

# ACMD

## Advisory Council on the Misuse of Drugs

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15 December 2016

Dear Home Secretary and Secretary of State for Health

### **ACMD report on Diversion and Illicit Supply of Medicines**

The Advisory Council on the Misuse of Drugs (ACMD) is pleased to enclose its report on Diversion and Illicit Supply of Medicines (referred to as 'DISM') for your consideration.

This report is in response to the Home Office's commissioning letter of September 2013, in which the then Home Secretary requested the ACMD to explore the potential for medical and social harms arising from the illicit supply of medicines – predominantly controlled medicines.

We are grateful to the ACMD's stakeholders, who provided presentations at the evidence gathering days as well as helpful written submissions (these are included in a separate attachment, alongside the main report on the ACMD website).

This report sets out to:

- explore the extent of DISM in the UK, to find out which drugs are being diverted;
- evaluate the extent of the medical and social harms of such diversion; and
- assess whether DISM displaces or replaces the use of known recreational drugs of abuse, such as heroin.

In recent years, DISM has become of increasing public concern across the globe, although the hard evidence for this constituting a major problem other than in the United States is hard to find.

### ***Key findings***

**Type of drug:** The most prevalent diverted drugs are opioids and benzodiazepines. Increasing amounts of gabapentin and pregabalin are being diverted. Cognitive enhancers could be susceptible to diversion in the future. Further attention needs to be given to the misuse of codeine in over-the-counter (OTC) preparations as a precursor to the misuse of prescription opioids.

**Source:** The nature and prevalence of diversion suggests that at the present time the major source of supply is by prescription prior to diversion. The Internet is an increasing illicit source of medicines with many unregistered online pharmacies supplying prescriptions and medicines unethically. There is little evidence of DISM facilitated by organised crime or of unethical prescribing by doctors /non-medical prescribers. Recent information suggests that diversion of wholesale supplies may be an important source of illicit benzodiazepines

**Prevalence:** There is a common perception that prevalence of DISM is increasing. The prevalence of females who abuse prescription-only medicines (POMs) is greater than males, the converse of traditional drug abuse. Quantifying the extent of DISM is difficult owing to a lack of suitable monitoring systems.

The number of people seeking treatment for addiction to prescription medicines has reportedly increased. As with other drug users those using prescription drugs often have other mental health problems to cope with. DISM via the Internet has appealing attributes to a wide demographic of people.

**Displacement:** DISM can supplement but does not lead to the use of traditional illicit drugs. Displacement from traditional drugs tends to be temporary and is dependent on the cost and availability of traditional drugs.

**Social and medical harms:** Use of illicitly-supplied medicines increases risk of accidental overdose, infections and blood-borne viruses (BBVs). Medicines supplied illicitly may be counterfeit or adulterated. DISM damages patient-doctor relationships and can create an atmosphere of distrust.

**Prisons:** Most prisons have reported an issue of diversion of medicines. Medicines sought tend to be depressants and tranquilisers due to the prison environment. Use of prescription only medicines (POM) in prisons may be circumstantial due to the reduced availability of other drugs.

The ACMD provides key recommendations in this report on public health and awareness, education and research. The production of this report has been greatly aided by valuable contributions from a wide range of organisations and experts and the ACMD is particularly grateful to those experts who provided written and oral evidence.

We will welcome an opportunity to discuss the report with you in due course.

Yours sincerely



**Professor Les Iversen**

Chair, ACMD

**Professor Ray Hill**

Chair, Diversion and Illicit Supply of Medicines Inquiry

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Nicola Blackwood MP (Parliamentary Under Secretary of State for Public Health and Innovation)

# ACMD

Advisory Council on the Misuse of Drugs

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## Diversion and Illicit Supply of Medicines

**December 2016**

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- Mr Terry L Boos - Drug Enforcement Administration (DEA) (USA)
- Dr Jody Green (Denver Health and Hospital Authority USA)
- General Secretariat of the Council (EU)
- Government of Sweden
- Medicines and Healthcare products Regulatory Agency (MHRA)
- National Institute for Health and Care Excellence (NICE)
- Public Health England (PHE)
- Home Office
- NHS England
- National Crime Agency (NCA)
- UK Border Force
- Veterinary Medicines Directorate (VMD)

## **List of abbreviations**

ABPI	Association of the British Pharmaceutical Industry
ACMD	Advisory Council on the Misuse of Drugs
ACPM	American College of Preventative Medicine
ADHD	Attention Deficit Hyperactivity Disorder
ADR	adverse drug reaction
BBV	blood-borne virus
BMA	British Medical Association
BNF	British National Formulary
CCG	Clinical Commissioning Group
CDAO	Controlled Drug Accountable Officer
CDC	Centers for Disease Control and Prevention
CDT	compulsory drug testing
CGL	Change Grow Live
CMS	Centers for Medicare and Medicaid Services
CNS	central nervous system
CNWL	Central and North West London
CPD	continuing professional development
CQC	Care Quality Commission
CRI	now known as: CGL (Change Grow Live)
CSEW	Crime Survey for England and Wales
DEA	Drug Enforcement Administration
DISM	diversion and illicit supply of medicines
DRD	drug-related death
EMCDDA	European Monitoring Centre for Drug and Drug Addiction
EU	European Union
FEWS	Forensic Early Warning System
GMC	General Medical Council
GP	General Practitioner
GPhC	General Pharmaceutical Council
H&J CRG	Health and Justice Clinical Reference Group
HMI Prisons	Her Majesty's Inspectorate of Prisons
HQ SG	Headquarters Surgeon General
IMG	Inter-ministerial Group

## *Diversion and Illicit Supply of Medicines*

LIN	Local Intelligence Network
MDMA	3,4-methylenedioxy-methamphetamine or Ecstasy
MDT	mandatory drug testing
MHRA	Medicines and Healthcare products Regulatory Agency
MIMS	Monthly Index of Medical Specialities
MOD	Ministry of Defence
MOJ	Ministry of Justice
NCA	National Crime Agency
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NPIS	National Poisons Information Service
NPS	Novel Psychoactive Substance
NPSAD	National Programme on Substance Abuse Deaths
NSAID	non-steroidal anti-inflammatory drugs
ONS	Office for National Statistics
OST	opioid substitution therapy
OTC	over the counter
PDMP	Prescription Drug Monitoring Program
PHE	Public Health England
PHW	Public Health Wales
POM	prescription-only medicine
PPO	Prisons and Probation Ombudsman
SOP	Standard Operating Procedure
UK	United Kingdom
UNGASS	United Nations General Assembly Special Session
UNODC	United Nations Office on Drugs and Crime
US	United States
WHO	World Health Organisation
YC	Yellow Card

## 1 Introduction

### 1.1 Scope of this review

- 1.1.1 This inquiry by the Advisory Council on the Misuse of Drugs (ACMD) was initiated in response to a commissioning letter from the Home Secretary in September 2013 noting that the Inter-Ministerial Group (IMG) on Drugs and the Home Affairs Select Committee both were concerned that medicines were becoming more widely available for misuse through diversion and illicit supply of medicines (referred to in this report as 'DISM'), including via the internet.<sup>1</sup>
- 1.1.2 The ACMD set up a Working Group (see Annex B for membership), under the chairmanship of Professor R G Hill (Imperial College London), with the following objectives:
- Consider the potential for medical and social harms arising from the illicit supply of medicines, predominantly controlled drugs (CDs).
  - Consider whether diversion and illicit supply displaces the misuse of 'classic drugs of abuse'.
  - Consider the prevalence of misuse of these medicines obtained through these means.
  - Consider the demographics of users.
  - Consider the most prevalent drugs being misused in this manner.
- 1.1.3 This report also identifies the key differences between the situation in the UK and consideration of the situation in other countries, particularly the US.

This report examines the following, in individual chapters:

- The types of drugs diverted
- Sources of diversion and supply
- Prevalence of DISM
- Demographics
- Displacement
- Social and medical harms associated
- Consideration of prescription drugs in prisons
- Comparison with the US and other countries

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[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/265396/Commissioning\\_letter\\_from\\_Home\\_Secretary\\_to\\_Les\\_Iv\\_ersen\\_2013-.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/265396/Commissioning_letter_from_Home_Secretary_to_Les_Iv_ersen_2013-.pdf)

1.1.4 The information base on DISM in the UK has limitations; much of the data collected was largely anecdotal and difficult to quantify (see separate attachment for submissions received). The Working Group gathered information through the following means, which are reflected in each chapter in this report.

- Available peer-review literature and national surveys.

This represents the evidence base in the form of in-depth studies and literature reviews.

- Written and oral submissions to the Working Group's 'call for evidence' from relevant governmental sources, professional bodies and organisations.

This was carried out with the intention to generate data suitable for quantitative analysis but in the event produced largely anecdotal information, opinion and suggestions for actions and recommendations (see Annex C for a list of those consulted).

As it is not possible to make the inquiry completely exhaustive, some drugs which are known to be diverted or used illicitly (such as those for treating erectile dysfunction and anabolic steroids), but which are outside the remit of our commission, have not been considered in this report other than as comparators.

## **1.2 Previous considerations by the ACMD**

1.2.1 The ACMD's Technical Committee was undertaking a preliminary scoping exercise of diversion of medicines prior to the September 2013 commission. The Technical Committee had considered information from a number of sources, including submissions from: the US Drug Enforcement Administration (DEA); Public Health England (PHE); the Department of Health, Social Services and Public Safety (DHSSPS, Northern Ireland), the National Institute of Drug Abuse (NIDA), and a report from the Executive Office of the President of the United States – *Epidemic: Responding to America's Prescription Drug Abuse Crises*.<sup>2</sup>

1.2.2 The commissioning letter from the Home Secretary was thus very timely.<sup>3</sup>

- The ACMD supports the response of government to the most recent Home Affairs Select Committee review of the misuse of prescription drugs (*Drugs: New Psychoactive Substances and Prescription Drugs*, 2014). Specifically, that the Royal College of General Practitioners (RCGP) should produce guidance for GPs who are treating addiction to prescription drugs and that all cases should be recorded on the National Drug Treatment Monitoring System (NDTMS) in order to further clarify the prevalence of prescription drug misuse.

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<sup>2</sup> Certain information has been omitted from this paper due to the security marking.

<sup>3</sup> <https://www.gov.uk/government/publications/home-secretary-letter-to-acmd-on-the-governments-work-priorities-for-2013-to-2014>

- The ACMD is pleased to note that a number of helpful actions have already been initiated by government in response to the Home Affairs Select Committee report:
  - The Medicines and Healthcare products Regulatory Agency (MHRA) published a learning module on benzodiazepines in April 2013 which highlighted the risk of dependence and advised clinicians on how people could be helped to withdraw.
  - PHE published a commissioning guide for addiction to medicine services in June 2013.
  - The Centre for Pharmacy Postgraduate Education published a learning module for pharmacists and others in August 2013.
  - The National Institute for Health and Care Excellence (NICE) includes among its Clinical Knowledge Summaries advice on benzodiazepine and z-drug<sup>4</sup> withdrawal.
  - In addition, the RCGP and Substance Misuse Management in General Practice (SMMGP) continues to run training for GPs on addiction to medicine and how to support patients to withdraw from long-term use.

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<sup>4</sup> Group of non-benzodiazepine drugs with effects similar to benzodiazepines, used to treat insomnia and most of whose names start with 'Z'.

## **2 Types of drugs diverted**

*The Working Group set out to determine which types of drugs were being diverted and supplied illicitly. Stakeholders' opinions and evidence from the literature indicated which classes of drugs were being sought and which groups of drugs were being diverted most commonly. Some specifically named substances were mentioned by multiple stakeholders as being most susceptible to diversion.*

### **2.1 Key findings**

- ❖ The most prevalent diverted drugs are opioids and benzodiazepines.
- ❖ Increasing amounts of gabapentin and pregabalin are being diverted.
- ❖ Drugs prescribed for ADHD or used for non-licensed indications could be susceptible to diversion in the future.
- ❖ Attention needs to be given to codeine in over-the-counter (OTC) preparations as a precursor to the misuse of prescription opioids. Other substances were reported as being misused or diverted by some of our respondents and it was suggested that these form the basis of a watch list (see later recommendation).

### **2.2 Summary of information received by this inquiry**

*From government departments/agencies and international agencies*

- 2.2.1 Information from one Scottish Health Authority suggested that the prescribed medications most commonly diverted in Scotland were dihydrocodeine and oxycodone, as well as methadone, diazepam and buprenorphine. One health board response (Scotland) noted that around half of those on Opioid Substitution Therapy (OST) were believed to be also taking diverted diazepam. Health services in Scotland have seen regular presentations with dependence on dihydrocodeine, as well as patients intoxicated with gabapentin and pregabalin.
- 2.2.2 The majority of opioid users who present for treatment in Jersey (Jersey Govt. Information) use drugs such as benzodiazepines, codeine, tramadol and fentanyl, obtained either by prescription or illicitly. Fentanyl was implicated in six deaths in the period 2006-07, while tramadol has been linked to one death recently. Benzodiazepines especially diazepam were the most commonly diverted, followed by dihydrocodeine, buprenorphine, tramadol, fentanyl and more recently pregabalin and gabapentin. Treatment data provided in the Jersey Government's submission also indicate an increase in the number of people who are abusing codeine-containing OTC medicines.
- 2.2.3 In the strictly-controlled military environment (information from Headquarters Surgeon General), the small number of cases of illicit use of medicines identified by the Ministry of Defence (MOD) were primarily benzodiazepines. It was noted that they have a category of accountable drugs, including those in Schedules 3 to 5, which provide greater control of drugs attractive for abuse, such as opioids, than can be found in a civilian environment. Furthermore within the military

environment, compulsory drug testing (CDT) acts as a significant deterrent to substance misuse.

- 2.2.4 In Northern Ireland, there had also been seizures, and reports of widespread availability from drug services and service users, of the Z-drugs, tramadol, opioids (particularly fentanyl), pregabalin/gabapentin and erectile dysfunction/performance-enhancing drugs. Northern Ireland is recognised as having significantly higher than UK average usage rates for benzodiazepines (DSSPS submission).
- 2.2.5 In Scotland, the most common medicines/drugs diverted and supplied illicitly were opiates, ranging from methadone, oxycodone, morphine sulphate and fentanyl, to weaker preparations such as co-codamol and dihydrocodeine. Scotland also suggested that the diversion and illicit use of methadone was less of an issue than that of gabapentin and pregabalin, which seems to be climbing significantly (submission from Scottish Government). The abuse of gabapentin and pregabalin is a recent phenomenon. When pregabalin was introduced to the EU in 2004 it was thought to have a low abuse liability (information from MHRA). It appears that pregabalin and gabapentin are especially sought after in a prison setting. In the community, the biggest increase in medications being misused and diverted seem to be pregabalin and gabapentin (submission from NHS England).
- 2.2.6 PHE and NHS England issued a joint statement on the potential for misuse of gabapentin and pregabalin (sent to all community pharmacies, prescribers and HCPs looking after patients who may be taking gabapentin or pregabalin) (Stannard *et al.*, 2014).<sup>5</sup>
- 2.2.7 The MHRA have recently drawn attention to the illegal diversion of POMs from the regulated supply chain into the criminal market. The commodities involved are mainly Misuse of Drugs Act 1971 Class 'C' benzodiazepines and other hypnotics/anxiolytics known as the 'Z-drugs' (zopiclone, zolpidem, etc.) across the UK and beyond.
- 2.2.8 A second referral was subsequently made by Police Scotland following the discovery of 750,000 diazepam tablets during a search. On examination, the diazepam tablets were identified as coming from the legitimate supply chain. The subsequent investigation identified the scale of regulated supply chain diversion by the individuals involved over a 12-month period amounting to many millions of doses. The products included diazepam, zopiclone and temazepam. Following the initial intelligence referral from Ireland, ten complex and potentially linked investigations had been instigated. All of these investigations involved the diversion of diazepam or zopiclone from the regulated supply chain towards an illegal market (ref: MHRA, personal communication 2016).

