when people are engaged in multiple risk behaviours, including smoking, chronic alcohol use, poly-drug use (see below), poor diet and lack of exercise.

4.2.3 As shown in the previous chapter, an increasing number of deaths involving heroin in England and Wales have involved other substances. Some of this increase may be attributable to improved recording of multiple substances involved. But the figures suggest that many recent heroin-related deaths have also involved alcohol, other opioids (including methadone) and/or benzodiazepines. It is well-known that some types of poly-drug use, particularly drugs with a sedative effect, increase the risk of death (Modesto-Lowe et al., 2010).

4.2.4 The interaction between the increasing age of the heroin-using cohort and their range of health problems, socio-economic circumstances and risk behaviours
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(including poly-substance use and injecting) is likely to be a driver of recent increases in opioid-related deaths.

4.3 Changes in the availability and purity of heroin

4.3.1 Around 2010, the amount of heroin that was available at street level in the UK reduced – a period that has come to be known as the ‘heroin drought’. According to the National Crime Agency, the purity of heroin at “local dealer level” fell to 18% in 2011 (NCA ENDORSE data, 2009-2016). Street prices were also reported to increase (Harris, et al., 2015).

4.3.2 Notwithstanding temporal variability in the extent of toxicological screening, Figure 6 on page 18 suggests that this change in the availability of heroin had an effect on the pattern of opioid-related deaths. Specifically, there was a reduction in the number of deaths involving heroin, and a simultaneous (but smaller) increase in deaths involving methadone.

4.3.3 Some people who use heroin reported temporarily reducing or stopping their use during this period. Some also reported adverse effects from higher levels of adulterants in the street heroin that they did use (Harris et al., 2015).

4.3.4 The causes of the heroin ‘drought’ are not well understood, but may have included weather and conflict in Pakistan and Afghanistan, crop failures in the Afghan poppy fields, as well as law enforcement interventions in the supply route through Turkey (Griffiths et al., 2012; United Nations Office on Drugs and Crime (UNODC), 2012).

4.3.5 Since the ‘heroin drought’, there have been significant increases in the availability and purity of heroin at street level. The recorded purity of local dealer level heroin climbed back up to 44% by 2015 (NCA ENDORSE data, 2009-2016).

4.3.6 While the purity of heroin, per se, may make a moderate contribution to increased risk of fatal overdose (Darke & Hall, 2003; Darke, et al., 1999), changes in purity may serve as an indicator of the wider availability of heroin. As availability of heroin declines, so does the purity of the heroin that is available to users. It therefore seems that the general availability of heroin may have an impact on the numbers of opioid-related deaths. It seems that this effect is not necessarily produced by increased dangers of using higher purity heroin. Rather, it seems that the availability and price of heroin affects whether users take it, the amount they take, how often they take it and therefore impacts on the rate of heroin-related death.

4.4 Socio-economic changes

4.4.1 There are various social factors – at both community and individual level – that are associated with drug-related risk behaviours and deaths (ACMD, 1998; Rhodes, 2009).

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6 The recorded purity in 2010 was 39%, but there was a change in the data collation procedure between 2010 and 2011. From 2011, the figures are calculated using data from seizures weighing less than 25g, with specific, user-level package sizes. Prior to 2011, the figures were taken from seizures weighing anything between 25g and 500g, including larger package sizes than 25g.
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4.4.2 Individually, risk factors for problematic drug use and DRD include long-term poverty, unemployment and homelessness (ACMD, 2000; Davidson et al., 2003; Hannon & Cuddy, 2006; Stevens, 2011; Wright, et al., 2005).

4.4.3 Figure 13 shows that drug misuse death rates are substantially higher in the most deprived areas. It also shows that recent increases in deaths have been largest in the most deprived areas. This probably reflects the fact that prevalence of problematic heroin use is higher in areas of high socio-economic deprivation (ACMD, 1998). These deaths will increase health inequalities that are already wide and growing; inequality in life expectancy between the richest and poorest men has been growing since 1993 (Mayhew & Smith, 2016). There are also known links between increased financial hardship and increases in suicide risk (Barr et al., 2012), and between suicidality and the risk of DRD (Bogdanowicz et al., 2016).

**Figure 14**: Age standardised mortality rates (drug misuse deaths per 1 million population) by lower super output areas sorted into quintiles of the Index of Multiple Deprivation (1 is the most deprived), 2001 to 2014 registrations (Source: Office for National Statistics)

![Figure 14: Age standardised mortality rates](image)

4.4.4 Economic change in the 1970s and 1980s, and especially the rise of unemployment and poverty in de-industrialised areas of the UK, has been identified as one of the factors causing the inflow of people into heroin use in the 1980s and early 1990s (MacGregor & Thickett, 2011; Pearson, 1987).

