Executive Summary
Opioids are gold-standard painkillers for acute (short-term), end-of-life, and cancer-related pain. Yet there is limited evidence for their usefulness in chronic (long-term) pain and growing awareness of side-effects including dependence and misuse.

Opioids and drug related deaths in the UK
Drug-related deaths (DRDs) in England and Wales are at their highest levels since records began in 1993 and are more than double the European average. Of the 3,756 DRDs recorded in 2018, 53% related to opioid use, which includes legal and illegal use.

Opioid availability, prescribing and related deaths have grown significantly in the UK over the past 20 years. Prescription of higher doses of opioids is correlated with a higher risk of unintended overdose. Greater rates of high-dose opioid prescribing are associated with larger GP practice list size, ruralness and deprivation, particularly affecting northern and coastal areas.

Understanding the opioid crisis
The opioid crisis is a complex phenomenon involving licit and illicit drug markets, driven by a combination of clinical need, drug availability and distribution, economic and social conditions, and organized crime.

Data from the US shows that opioid misuse is more likely for individuals who were first prescribed opioids, as well as indicating that unemployment and housing instability are linked to the opioid crisis. The recent development of clandestine markets on the ‘dark web’ has provided a small but growing source for illicit drugs, including opioids.

The UK opioid crisis is unlikely to escalate to the same scale as the US crisis
Opioid availability and overdose figures in the UK are substantially lower than in the US. This may be a result of factors including the prohibition of direct advertising of drugs to patients in the UK, less consumer control over healthcare, the requirement for GP registration which doesn’t allow ‘doctor shopping’, and fentanyl doesn’t currently have a significant presence in the UK illicit opioid market.

Nevertheless opioid related deaths in England and Wales are considerably higher than the OECD average. Addressing opioid dependence, misuse and overdoses in the UK requires policy coordination across health, social and criminal justice systems.

Key interventions might include:
- Improved evidence-based opioid prescribing practices and systematic outcome monitoring
- Further opioid use disorder (OUD) healthcare services
- New research and development in pain management
- Public health campaigns
- Increased availability of naloxone and naltrexone, especially for all first responders
- Needle exchange programs
- Overdose prevention sites and/or heroin-assisted treatment
- Better coordination between health, social and criminal justice sectors
- Housing and employment intervention
Opioids are gold-standard analgesics for acute, end-of-life and cancer-related pain, but there is limited evidence for widespread usefulness in chronic pain syndromes and growing awareness of side-effects including dependence and misuse.

Opioid pain medications (OPMs) are a class of drugs widely and successfully used for the treatment of acute, end-of-life and cancer-related pain. Acute (short-term) pain states tend to be predictable, linear and responsive to opioids in a dose-responsive manner. Chronic (long-term) pain states become more closely associated with emotional and psychosocial factors and are often non-responsive to opioids over time. The prescribing model known as the WHO analgesic stepladder (1986) provides a pain management pathway by which the dose and frequency of analgesic drugs can be titrated upwards according to the severity of the acute pain syndrome. This model has been particularly helpful in palliative care. Its inappropriate use in the management of chronic pain has contributed to an international epidemic of opioid over-prescription, dependence and related death, particularly in the United States.¹

Chronic pain syndromes are highly debilitating for the patient, notoriously difficult to treat and responsible for a vast public health burden. A meta-analysis of 96 randomised controlled trials reported that OPM use had a limited benefit in the management of chronic noncancer pain but that these benefits were similar to non-opioid alternatives.² The Faculty of Pain Medicine of the Royal College of Anaesthetists posit that OPMs do work for chronic pain in selected patients as part of a comprehensive pain management plan, but that the drugs should be prescribed in low doses with close monitoring.³ Intermittent use carries lower risks than continuous use; doses in excess of 120mg morphine/day (or the equivalent dose with other OPMs) are considered high-dose and high-risk. Since 2010, UK clinical guidelines have recognised the risks of OPMs in long-term care and recommended that patients “being considered for long term treatment with opioids should have a carefully supervised trial of opioid therapy with evaluation of analgesic efficacy and adverse effects”.⁴