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<sup>5</sup> [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/385791/PHE-NHS\\_England\\_pregabalin\\_and\\_gabapentin\\_advice\\_Dec\\_2014.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385791/PHE-NHS_England_pregabalin_and_gabapentin_advice_Dec_2014.pdf)

*Peer-reviewed literature/surveys and information*

- 2.2.9 An internet survey conducted in the UK in July 2014 looked at prescription medicine misuse and illicit drug use in 2,499 individuals (Wood *et al.*, 2015; Dargan *et al.*, 2015).. The reported use of any illicit drug in the past year was reported as 8.6%. Of the 2,499, 968 (38.7%) respondents reported lifetime non-medical use of at least one prescription opioid; the reported lifetime prevalence of non-medical use was highest for dihydrocodeine/codeine (21.0%), followed by fentanyl (4.9%), tramadol (3.3%) and buprenorphine (3.1%) (ibid).
- 2.2.10 Fifty-seven respondents (2.3%) reported lifetime non-medical use of at least one benzodiazepine; the reported lifetime prevalence of non-medical use was highest for diazepam (1.4%), followed by temazepam (0.6%), and lorazepam (0.4%) (Wood *et al.*, 2015; Dargan *et al.*, 2015).
- 2.2.11 Since 2009 there have been increasing numbers of reports of misuse of gabapentin and a warning notice was included in the UK label in 2010, yet monitoring indicates that misuse was still increasing up to the end of 2013 (Kapil *et al.*, 2013). In this survey-driven study, the misuse of pregabalin and gabapentin in the UK was confirmed and it was also found that baclofen was being used by the same population of users (Kapil *et al.*, 2013). The lifetime prevalence of misuse of pregabalin (8 or 0.32%), gabapentin (10 or 0.40%) and baclofen (6 or 0.24%) was low (Wood *et al.*, 2015; Kapil *et al.*, 2013). Recent systematic reviews (Schjerning *et al.*, 2016; Smith *et al.*, 2016) stress the abuse potential of gabapentin and pregabalin, and cases of abuse, dependence and withdrawal from gabapentin, especially in those who are being treated for abuse of other substances, are now in the literature (Mersfelder *et al.*, 2016).
- 2.2.12 The 2015-16 Crime Survey for England and Wales (CSEW) estimated that in the last year 7.5% of adults aged 16 to 59 had taken a prescription-only painkiller not prescribed to them: 7.4% (around 2.4 million adults) said that they had taken the painkillers purely for medical reasons, while a small proportion (0.2% or 33,000 adults) said it was just for the feeling or experience it gave them. A further very small number of adults said it was for both. This tendency was also true for young adults aged 16 to 24.<sup>6</sup>
- 2.2.13 Of the 16 to 59 year olds who had reported misuse of prescription-only painkillers, 15.3% reported having taken another drug in the last year. This is in contrast with users of NPS (85% had used another drug in the last year).
- 2.2.14 The use of non-prescribed prescription-only painkillers for medical reasons did not increase with higher frequency of alcohol consumption (7.6% of those who drank less than once a month, including non-drinkers, compared with 6.8% of those who drank on three or more days a week in the last month).

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<sup>6</sup> The 2015-16 CSEW figures for prescription painkillers cannot be compared with 2014/15 due to changes in the questions

- 2.2.15 The 2014 DrugScope Street Drug Survey (now known as DrugWise) also highlighted the misuse of gabapentinoids as a particular problem among opioid users and prison populations (Daly, 2015).
- 2.2.16 In the Guardian survey (2014), the most common misused drugs were diazepam, temazepam, co-codamol and tramadol.<sup>7</sup>
- 2.2.17 A recent survey of addiction to medicines in Cheshire and Merseyside (Bates *et al.*, 2015) found that the most common suspected addictions were to benzodiazepines/z-drugs, weak opioid analgesics and antiepileptic/neuropathic pain medicines (gabapentinoids). The authors highlighted the danger of paracetamol toxicity when compound medicines containing codeine are taken in high doses.
- 2.2.18 According to data from the National Crime Agency (NCA), between 2013 and 2014 most police forces in the United Kingdom have reported seizures of prescription medicines in conjunction with seizures of illicit Class A drugs. The most commonly encountered prescription medicines were benzodiazepines and opiates.
- 2.2.19 Although there was little information provided to our inquiry on the misuse of drugs used to treat ADHD, it is clear that the student community in particular is interested in using these agents for cognitive enhancement (Sahakian and Morien-Zamir, 2007; Singh *et al.*, 2014). In a survey of students in the UK and Ireland, around 30% of those surveyed were interested in using these drugs, although only about 10% had actually used the drugs and between 0.3 and 4% were current users at the time of the survey (*ibid*).
- 2.2.20 It was more common to obtain the drugs from friends than to buy them from a dealer or on the internet, although a small number (n=14) of UK respondents to a survey by Nature (Maher, 2008) suggested that the majority of these drugs were obtained via the internet. The interest in these drugs is increasing (see Sahakian *et al.*, 2015; Sahakian and Morein-Zahir, 2015) and their potential for misuse suggests it would be prudent to add them to any watch list that may be put in place.

*Submissions from stakeholders / anecdotal reports*

- 2.2.21 There was consistency in the views presented to the Working Group by those providing information on the substances that were most likely to be the subject of DISM (see Table 1 below).

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<sup>7</sup> <https://www.theguardian.com/society/2014/oct/05/sp-drug-use-is-rising-in-the-uk-but-were-not-addicted>

**Table 1: Prescription medicines most susceptible to DISM**

<b>Drug type</b>	<b>Number of submissions received which mentioned the class of drug</b>
Opioids	27
Benzodiazepines (including the related Z-drugs)	24
Other individual named compounds	20
Pregabalin and gabapentin	13
Anti-psychotics	10
Erectile dysfunction / performance enhancing drugs	9
Anti-depressants	7

2.2.22 There are anecdotal reports that less obvious drugs, like cimetidine, for example, are diverted and being used to potentiate the effects of methadone by increasing the plasma concentration (submission from Scottish Government).

### 2.3 Specific substance advice

#### *Advice on opioids*

2.3.1 A large body of research has focused on the mechanisms of opioid tolerance and dependence (see Trang et al 2015) but at present there is no treatment regimen which allows the safe and effective use of opioid analgesia for long periods of time. The situation is complicated by the role of endogenous opioid activity in depressive disorders which are often comorbid with chronic pain (Hsu et al, 2015). It is necessary to accept that long term use of opioids is likely to prove ineffective for pain relief (see Franklin 2014; Kotecha and Sites 2013) and be associated with the patient developing tolerance and probably dependence. A recent systematic review (Vowles et al, 2015) suggested that rates of misuse of opioids in patients treated for chronic pain ranged from 21 to 29% and that addiction resulted in between 8 and 12%. In particular opioids are unsuitable for management of chronic pain in the elderly and should only be used if NSAIDs, paracetamol or cognitive behavioural therapy have failed (Reid, 2015). It has recently been pointed out that chronic pain has been mistakenly treated in a manner appropriate only for acute pain (Ballantyne et al, 2016). Short lived pain states exhibit a predictable and linear trajectory, tending to respond well to opioids titrated against pain intensity. Chronic pain does not have a predictable trajectory and often does not respond well to opioids other than in the early phase of treatment (ibid). Chronic pain is difficult to treat and prescribers and patients want to try the strongest medications available (Ballantyne, 2015). Although the evidence is clear that opioids are poorly effective in the treatment of chronic pain, once started, patients and prescribers are reluctant to stop the drugs even when they are ineffective as there are usually few alternatives for managing symptoms.

2.3.2 Although the evidence is clear that opioids are poorly effective in the treatment of chronic pain, once started, patients and prescribers are reluctant to stop the drugs

even when they are ineffective as there are usually few alternatives for managing symptoms. Persistent use of opioids can lead to dependency for the individual (Ballantyne, 2015) such that they believe they need opioids even when they have stopped providing good pain relief, leading to statements such as “*you see they work, when I stop them I get worse*”. This situation may increase the risks of diversion and misuse.

- 2.3.3 Attention needs to be given to codeine in OTC preparations as a precursor to the misuse of prescription opioids (see MHRA, 2009) and it may be time to ask whether this drug still has a therapeutic niche in 2016. The misuse of OTC codeine continues to be major problem (see Cooper, 2013a,b). Although users admit their addiction “*I have stopped taking codeine before and for the past few days I have had cold sweats and palpitations and had withdrawal symptoms. So the physical symptoms suggest that I am addicted to it and also the psychological*”. Most participants in Cooper’s survey described a genuine reason for initial use of a product that lead eventually to the medicine being taken for different reasons. Typically for codeine this was the ‘buzz’ or ‘calm’ associated with its use and the ability to cope with life events (*ibid*). It is necessary to clearly establish which conditions opioids should / should not be prescribed for in the minds of all prescribers. This should lead to establishing best practice of the type advised by the recent Faculty of Pain Medicine website.<sup>8</sup> Guidelines per se are probably not sufficient and further research on how to ensure successful implementation is needed. This situation is illustrated by the recent observation that more than 90% of patients who survive a prescription opioid overdose continue to be prescribed opioids (Gregg, 2015; Larochelle *et al.*, 2015b). The American Medical Association has named prescription drug abuse and addiction as one of its top nine issues affecting physicians in 2016, and stated that the AMA Task Force to reduce opioid abuse will continue to provide leadership to help turn the tide on this public health crisis (Brooks, 2016).
- 2.3.4 The 2014 report *Medications in Drug Treatment: Tackling the Risks to Children* by Adfam,<sup>9</sup> examined cases where children have died or come to harm from ingesting OST medicines prescribed to help people overcome drug addiction. This report concluded that existing clinical guidelines do mention the need to consider the risks to children (alongside other factors like diversion into the illicit market) when making decisions about OST; however, Adfam research suggests that safeguarding concerns may not be properly prioritised in reality and that there is a need for more accessible guidance for frontline practitioners and a greater emphasis on implementation at the local level.
- 2.3.5 The Faculty of Pain Medicine of the Royal College of Anaesthetists has reviewed the use of prescribing of opioids in great detail. A comprehensive guideline for

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<sup>8</sup> <http://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware>

<sup>9</sup> [http://www.adfam.org.uk/cms/docs/adfam\\_ost\\_fullreport\\_web.pdf](http://www.adfam.org.uk/cms/docs/adfam_ost_fullreport_web.pdf)

prescribers went live on the Faculty of Pain Medicine, Royal College of Anaesthetists website in Dec 2015.<sup>10</sup>

- 2.3.6 All opioids prescribed in the UK come under the control of the Misuse of Drugs Act 1971, so re-scheduling per se other than in cases such as tramadol where controls were clearly inadequate (ACMD, 2013b) is probably not a remedy for DISM.

*Advice on benzodiazepines*

- 2.3.7 The misuse of benzodiazepines has long been recognised and guidelines for appropriate prescribing have been in place in the UK since the early 1990s, yet abuse is still widespread. Our Working Group received information to suggest that only some of the misused benzodiazepines are a result of DISM; much is being obtained via the internet and bulk supplies are also being imported by dealers. Anomalies in the scheduling of some benzodiazepines and Z-drugs have now been rectified and all legally prescribable drugs now have an appropriate level of legal control. The way to control misuse is far from clear, but probably lies with effective education of prescribers and users/abusers rather than with more draconian control measures. Specific attention to how the diversion of wholesale supplies is occurring is an urgent matter for attention by the relevant authorities.

*Advice on gabapentinoids*

- 2.3.8 Gabapentin and pregabalin were the major emerging drugs to be subject to DISM during the period of our inquiry. Although undoubtedly capable of inducing drug-seeking behaviour, especially when combined with opioids, they are also essential drugs with a unique role in treating some forms of epilepsy, neuropathic pain and generalised anxiety disorder (Finnerup *et al.*, 2015). They are now recommended as first-line therapies for neuropathic pain (*ibid*). The problem of abuse is exacerbated by the fact that currently patients in drug abuse treatment programmes are not routinely tested to see if they have taken gabapentin or pregabalin so taking these drugs will not disqualify an individual from treatment (Lowry, 2015). It is also possible for patients to obtain gabapentin or pregabalin from their family practitioner to add to the OST (usually buprenorphine / naloxone) and benzodiazepine that they are prescribed as part of their addiction treatment (*ibid*). Identifying cases of prescription medicine misuse and/or diversion is a problem for clinicians especially for those psychiatric indications that lack an objective diagnosis. Prescribers may thus inadvertently supply medication for the illicit market. For example, some patients present to GPs with very plausible symptoms, such as neuropathic pain or generalised anxiety, for which objective diagnostic tests are lacking but which often require maximum doses of 'desirable' medication, including the gabapentinoids. However, a recent review of pregabalin prescribing in the UK suggests that most prescriptions are consistent with product labelling (Asomaning *et al.*, 2016).

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<sup>10</sup> Opioids Aware: A resource for patients and healthcare professionals to support prescribing of opioid medicines for pain. <http://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware>.

2.3.9 In December 2014, advice for prescribers was issued (Stannard *et al.*, 2014) in recognition that abuse of gabapentinoids had become established in the UK. Separately, in January 2016, the ACMD recommended that both pregabalin and gabapentin are controlled under the Misuse of Drugs Act 1971 as Class 'C' substances, and scheduled under the Misuse of Drugs Regulations 2001 (as amended) as Schedule 3, so as not to preclude legitimate use on prescription (ACMD, 2016). The ACMD concluded that pregabalin and gabapentin present a risk of addiction and a potential for illegal diversion and medicine misuse.

2.3.10 It might be helpful to review recent case histories where prescription drugs have been found to be abused (for example tramadol and the gabapentinoids) to see how close to best practice we are and whether response time to providing advice to prescribers and/or re-scheduling could be improved. It should be noted that comprehensive guidelines for best practice have been available for some time (e.g. ACPM, 2011; CMS, 2014) but have not made a major difference to the problem.

#### *Advice on other substances*

2.3.11 A number of other substances emerged in the information we received but not sufficiently often to have a clear picture of the diversion and misuse of the substances. Such substances included baclofen, quetiapine and mirtazapine. We recommend that these substances form the basis of a watch list to see if misuse increases.

2.3.12 Also being diverted are:

- benzodiazepines;
- Z-drugs and other sedation medications, including antihistamines such as promethazine;
- anti-depressants, e.g. mirtazapine; and
- anti-psychotics, such as quetiapine.