4.4.5 Economic changes since the financial crash of 2008 have further worsened some forms of socio-economic deprivation. Real wages have been depressed (Belfield et al., 2014) and, in England, the number of homeless people has increased (Department for Communities and Local Government, 2016; Fitzpatrick et al., 2016). While employment has increased, this has largely been in part-time work and self-employment (ONS, 2016a, 2016b; Resolution Foundation, 2016). Such jobs are less
likely to provide the longer-term stability that is supportive of recovery from problematic drug use.

4.4.6 Policy changes that have been made since 2010 have also affected individuals and areas that suffer most from socio-economic deprivation. The areas that experience the highest rates of DRDs are among those that have experienced the greatest reductions in funding for local authority services and welfare benefits for working age adults (Beatty & Fothergill, 2016; Hastings et al., 2015). It is projected that rates of absolute poverty will increase between the years ending 2015 to 2016 and 2020 to 2021, partly due to the effect of changes to taxes and welfare benefits (Browne & Hodd, 2016). This means that both the incomes of many people who use drugs and the services provided to them by local authorities have been, and will continue to be, cut.

4.4.7 Increasing the socio-economic deprivation of vulnerable people and of the areas that they live in, while reducing public services in these areas, would be expected to increase their social isolation, their experience of poverty and so their risks of DRD. Warnings were given about the potential effects of such changes on the health of people who use drugs (MacGregor & Thickett, 2011; ACMD, 2015).

4.4.8 An increase in DRDs has been observed, although it is not possible – given the current research base – to establish a causal relationship between socio-economic conditions and trends in DRDs in each area.

4.5 Drug treatment and commissioning practices

4.5.1 There has been concern for several years that treatment services were not providing optimal doses of OST medication, leading to risks of patients using heroin in combination with OST and so an increased risk of overdose (ACMD, 2015).

4.5.2 Since the late 2000s, there has been an emphasis in the UK and Scottish drug strategy documents (although less so in Wales) on the promotion of recovery in drug treatment (HM Government, 2010; The Scottish Government, 2008; Welsh Government, 2008; Department of Health, Social Services and Public Safety, 2011; Lloyd, 2009). Increasing emphasis has been placed – in both policy documents and commissioning practice – on getting people to leave treatment abstinent from all drugs, having completed OST (e.g. Inter-Ministerial Group on Drugs, 2012). While ACMD fully supports the aim of recovery from heroin misuse, we have previously reported evidence that heroin dependence is prolonged and relapse is common after leaving treatment, even if a service user wants to achieve abstinence (ACMD, 2014).

4.5.3 As periods of transition both into and out of treatment are associated with increased risk of overdose and death (Cornish et al., 2010; Pierce et al., 2016), encouraging people to leave treatment may increase their risk of dying if they are not able to sustain abstinence.

4.5.4 Changes to commissioning practices have increased the frequency of recommissioning of drug treatment services. The ACMD is concerned that frequent recommissioning diminishes the quality of services and reduces their ability to retain
patients in treatment (ACMD, 2015). The ACMD has also received evidence of arbitrary changes to the conditions attached to treatment of individual patients that are caused by changes in the provider of the treatment service, rather than being based on clinical need.

4.5.5 There is also emerging evidence that some drug treatment services may not be providing services in a way that will enable both the reduction of drug-related harm and the achievement of recovery (Dennis, 2016; Floodgate, 2016). Practices which could increase risk to patients would include:

- encouraging patients to reduce their dosage of OST before they are ready and regardless of clinical need;
- imposing arbitrary limits on the length of time that patients can spend in OST (against national guidelines);
- reducing or ending OST on the grounds of relatively minor non-compliance with the treatment programmes (e.g. not attending appointments); or
- encouraging patients to participate in forms of treatment that do not involve OST when they have a clinical need for OST.

4.5.6 In answer to queries about the experiences of drug users in treatment, the ACMD has received reports of each example of these kinds of practice occurring in treatment services, but has no way of quantifying how widespread they are.

4.5.7 Treatment practices, and the reputations of treatment services among opioid users, are important for the reduction of DRDs. If services have a reputation that they want everyone to ‘come off OST within a set time’ or are not seen as not useful to those who may seek treatment, this may put potential opioid service users off treatment, placing them at greater risk of overdose and potentially increasing the rate of DRDs.

4.5.8 The ACMD has also received evidence that many drug treatment services are working hard to try and protect the health of their patients by providing optimal dosing in OST and providing individualised support to their recovery (ACMD, 2016). Such treatment will be effective in attracting and retaining vulnerable people. The treatment services that are most effective will be those that combine harm reduction services with support to recovery.

