Question 1

Opioids are synthetic or natural compounds known for their **analgesic properties**, as they bind to opioid receptors within the central nervous system, effectively alleviating sensations of pain [3].

- Opioids, often combined with other substances, remain the **primary cause** of drug-induced deaths.
    - Drug-induced deaths refer to those directly caused by the consumption of drugs.
- While **heroin** is a significant factor, it's important to recognize the growing role of various other opioids in these fatalities. [18].
- Furthermore, nearly **80% of drug-related deaths** can be attributed to opioids, and approximately a quarter of these deaths result from opioid overdoses.[5]

This phenomenon is primarily driven by the susceptibility of opiates to misuse and addiction.

The surge in **misuse** is linked to

a. the large availability of prescription opioid analgesics,
b. the heightened purity of heroin,
c. the escalating number of opioid overdose fatalities,
d. the introduction of potent illicit fentanyl compounds [3].

Various risk factors contribute to the prevalence of extra-medical prescription opioid and illicit opioid use, including genetic, early life, and environmental factors [6].

Opioids work by **activating receptors** in the brain, spinal cord, and organs linked to pain and pleasure.

- This can intensify the **craving** for the drug and the desire to repeat the experience.
- Prolonged opioid exposure can permanently **change brain** regions linked to reward and motivation, leading some people into a lifelong cycle of compulsive drug use.
- These lasting changes are partly due to **alterations in gene expression** through epigenetic modifications in specific brain areas.

- Even when taken as prescribed, prescription opioids can lead to substance use disorders.

- Opioid addiction leads to withdrawal symptoms like muscle pain, sleep problems, digestive issues, and strong cravings

Investigations into how opioids affect the **epigenetic** landscape are gradually emerging.

- While most research on the role of epigenetic modifications in addiction has focused on psychostimulants such as cocaine,
- This is a key area that aids the understanding of the harms illicit drugs use can induce.
- However, there are both data availability and methodological issues, finding considerable areas of uncertainty. Consequently, any conclusions drawn within this context must be made with prudence [1].

Gap?

- **Methodological limitations** likely result in underreported numbers, and international comparisons are cautioned due to varying reporting capacities.

- The lack of **detailed toxicological data** limits the understanding of how different drugs contribute to such fatalities over time. Notably, benzodiazepines are often found alongside opioids in drug-induced deaths, potentially intensifying their effects.

- In fact, **polydrug use** significantly contributes to drug-related deaths, emphasizing the need for better toxicological information.

- Additionally, statistics on drug-induced deaths do not account for **mortality** from accidents, violence, non-drug-related suicides, or chronic diseases where drug use may have played a role [1].

To address these issues, **resources should be invested** in accurately recording and monitoring opioid prescriptions and drug-induced deaths, with Prescription Drug Monitoring Programs offering potential solutions for **identifying drug-seeking behaviour and patient safety concerns [3].**

Social and environmental factors that relate to opioid addiction

Prescription practices	Family history and genetics	trauma and adverse childhood experiences	stigma and discrimination equal no seek help.

Availability of illicit opioids	Lack of education and awareness	peer influence	Access to healthcare, addiction treatment and mental health services.

Economic factors: Socioeconomic status plays a role in opioid addiction. Individuals facing economic hardship, unemployment, or financial stress may be more vulnerable to opioid misuse as a way to cope with their circumstances.

Some circularity over the surge in misuse linked to overdose fatalities - surely its the other way round?

While the surge in opioid misuse contributes to overdose fatalities,

- the increasing number of overdose deaths can also lead to responses and interventions that address the root causes of opioid misuse.

It's essential to tackle both aspects of the issue simultaneously by addressing the underlying social and environmental factors contributing to opioid misuse and by implementing **harm reduction and addiction treatment strategies** to reduce overdose fatalities.

This multifaceted approach is crucial in breaking the cycle of harm associated with opioid addiction.

What are these other polydrug substances?

- **Benzodiazepines**: These are a class of prescription medications used to treat anxiety and sleep disorders. When used in combination with opioids, they can enhance the effects of each other, which can increase the risk of overdose.
- **Alcohol**: The concurrent use of alcohol and opioids can be particularly dangerous because both substances depress the central nervous system. This combination can lead to respiratory depression, a significant risk factor for fatal opioid overdoses.
- **Cocaine**: In some cases, individuals use opioids and cocaine together. This combination is sometimes referred to as "speedballing." While opioids can suppress the stimulant effects of cocaine, the mixture can still pose substantial health risks.
- **Methamphetamine**: Similar to cocaine, methamphetamine is a stimulant, and its combination with opioids can result in unpredictable and potentially harmful effects.
- **Other prescription drugs**: Some individuals combine opioids with other prescription medications, such as muscle relaxants, to enhance the euphoric or sedative effects.

- **Marijuana**: While not typically considered a high-risk combination, some individuals may use marijuana alongside opioids, which can influence the overall effects and side effects.

What are the other problematic opioids?

Historically, prescription opioids like **codeine, tramadol**, and others have been associated with misuse and addiction. However, illegal opioids like **heroin and synthetic opioids (e.g., fentanyl)** are also problematic and can result in fatal overdoses.

In recent years, efforts have been made to address the issue of prescription opioid misuse by **tightening regulations and increasing awareness among healthcare providers**. Still, the availability of illegal opioids remains a significant concern, and fentanyl-related deaths have been on the rise in various parts of the UK and other countries.

Which is more problematic in TH UK - prescriptions or illegal drug use?