The misuse of benzodiazepines and Z-drugs seems especially prevalent (see Kapil *et al.*, 2014).

### 3 Sources of diversion and supply

#### 3.1 Key findings

- ❖ The nature and prevalence of DISM suggests that currently the major source of supply is by prescription prior to diversion.
- ❖ The internet is an increasing illicit source of medicines with many unlicensed online pharmacies supplying prescriptions and medicines unethically.
- ❖ It has not been possible to find hard information on DISM facilitated by organised crime.
- ❖ It has not been possible to find hard information on DISM facilitated by unethical prescribing by doctors / non-medical prescribers.
- ❖ Recent information from the MHRA shows that diversion from wholesalers or retailers of medicines may be a source of supply.

#### 3.2 Summary of submissions and information received by this inquiry

*From Government departments/agencies and international agencies*

- 3.2.1 In the first major report on non-medical use of prescription drugs, the United Nations Office on Drugs and Crime (UNODC) (2011a) listed the possible ways in which prescription medicines could be diverted for illicit use:
- from family and friends;
  - over-prescribing by physicians;
  - multiple prescriptions from a physician;
  - forged prescriptions;
  - illegal online pharmacies;
  - theft from hospitals and pharmacies;
  - sale by unscrupulous physicians.
- 3.2.2 **Family and friends:** The Scottish Government submission suggested that family and friends with a legitimate prescription may be the source of diverted prescribed medicines for drug users. At times, individuals may mistakenly assume that because the drug is prescribed it is 'safe'.
- 3.2.3 **Legitimate prescriptions:** In Wales, DISM is occurring with the traditional source of supply being the sale of drugs to the user by patients with legitimate prescriptions. It has been suggested that this may be exacerbated by the lack of a prescription charge in Wales (Kyrie James, personal communication). It was reported that there is no evidence of corrupt doctors in Wales writing unnecessary prescriptions to feed DISM and this should have been detectable by their monitoring systems (written submission of information from a seconded officer).

- 3.2.4 **Police seizures:** Recent information from police drug seizures reveals that prescription medicines are being detected. As some of these are described as white powders rather than proprietary dosage, at least part of what is seized is likely being purchased via the internet rather than being due to DISM (data supplied by the NCA 14 Jan 2015 and updated June 2015).
- 3.2.5 **Organised groups:** In Northern Ireland organised crime groups are also obtaining prescription drugs via the internet for sale alongside the other drugs they supply, but details of this were not provided. Theft of drugs from either pharmacies or from patients seems to be only opportunistic. Recent investigations into drug trafficking resulted in seizure of products which originated from the legitimate supply chain in the UK. Further examination then unearthed significant levels of diversion of these products out of the regulated supply chain and identified the diversion of multi-million doses to one source. The purchaser, owning a number of pharmacies in England, when questioned about the product stated that it had been sold for cash with no audit trail or paper work (correspondence from MHRA, 24 June 2016).
- 3.2.6 **Diversion of legitimate wholesale supplies:** In June 2016, the MHRA informed the ACMD of the illegal diversion of POMs from the regulated supply chain into the criminal market. The issue of diversion of POMs, further controlled under the Misuse of Drugs Act 1971, into illegal markets was first brought to the attention of the MHRA by the Irish medicines regulator, Health Products Regulatory Authority (HPRA). Investigations into the prolific drug trafficking and misuse of benzodiazepines and Z-drugs in Ireland resulted in the seizure of products that appeared to originate from the legitimate supply chain in the UK. Intelligence work was carried out and the products were identified as originating from a UK wholesaler. As a result, an inspection of this wholesaler took place and the top ten sales of benzodiazepines and Z-drugs were examined. This examination then started to unearth significant levels of diversion of these products out of the regulated supply chain. The first significant step in this enquiry identified the diversion of multi-million doses to one source. The medicines were apparently sold to another business which had had their wholesale dealer's authority suspended. The location of this huge amount of medicines has never been identified but it is the investigative hypothesis that they had been sold into the illegal market.
- 3.2.7 Following the initial intelligence referral from Ireland, ten complex and potentially linked investigations had been instigated. All of these investigations involve the diversion of diazepam or zopiclone from the regulated supply chain towards an illegal market. Investigation linked to the sale of such products, diverted from the regulated supply chain, on the internet with links to the above described cases had so far resulted in a number of arrests and the seizure of large volumes of diazepam, tramadol and zolpidem. The entire product was from the regulated supply chain. Investigation into the offer to supply benzodiazepines diverted from the regulated supply chain resulted in another large seizure of diazepam and the arrest of a suspect.
- 3.2.8 The scale of the diversion, use and abuse of such Class 'C' products has been recognised by the media: (June 2016 BBC programme, Drugs Map of Britain 3.

Scotland: Valium Crisis: [www.bbc.co.uk/iplayer/episode/p03wbn39](http://www.bbc.co.uk/iplayer/episode/p03wbn39) (programme available until 8 June 2017).

- 3.2.9 It is the assessment of the MHRA that the number of similar investigations is likely to increase as dedicated work unearths new lines of inquiry and further abuses of the regulated supply chain.
- 3.2.10 Doctor shopping as a way to obtain drugs for sale is thought to happen but the extent is unknown and not adequately picked up by current tracking methods. Guidelines are in place to help GPs detect patient registration fraud (NHS Protect, 2010) but contain an example of one woman who managed to register with over 40 separate identities to obtain drugs from multiple GPs. One specific example that was brought to the ACMD's attention (NHS England H&J CRG) is of people touring NHS walk-in centres in Yorkshire and Humberside and obtaining a week's worth of opioid medication at each centre.
- 3.2.11 There is information that DISM in Jersey is supported by individuals 'doctor shopping' with evidence also pointing to the use of physicians in France or elsewhere in the UK to obtain prescriptions. Care is needed with extrapolation of this data as the healthcare system in Jersey is not exactly the same as in the rest of the UK and the geographical proximity of France is also a unique feature. Imported buprenorphine prescribed in France and, to a lesser extent, from the UK is a growing concern. One 8 mg Subutex tablet on the streets sells for £80 in Jersey (written submission received from Jersey).
- 3.2.12 **Internet and social media:** There is also information on prescription medicines being purchased online and imported through the post. A large proportion of street diazepam is trafficked into Scotland from overseas, with some tablets also being illicitly produced within Scotland (information from Robert Gordons and Abertay Universities working with Police Scotland). Overall, the internet and social networking sites are rapidly growing in size and are becoming a significant determinant in marketing, sale and distribution of POMs (EMCDDA, 2014).

*Peer-reviewed literature/surveys*

- 3.2.13 **Legitimate prescriptions:** A survey study (Winstock *et al.*, 2014) explored the source of misused tramadol in the UK. In 2012, 7,360 individuals completed this survey and 369 reported misuse of tramadol in the previous year. Of these tramadol users, 235 (64%) reported that the drug had been prescribed for them, 124 (34%) reported obtaining it from a friend, 12 (3%) reported buying it from a dealer and 10 (2.7%) bought it from the internet.
- 3.2.14 **Internet:** The internet, particularly with the introduction of the web 2.0, has facilitated the transformation of the 'street market' into a 'virtual marketplace', characterised by both a quasi-legal appearance (Power, 2013) and ease of access to a virtually unlimited variety of medicines/drugs.
- 3.2.15 In the United Kingdom, there are strict legal controls on the retail sale, supply and advertisement of medicinal products. Like all registered pharmacies, internet or

online pharmacies are registered with and regulated by the General Pharmaceutical Council (GPhC) or the Pharmaceutical Society of Northern Ireland. The Care Quality Commission in England regulates digital providers providing on-line prescribing services and the MHRA regulate the products including their sale and supply. Any pharmacy, including those providing services at a distance, for example on the internet, must receive a legally valid prescription before supplying prescription only medicines.

3.2.16 Registered pharmacies that are regulated by the GPhC and meet their standards can use the GPhC voluntary internet pharmacy logo. Also from 1 July 2015 anyone in the UK selling medicines to the public via a website also needs to be registered with the MHRA and to be on the MHRA's list of UK registered online retail sellers. They also need to display the Distance Selling logo on every page of their website offering medicines for sale.

3.2.17 However, the number of unregistered 'no-prescription-required' online pharmacies has increased substantially over the past decade (Orizio et al., 2009a; 2009b). Typically, these unlicensed online pharmacies are just computerised systems designed to handle business transactions from remote sites (Gondim and Falcao, 2007). Most of them provide a 'prescription service', e.g. customers are required to fill in an online medical questionnaire which is then allegedly assessed by a 'cyber-doctor', often a computer programme designed to guide patients towards those responses which are needed to justify a prescription (Weiss, 2006). Quite often, this procedure does not take into account the possible presence of medication warnings/contraindications (Schifano, 2014).

3.2.18 Most medicine vending websites present with aggressive marketing strategies, including:

a) special offer sales/discounts and provision of free medicines samples, with promotions made through unsolicited emails/advertisements;

b) free/fast delivery;

c) availability of consumers' reviews; and,

d) guarantee of privacy protection (Orsolini et al, 2014).

3.2.19 Virtually any psychoactive/non-psychoactive molecule is being made available for the online purchase, including: scheduled drugs; and prescription medications (Van Hout et al., 2013). A recent internet snapshot survey (Ho et al 2015) identified 37 websites selling zopiclone tablets in quantities up to 2000 and 35 of these also sold other benzodiazepines/ Z -drugs and 15 offered bulk discounts.

3.2.20 Although some drug vending websites present with an appearance which is fairly stable over time (Bachhuber et al., 2013), most of them show high levels of fluidity in their layouts, with frequent changes in their names, IP, and postal address (Orsolini et al, 2014). When comparing a range of drug vending websites, high levels of similarities between them may be identified, including: homepage

appearance, site organisation, available products, and purchase conditions, so that one could argue that just a few owners are behind a large number of vending websites (Schifano et al., 2006). Most often, the 'no prescription' websites do not provide their customers with any elements suggesting the possession of a retailer legitimacy status, including: owners'/directors' names; landline telephone number; and geographical location. Conversely, some sites try to mislead their customers providing logos of either professional/governmental agencies and/or of the main credit card circuits (Orsolini et al., 2014).

3.2.21 In being supported by the creation of a personal account, the relationship between vendors and consumers has been described as based on alleged 'cyber levels of trust and professionalism' (Van Hout et al., 2013). Most cyber pharmacies require credit card/Western Union/ MoneyGram's payments (Orsolini et al, 2014). Some websites use popular/renowned professional carriers offering to deliver internationally/overseas, although the exact amount of shipping costs is often not known until the end of the transaction (Levaggi et al., 2012).

#### *Submissions from stakeholders / anecdotal reports*

3.2.22 Responses to our questionnaire and data in the literature indicated that the most common source of prescription drug used illicitly is prescribed medicine either for the individual abusing it once the medical needs have ceased or prescribed for a family member or friend. Medicines obtained by street or internet supply may be becoming more important.

3.2.23 Of the 706 drug-related deaths reported in Scotland in 2015, methadone was implicated in, or potentially contributed to, 251 deaths (National Records of Scotland, 2016). Responses from users indicate that illicit methadone consumption is largely the result of the diversion of prescribed medicines, as opposed to supply from organised crime. There are anecdotal reports that dihydrocodeine and similar drugs are traded by patients in exchange for alcohol. Cases of individuals being approached in pharmacies for sale of their prescription were also noted.

3.2.24 Anecdotal information suggests that long-term prescription of some medicines and poor patient compliance may lead to significant quantities of medicines not being returned or disposed of in the correct manner. This may provide access to these medicines for relatives and others to use recreationally. Control of prescribing practice and effective disposal of supplies once no longer needed appear to be the best control measures.

In 2006, NICE published updated guidance on safe handling of CDs in the NHS, and reiterated the advice to the public to return their unused medicine to their pharmacist for safe disposal when no longer required. And there is professional guidance for pharmacists on managing the patient returned CDs in their pharmacies. ('Controlled drugs: safe use and management' (April 2016), *NICE NG46*, <https://www.nice.org.uk/guidance/ng46>.)

3.2.25 Although the data are soft and incomplete there is little evidence of organised crime being involved in DISM or of unethical prescribing by doctors or non-medical prescribers. Information from the GMC under their Fitness to Practice procedures indicates that there were no allegations of malpractice attributable to DISM per se in the period 2009-13. The most common instances of malpractice related to DISM were opioid-dependent doctors self-prescribing or fraudulently prescribing under the name of a relative or a patient in order to obtain drugs for personal use. The GMC commented that they have no strong evidence with which to assess the scale of DISM, but they are not complacent and will act on any concerns that emerge from this exercise. Disciplinary action by professional bodies and the regulator related to DISM appears mostly related to practitioners obtaining supplies for their own misuse rather than for supply to others.

*Actions and recommendations suggested by stakeholders and other bodies*

3.2.26 The Medical Royal Colleges, PHE, NHS England and CQC are collaborating to develop a definitive Opioid Prescribing Resource to support prescribers in making safe decisions in relation to opioid prescribing and to improve recognition and management of misuse and diversion.

3.2.27 The Home Affairs Select Committee report: *Breaking the Cycle* (2012) highlighted that it is ultimately the responsibility of the medical profession to ensure that their prescribing decisions do not lead patients into drug dependency. The report further noted that the police and public should be aware of this deeply concerning trend, so they too can be vigilant in seeking to prevent it.

3.2.28 There is a recommendation that medical practices start an anonymous data collection of those patients who have been proven to be, or a medical professional has reasonable suspicion of being, addicted to prescription drugs and determine how they are being supplied, can be implemented and further used. This practice must be formalised in order for it to continue with the structural changes in healthcare in the UK (House of Commons, Home Affairs Committee 12<sup>th</sup> report of session 2013/14: *Drugs: new psychoactive substances and prescription drugs*).

3.2.29 There is a recommendation that NHS England should issue guidance to local Clinical Commissioning Groups (CCGs), which will lead to them taking central responsibility for the collation of data on patients visiting multiple practices to request specific drugs. The administrative part of the CCGs should be strengthened in order for them to facilitate sharing this information with all practices and thus informing all healthcare professionals in their areas (House of Commons, Home Affairs Committee 12<sup>th</sup> report of session 2013/14).

3.2.30 There is a recommendation that the Medical Royal Colleges establish a joint Working Group to assess the effectiveness of their consensus statement and to examine whether local area health teams are effectively communicating concerns around individuals visiting multiple practices to request specific drugs following the introduction of the new health service structure. This Working Group should also be responsible for starting the collection and collation of data by local healthcare practices. Centrally-collected prescriptions data do not record the number of

people receiving particular drugs. Furthermore, the British Medical Association (BMA) have since published an analysis report (BMA, 2015) by the Board of Science of the BMA on involuntary dependence to prescription medications (*ibid*).