4.5.9 The recent inquiry by the Local Government Association and Public Health England (2016a) found that it was not possible to draw a conclusive link between treatment policy and trends in deaths. Data are available in England on the treatment status of those people who have died. Figure 15 below shows that there has been an increase in deaths among people recorded as being in treatment since 2008. In 2013, there was also a small increase in deaths among those who had recently left treatment. Most recently, Public Health England (2016b) has reported an increase of 14% in the overall number of people who died while in contact with treatment services; from 2,393 deaths in 2014/1, to 2,689 deaths in 2015/16.
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Figure 15: Breakdown of opiate misuse deaths by treatment status, 2008-2013 (reproduced from Public Health England, 2016c)

Note: figures for 2013 should be regarded as partially incomplete.

4.5.10 Figure 15 also suggests that large proportions of deaths continue to occur among those who are recorded as having had no contact with treatment. It is therefore important to know whether treatment services and commissioners are doing as much as they could do to attract and retain vulnerable people.  

4.6 Conclusion

4.6.1 From this brief review of the potential causes of recent trends in DRD, we can assert with a good degree of confidence that the increasing vulnerability of the UK’s ageing cohort of heroin or opioid users with increasingly complex health needs (including long-term conditions and poly-substance use), social care needs, and continuing multiple risk behaviours is highly likely to have contributed to recent increases in DRDs.

4.6.2 Other factors, including changes in the availability of street heroin, socio-economic changes (including cuts to health and social care, welfare benefits and local authority services) and changes in treatment services and commissioning practices may also have contributed to these increases.

7 It is possible that this proportion is over-estimated, due to problems in matching individuals who appear in treatment records with those who have died. If these peoples’ details are recorded differently in each dataset, they would not be matched, so inflating the proportion of people who are estimated to have died who have not been in contact with treatment.
5 Policy and treatment responses to prevent opioid-related deaths

5.1 Introduction

5.1.1 Previous chapters of this report have demonstrated that opioid-related death is a serious and rising public health problem which has complex causes. This chapter will discuss the policy and treatment responses that can be used to reduce the numbers of opioid-related deaths.

5.1.2 The responses covered in this chapter include those that are already being used in the UK and elsewhere. The chapter uses the international evidence on these responses, with a focus on evidence from systematic reviews, high-quality randomised controlled trials and large observational studies.

5.1.3 The scale of the challenge, and the limits to current interventions, also requires that investment be made in developing and evaluating new, innovative approaches for the reduction of opioid-related death.

5.1.4 Responses are grouped into six sections:

- Supply reduction.
- Support for abstinence and recovery from dependence.
- Opioid substitution therapy (OST).
- Prevention and treatment of overdose.
- Social and integrated responses.
- Research.

5.2 Supply reduction

5.2.1 From experience in the UK and elsewhere, it seems that changes in the availability and price of street heroin can have an effect on opioid-related deaths. Reductions in price (but not increases in purity) were associated with increased heroin overdose hospitalisations in the USA between 1992 and 2008 (Unick et al., 2014). Reductions in the availability of heroin were associated with reduced overdoses in Australia and western Canada in 2001 (Degenhardt et al., 2006; Weatherburn et al., 2003; Wood et al., 2006). This also appears to have occurred in the UK from 2010 to 2012 (see chapters 3 and 4 of this report).

5.2.2 However, the interventions and circumstances that led to these heroin shortages are not well understood. They may have had more to do with trends in global heroin supply than with law enforcement in countries of consumption (Degenhardt & Hall, 2006; Griffiths et al., 2012; Jiggens, 2008; Wood et al., 2006). They may therefore be difficult to reproduce. Any shortages that are produced may also be difficult to sustain, due to the wide variety of potential areas of production and routes of transit. Heroin markets have frequently reconfigured themselves in the past in response to
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government interventions (Paoli et al., 2012). The limited evidence available suggests that simply increasing arrests, incarcerations or seizures may not have the desired effect in reducing availability and deaths (Pollack & Reuter, 2014).

5.2.3 Even if reductions in the availability of heroin can be produced, the effect in reducing deaths may be reduced if users move to other potentially harmful substances. During the Australian heroin ‘drought’ of 2001, an initial increase in use of cocaine, benzodiazepines and methamphetamine was observed (Degenhardt et al., 2005). And, as discussed above, the UK heroin ‘drought’ from 2010 to 2012 coincided with an increase in deaths related to methadone as users sought alternative opioids. It should, however, be noted that there was an overall, short-term reduction in deaths in both these cases.

5.2.4 It is unlikely that allowing a regulated market for heroin – outside the confines of medical prescription for a tightly defined group of patients – would reduce deaths. Drug law enforcement probably does have an effect in containing, if not eradicating, the illicit heroin market and so in increasing the price of street heroin (Pollack & Reuter, 2014; Windle & Farrell, 2012). The USA and Canada have seen very substantial increases in deaths from prescribed opioids (King et al., 2014). This does not suggest that the number of lives saved by the provision of pure, uncontaminated opioids would be enough to offset the increases in deaths that would arise from the increased use of these substances if they were to be more widely prescribed or sold (Darke & Farrell, 2014).