Opioid availability, prescribing and deaths have grown in the UK over 20 years

A 2019 report by the OECD, which drew from 25 countries (including England & Wales), reported that the average availability of OPMs has grown steadily over the past 15 years.⁵ Across the OECD countries, OPM availability grew by more than 58% between 2002-4 and 2005-7. ⁵ OPM availability in the UK increased by 68% between 2013-16, associated with increasing prescriptions. ⁵ High rates of over-prescribing were not necessarily associated with higher overdose deaths, but prescription of higher doses of opioids is correlated with 32-188% higher risk of unintended overdoses.⁵

A 2018 review found that primary care prescriptions of OPMs in England (measured in oral morphine equivalents) increased by 127% between 1998 and 2016 but fell from 2016 to 2017.⁶ Greater rates of high-dose prescribing were associated with larger practice list size, ruralness and deprivation; particularly affecting northern and coastal areas. There was wide variation between Clinical Commissioning Groups (CCGs) on which opioid medications were more frequently prescribed.

Drug-related deaths (DRDs) in England and Wales are at their highest levels since records began in 1993 and are more than double the European average.⁷ In 2016, the UK accounted for almost a third of all overdose deaths in Europe.⁸ Numbers of deaths from opioid poisoning have increased by 468% from 1993 – 2018, or by 336% per million inhabitants.⁷ Since 2006, more than half of drug overdose deaths have related to opioid use.⁷ Opioid-related deaths in England and Wales rose from 28.4 per million inhabitants in 2011 to 40.9 in 2016;⁹ in 2017, rates were as high as 160 per million inhabitants in the most affected regions of the UK. These poisoning rates account for both licit and illicit use of opioid drugs.
The situations in the UK and the US differ in several important ways and the UK may be at lower risk of an opioid epidemic on the same scale

Twenty-five years of over-prescription, misuse and unauthorized distribution of opioids in the United States has resulted in an epidemic of dependence and related harms.\textsuperscript{10} Table 1 provides a comparison of the opioid crisis in the U.K, the US and the average values of the 25 countries assessed in the OECD report.\textsuperscript{5} While the situation in the UK is certainly worthy of concern, particularly the increasing trends in availability, prescribing and related deaths, the figures are substantially lower than those in the US after controlling for population size.

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Table 1: Figures in green are lower than the OECD average and those in red are higher than the OECD average. Availability of prescribed opioid medicines for pain is significantly higher in the United States than in the United Kingdom, but has decreased since 2013, while availability in the UK has increased. Seizures of black-market opioids are also significantly higher in the United States after controlling for population differences. In the United States, opioid-related deaths per million inhabitants have consistently been more than double the rate of deaths in the UK and in 2016 were at more than three times the rate.

\textbf{S-DDD:} Defined daily doses for statistical purposes

\textbf{Source:} OECD.\textsuperscript{5} Original data tables available at: https://doi.org/10.1787/888933925654; https://doi.org/10.1787/888933925692; https://doi.org/10.1787/888933925711

There is a growing concern about the over-prescription of OPMs in the UK, which has increased over the past two decades, but for the following reasons the NHS may better protected against an epidemic than the U.S:

- The UK does not permit direct advertising of drugs to patients
- Patients have less consumer control over their healthcare in the UK
- Registration with a single primary care physician in the UK reduces the phenomena of ‘doctor shopping’
- Fentanyls do not presently have a significant presence in the UK illicit opioid market
- The UK has the opportunity to learn from the US

Public Health England (PHE) are soon to publish a Prescribed Medicines Review (PMR)

PHE are preparing a Prescribed Medicines Review (PMR) looking at opioids\textsuperscript{11}, Z drugs, benzodiazepines, gabapentinoids and antidepressants associated with dependence and withdrawal. It will provide the first comprehensive analysis of the number of patients with long-term dependency. No publication date has been announced but it is expected within weeks. With regard to OPMs, the PRE aims to answer the questions:

What are the causes, harms associated with, and responses to:

1. dependence on opioids for chronic pain; and
2. discontinuation/withdrawal syndrome in relation to these prescribed drugs.
Other relevant upcoming reports include a review of deprescribing commissioned by the Secretary of State for Health and Social Care, led by Dr Keith Ridge, and an analysis of Clinical Practice Research Datalink (CPRD) data from GPs showing long term trends in the same medicine categories as the PMR, conducted by NatCen. The Faculty of Pain Medicine of the Royal College of Anaesthetists and the Royal College of Surgeons are presently looking at the problem of post-operative OPM prescribing in the UK.