- 3.2.31 **Enhanced links between community pharmacies and clinicians should also be encouraged.** The community pharmacist may be the first professional to identify an issue through, for example, early requests for repeat supplies, excessive consumption of OTC medications and repeated requests for emergency supplies. Concerns should be reported to the local Controlled Drugs Accountable Officer (CDOA).
- 3.2.32 Safe disposal of waste medicines is an essential service within the community pharmacy contractual framework to be provided by all community pharmacies in England (NICE, 2016).
- 3.2.33 **Stricter guidelines around the prescription of certain medicines may reduce misuse and diversion.** For example, daily dispensing, more frequent prescriptions for smaller amounts, and contacting the police (or encouraging patients to contact the police) when tablets are 'stolen' are associated with higher economic costs.
- 3.2.34 It is important that current and future systems used by the healthcare sector to review and monitor repeat prescription, particularly with regard to methadone, benzodiazepines and other similar drugs, are robust and can effectively identify the diversion of prescribed medicines (NICE, 2016).
- 3.2.35 Regular information on trends of misuse and the street value of 'desirable' medicines could aid these processes by increasing awareness among prescribers. For example, see England (2013), who interviewed inmates at Holloway to find those prescription drugs which were liked and/or had street value; the list included quetiapine, mirtazapine, carbamazepine, gabapentin and pregabalin, as well as opioids and benzodiazepines – all substances named by respondents to our inquiry.
- 3.2.36 There should be improved support and information for patients about why prescribers have concerns about potential misuse of medications to promote a culture where discussions about risks of misuse are an integral component of safe prescribing.

## **4 Prevalence**

### **4.1 Key findings**

- ❖ There is a common perception that prevalence of DISM is increasing.
- ❖ Quantifying the extent of DISM is difficult due to a lack of suitable monitoring systems, and available information is largely anecdotal.
- ❖ People seeking treatment for addiction to prescription medicines has reportedly increased.

### **4.2 Summary of submissions and evidence received by this inquiry**

#### *Submissions from stakeholders / anecdotal reports*

- 4.2.1 Responses from stakeholders indicated that the diversion and illicit supply of medicines varied from area to area, due to differences in supply, demand and the preference of users within the geographical area.
- 4.2.2 Information from stakeholders suggested that DISM was prevalent. However, over half of the respondents perceived that the extent was unknown and over half of the impressions were anecdotal.
- 4.2.3 Information from NHS Protect suggests that the majority of diversion of NHS drugs does not come to their attention and that the true nature and scale of DISM is not known or possible to estimate at this time. In addition, it is difficult to be certain when a medicine is being diverted for illicit use or when a chemical that also happens to be a medicine is being purchased in bulk then sold for misuse. This is often an evolution and a good example is ketamine where misuse started with the drug being diverted from legitimate medical and veterinary supplies and which is now mainly supported by drug imported in bulk from overseas chemical suppliers (ACMD, 2013a). Collated data from a variety of sources are needed to address this, including traditional prescribing data (and it is noteworthy that the recent inclusion of controlled drug (CD) prescribing in electronic prescribing systems may offer additional evidence collection opportunities) together with information from properly conducted surveys of street level availability, service users and providers.

The intelligence information from NHS Protect suggests that most diversion takes place at the level of the community pharmacy by patients or third parties where alterations and additions to genuine prescription stationery are made. It is possible that other diversion strategies, which occur after a prescribed medication has been lawfully dispensed and provided to a patient or authorised third party, are not being detected since systems to monitor or survey such activities do not exist and this is an area that deserves further study. Other strategies that have also been reported include instances of multiple scripting, obtaining repeat prescriptions where there is no longer a clinical need and theft of prescription pads. Thefts of NHS drugs from hospitals, pharmacies, surgeries and drug treatment centres appear to be rare. In the period April 2012 to March 2014, there were only 147 crimes involving CDs where the NHS was the victim.

- 4.2.4 The misuse of prescription drugs has been recognised as a growing area of concern in Northern Ireland (written submission of information) and the issue of how to deal with this has become part of their strategy to prevent and address the harms resulting from alcohol and drug misuse. DHSSPS (Northern Ireland) is working to improve the information base in relation to the misuse of prescription and OTC medicines to reduce inappropriate prescribing, tackle diversion, illicit markets and internet markets. At present, it is very difficult to quantify the problem in Northern Ireland but it is believed that DISM is a direct cause of prescription drug misuse. Survey data shows that use of sedatives, anti-depressants and tranquillisers is high (~20%) and increasing, and is approximately twice that of individuals in the Republic of Ireland (*ibid*).
- 4.2.5 Law enforcement personnel (Metropolitan Police) suggested that DISM was seen as a live and increasing trend within England, Wales and Northern Ireland. Although it was perceived to be a growing problem, there was a shortage of research to support this view or properly assess it. The primary sources were stated to be users of illicit drugs obtaining prescribed medication for their own use then selling this onward to others to provide cash to support their illicit drug use (Met Police). Police Scotland seizures suggest that the illicit supply of medicines is a known problem within Scotland.
- 4.2.6 In the controlled environment of the armed services, where a policy of compulsory drug testing (CDT) is in place, information provided by the Headquarters Surgeon General (HQ SG) shows a very small number of individuals testing positive for prescription medicines (largely benzodiazepines) that were not prescribed for that person. Some were found to be as a result of medicines passed on from friends or family members but others were probably the result of internet or illegal sales. It was noted that prescribing and dispensing is very strictly controlled in the military environment but that, even here, once a medicine has left the pharmacy there is no way of knowing if it is being used appropriately or not (submission from HQ SG).

*Peer-reviewed literature/surveys*

- 4.2.7 Survey data from GPs, pharmacists, drug treatment services and police suggest that their perception of the nature of the misuse of prescribed medication, including DISM, takes a number of forms. This includes:
- consumption in excess of the prescribed regime;
  - continuing to consume or to divert to others when there is no longer a clinical need;
  - abuse of the prescribed medication to obtain a 'high'; and,
  - diversion to others including to friends and family.
  - Medicines are also being prescribed for people who do not need them but persuade their GP to prescribe for them.

4.2.8 Drug treatment services have seen an increase in the number of patients presenting with addiction to prescribed medicines. This may be through excessive consumption of legitimately prescribed medicines or diverted/illicitly-supplied medicines (Bates *et al.*, 2015). The position is complicated by poly-drug use in which the mixture of drugs taken can be driven by price and availability, such that a heroin user may prefer this drug when it is available and affordable but may use oxycodone diverted from prescription supply when it is not. People who have problems with drugs (including prescribed medicines) may be deterred from seeking treatment if they see it as only being for criminally-involved heroin users (Radcliffe and Stevens, 2008). Such treatment services should be provided in settings, including primary care services, which are not associated exclusively with this group.

*Actions and recommendations from stakeholders and other bodies*

4.2.9 **All sectors should work together to collect and critically appraise information.** Presently this is done to some extent in Scotland through Drug Death Groups (consisting of representatives from Alcohol Drug Partnerships, pharmacy, medicine, substance misuse, public health, police, ambulance service and social work) and Local Intelligence Networks (LINs) (consisting of representatives from private healthcare, prison, police, GPhC, and health). However, further links between other relevant agencies also need to be developed (for example, in England with Controlled Drugs Accountable Officers (CDAOs) and Local Intelligence Networks (LINs)).

4.2.10 The NHS has a comprehensive system in place to ensure good clinical governance in the treatment of patients and the prescribing of CDs. 'Safeguarding Patients' was the Government's response to the recommendations of the Shipman Inquiry's fifth report and to the recommendations of the Ayling, Neale and Kerr/Haslam Inquiries and was published in 2007 as a command paper.

The government issued a command paper 'Safer management of controlled drugs: the Government's response to the Fourth Report of the Shipman Inquiry' in December 2004 proposing a series of governance measurements to strengthen arrangements already in place. The Fourth report focused on the methods used by Shipman to divert large quantities of CDs for a considerable period of time without detection. Since 2007, the introduction of CDAOs in designated healthcare organisations who have responsibility for all aspects of the management of controlled drugs within their organisation, and are also required to share both incidents and concerns with other organisations and stakeholders brought together in LINs.

4.2.11 These changes bring a range of local interests (including regulators, health providers, local authorities and the police) together to share information and intelligence on problems concerning CDs and to take appropriate action. These regulatory assurances, coupled with the high standard of practice by NHS professionals, should mean that people can have a high degree of confidence in safe governance and prescribing practice in the UK. This needs to be

demonstrated to be true by monitoring results and this is reinforced in the new NICE guidelines (NICE, 2016). When there are doubts of a doctor's fitness to practice, for whatever reason, the GMC exists to rule on whether they can continue in practice and with what additional constraints, if any.

## 5 Demographics

### 5.1 Key findings

- ❖ The prevalence of females who abuse POMs is greater than males, the converse of traditional drug abuse.
- ❖ There are strong links between POM abuse and mental health issues.
- ❖ DISM via the internet has appealing attributes to a wide demographic of people.
- ❖ The rise in prescribing opioid medication in the UK is almost wholly attributable to increased prescribing for chronic pain.
- ❖ DISM shows marked regional variation coinciding with the highest rates of prescribing in the North East and the lowest in London.

### 5.2 Summary of submissions and information received by this inquiry

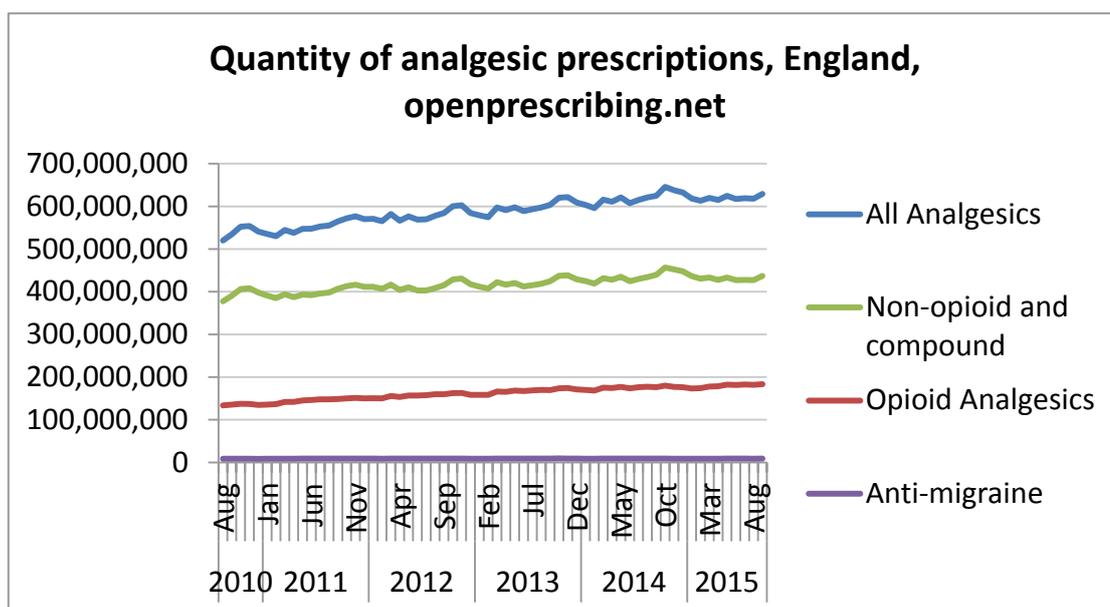
*From government departments/agencies and stakeholders / anecdotal reports*

- 5.2.1 DISM could affect a wide demographic of people depending on the substances involved. The seemingly social acceptability of misuse of POMs is highlighted by the findings that people are less likely to seek treatment for addiction to POMs than to traditional drugs of misuse as they are perceived as separate issues. (see stakeholder responses).
- 5.2.2 A major global study on misuse of prescription medicines (UNODC, 2011a) identified women and young girls, young people generally, older adults and healthcare workers, as those groups most at risk. It also pointed to groups where there were less solid data but some evidence for abuse of prescription medicines including incarcerated criminals, patients being treated for pain, those with mental health problems, and those who are already dependent on alcohol or illicit drugs (*ibid*).
- 5.2.3 In nearly all worldwide and country surveys on drug users, the number of men using illicit drugs vastly outnumbers the number of female users; however, when misuse of prescription medicines is considered, the position is reversed with a preponderance of female users (UNODC, 2014). When data from five surveys were pooled, approximately half of female users had abused a prescription drug in the last 12 months compared with one-third of male drug users (*ibid*).
- 5.2.4 The social class of those taking illicit prescription drugs is hard to determine. It is clear that illicit use of prescription opioids is seen in very prosperous countries such as the US, Canada and Australia, but it is also seen in middle income countries, such as Nigeria and Pakistan, where there is low use of prescription opioids for treating pain (UNODC, 2014). It is likely to be a mixture of price and availability combined with the relative laxity of prescription regulations in different countries that drives whether or not prescription drugs are misused.

5.2.5 Information on demographics of use in Scotland is incomplete, although stakeholders suggested that DISM affects a wide range of ages and types of user depending upon the substance being misused. Each drug has its own unique trend linked to its effects and demand from varying types of drug user, e.g. recreational or occasional drug users and according to environment, especially whether within or outside the criminal justice system.

5.2.6 Figure 1 illustrates that, overall, prescriptions for both non-opioid analgesics and opioids are increasing. This is in line with trends for other types of medicines, reflecting a greater demand on the health service.

**Figure 1: Trends in prescribing analgesics, 2010-15**



*Peer-reviewed literature/surveys*

5.2.7 An earlier inquiry on dependence on prescription medicines in the UK during 2007 (Reay 2009; and also Hsu *et al.*, 2015) found that:

- many individuals with dependency problems had other mental health conditions, such as depression;
- addiction to prescription medicines was considered to be relatively common but that it was reported anecdotally and there were no official statistics to work from;
- benzodiazepine misuse in females was a major problem;
- there was also much benzodiazepine use in those addicted to alcohol;
- within both prisons and the wider community, substance misuse and mental health problems were strongly linked.

5.2.8 It should be noted that addiction per se is not evidence of DISM and can result from a legitimate supply of drugs on prescription (Bates *et al.*, 2015; Ballantyne, 2015). The Bradley review of people with mental health problems or learning

disabilities in the criminal justice system (Bradley, 2009) highlighted the strong relationship between substance misuse and mental health problems as the majority of users of drug services (74.5%) also experienced mental health problems (Weaver *et al.*, 2003).