5.2.5 The ACMD will shortly publish a report on the diversion and illicit supply of medicines which includes a recommendation for reducing supply of opioids through these routes. The ACMD also brings readers attention to the 2016 NICE document, Controlled drugs: safe use and management.

5.2.6 The reduction in deaths from tramadol that was registered in England and Wales in 2015 may suggest that tighter controls on its prescription that were introduced following an ACMD recommendation in 2013 (ACMD, 2013a) have had the intended effect of reducing deaths involving this medicine, but this should be closely monitored for longer term changes.

5.2.7 Professional experience suggests that the key to reducing the illicit supply of heroin lies in targeting those who are bringing large quantities into the UK and disrupting the activities of their organised criminal networks, which may often be international. Such targeting may require substantial international cooperation and a complex range of tactics, as well as a considerable effort in time and money.

5.3 Support for abstinence and recovery from dependence

5.3.1 Most people who enter treatment for heroin use want to stop (McKeganey et al., 2006). Abstinence – when it is sustained – is the most certain way of reducing the risk of overdose and death. The ACMD fully supports the aims of the UK government to help people recover from drug dependence, but has also cautioned government to be realistic with regard to the ageing cohort of heroin users, with complex health and social care needs and poor recovery capital.
5.3.2 It is known that dependence on heroin is a chronic disorder with very high rates of relapse. Typically, a minority (estimated at less than 30%) of heroin users who enter treatment will achieve stable abstinence in 10 to 30 years (Hser et al., 2015). Many people who become abstinent will not sustain it but will relapse to opioid use. This is a known risk for overdose and death, as users lose tolerance to opioids during periods of abstinence.

5.3.3 The English drug treatment system has increased the number of patients who leave treatments free of drug use from less than 15,000 in the year ending 31 March 2006 to about 30,000 in the year ending 31 March 2011, but this number has since stabilised. The proportion of people leaving treatment drug-free in Wales has also stabilised, at around 13%, in recent years. However, it should be noted that the type of completion of drug treatment, whether drug-free or not, does not seem to affect the risks of subsequent fatal overdose (Pierce et al., 2016).

5.3.4 Some people can achieve recovery through outpatient treatment alone, but others can benefit from residential treatment in order to achieve their goals (Vanderplasschen et al., 2013). The evidence for the use of residential services to support abstinence remains under-developed, and high rates of drop-out and relapse have been found (National Collaborating Centre for Mental Health, 2008; Malivert et al., 2012). The long-term effectiveness of residential treatment may be boosted by the provision of follow-on ‘recovery housing’ (Reif et al., 2014).

5.3.5 Contingency management (i.e. the use of monetary or other rewards to incentivise progress in treatment) has evidence of effectiveness in supporting abstinence, at least in the short term (National Collaborating Centre for Mental Health, 2008; Benishek et al., 2014; NICE, 2007), but it is rarely used in treatment services in the UK.

5.3.6 It is known that a range of other services including support to housing, employment and family relationships can help people who use heroin to recover from dependence (ACMD, 2012, 2013b), as was recognised in the 2010 drug strategy.

5.3.7 There are medicines, such as naltrexone, which are used to support patients’ decisions to abstain from heroin. Evidence on the effectiveness of this treatment is so far weak and mixed (Minozzi et al., 2006; Lobmaier et al., 2010; Tait et al., 2008; Larney et al., 2014). A recent Australian study which compared patients who received oral naltrexone to methadone treatment found that rates of death were 3.5 times higher in those prescribed naltrexone (Degenhardt et al., 2015). Naltrexone implants may provide better effects for some patients (Larney et al., 2014).

5.3.8 There are risks associated with the move towards abstinence. For example, there is a higher risk of death for heroin users who have left OST than for those who stay in it, especially in the first few weeks (Bauer et al., 2008; Cousins et al., 2016; Pierce et al., 2016). As Hickman et al. (2011, p. 332) noted, “Premature or excessive zeal in movement towards recovery with an excessive focus on total ‘abstinence’ can actually stall progress, or trigger further decline.”
5.3.9 The ACMD recommends that central and local governments implement strategies to protect the current levels of investment in evidence-based drug treatment which can enable people to achieve a range of recovery outcomes, including sustained abstinence from opioids.

5.4 Opioid substitution therapy (OST)

5.4.1 Opioid substitution therapy involves the prescription of medicines, such as methadone, buprenorphine, diamorphine (pharmaceutical heroin) or hydromorphone to people who are dependent users of street heroin.

5.4.2 Many systematic reviews, randomised trials and large-scale observational studies have found OST to be effective in retaining patients in treatment, reducing use of street heroin, reducing offending, and improving health including reducing the transmission of HIV and viral hepatitis, as well as rates of death among heroin users while they are in OST (Mattick et al., 2009; Brugal et al., 2005; Clausen, Anchersen, & Waal, 2008; Gisev et al., 2015; Pierce et al., 2015; Cousins et al., 2016; Degenhardt et al., 2009).