The opioid crisis is a complex phenomenon involving licit and illicit drug markets, driven by a combination of clinical need, drug availability and distribution, economic and social conditions, and organized crime

The opioid crisis involves both the licit distribution of prescription medicines and the illicit trade in opioids for non-medical use, which has grown globally over the past two decades. Prices have gone down while availability and purity have gone up. The recent development of clandestine markets on the "dark web" has provided a small but growing source for illicit drugs, including opioids.

This short report cannot address the complex associations between the licit and illicit opioid markets in detail, but data from the US indicates that over-prescription of OPMs increases demand and supply on the illicit market. For instance, the majority of US high school seniors with a history of nonmedical opioid use had first gained access to opioids through prescription and the incidence of heroin initiation is almost twenty-fold greater for individuals who have previously used painkillers recreationally. Rapid and widespread deprescribing may shift demand to illicit markets without reducing dependency and should be supported by increased funding of addiction services.

Economic and social conditions such as unemployment, housing, deprivation and exclusion are also linked to the opioid crisis. Data from the United States indicates that for every 1% increase in county unemployment rates, the opioid death rate increases by 3.6% and the overdose emergency department visit rate increases by 7%. The literature provides no consistent evidence regarding the arrow of causality. Economic recession also correlates with increases in drug use and substance use disorders. Unstable housing situations increase the rate of problematic use of opioids, reduce opportunities to access treatment and negatively affect treatment retention rates and effectiveness. To address the problem, policy must involve coordination across health, social and criminal justice systems.

The biggest risk factors for opioid dependency after surgery in the US are the use of modified-release opioid prescriptions, repeat prescriptions for the treatment of acute pain, and the duration of the prescription. Greater risks are associated with longer exposure and larger doses. Some patients benefit from the management of pain rather than treatment for it and the perception of undertreatment of pain accounts for some opioid over-prescribing practices. Dose escalation indicates a lack of clinical benefit to the patient.

To manage the problem, we should consider improved evidence-based prescribing practices, systematic outcome monitoring, further opioid use disorder (OUD) healthcare services, new research and development in pain management, public health campaigns, increased availability of naloxone and naltrexone, needle exchange programs, overdose prevention sites and/or heroin-assisted treatment, better co-ordination between health, social and criminal justice sectors, and social interventions around housing and employment.

The OECD recommend four broad areas for improvement to reduce the harmful impacts of opioid overprescription:

1) **Better prescribing.** Improved prescribing practices through evidence-based clinical guidelines (e.g. for opioid prescription, for adequate medication-assisted therapy for OUD patients), prescribers training, surveillance of opioid prescriptions, regulation of marketing and financial relationships with opioid manufacturers, and public education and awareness interventions to enhance opioid-related literacy and reduce stigma.
2) **Better care.** Expansion of coverage for long-term medication-assisted therapy (e.g. methadone, buprenorphine, naltrexone), specialised services for infectious disease management and psychosocial interventions. Availability of overdose reversal medications for all first responders, needle and syringe programmes and medical supervised consumption centres.

3) **Better approach.** Improved coordination across health, social and criminal justice systems, (e.g. coordination networks across sectors aiming to facilitate access to integrated services for OUD patients). Change needs to be supported by social interventions around housing and employment and law enforcement uptake of a public health approach.

4) **Better knowledge and research.** Big data and impact evaluations with advanced analytics. Quality of care measurement should be enhanced in areas such as opioid prescription, OUD healthcare services and patient reported indicators. R&D in new pain management modalities and OUD treatments.

For more information contact Dave King, Senior Researcher at the CDPRG: David.King@cdprg.co.uk

**Endnotes**

9 Figure 3.4. Opioid-related deaths per million inhabitants, 25 OECD countries, 2011-16. https://doi.org/10.1787/888933925711. From OECD (2019), see ref. 4.
11 Opioids included in the upcoming review are: Buprenorphine; Codeine; Co-codamol; Dextromoramide; Diamorphine; Dihydrocodeine; Co-dydramol; Dipipanone (with cyclazine); Fentanyl; Hydromorphone; Meptazinol; Methadone; Morphine; Morphine plus cyclazine; Oxycodone; Oxycodone with naloxone; Papaveretum; Pentazocine; Pethidine; Tapentadol; and Tramadol.