- 5.2.9 Furthermore, a pattern of 'adverse selection' in prescribing has been noted whereby patients with mental health problems and current or past history of substance misuse are more likely to receive prescriptions for opioid drugs and are more likely to be prescribed higher, more harmful doses (Weisberg *et al.*, 2014).
- 5.2.10 The rise in prescribing opioid medication in the UK is almost wholly attributable to increased prescribing for chronic pain (Zin *et al.*, 2014). Prescription patterns show marked regional variation with the highest rates of prescribing in the North East and the lowest in London. These differences are mirrored exactly in the regional variation seen in benzodiazepine prescribing and, to date, prescribing of gabapentin and pregabalin. It is likely that these differences relate to socio-demographic variables rather than regional variation in prevalence of the clinical indications for which they are prescribed (*ibid*).
- 5.2.11 Prevalence rates for the use of sedatives/tranquillisers and for benzodiazepines are higher for older (35 to 64 years) individuals than for the younger (15 to 34 years) age group. Especially high rates are seen among those who are divorced, widowed or bereaved. The majority of survey respondents reported that they had obtained their drugs on prescription, but prescription drugs were also being obtained illicitly via the internet and the postal system usually from Asia (especially Pakistan). Overall, higher levels of education may be associated with online search of health-related information (Chiauzzi *et al.*, 2013). Conversely, subjects with low literacy levels may be more prone to purchase from 'rogue' internet pharmacies (Orsolini *et al.*, 2014). A range of determinants/variables may be taken into account in profiling the 'generic online drug consumer' (Gurau, 2005).
- 5.2.12 Overall, however, typical unlicensed online pharmacy customers were found to be young, Caucasian and male (Orsolini *et al.*, 2014; Chiauzzi *et al.*, 2013). There are variations in gender/age according to the type of drug purchased, with males most typically interested in purchasing sexual performance-enhancing drugs (Orizio *et al.*, 2010) and females carrying out online acquisitions of contraceptives (Kaskowitz *et al.*, 2007).
- 5.2.13 A recent paper (McCarthy, 2015) comments on reports of the rising death rate among middle-aged white people in the US and points to the increased availability of opioid prescriptions for pain as one of the contributory factors.
- Use of non-prescribed prescription-only painkillers for medical reasons was higher among men (7.9%) than women (6.8%).
  - The use of non-prescribed prescription-only painkillers for medical reasons decreases as life satisfaction increases; 12.7% of those with low levels of life satisfaction reported use in the last year, compared with 5.7% of those with very high levels of life satisfaction.

### *Diversion and Illicit Supply of Medicines*

- However, across other demographic factors, patterns of use diverge from those seen in the use of other drugs.
- Use of non-prescribed prescription-only painkillers for medical reasons was similar in different age groups (7.7% of those aged 16 to 24, compared with 7.3% of those aged 25 to 59).
- Over twice as many people with a long-standing illness or disability reported use of non-prescribed prescription-only painkillers for medical reasons (13.7%) compared with those with no long-standing illnesses (6.3%).

## **6 Displacement**

### **6.1 Key findings**

- ❖ There is no evidence that diverted prescription drugs are replacing traditional street drugs of choice.
- ❖ DISM can supplement the use of traditional illicit drugs.
- ❖ Displacement from traditional drugs tends to be temporary and is dependent on the cost and availability of traditional drugs.
- ❖ DISM does not appear to lead to the use of traditional illicit drugs.

### **6.2 Summary of information**

*From government departments/agencies and international agencies*

- 6.2.1 There is no evidence at present that diverted prescription drugs are replacing traditional street drugs of abuse. A recent Forensic Early Warning System study of drug use at a music festival (FEWS, 2015) detected use of a number of expected substances such as cocaine and MDMA together with a variety of ‘novel psychoactive substances’ but, other than diazepam, none of the medicines reported to our inquiry were detected. This was not due to an inability to detect prescription drugs as oxytetracycline, propranolol, sildenafil, ibuprofen and a number of other medicines were detected in the samples taken.
- 6.2.2 Some studies have suggested that young people may be moving from illicit drugs to prescription drugs, especially in the US (UNODC, 2011b; 2014) as they are more readily available and may be seen as more socially acceptable.
- 6.2.3 In 2009, the MHRA issued a public assessment report on minimising the risk of addiction to codeine and dihydrocodeine-containing medicines outlining a number of risk minimisation tools, and it is keeping the risk balance of these medicines under review (MHRA, 2009).
- 6.2.4 Due to the high costs of illicit drugs in Jersey compared with the rest of the UK (information from Jersey Government), prescribed and diverted medicines are widely abused by drug users either to complement the effects of drugs such as heroin and cocaine or to ‘tide them over’ by alleviating withdrawal symptoms until they can afford to access Class ‘A’ drugs.

*Submissions from stakeholders / anecdotal reports*

- 6.2.5 Medicines are being diverted and supplied illicitly in the UK, but quantities involved are currently modest compared with those of known illicit drugs such as cannabis, cocaine and heroin.
- 6.2.6 Use of prescription medicines to manage the ‘come down’ from illicit stimulant drugs seems to involve purchase of the drugs from a ‘friend’ who may have

obtained them by legitimate prescription. Existing drug addiction issues create a ready market for prescribed medicines, such as benzodiazepines, methadone, and other opiates, whether diverted or illicit (Green *et al.*, 2014).

- 6.2.7 Addiction clinics and therapists in the UK reported, anecdotally, that they sometimes see opioid-addicted clients who first developed a dependency on OTC codeine, which becomes very costly and time consuming to purchase from multiple outlets. These clients may then present to their local GP clinic with a serious addiction, which they conceal in the consultation, in order to procure a more regular, cheaper, supply of prescribed opiates (Graham – personal communication). It has been suggested that the use of codeine as a cough suppressant should be more tightly controlled (Brown, 2015).

## **7 Social and medical harms associated**

### **7.1 Key findings**

- ❖ Use of illicitly-supplied medicines increases risk of accidental overdose.
- ❖ Intravenous use increases the risk of infections and blood-borne viruses (BBVs).
- ❖ DISM damages patient-doctor relationships and can create an atmosphere of distrust.
- ❖ Medicines supplied illicitly may be genuine or may be counterfeit or adulterated.

The most serious problems DISM causes to the public, patients and clinicians are:

- mortality;
- criminality and recidivism;
- failure of recovery; and
- unintended child exposure and child mortality.

The knowledge that certain drugs are abused may compromise the clinician's willingness to prescribe them.

DISM risk mitigation includes:

- advice about the need for regular medication reviews;
- support in stopping ineffective medicines; and
- education for prescribers and patients about the lack of effect of long-term opioids (and other medications for pain) and the harms of prolonged use.

### **7.2 Summary of submissions and evidence**

*From government departments/agencies and international agencies*

7.2.1 Evidence from Scotland (Scottish Health Authority) suggests:

- Those who misuse prescription drugs opened themselves to a number of risks associated with misuse of medications, including adverse drug interactions and accidental overdoses, with opioid drugs carrying the highest risk.
- When patients consume POMs without a medical assessment or intervention, there is the potential for sub-therapeutic or excessive doses. Patients diverting their prescribed medication may also be at risk of sub-therapeutic dosage. Patients taking in excess of the prescribed doses of medicine through illicit supply are difficult to treat effectively as clinicians are unable to establish the true extent of their misuse.

7.2.2 The MHRA kindly interrogated their Yellow Card (YC) database from 2013 to the end of 2015 for those classes of medicines that were mentioned by the respondents to our request for information (Table 2).

**Table 2: Number of suspected adverse drug reactions (ADRs) in the YC database related to drug abuse, dependence and withdrawal, 2013-15**

<b>Class of medicines</b>	<b>Number of reports</b>
Opioids	511
Benzodiazepines	166
Anti-depressants/anti-psychotics	93
Gabapentinoids	163
ADHD medicines	4

7.2.3 The usual YC caveats apply when interpreting this data because it relies on spontaneous reports. These can be summarised as follows:

- a) **The frequency of an ADR cannot be estimated from YC data.** This is because there is limited information about how many people have taken the medicine without experiencing a reaction. Reporters are asked to submit YC reports even if they only have a suspicion that the medicine may have caused the ADR. The existence of an ADR report on the database does not necessarily mean that the medicine has caused the reaction.
- b) **It may be difficult to tell the difference between something that has occurred naturally and an ADR.** Sometimes reactions can be part of the condition being treated rather than being caused by a medicine.

7.2.4 Many factors have to be considered when assessing whether a medicine has caused a reported ADR. When monitoring the safety of medicines, MHRA staff carry out careful analysis of these factors. It is not possible to compare the risks of different medicines by comparing the numbers of reports in the YC database. For example, there are relatively few reports of dependence with benzodiazepines, but this is likely to be due to very high under-reporting by clinicians because this is such a well-recognised side effect of these medicines that clinicians may not perceive there is any benefit in reporting it. Even with the above caveats, this analysis adds further support to the conclusions we have drawn in this report, but also see Chaplin (2006) and Hazell and Shakir (2006).

7.2.5 In Jersey, the misuse of benzodiazepines among heroin users is associated with increased needle sharing, transmission of BBVs and accidental overdoses. Tablets are often crushed and injected resulting in thrombosis and venous abscesses. Patients are less likely to present for treatment if diverted medicines are readily available, and those who do are more likely to resist treatment.

#### *Peer-reviewed literature/surveys*

7.2.6 There were 3,674 poisoning deaths registered in England and Wales in 2015 (ONS 2016 – see table 3). There are caveats which apply to this data; it is not possible to:

- distinguish between street supplied drug and DISM,

- distinguish the proportion due to overdose of legitimate medication from those due to DISM,
- compare data with previous years.

**Table 3: Number of drug-related deaths registered in 2011-15 with selected medicinal substances mentioned on the death certificate (ONS)**

England and Wales					
	2011	2012	2013	2014	2015
All drug poisoning deaths	2,652	2,597	2,955	3,346	3,674
Paracetamol <sup>4</sup>	207	182	226	200	197
Antidepressants	393	468	466	517	447
Tricyclic antidepressants	200	233	235	253	215
Selective serotonin re-uptake inhibitors	127	158	150	159	150
Other antidepressants	84	104	124	155	133
Antipsychotics	104	102	107	126	101
Zopiclone or Zolpidem	71	83	86	100	87
Propranolol	32	39	46	54	55

Source: Office for National Statistics

Notes:

1. Cause of death was defined using the International Classification of Diseases, Tenth Revision (ICD-10) (see the Quality and Methodology Information for more details).
2. Figures are for deaths registered, rather than deaths occurring in 2011-2015.
3. Figures for England and Wales include deaths of non-residents.
4. Dextropropoxyphene is very rarely ingested except in combination with paracetamol, therefore figures include dextropropoxyphene mentioned without paracetamol.

7.2.7 In England and Wales, deaths involving tramadol fell for the first time in 2015, to 208 from 240 in 2014 (ONS, 2016). Although paracetamol-related deaths were similar in 2014 and 2015, deaths involving zopiclone/zolpidem, anti-depressants and anti-psychotics fell in 2015.

7.2.8 Prescription opioid abuse is probably the cause of more adverse experiences than any other class of drug. The increase in opioid prescribing in the UK, although not of the magnitude seen in the US, correlates with an increase in opioid-related deaths (Giraudon *et al.*, 2013). However, this has been contested in recent publications (Ekholm *et al.*, 2014; Weisberg *et al.*, 2014) which claim that the increase in opioid prescribing in the UK and Denmark has not resulted in an increase in deaths. All authors recommended that the situation is monitored closely to avoid the explosion in opioid availability seen in the US which has fuelled prescription opioid abuse (Volkow, 2014).

7.2.9 In 2015, benzodiazepines were:

- associated with 366 deaths in England and Wales with 252 (69%) of these implicating diazepam;

- implicated in, or potentially contributed to, 191 deaths in Scotland.

7.2.10 In Scotland there were 706 drug-related deaths registered in 2015; opioids as a whole were implicated in 606 of these, with heroin or morphine attributed to 345 and methadone to 251.

7.2.11 Information from the Coroners' Society (England and Wales) suggests DISM associated with drug-related deaths is due to supplies obtained via the internet purchased from the US, Europe and Far East including China, or via hoarding of prescribed medicines.

#### *Submissions from stakeholders / anecdotal reports*

7.2.12 Stakeholders were asked what problems DISM has caused for patients and clinicians.

7.2.13 In 2014, a report by the National Poisons Information Service (NPIS) surveyed telephone enquiries involving pregabalin, gabapentin, quetiapine, mirtazapine and memantine and quantified those for the period January 2007 to 23 October 2014 (Hawkins and Thomas, 2014). It is not possible in most cases to differentiate using NPIS data those enquiries relating to exposure to illicit/diverted drugs from those involving legitimately prescribed medicines. Recreational drug abuse and route of exposure are, however, both recorded separately. Therefore data are provided as total telephone enquiries by year. These are all enquiries from an NHS health professional to NPIS involving an exposure to any of the five drugs studies in this report under any circumstances. Note that the majority of these enquiries are intentional or accidental overdoses of legitimately prescribed drugs.

7.2.14 Enquiries by year flagged as recreational abuse were also recorded. This requires recognition from the enquirer and/or the NPIS poisons information specialist handling the call that the drug has been used for recreational purposes. Because this may not be recognised in a substantial proportion of cases, these data are likely to underestimate the extent of the problem.

7.2.15 Enquiries where the route of administration is recorded as non-oral were also recorded. These data are provided because non-conventional routes of administration are more likely to represent recreational use. Telephone enquiry data was only collected consistently onto a national database from 2008, so data for 2007 is incomplete and should not be used for time trend analysis.

7.2.16 Over the duration of the study, there were 12,334 telephone enquiries of all types relating to the five drugs of interest with numbers increasing from 1,260 in 2008 to 2,024 in 2013, the earliest and most recent full years for which complete national data are available. Of those enquiries, 107 (0.9%) were identified as recreational and in 11 (0.1%) a non-oral route of administration was recorded. Recreational enquiries have increased over the period of study from 3 (0.2% of the total) in 2008 to 25 (1.2% of the total) in 2013, with the largest incremental increase

between 2011 and 2012. For each of the five individual drugs, recreational or non-oral use constituted only a small minority of all telephone enquiries relating to that drug. Pregabalin was most commonly identified as associated with recreational use (36 or 1.9% of all pregabalin enquiries), with quetiapine (27 or 0.64%), gabapentin (24 or 1.6%) and mirtazapine (20 or 0.44%) implicated less frequently. There were no recreational enquiries identified for memantine.

7.2.17 For all drugs, overall, enquiries more commonly involved female than male patients; however, for three of the four drugs implicated, recreational or non-oral users were more frequently male, the exception being pregabalin. For all implicated drugs, the median ages of recreational or non-oral users were younger than those involved in NPIS enquiries overall. <sup>11</sup>Enquiries relating to recreational and/or non-oral use of the four implicated drugs have increased between 2008 and 2013, although remain a small proportion of total enquiries for each. Recreational or non-oral users are younger and, with the exception of pregabalin, more commonly male. The proportion of recreational or non-oral exposures that arise from health professionals working in prisons or with the police is substantially larger than for general NPIS enquiries.

7.2.18 Aside from the wider societal effects of drug misuse and illicit supply networks, medicine diversion may cause damage to the professional/patient therapeutic relationship (Hurwitz, 2005). Strategies implemented to restrict access to medications may bring unanticipated consequences. For example, tight restrictions may create an atmosphere of distrust between patient and clinician when prescribing a specific drug (*ibid*). In extremes, this may create barriers to access and treatment, as patients may be reluctant to accept a medicine perceived to be one associated with abuse. All of these real or perceived problems may have implications for the patient, clinician and the wider community. The most serious problems that DISM causes to public, patients and clinicians are:

- mortality;
- criminality and recidivism;
- failure of recovery; and
- unintended child exposure and child mortality.