5.4.3 Not only is there a higher risk of death for heroin users who are not in any form of treatment, there is also a higher risk of death for those who are in treatments which do not include OST (Pierce et al., 2016).

5.4.4 There has been considerable expansion in the use of OST in the UK since the mid-1990s. It is likely that this has had a substantial effect in limiting the increase in DRDs that would otherwise have occurred. For example, in England, it has been estimated that the provision of drug treatment, the majority of which involves OST, saved approximately 880 lives per year in 2008 to 2011 (White et al., 2015).

5.4.5 OST can also be effective when provided to prisoners in reducing the risk of death on release (Dolan et al., 2005; Kinlock et al., 2009). It is important that effective OST be available on the basis of clinical need within and on release from prison.

5.4.6 There is a danger that prescribed opioid substitutes are diverted for use by other people. Data collected by the National Programme on Substance Abuse Deaths indicates that many people whose death was related to methadone were not themselves being prescribed this medication (Claridge & Goodair, 2015). Consumption of the substitute can be supervised in order to reduce this risk (Independent Expert Working Group, 2016). This issue has also been considered by the ACMD in its forthcoming inquiry into the diversion and illicit supply of medicines.

5.4.7 Expansion of supervised consumption of methadone was followed by significant reductions in methadone-related deaths in both England and Scotland (Strang et al., 2010). But a longer period or higher frequency of supervision may be less effective in retaining patients in treatment (Cousins et al. 2016; Holland et al., 2014).

5.4.8 For some patients, it may be safer to prescribe buprenorphine than methadone, as some studies have shown lower rates of death with buprenorphine (Marteau et al., 2015; Bell et al., 2009). However, the improved safety of buprenorphine is counter-
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balanced by some evidence that it is less effective than methadone in retaining patients in treatment (Mattick et al., 2008; Degenhardt et al., 2009).  

5.4.9 Cornish et al., (2010) have investigated whether provision of specific types of OST in a primary care setting is associated with different risk of death due to any cause. Additional work, led by the University of Bristol is investigating this area further, using primary care data.

5.4.10 The draft updated clinical guidance on the treatment of drug dependence has considered the issue of which type of pharmacotherapy to use in individual cases, and the ACMD refers readers who are involved in drug treatment services to this guidance (Independent Expert Working Group, 2016).

5.4.11 Heroin-assisted treatment (HAT) is a specialist service that is provided to people for whom other opioid substitutes have not been effective (Uchtenhagen, 2008). Multiple randomised trials of HAT have shown that it is effective in reducing the use of street heroin and related negative outcomes – but with a higher risk of adverse events than other forms of OST – for people for whom these forms of OST have not been effective (Strang et al., 2015; Ferri et al., 2011).

5.4.12 As HAT is more effective in retaining in treatment those people for whom other forms of OST have not been effective, it is also highly probable that HAT reduces rates of death among this group. Lower rates of death have also been observed among patients in HAT than in other forms of OST (Rehm et al., 2005).

5.4.13 In England, pilot studies showed that HAT is more cost-effective than optimised methadone treatment for this target group (Byford et al., 2013). There is a recent proposal to introduce HAT in Glasgow (NHS Greater Glasgow and Clyde, 2016).

5.4.14 In 2009, the Injectable Opiate Treatment Expert Group considered the available evidence on the effectiveness and cost-effectiveness of HAT. It recommended that this treatment be expanded to cover a larger proportion of the minority of opioid-dependent persons who need this treatment. It also noted that central funding and coordination would be necessary to support the availability of this treatment (Injectable Opioid Treatment Expert Group, 2009). Despite this advice, central funding for HAT in England was ended in 2015. This funding was not replaced at local level and the three clinics that were providing HAT closed down.

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8 Unfortunately, complete time-series data for prescribing are only available for relatively small cohorts of individuals newly starting treatment (albeit that as time elapses, these cohorts will grow). Thus, the numbers of drug-related deaths that occur in these cohorts are rather small and they are unlikely to provide sufficient statistical power to ascertain whether there are associations specifically between DRD and prescribing patterns. Moreover, this type of observational study is unable to determine whether there are causal links between the type of pharmacotherapy that is provided and the risk of DRD. There is evidence that patients who have lower severity of dependence, less complex problems, and greater recovery capital are more likely to be provided with specific types of pharmacotherapy than others (Marsden et al., 2014). These patients may be at lower risk of drug-related death anyway, irrespective of the type of treatment that they receive; hence any difference in risk that might be observed could not be ascribed directly to the type of pharmacotherapy that they receive.
5.4.15 While concerns have been expressed that some patients have been in OST for several years, there is also concern that many patients experience quite short durations of treatment. As entry to and exit from OST are times of heightened risk, this may increase their vulnerability. Recent work in Scotland by the Scottish Drug Forum, the Scottish Government, and Hepatitis Scotland concluded that retention in services is key in reducing DRDs (Scottish Drugs Forum, 2016).

5.4.16 Both the ACMD (2012a, 2015) and the Recovery Oriented Drug Treatment Expert Group (2012) have made recommendations for improving recovery outcomes in drug treatment. Both bodies have advised that OST retains a vital place in protecting people’s health while they move towards recovery.

5.4.17 The ACMD is concerned with the effects of unnecessary re-procurement of drug treatment services, as this may damage continuity of optimised harm reduction and treatment services.

5.4.18 **The ACMD recommends that:**

- **governments continue to invest in high-quality OST of optimal dosage and duration delivered together with interventions to help people achieve wider recovery outcomes including health and well-being, in order to continue to reduce rates of DRD;**

- **drug treatment services should follow national clinical guidelines on OST and provide tailored treatment for individuals for as long as required;**

- **central government funding should be provided to support HAT for patients for whom other forms of OST have not been effective.**

5.5 Prevention and treatment of overdose

5.5.1 As stated in chapter 4, there are many social and individual-level factors that influence the risk of overdose. At the individual level, these include behaviours that can be changed, such as injecting rather than smoking heroin.

5.5.2 The proportion of deaths from overdoses that do occur can be reduced by prompt medical responses, including administering naloxone to reverse the effects of opioid overdose.

5.5.3 For people who continue to use heroin and other drugs by injection, it may be safer for them to do so under medical supervision.

5.5.4 In its 2000 report on reducing DRDs, the ACMD recommended the expansion of services to help people move away from injecting. The prevalence of injecting varies widely across areas. Judging from the proportion of patients who report injecting at entry to treatment, there appears to have been a decline in injecting in England. The pattern in other parts of the UK is not clear.

5.5.5 In environments that are risky for people who use heroin (Rhodes, 2009), the influence of specific interventions to reduce injecting may be limited. However, entry
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to drug treatment can promote transition from injecting to smoking, even for those who continue to use street heroin (Gossop et al., 2004). OST is also effective in reducing drug injections (Gowing et al., 2011).

5.5.6 There are also specific interventions that can help to prevent initiation into injecting and promote transition away from injecting. Given the ageing profile of UK heroin users, the latter are more likely to have an impact in reducing DRD. Such interventions include the provision of foil by needle exchanges. Initial evidence suggests that this has been positively accepted since it became legal to distribute foil in 2013 (Ryan-Mills & Stephenson, 2016). Local authorities can include this and other such services in the local provision of drug treatment when commissioning services.

5.5.7 The ACMD (2012b) previously recommended wider use of naloxone, including by people other than medical staff. Naloxone is a medicine that reverses the effects of an opioid overdose (Strang et al., 2013). There is strong evidence for its effectiveness in preventing DRDs (Clark et al., 2014; Giglio et al., 2015; EMCDDA, 2015; McDonald & Strang, 2016). It can be provided by medical staff, and drug treatment and hostel workers. Studies have shown that it can also be effectively delivered between peers who use drugs (Dwyer et al., 2016). A US study has estimated that providing naloxone saves more money than it costs (Coffin & Sullivan, 2013).

5.5.8 Naloxone can be provided for intramuscular or intranasal administration (Kerr et al., 2009); however, currently used intranasal preparations may not be as effective as when injected (Strang et al., 2016). No intranasal preparations of naloxone are yet licensed for use in the UK.

5.5.9 The provision of naloxone is particularly important at points of transition between residential settings and when leaving treatment, given that we know there is an increased rate of death among heroin users who are released from prison (Farrell & Marsden, 2008), in-patient drug-free treatment and detoxification (Ravndal & Amundsen, 2010; Strang et al., 2003) and hospital (S. White et al., 2015), and when people leave specialist drug treatment, including OST (Cornish et al., 2010; Davoli et al., 2007).

5.5.10 Other countries including Italy, Australia and the USA have enabled pharmacists to provide naloxone to people who may need to use it, including by over-the-counter sale without prescription (Lenton et al., 2016). In the UK, it is unlikely that naloxone would be approved for OTC sale in injectable form, so a company would first have to gain a license for an intranasal preparation before being able to get permission for such sales.

5.5.11 The proportion of users of needle exchange services in Scotland who had been prescribed naloxone in the past year was estimated at only 32% in the year ending 31 March 2014 (when the National Naloxone programme distributed 4,735 take-

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9 Providing foil can help users move from injecting to ‘chasing’ heroin fumes off heated foil (Pizzey & Hunt, 2008; ACMD, 2010).
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home naloxone kits), although this had increased substantially since the year ending 31 March 2012 (when it distributed 2,750 such kits) (McAuley et al., 2016; ISD Scotland, 2016b). It is not known how many of the people who inject opioids currently have immediate access to naloxone in the places where they use opioids.