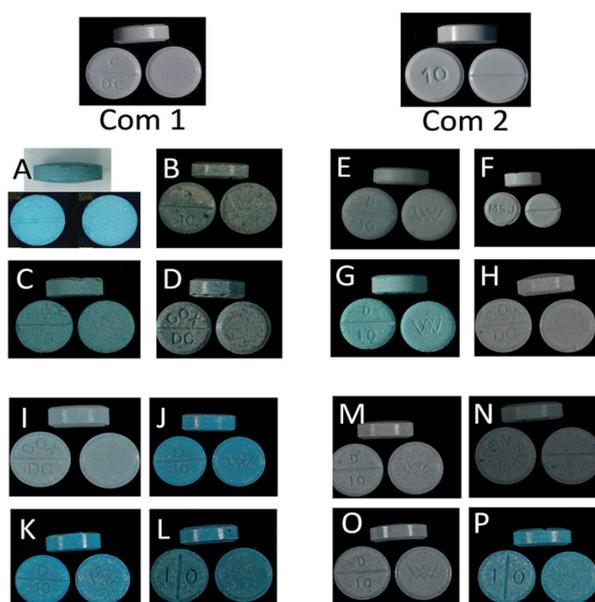
7.2.19 Medicines obtained through diversion are likely to be pure and unadulterated, but those from illicit sources may be counterfeit and contaminated, inconsistent or contain adulterants. For example, diazepam tablets purchased on the street may contain varying levels of the drug, as well as other substances, such as etizolam, phenazepam, amitriptyline or warfarin (or a combination). In a recent survey of drugs bought as purporting to be blue diazepam tablets, the 43 cases that were studied between 2006 to 2013 (submission from Robert Gordons and Abertay

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<sup>11</sup> NPIS data are of limited value for studying patterns of drug diversion and illicit supply, but do give an indication of the frequency of episodes of toxicity presenting to UK health professionals associated with recreational use of licensed medicines.

Universities working with Police Scotland) showed that ten samples contained between 9-11 mg of diazepam and lactose in tablets of a pharmaceutical grade that may have been diverted. There were also tablets of a chalky appearance that contained approximately 8 mg of diazepam and were probably counterfeit. In a number of cases, counterfeit tablets that looked like genuine 10 mg diazepam tablets were found to contain between 20-25 mg of diazepam. Perhaps most worryingly, in two cases tablets contained no diazepam but instead contained the potent benzodiazepines phenazepam or etizolam instead. This mixture of real and counterfeit versions of prescription medicines illustrates the difficulty faced in our attempts to accurately estimate the magnitude of DISM (see Figure 1 for tablet appearance). Risk of accidental overdose is also increased by uncertainty over purity and strength of medicines purchased illicitly (Personal correspondence from Kenny Simpson, Police Scotland).

**Figure 2: Photographs of licit (Com 1 and Com 2) and illicit ‘diazepam’ tablets; individual Cases A to P included**



7.2.20 The misuse of prescription drugs is prevalent in Scotland and by the far the greatest illicit market demand is for benzodiazepine 'type' tablets. Accurate assessment of the number of tablets in circulation is impossible; however, it is assessed by police that there were significant amounts and types of tablets circulating which had been diverted from lawful manufacture or produced without regulation. Blue, yellow and white tablets purporting to be diazepam had been found to contain etizolam, diclazepam, flubromazepam and other benzodiazepine-type drugs. Other blue tablets bearing the markings NTZ, EZ or 1.0 have been found to contain etizolam, and the drug U-47,700 has been identified in a variety of tablets perceived to contain diazepam. Perception is a significant factor exploited by those involved in the illicit production of these tablets. There is currently no guarantee that any tablet on the illicit market purporting to be diazepam, may actually contain that drug. Tablets sold as benzodiazepines currently sell for 50p to £1 each on the illicit Scottish drug market and are widely available (Personal correspondence from Kenny Simpson, Police Scotland)..

7.2.21 Identifying cases of prescription medicine misuse and/or diversion is a problem for clinicians, especially for those psychiatric indications that lack an objective diagnosis. Prescribers may thus inadvertently supply medication for the illicit market. For example, some patients present to GPs with very plausible symptoms, such as neuropathic pain or generalised anxiety, for which objective diagnostic tests are lacking but which often require maximum doses of 'desirable' medication.

*Actions and recommendations suggested by stakeholders and other bodies*

Stakeholders suggested that clinicians can improve practice by:

- **closer monitoring** of commonly abused prescription drugs;
- implementing regular **medication reviews**; and
- **developing guidelines** on what action to take if diversion is suspected.

## 8 Consideration of prisons

*Within the prison environment, factors leading to DISM include high levels of prescribing medicines liable to abuse, poor supervision of medication queues and lack of secure in-cell storage. The unique prison environment and demographics mean a number of factors have to be taken into account when comparing the findings to that of the wider community.*

### 8.1 Key findings

- ❖ Most prisons have reported an issue of diversion of medicines.
- ❖ Medicines sought tend to be depressants and tranquillisers due to boredom in the prison environment.
- ❖ Buprenorphine has been a drug of misuse in prison for several years.
- ❖ Misuse of POMs in prisons may be due to the reduced availability of other drugs.

### 8.2 Summary of submissions and evidence

*From government departments/agencies and international agencies*

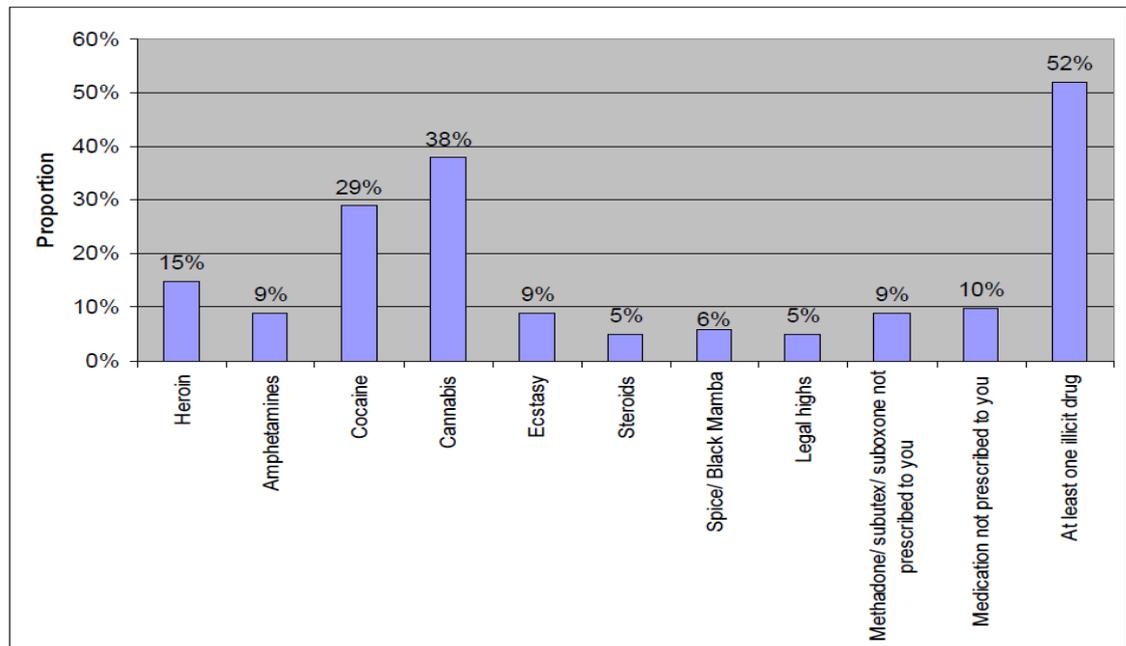
8.2.1 In recent years, Her Majesty's Inspectorate of Prisons for England and Wales (HMI Prisons) has raised concerns about the diversion of medications in prisons.

2015	Diversion of medications is a serious problem in prisons ( <i>Changing patterns of substance misuse in adult prisons and service responses</i> , HMI Prisons, 2015).
2013	Reiterated concerns raised in 2012 about the use of prescribed medications within establishments highlighting inflexible prescribing and a lack of secure storage for in-possession medications as contributing to the rise in diverted medications (HMI Prisons, 2013).
2012	Diversion of prescribed medication had spread to mainstream populations and was being reported at most prisons inspected ( <i>The 2012 report</i> , HMI Prisons, 2012).
2011	First highlighted the issue of diverted medications in its 2010-11 annual report (HMI Prisons, 2011), noting that the diversion of medication was a major issue in high security and vulnerable prisoner populations.

8.2.2 HMI Prisons 2012-13 prisoner survey, conducted in 38 establishments, included a question about diverted medication for the first time. Of adult prisoners surveyed, 7% reported that they had developed a problem with diverted medications within their current establishment. The highest percentage was reported in the women's estate (10%) compared to only 2% within adult male open prisons and young adult male establishments. On the whole, similar percentages of prisoners reported developing a problem with diverted medications as did a problem with illegal drugs (6%), and again the highest percentage (9%) was reported by women.

- 8.2.3 Undiagnosed/untreated mental health problems could in part explain the use of benzodiazepines and other anti-depressants within the prison population. The Department of Health issued guidance on managing prisoners with dual diagnosis in 2009: [http://www.nta.nhs.uk/uploads/prisons\\_dual\\_diagnosis\\_final\\_2009.pdf](http://www.nta.nhs.uk/uploads/prisons_dual_diagnosis_final_2009.pdf) This guidance recommends that those who present with a dual diagnosis be managed through a coordinated care plan approach and that any prescribing is monitored by both substance misuse and mental health teams. Recent guidance on pain management prescribing has also been produced by PHE. This work highlights the particular challenge of prescribing abusable medications in secure settings and sets out practical guidance on assessment (*Managing persistent pain in secure settings*, PHE, July 2013).
- 8.2.4 Guidance for prisons developed by NHS England in partnership with National Offender Management Service (NOMS) and PHE provide additional support for pain management, including a prison pain management formulary and related publications (NHS England 2015: <https://www.england.nhs.uk/commissioning/health-just/pain-formulary/>
- 8.2.5 The Prisons and Probation Ombudsman (PPO) reported in 2011-12 that 6% of all fatal incidents investigated were due to drug toxicity (submission received from HMIP). Recurring factors in the investigated deaths included trading in prescribed or smuggled drugs, the hoarding of drugs for later use, and the combined effects of prescribed medication and illicit drug use.
- 8.2.6 The Prison Service has been a valuable source of information from all parts of the UK (written submission from HMIP). Drug misuse was reported by 70% of offenders prior to entering prison and 51% of inmates reported drug dependency (*ibid*). Offenders coming into prison reported DISM with drugs purchased over the internet, drugs extorted or purchased from patients exiting pharmacies or obtained by 'doctor shopping'. In the latter case it has been reported that doctors were receptive to excuses such as theft or loss of a prescription or accidental disposal of the drugs. There were also occasional reports of community pharmacy staff selling POMs illicitly.
- 8.2.7 Most medications diverted in prisons were those which had a depressant effect. Buprenorphine has been the prime drug of misuse in prisons for years, usually as Suboxone or Subutex (*Changing patterns of substance misuse in adult prisons*, HMI Prisons, 2015).

**Figure 3: Reported drug use in the two months prior to prison by type of drugs (N=1,384) from HMI Prisons thematic survey, ‘Changing patterns of substance misuse in adult prisons and service responses – a thematic review’ (2015)**



*Peer-reviewed literature/surveys*

- 8.2.8 The trend towards diverted medications can in part be explained by reductions in the availability of illicit drugs within prisons as security departments become more adept at reducing the supply of illicit drugs into prisons (Tompkins *et al.*, 2013).
- 8.2.9 Within prisons in England and Wales, even though the range of drugs available is restricted, inmates have learnt to describe the symptoms of specific disorders (e.g. neuropathic pain or anxiety) in order to obtain drugs with abuse potential. Notably, many of the symptoms presented are associated with disorders for which no reliable and objective diagnostic test is available and this makes diagnosis solely dependent upon patient-reported symptoms. Where particular drugs are requested by name, this is a warning that abuse may be a possibility (HMIP, 2013).
- 8.2.10 Along with the increased misuse of opioid substitution medications, there has also been a reported increase in the misuse of other prescribed medication in prisons including benzodiazepines, anti-depressants and painkillers (Penfold *et al.*, 2005; Plugge *et al.*, 2009), because of their low cost, availability, undetectability and guaranteed effect. The principal source of these medications is believed to be through the diversion of in-prison supplied medication. There are substantial challenges for prescribers in prisons in distinguishing patients who present with genuine clinical need for medications and those who seek prescriptions for abusable medications for personal use or as a commodity for trade.
- 8.2.11 In the UK prescribing per capita of pregabalin and gabapentin in secure settings is double that in the community and this appears unlikely to represent differences in

prevalence of the licensed indications for the drugs in these populations (see Stannard *et al.*, 2014).

8.2.12 Misuse of medications is not restricted to the nature of the medications themselves; prisoners have also reported new routes of administration. For example, prisoners have reported snorting buprenorphine for an initial euphoric effect with a longer-term narcotic effect (Tompkins *et al.*, 2009). Previous research has also revealed methadone syrup being injected (Gossop *et al.*, 2000), although the likelihood of this occurring within prisons is slim given the general low level of injecting practices within prisons.

*Submissions from stakeholders / anecdotal reports*

8.2.13 There is no single source which can tell us the scale of drug use within prisons. The mandatory drug testing (MDT) panel is limited in that it does not include all medications which are prescribed or abused within prisons. Therefore, the scale of medication use is relatively unknown in contrast to the better known extent of the use of illicit drugs within prisons. However, MDT figures and finds reported in recent inspection reports suggest that cannabis and buprenorphine may now be the most commonly misused substances in prison (2012-13 HMIP annual report).

8.2.14 To minimise the risk of diversion of prescribed buprenorphine it is crushed and administered daily under supervision (PSI IDTS 2010/45). This means that any intact tablets seized within prisons can be considered to originate from non-prescribed supplies. Crushed doses are also more difficult to divert.

8.2.15 While there are no definitive figures on the number of prisoners who misuse drugs while detained, the fact that 70% of offenders report drug misuse prior to prison and 51% reported a drug dependency can be used to infer the scale of the problem (quote from written submission from HMIP).

8.2.16 A report of the NPIS showed that there were 112 unique enquiries identified as arising from recreational or non-oral use of pregabalin, of which a substantial minority were recorded as originating from prisons (25 or 22%) or the police (5 or 4.5%). Of all NPIS telephone enquiries received, fewer than 2% arise from prisons (Hawkins and Thomas, 2014).

## **9 Comparison with the US and comment on other countries**

- 9.1** The public health implications of DISM in the US have been well described over a number of years and it is clear that the rise in prescribing of abusable medicines, particularly opioids, has paralleled the rise in medication misuse. Similar trends in prescribing are seen in the UK, and stakeholder responses gathered for this report are consistent in suggesting that DISM is an increasing problem in the UK although this has been very difficult to quantify.
- 9.2** An objective of this study was to compare the current situation in the UK with the extent and nature of DISM in the USA. DISM is a well-established issue in the US and, although minimal in the UK, it is important to look at any trends evident from the US to assist with suitable monitoring and effective recommendations.
- 9.3** In recent years, DISM has become of increasing public concern across the globe, although the evidence for this constituting a major problem other than in the US is hard to find. In the US overdose deaths involving prescription opioids have quadrupled since 1999<sup>12</sup>, and so have sales of these prescription drugs<sup>13</sup>. From 1999 to 2014, more than 165,000 people have died in the US from overdoses related to prescription opioids (CDC, 2014a).
- 9.4** The prevalence of opioid use remains high in North America (3.8%) in relation to the global average (UNODC, 2015). In the US, it has been claimed that prescription medications, such as those used to treat pain, attention deficit disorders and anxiety, are being abused at a rate second only to cannabis among illicit drug users (Volkow, 2014). The increase in prevalence of medication misuse in the US has been paralleled by a sharp and sustained increase in the prescription of opioid medications in the US over the past 25 years. Recent reports suggest that similar trends in opioid prescribing in the UK and Denmark do not appear to have been accompanied by proportionate rises in misuse of prescription opioids (Ekholm *et al.*, 2014; Weisberg *et al.*, 2014) and this issue clearly needs to be further studied.
- 9.5** In comparison in the US in 2014 there were more than 14,000 deaths attributed to prescription opioid overdoses. The most common were methadone, oxycodone and hydrocodone (CDC, 2014c).