5.5.12 Medically-supervised drug consumption clinics are facilities where people can come to use illicit drugs (that they have purchased elsewhere) in a hygienic and medically-supervised setting. The presence of medical staff means that overdose events can be detected early and treated professionally.

5.5.13 Most of the research literature on this topic relates to the medically-supervised injecting facilities in Vancouver and Sydney. These focus on providing a place for people to inject heroin. In some European countries, there are also services for safer use by smoking (Bridge, 2013).

5.5.14 Research on the effects of medically-supervised drug consumption clinics has shown that they reduce injecting risk behaviours and overdose fatalities (Potier et al., 2014). They have been estimated to save more money than they cost, due to the reductions in deaths and HIV infections that they produce (Andresen & Boyd, 2010; Bayoumi & Zaric, 2008; Pinkerton, 2010).

5.5.15 Such facilities have not been found to increase injecting, drug use or local crime rates. In addition to preventing overdose deaths, they can provide other benefits, such as reductions in blood-borne viruses, improved access to primary care and more intensive forms of drug treatment. No deaths from overdose have ever occurred in such facilities (Potier et al., 2014; NHS Greater Glasgow and Clyde, 2016).

5.5.16 The effect of such centres can be highly localised. There was a 35% reduction in the rate of fatal overdoses within 500 metres of the Vancouver site after it opened. The reduction in deaths outside this zone was much smaller at 9% (Marshall et al., 2011) Similarly, there was a significant reduction in the rate of ambulance call outs for opioid overdoses in the immediate vicinity of the Sydney supervised injecting facility after it opened (Salmon et al., 2010).

5.5.17 Proposals are already in place to create a medically-supervised injecting facility in Glasgow, partly as a response to an outbreak of HIV among people who inject drugs in public places in the city centre (NHS Greater Glasgow and Clyde, 2016).

5.5.18 The ACMD recommends that:

- **naloxone be made available routinely, cheaply and easily to people who use opioids, and to their families and friends;**

- **consideration be given – by the governments of each UK country and by local commissioners of drug treatment services – to the potential to reduce DRDs and other harms through the provision of medically-supervised drug consumption clinics in localities with a high concentration of injecting drug use.**
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5.6 Social and integrated responses for the reduction of health inequalities

5.6.1 In its 2000 report on DRD, the ACMD noted that “deprivation can breed social conditions which encourage the more dangerous forms of drug misuse, and which thus enhance the risk of DRD”. As stated in that report, “there is a need for continued and strengthened action directed at the amelioration of social deprivation”.

5.6.2 As discussed in chapter 4, vulnerability to DRDs is exacerbated by socio-economic deprivation at both individual and area level. The people who are most at risk from opioid-related deaths are likely to experience complex needs that require integrated approaches across different public services.

5.6.3 It is particularly concerning that drug treatment and prevention services in England are planned to be among those public health services that receive the most substantial funding cuts as a consequence of the government’s decision to cut the public health grant. Planned spending by English local authorities on treating and preventing adult drug misuse and related harms is falling by over 16% – more than £72 million – between the years ending 2015 to 2016 and 2016 to 2017 (DCLG, 2015, 2016). The ACMD Recovery Committee’s recent work also suggests that there will continue to be substantial cuts in funding through to the year ending 31 March 2021 (ACMD Recovery Committee’s forthcoming report on commissioning). This work establishes that “reductions in funding are the single biggest threat to local areas enabling service users and community to achieve recovery outcomes and reduce health inequalities”.

5.6.4 In Scotland, cuts in central government funding for drug services have been absorbed by health boards without affecting drug treatment services, but the funding position is uncertain from 2017 onwards. Funding is more stable in Wales, under the current Substance Misuse Delivery Plan, which runs to 2018.

5.6.5 Homeless heroin users are particularly vulnerable (ACMD, 2000; Wright et al., 2005; Hetherington & Hamlet, 2015; Morrison, 2009). There is some, although limited, evidence that the provision of housing can help patients to stay in treatment and sustain recovery, although more support is needed as well as just the provision of accommodation (Kirst et al., 2015; Reif et al., 2014).

5.6.6 Other health issues, including mental health problems, cardiovascular conditions, respiratory problems and the health impacts of chronic alcohol use and poor diet are relatively common among long-term users of heroin. These complex needs require responses from multiple agencies, and therefore require services to be integrated across professional discipline and organisational boundaries. Examples of such service integration include the incorporation of naloxone distribution and training into primary care services, hospitals, hostels and police services (Wagner et al., 2016).

5.6.7 There is a particular problem of opioid-related deaths among people who have problems with heroin but who are not in contact with drug treatment services. Many of them are homeless and/or have mental health problems and/or other problems (ACMD, 2000; Hser et al., 2015).
5.6.8 In the field of mental health, the assertive outreach approach has been found to be effective in engaging people who are in need of treatment but not in contact with such services (Commander et al., 2008; Sood & Owen, 2014). Assertive outreach can also be effective in engaging people with co-occurring substance use and mental health problems, including those who are homeless (Fisk et al., 2006; Place, 2010; van Vugt, Kroon et al., 2014; Wright & Tompkins, 2006).