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<sup>12</sup> CDC. Wide-ranging online data for epidemiologic research (WONDER). Atlanta, GA: CDC, National Center for Health Statistics; 2016. Available at <http://wonder.cdc.gov>.

<sup>13</sup> . Frenk SM, Porter KS, Paulozzi LJ. Prescription opioid analgesic use among adults: United States, 1999–2012. NCHS data brief, no 189. Hyattsville, MD: National Center for Health Statistics. 2015.

## 9.6 Context of evidence

- 9.6.1 It is important to contextualise the evidence from the US as there are a number of important cultural and healthcare differences between the US and the UK that may be respectively permissive and protective in relation to DISM.
- 9.6.2 In the UK, patients have a registered general practitioner (GP) in the majority of cases within the NHS, who is well known to the patient, and practices have information systems that will indicate the frequency and dose of prescriptions. However, patients may increasingly obtain prescriptions from out of hours services and drop-in centres. Less than 0.1% of opioid prescriptions are issued privately in the UK (CQC, 2015). Unlike the UK, the US does not have a national system of medical records for individual patients. This means that it is much easier in the US, and in some other countries, for an individual to visit different prescribers to obtain multiple prescriptions for the same medicine. The experience of these other countries is not necessarily applicable to the UK. In the most extreme cases in the US, 'pill mills' are being run by unscrupulous physicians prescribing so irresponsibly that two of them are now on trial for murder (Dyer, 2015). They were part of a group of 13 doctors which prescribed over 20 million oxycodone tablets and their business model was described as "get the customers in, get their \$150, give them what they want and move them out". Customers paid cash and the clinic did not accept insurance patients.

## 9.7 Types of drugs

### *Opioids*

- 9.7.1 In the US, opioids are most commonly diverted, followed by benzodiazepines (Inciardi *et al.*, 2006). A survey of drug dealers in South Florida (Rigg *et al.*, 2012) revealed the prescription medicines that they obtained for sale were most commonly prescription opioid analgesics with, to a lesser extent, benzodiazepines. In the US, Zosel *et al.* (2013) found that the most frequently misused prescription drugs in adolescents (median age 16.6 years) were hydrocodone, amphetamine, oxycodone, methylphenidate and tramadol.
- 9.7.2 A very large survey based on data from 472,200 subjects (aged 18 to 64) who participated in the US 2003-13 National Survey on Drug Use and Health suggests that the prevalence of non-medical use of prescription opioids decreased slightly from 5.4% in 2003 to 4.9% in 2013, but that the prevalence of opioid use disorders increased from 0.6% to 0.9% over this period (Han *et al.*, 2015).
- 9.7.3 Recent data points to less use of oxycodone in the US driven by the introduction of tamper-proof formulations and the ready availability of cheap heroin on the street (UNODC, 2014). From 1999 to 2006, the proportion of individuals aged over 20 in the US using a prescription opioid in the last 30 days increased from 5% to 6.9%, but this figure remained stable at 6.9% from 2003 to 2012 (Frenk *et al.*, 2015).
- 9.7.4 In the US in 2010, over 5 million people abused prescription pain relievers and those with the most severe dependence on prescription opioids were 7.8 times

more likely to have also used heroin in the last 12 months than the general population (UNODC, 2014).

- 9.7.5 Conversely, in 2012 it was found that those who had used heroin were five times more likely to have used analgesics for non-medical reasons (*ibid*) and that one-third of this group had misused OxyContin (a commercial brand of oxycodone). Of those who had presented as having abused OxyContin, one-quarter had also used heroin. In contrast, a recent study suggested that the illegal use of prescription opioids may not be a primary cause of subsequent heroin use (Lipari and Hughes, 2015). A recent trend is for increased use of fentanyl and fentanyl analogues but usually as a result of bulk illicit drug supply rather than DISM (Cassels 2015), with amounts up to 12 kg being seized in California in 2014.
- 9.7.6 A recent analysis of the records of 22,142 adults receiving chronic opioid therapy in the US over a 7-year period (Palmer *et al.*, 2015) suggested that 9.4% were 'problem users' at risk of addiction. A similar survey of more than 100,000 patients from Veterans Administration (VA), Baylor Scott and Henry Ford Health systems between 2000 and 2012 indicated that the risk of new onset depression increased in patients treated with opioids and the risk increased with duration of opioid treatment (Mayor, 2016).

#### *Other central nervous system (CNS) depressants*

- 9.7.7 The most common misused sedatives were benzodiazepines and the Z-drugs (Frenk *et al.*, 2015).

In the US, benzodiazepine prescribing continues to rise (Bachhuber *et al.*, 2016); whereas in the UK, education has led to a downward trend in prescribing with consumption of benzodiazepines per capita being one-quarter of that in the US. The FDA has recently issued a drug safety communication (31 August 2016) warning about serious risks and death when combining opioid medicines with benzodiazepines (see <http://www.fda.gov/Drugs/DrugSafety/ucm518473.htm>).

#### *CNS stimulants*

- 9.7.8 Although stimulant drugs used to treat ADHD in the UK were mentioned individually in the responses to our inquiry, DISM did not seem to be a major issue for those bodies we consulted (in spite of many reports in the press and broadcast media that these drugs were being used extensively by the student community in particular). In the US this is seen as a prevalent and growing issue with between 2 and 8% of college students using these drugs to improve academic performance with a disregard of potential adverse effects (Benson *et al.*, 2015; DeSantis and Hane, 2010; Sahakian and Morein-Zamir, 2015; Wilens *et al.*, 2007). This seems to be fuelled by competition with peers who are taking these drugs on prescription (*ibid*). A wide range of agents were being used including methylphenidate, atomoxetine (Chamberlain *et al.*, 2007) and dexamphetamine. Modafinil seems particularly popular and may have the best risk/benefit ratio of current agents (Porsdam-Mann and Sahakian, 2015).

- 9.7.9 Prior use of ADHD drugs on prescription does not increase the risk of the individual later pursuing substance abuse and indeed the risk of this may be reduced in childhood users of ADHD medications (Wilens *et al.*, 2003). The abuse of the OTC stimulant pseudoephedrine and sedative antihistamines has also been reported in the literature (Cooper, 2013a,b). Up to 90% of all modafinil use may be 'off label' (Sahakian *et al.*, 2015).

## **9.8 Sources**

- 9.8.1 A review of opioid poisonings in the US demonstrated that fewer than half of patients had been prescribed opioids legitimately and 20% had received prescriptions from multiple sources, also known as 'doctor shopping' (Rudd, 2015).
- 9.8.2 In addition to the ready availability of legitimate prescriptions from multiple prescribers, prescriptions were available from fraudulent practitioners, known as 'Pill Mills' (Dyer, 2015).
- 9.8.3 Data from Ohio (Inciardi *et al.*, 2007) indicated that healthcare workers were involved in the diversion of drugs for illicit use, with three-quarters of those cases coming to court involving nurses, nursing assistants and medical assistants. Hospitals were the most common source, followed by pharmacies. A survey of adolescent users in the US indicated that the source of their drugs was usually a family member or friend who had a legitimate prescription for the drug in question (Zosel *et al.*, 2013).
- 9.8.4 A detailed investigation in the US suggested that while 'doctor shopping', unscrupulous physicians and supplies via the internet were present, there were also street markets involving patients, Medicaid recipients and pharmacies (Inciardi *et al.*, 2007). In addition, they found that residential and pharmacy robberies were perhaps underestimated as a source of diverted medicines. A more recent investigation in South Florida used interviews with drug dealers to establish where their supplies originated – visiting multiple pain clinics to obtain prescriptions, working with pharmacy employees to steal medicines and purchasing medicines from indigent patients were the most common among a wide range of strategies (Rigg *et al.*, 2012).

## **9.9 Prevalence**

- 9.9.1 Volkow (2014) reported that in 2012 over 5% of the US population aged 12 years or over used opioid pain relievers for non-medical reasons and many people reported that a prescription medication was their first drug of abuse. Significant social harms have resulted from the ready availability of opioids and, for example, there has been a four-fold increase in neonatal abstinence syndrome between 2004 and 2013 (McCarthy, 2015).

## **9.10 Social and medical harms**

- 9.10.1 Almost one-third of prescription opioid deaths in the US relate to use of methadone for chronic pain. The uncertain pharmacokinetics of the drug,

particularly in the early days of dosing and the long half-life in relation to respiratory depression, make it particularly hazardous when co-administered with other centrally acting drugs. The per capita prescribing of methadone in the UK is similar to the US, but around 97% of prescribing in the UK is in the supervised context of OST with the small remainder being prescribed for pain. In the US, it is also common to use opioid analgesics during pregnancy, although this is strongly associated with neonatal complications (Patrick *et al.*, 2015; Volkow, 2016). A set of guidelines on opioid prescribing for chronic pain have now been issued by CDC (Ault, 2015; Dowell *et al.*, 2016).

9.10.2 The use of opioids in conjunction with benzodiazepines presents a particular overdose hazard (Babalonis and Harris, 2015; Park *et al.*, 2015) and this is reflected in drug poisoning data in the US where benzodiazepine prescribing continues to rise (Bachhuber *et al.*, 2016). In the UK, concerted efforts to educate prescribers of the hazards of long-term benzodiazepine use have led to a downward trend in prescribing with consumption of benzodiazepines per capita being one-quarter of that in the US.

9.10.3 The US Government does not track death rates for every drug. However, the National Centre for Health Statistics at the CDC does collect information on many of the more commonly used drugs.

9.10.4 In the US, from 2001 to 2014, there was:

- a 2.8-fold increase in the total number of deaths involving prescription drugs;
- a 5-fold increase in the total number of deaths involving benzodiazepines;
- a 3.4-fold increase in the total number of deaths from prescriptions opioid pain killers (CDC, 2015).

9.10.5 In the US, Prescription Drug Monitoring Programs (PDMPs) are state-wide electronic databases used to track the prescribing and dispensing of controlled prescription drugs to patients. PDMPs improve the prescribing of opioids and can monitor information for suspected abuse or diversion. They also provide critical information about a patient's prescription history to prescribers and pharmacists, which help them to identify at-risk patients and provide early intervention.

9.10.6 Evaluation of PDMP effects on prescribing has been mixed, but are likely to be contributing to:

- changed prescribing behaviour;
- identifying 'doctor shopping' by patients; and,
- a reduction in substance abuse treatment admissions (CDC)

9.10.7 The British Pain Society together with the Royal College of Anaesthetists have recommended that non-pharmacologic and non-opioid pharmacologic therapy should be preferred for chronic pain and that when using opioids short-acting rather than long-acting agents should be used. The CDC made a similar recommendation independently.

## 9.11 Displacement

9.11.1 It has been found that individuals in the US who misuse prescription opioids are more likely to progress to the use of heroin than the general population although this conclusion has been questioned by others (Muhuri *et al.*, 2013). It does appear clear that most heroin users also have a history of non-medical use of prescription opioid pain relievers, and the increase in the rate of heroin overdose deaths in the US has been concurrent with the increase in prescription opioid overdoses (CDC, 2015; Lipari and Hughes, 2015). Between 2002 and 2013 there was an increase from 17.8 per 1000 to 42.4 per 1000 in heroin use by the non-medical opioid users, but prior cocaine users had a heroin use rate of 91.5 per 1000 over the same time period (*ibid*). Mortality assessed by drug overdose death rates in the US increased from 4.5 per 100,000 to 7.8 per 100,000 over the period and frequency of opioid use also increased (Han *et al.*, 2015). It is also noteworthy that the number of babies born in opioid withdrawal has increased 4-fold in the US between 2004 and 2013 (McCarthy, 2014b).

9.11.2 Although it was found to be true that people misusing prescription opioids were more likely to progress to heroin than those who had not, the vast majority of prescription opioid misusers did not progress to heroin (Lipari and Hughes, 2006). There is evidence for a dynamic interaction between the misuse of prescription opioids and that of heroin illustrated by the situation after the introduction of abuse-deterrent formulations of oxycodone (Laroche *et al.*, 2015). In 2010, propoxyphene was withdrawn from the US market and abuse-resistant oxycodone was introduced. In order to assess the effects of this change, the claim records of 31 million individuals insured by a major US provider were analysed between 2003 and 2012 (*ibid*). Opioid dispensing and prescription opioid overdose decreased after 2010 but heroin overdose rates continued to increase (Laroche *et al.*, 2015). It is also clear that abuse-resistant formulations have a limited efficacy in reducing opioid misuse in the longer term (Cicero and Ellis, 2015).

9.11.3 The illicit use of prescription opioids shares a market with other substances, including heroin, with the price and availability of each substance influencing misuse prevalence. Greater access to OST and facilitated retention in opioid substitution programmes may also be protective in the UK, whereas in the US, users may turn to the illicit prescription market to maintain an opioid addiction. Ready access to relatively cheap heroin and accessibility of OST may restrict the market for illicit prescription opioids in the UK compared to the US.

## 9.12 Demographics

9.12.1 Data obtained from poison centres in the US indicate that there is a high level of misuse of prescription drugs by adolescents (median age 16.6 years) (Zosel *et al.*, 2013). There are indications that the more highly educated college students are the ones most likely to use prescription rather than street drugs (UNODC, 2011a).

## **9.13 Consideration of rest of the world**

9.13.1 The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) identified an increasing trend in misuse of prescribed medications in Europe.

9.13.2 Apart from the single case of opioid substitution drugs (UNODC, 2011a), in Europe the non-medical use of prescription drugs has not to date been considered a major concern. Only some countries in Europe monitor the prevalence and patterns of DISM, since the main efforts at monitoring substance use and abuse have focused on illicit substances as well as alcohol and tobacco, and hence the magnitude of DISM is not properly known.

9.13.3 The European Drugs Report (EMCDDA, 2014) indicated that:

- illicit use of medicines is increasing in the EU;
- as well as prescription opioids (principally methadone, buprenorphine and fentanyl), pregabalin, tropicamide and carfentanil had all been detected as being used by the opioid addiction community;
- in addition, drugs which are licensed for prescription use elsewhere in the world are appearing in the EU such as phenazepam and phenebut (*ibid*);
- misused medicines are diverted from the regulated market but are also imported as bulk drugs from outside the EU, typically from China, then packaged and distributed locally. They may get to the end user by way of the illicit drug trade, the 'legal highs' trade or by way of the internet.

9.13.4 The European Drugs Report (*ibid*) stated that the role these drugs play in overdose deaths in Europe is poorly understood and there are concerns about misused benzodiazepines and other medicines, including OST medications, which had been diverted from therapeutic providers or obtained from unlicensed sources. Regulatory frameworks and clinical guidelines can help reduce the risk of diversion of medicines from appropriate therapeutic uses.

9.13.5 The EMCDDA has reported that the countries in Europe with a substantial proportion of treatment demand for sedatives and tranquillisers are Sweden, Norway and Finland. The use of benzodiazepines is common among drug users across Europe, including by OST clients.

9.13.6 A systematic review of the literature between 2001 and 2011 (Casati *et al.*, 2012) indicated that:

- heterogeneity in medicine misuse across the EU indicating that country-by-country prevalence studies are needed; and
- analgesics were the most common class of drug being misused, both prescription and OTC.

9.13.7 The most frequently abused drugs were codeine, tramadol and fentanyl. Opioid substitution drugs (methadone and buprenorphine) were also prone to misuse.

When 309 patients who were attending opioid treatment programmes in Germany or Italy were surveyed, 36% reported that prescription opioids were the primary drugs used to get high including buprenorphine and methadone (Green *et al.*, 2014).

- 9.13.8 UNODC reported that in some parts of Europe, heroin users had switched to fentanyl, owing to the declining availability of heroin (UNODC, 2014).
- 9.13.9 There has also been a recent increase in abuse of fentanyl in the US, sometimes in a mixture with heroin (Cassels, 2015) and its high potency has resulted in an increase in the number of overdose deaths in the US, Russia, Ukraine, Sweden and Denmark. This does not seem to be by way of diverted prescription medicine but from bulk supplies produced in laboratories in Mexico and elsewhere (Cassels, 2015). It has been pointed out that the cycle of abuse between illicit and prescription opioids requires us to recognise that society does not face distinct heroin or prescription drug problems but faces an overarching addiction problem (Rannazzisi, 2014). Which drugs are being taken at a given time is price dependent (*ibid*) and typically black market sales of prescription drugs in the US are at 5-10 times their retail value with the stronger opioids demanding higher prices. For example, hydrocodone can be purchased at \$7-10 per tablet whereas oxycodone can command \$40-80 a tablet (Rannazzisi, 2014). Some users have turned to heroin as a much cheaper opioid (typically \$10 per bag) which gives a similar high and suppresses withdrawal symptoms (*ibid*).
- 9.13.10 In 2011, the UNODC report '*Ensuring availability of controlled medications for the relief of pain and preventing diversion and abuse*', concluded that while in most countries there is little or no access to opioids, in some countries, the misuse of controlled medicines represents a significant public health problem (UNODC, 2011c). In UN Resolution 53/4, the Commission acknowledged that an increase in the licit supply of internationally controlled substances may raise the risk of diversion and abuse.
- 9.13.11 In April 2016, the United Nations General Assembly Special Session (UNGASS) outcomes document recommended measures to address demand and supply reduction, and to improve access to controlled medicines while preventing diversion.<sup>14</sup>

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<sup>14</sup> <http://www.unodc.org/wdr2016/>

## **10 Recommendations**

1. Maintain a watch list of emerging prescribed substances with the potential for DISM.

ACMD will develop a SOP for monitoring substances on the watch list in order to make timely recommendations on revisions to control status should that be warranted.

ACMD will review the case histories leading to the recommendations for re-scheduling the gabapentinoids and tramadol in order to establish best practice guidelines.

Government agencies with information and statistics relevant to substances on the watch list to make them available to ACMD in line with the SOP.

**Lead: NHS Digital and NHS Protect, Home Office, ACMD**

2. Ensure appropriate education of medical students / non-medical prescribers and, by CPD, existing practitioners so that controlled drugs subject to DISM are not prescribed to patients who no longer derive a therapeutic benefit from them.

**Lead: Clinical Commissioning Groups (in conjunction with Medical Royal Colleges, Royal Pharmaceutical Society, General Pharmaceutical Council, Medical Schools Council and GMC)**

3. Monitor the implementation of the NICE Guidelines on the Safe Use and Management of Controlled Drugs to ensure that prescribers follow best practice in reviewing repeat prescribing of medicines on which people may become dependent, ensuring patients are appropriately aware of the risks and benefits of such medicines and understand the need for safe and timely disposal of unused medicines.

**Lead: Professional Bodies, Regulators, CCGs and Devolved Administrations**

4. Support the development of tailored treatment for those who misuse or have become dependent on prescription or over-the-counter medicines (whether or not this involved DISM).

**Lead: Public Health England (PHE), NHS England, Public Health Wales (PHW) and NHS Health Scotland, Department of Health, Social Services and Public Safety (Northern Ireland).**

5. Ensure up to date and relevant survey information is available on those drugs subject to DISM. This might be by way of a review and revision of the annual Crime Surveys to increase available prevalence information on DISM.

**Lead: Home Office, Office for National Statistics**

6. Continue to monitor closely the safety of OTC codeine and dihydrocodeine-containing medicines and to ensure that appropriate measures are in place to minimise the risk of abuse.

**Lead: MHRA Self Medication Unit**

7. The British National Formulary (BNF), the Monthly Index of Medical Specialities (MIMS, providers of electronic prescribing and dispensing system software to consider including 'cautionary information' in relation to controlled drugs subject to the risk of DISM following identification of such 'watch list' drugs.

**Lead: ACMD, BNF, MIMS**

8. The ACMD supports the efforts by NHS England in developing standard specifications for prison healthcare systems. The ACMD recommends that prison health care commissioners including NHS England should embed responsibility for protecting against the diversion of and treatment of addiction to prescribed medication into prison healthcare provider specifications. This requires action by prison Governors to deliver improved safety in partnership. Practical solutions include;
  - (a) good medicine management policy protocols (including prescribing of medicines, appropriate monitoring and supervision of queues);
  - (b) enhancing the storage provision for in-possession medications and
  - (c) effective assessment and management of chronic pain

**Lead: NHS England, devolved administrations Prison Healthcare Commissioners and prison Governors**

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<http://dx.doi.org/10.1016/j.jaac.2012.11.014>

## Annex A

### Top ten by items prescribed in the community in 2015 for Schedule 2 and 3 controlled drugs, for the period 2005-15

Chemical name	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Tramadol Hydrochloride	3,854,695	4,487,567	5,036,152	5,620,595	6,142,087	6,668,249	7,167,784	7,608,409	7,913,030	7,909,333	7,542,483
Morphine Sulphate <sup>1</sup>	805,722	908,490	1,054,818	1,200,067	1,344,745	1,496,005	1,716,713	1,973,396	2,197,778	2,414,076	2,582,490
Methadone	2,043,974	2,277,066	2,491,912	2,737,987	2,967,960	3,098,071	2,975,499	2,799,228	2,643,986	2,540,440	2,453,897
Buprenorphine <sup>2</sup>	738,526	958,012	1,182,018	1,428,438	1,727,509	1,931,975	2,162,975	2,420,477	2,638,648	2,859,748	2,977,292
Temazepam	3,492,913	3,321,581	3,254,797	3,122,239	2,969,038	2,813,955	2,627,679	2,367,115	2,010,997	1,681,325	1,423,531
Oxycodone <sup>3</sup>	295,677	387,607	500,723	622,795	788,454	961,173	1,073,192	1,157,179	1,250,227	1,357,178	1,490,868
Fentanyl <sup>4</sup>	392,349	512,700	659,721	794,915	901,988	990,014	1,062,936	1,119,380	1,161,648	1,206,800	1,230,050
Methylphenidate	389,186	456,909	535,328	573,397	610,194	661,463	714,820	786,358	859,035	922,206	993,994
Phenobarbital <sup>5</sup>	291,623	285,072	283,746	280,381	274,317	269,713	264,730	257,694	247,253	237,502	226,302
Midazolam <sup>6</sup>	38,106	42,320	55,385	66,660	94,482	122,413	142,633	177,358	193,786	214,953	236,728
<i>All other Schedule 2 &amp; 3 controlled drugs</i>	297,464	296,380	302,260	300,472	296,077	289,056	287,890	295,105	307,707	335,673	373,638
<b>Total</b>	<b>12,640,235</b>	<b>13,933,704</b>	<b>15,356,860</b>	<b>16,747,946</b>	<b>18,116,851</b>	<b>19,302,087</b>	<b>20,196,851</b>	<b>20,961,699</b>	<b>21,424,095</b>	<b>21,679,234</b>	<b>21,531,273</b>

#### NOTES

1. Morphine Sulphate includes Morphine Hydrochloride
2. Buprenorphine includes Buprenorph HCl / Naloxone HCl and Buprenorphine Hydrochloride
3. Oxycodone includes Oxycodone HCl / Naloxone HCl and Oxycodone Hydrochloride
4. Fentanyl includes Fentanyl Citrate
5. Phenobarbital includes Phenobarbital Sodium
6. Midazolam includes Midazolam Hydrochloride and Midazolam Maleate

## **Annex B: Diversion and Illicit Supply of Medicines Working Group Membership**

### **Membership from the ACMD:**

Prof Ray Hill (Inquiry Chair)  
Dr Kostas Agath  
Ms Gillian Arr-Jones  
Dr Roger Brimblecombe  
Prof Paul Dargan  
Ms Sarah Graham  
Prof Les Iversen (ACMD Chair)  
Ms Kyrie James  
Prof Fabrizio Schifano  
Prof Ben Whalley

### **Co-opted members:**

Ms Anita Gundecha (CNWL Addictions Service Line)  
Dr James Coulson (Cardiff University)  
Dr Simon Noble (Aneurin Bevan Health Board – Palliative Medicine)  
Dr Simon Thomas (NPIS)  
Dr David Wood (Guys & St Thomas Hospital Trust)  
Mr Ric Treble (LGC Forensics)  
Dr Catherine Stannard (British Pain Society)  
Mr Alexandra Chadd (Seconded to Welsh Government)

### **Secretariat:**

Mohammed Ali (Working Group Secretary)  
Zahi Sulaiman (ACMD Secretary)  
Linsey Urquhart (ACMD Secretariat)  
Jo Wallace (Home Office Science Secretariat)  
Caroline Wheeler (Science Secretariat)

## **Annex C: Sources of information - Written information submitted by:**

1. General Secretariat of the Council of the European Union Justice and Home Affairs
2. Adfam
3. US Drug Enforcement Administration (DEA)
4. Government of Sweden
5. HMP Leeds
6. HMI Prisons
7. College of Paramedics
8. British Association for Psychopharmacology
9. NHS Protect
10. HM Senior Coroner Inner West London
11. NHS England
12. Chief Coroners
13. British Pain Society
14. Metropolitan Police / ACPO
15. NAPP Pharmaceutical Ltd
16. Department of Health, Social Services and Public Safety (Northern Ireland)
17. United Kingdom Clinical Pharmacy Association (UKCPA)
18. Matt Griffiths (Royal College of Nurses)
19. Royal Pharmaceutical Society
20. Guild of Healthcare Pharmacists
21. Health and wellbeing - States of Jersey
22. Association of the British Pharmaceutical Industry (ABPI)
23. British Pharmacological Society
24. Walgreens Boots Alliance (formerly Alliance Boots)
25. General Pharmaceutical Council (GPhC)
26. Royal College of Veterinary Surgeons
27. Scottish Government
28. General Medical Council (GMC)
29. RB Pharmaceuticals Ltd
30. All Wales Therapeutics & Toxicology Centre
31. Headquarters Surgeon General
32. Staffordshire Police
33. Medicines and Healthcare Regulatory Agency
34. Welsh Government (Seconded Police Officer)
35. Department of Health, Social Services and Public Safety (Northern Ireland)
36. Ms Cathryn Kemp

## Verbal information (March to November 2014)

1. CRI (now Change Live Grow), June 2014
2. Adfam, June 2014
3. Addaction, June 2014
4. Royal Society of Chemistry, June 2014
5. Rickett & Benkiser, September 2014
6. Metropolitan Police, June 2014
7. HMI Prisons, June 2014
8. PHE, April 2014
9. Home Office, April 2014
10. All Wales therapeutics and toxicology centre, September 2014
11. US DEA, March 2014
12. Prof Matt Griffiths, June 2014
13. Northumbria NHS Trust, June 2014
14. Scottish Government, April 2014
15. Jamie Monroe (USA), April 2014
16. Aneurin Bevan Health Board, April 2014
17. Central and North West London NHS (CNWL), March 2014
18. The Researched Abuse, Diversion and Addiction-Related Surveillance (**RADARS®**) System)  
(Feb 2016 – Dr Jody Green)

## Annex D: Members of the Advisory Council on the Misuse of Drugs

Professor Leslie Iversen (Chair of ACMD)	Neuropharmacologist and Visiting professor of pharmacology, Oxford University
Dr Kostas Agath	Consultant Psychiatrist (Addictions), Medical Director of Addiction
Ms Gillian Arr-Jones	Pharmacist and expert reviewer and pharmacist consultant in health and social care
Fiona Bauermeister	Assistant Chief Officer with London Community Rehabilitation Company
Mr Simon Bray	Commander in the Metropolitan Police, Specialist Operations
Dr Roger Brimblecombe	Pharmacologist
Ms Annette Dale-Perera	Independent consultant
Professor Paul Dargan	Consultant physician and clinical toxicologist, clinical director, Guy's and St Thomas' NHS Foundation Trust  Professor of Clinical Toxicology, King's College London
Dr Emily Finch	Clinical director of the Addictions Clinical Academic Group, Consultant psychiatrist for South London and Maudsley NHS Trust
Professor Simon Gibbons	Professor of Medicinal Phytochemistry, Research Department of Pharmaceutical and Biological Chemistry, UCL School of Pharmacy
Ms Sarah Graham	Director, Sarah Graham Solutions
Professor Raymond Hill	Neuropharmacologist and Visiting Professor of Pharmacology, Imperial College London

Ms Kyrie LI James	First Tier Tribunal (Immigration and Asylum Chambers)
Mr David Liddell	Chief Executive Officer at the Scottish Drugs Forum
Professor Fiona Measham	Professor of Criminology in the School of Applied Social Sciences, Durham University
Mrs Jo Melling	Head of Performance and Delivery, NHS England (Midlands)
Dr Tim Millar	Senior Research Fellow and Addiction Research Strategy Lead, University of Manchester
Mr Richard Phillips	Independent consultant in substance misuse
Mr Rob Phipps	Former senior policy official (drugs and alcohol), DHSSPS, Northern Ireland
Dr Steve Pleasance	Analytical chemist and Head of Industry at the Royal Society of Chemistry
Professor Fabrizio Schifano	Consultant psychiatrist (addictions), CRI Hertfordshire Drug and Alcohol Recovery Services  Professor of Clinical Pharmacology and Therapeutics, University of Hertfordshire
Professor Alex Stevens	Professor of Criminal Justice  Deputy Head of the School of Social Policy, Sociology and Social Research, University of Kent
Professor Harry Sumnall	Professor in Substance Use, Liverpool John Moores University
Professor Ben Whalley	Professor of Neuropharmacology, University of Reading