5.6.9 Such work requires a partnership approach between agencies in order to identify and meet the multiple needs of this group. As these people are likely to present themselves frequently to acute services (including police, ambulance, in-patient psychiatric care, and accident and emergency departments), it is likely that earlier outreach to them will save money by reducing the number of acute episodes that have to be dealt with, including overdoses and deaths.

5.6.10 There is a particular need, given the health problems caused by the combination of long-term heroin use and smoking of tobacco, to provide integrated services for smoking cessation and tobacco harm reduction.

5.6.11 The people who are most vulnerable to opioid-related death are also a group that experiences high rates of infection by hepatitis C virus (HCV). Effective treatments exist for HCV and even currently injecting drug users can benefit from them (Bruggmann & Grebely, 2015). Integrating HCV treatment with OST can be particularly effective. For example, a German study found rates of HCV treatment adherence of over 90% in a group of patients who were in HAT (Bernd et al., 2010).

5.6.12 The Welsh Government (2015) has issued guidance to commissioners of substance misuse services advising them to combine recovery orientation, harm reduction and partnership with other agencies. There is no such national guidance in England.

5.6.13 Research in this area suggests that services to meet complex needs at local level require a clear focus, inter-disciplinary collaboration, giving local areas greater flexibility to innovate while also providing some central government support (Wilson et al., 2015).

5.6.14 Governments and local authorities could reduce deaths by supporting innovation to develop inter-disciplinary, multi-agency responses to the complex needs of people who are vulnerable to opioid-related death. These should include integration of drug treatment with services for homelessness, mental health problems (including assertive outreach), chronic alcohol use, smoking cessation, tobacco harm reduction and HCV treatment.

5.6.15 The ACMD recommends that central and local governments provide an integrated approach for drug users at risk of DRD, and prioritise funding and access to physical and mental health and social care services.
5.7 Research

5.7.1 In the course of writing this report, members of the working group have come across a number of gaps in the evidence base that hamper more effective responses to opioid-related deaths. These gaps include:

- Rigorous analysis of the causes and drivers of trends in opioid-related deaths.
- Evaluation to establish the most effective strategies for reducing the illicit supply of heroin and other opioids.
- Research to test and improve the effectiveness of drug treatment and other services in supporting sustained abstinence. This should study both outpatient and residential services, including contingency management, as well as support to housing, employment and the family relationships of people who want to put drug dependence behind them.
- Evaluations of interventions – in addition to OST and other forms of treatment – that may be effective in reducing the use of opioids by injection.
- Reliable estimates for each country of the UK of the proportion of the people who use opioids who have immediate access to naloxone at the times and places where they are using opioids.
- Research on the effectiveness of intranasal preparations of naloxone.
- Evaluation of national and local initiatives aimed at the reduction of opioid-related deaths.

5.7.2 The ACMD recommends that governments fund research to fill important gaps in the literature on the causes and prevention of opioid-related deaths.
6 Recommendations

In order to reduce opioid-related deaths in the UK, the ACMD recommends:

1. Improving the current processes by creating data standards for local reporting that feed into national systems. This may include: coroners reporting; toxicological assessments to understand poly-substance use; local partnership investigations and information sharing on DRDs and non-fatal overdoses; and strengthening links between national datasets including death registrations and national treatment monitoring systems (see section 2.7.6).

2. Central and local governments implement strategies to protect the current levels of investment in evidence-based drug treatment which can enable people to achieve a range of recovery outcomes, including sustained abstinence from opioids (section 5.3.9).

3. Central and local governments continue to invest in high-quality OST of optimal dosage and duration, delivered together with interventions to help people achieve wider recovery outcomes including health and well-being, in order to continue to reduce rates of DRD (section 5.4.18).

4. Drug treatment services should follow national clinical guidelines on OST and provide tailored treatment for individuals for as long as required (section 5.4.18).

5. Central government funding should be provided to support heroin-assisted treatment for patients for whom other forms of OST have not been effective (section 5.4.18).

6. That naloxone is made available routinely, cheaply and easily to people who use opioids, and to their families and friends (section 5.5.18).

7. Consideration is given – by the governments of each UK country and by local commissioners of drug treatment services – to the potential to reduce DRDs and other harms through the provision of medically-supervised drug consumption clinics in localities with a high concentration of injecting drug use (section 5.5.18).

8. Central and local governments provide an integrated approach for drug users at risk of DRD, and prioritise funding and access to physical and mental health and social care services (section 5.6.15).

9. Governments fund research to fill important gaps in the literature on the causes and prevention of opioid-related deaths (section 5.7.2).
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7 References


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8 Appendix A: Contributions to this Review

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