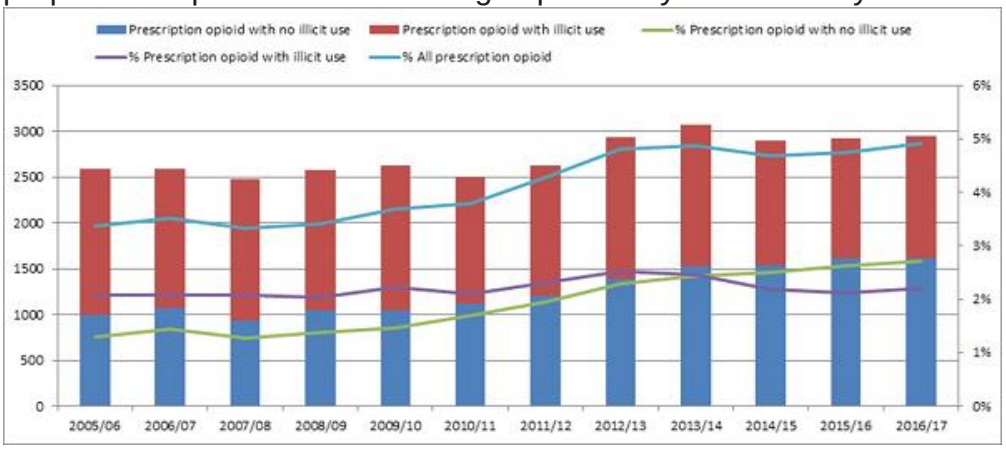
The relative impact can vary by region and change over time. Changes in prescribing practices and the availability of illicit drugs. However, **prescriptions** have increased over time.

Office for National Statistics Data:

two populations presenting to drug services:

1. patients addicted to **prescription opioids** as their sole drug of dependency
2. those who use prescription opioids as part of a **polysubstance misuse** (ie, in combination with illicit drugs).

While the number of patients using prescription opioids in conjunction with illicit drugs (2) has remained relatively stable, the proportion of individuals who use prescription opioids (1) as their sole drug has increased and this group represents an increasing proportion of presentations to drug dependency and recovery services.



What changes lead to opioid dependence and addiction and why don't all drugs do this?

Effect on Brain Chemistry: Opioids, whether prescription pain medications or illegal substances, have a powerful **impact** on the brain's **reward and pleasure centers**. They mimic the body's natural pain-relief mechanisms and release large amounts of **dopamine**, a neurotransmitter associated with pleasure. This intense euphoria and relief from pain can create a strong reinforcement for continued opioid use.

Not all drugs have the same addictive potential because they don't necessarily affect the brain in the same way.

- Some drugs, like opioids, **stimulate the brain's reward** centers more intensely due to their chemical properties, leading to a higher risk of addiction.
- The **route of administration** can also affect addiction potential. Intravenous drug use, which delivers a substance directly into the bloodstream, can be more addictive than oral consumption.

Physical Dependence, Tolerance, Psychological Factors and mental health, rapid onset, Availability and Legitimacy.

What specific health harms are involved eg in an overdose versus chronic problems?

Acute Opioid Overdose	Chronic, long-term use
Respiratory depression	Physical dependence & tolerant
Loss of consciousness	Psychological distress & mental issues
Hypoxia, no oxygen, organ damage	Financial problems
Cardiovascular problems, low blood pressure	Social consequences
Small pupils	Legal issues
Death	Risk of infectious diseases (HCV, HIV)
	Overdose risk
	Chronic health conditions & cognitive impairment

How big a problem do you think epigenetic causes are versus what gets people involved with drugs in the first place? Do you think a genetic predisposition is a stronger driver towards opioid addiction than social and economic circumstances?

Epigenetic causes involves **modifications to DNA** and associated proteins,

- which can be **influenced** by various factors, including environmental exposures, early life experiences, and behaviors.

While **genetic predisposition** certainly play a role in addiction susceptibility, they **do not act alone**. Environmental and behavioral factors also significantly contribute to the development of addiction.

For example, exposure to stressful environments or drug use can lead

- to specific epigenetic changes that may increase the risk of addiction in individuals with a genetic predisposition.
- Do not wake up one day saying I want to do drugs, but if they find themselves in the environment, they will have a higher risk of becoming addicted

Differentiating prevalance of addiction from drug deaths/ hospitalisations would be helpful as well as some information on the prevalence of health harms that are chronic.

Opioid-related hospitalisations increased by 48.9%, from 10,805 admissions in 2008 to 16,091 admissions in 2018, with total treatment costs of £137 million. The growth in opioid-related hospitalisations was 21% above the corresponding rate for all other emergency admissions in England. Relative changes showed that hospitalisations increased most for individuals older than 55 years (160%), those living in the most affluent areas of England (93.8%), and suffering from four co-morbidities (627.6%) or more. Hospitals reduced mean patient length of stay from 2.8 days to 1.1 days over 10 years. Mean in-hospital mortality was 0.4% and mean 30-day readmission risk was 16.6%.

For deaths registered in 2021, a total of 2,219 drug poisoning deaths involved opiates; this was 1.9% lower than in 2020 (2,263 deaths). Opiates were involved in just under half (45.7%) of drug poisonings registered in 2021, increasing to 61.0% when we exclude deaths that had no drug type recorded on the death certificate. England.

Do we know the relapse rate for individuals on OST programmes?

It is difficult to give a specific relapse rate for every OST programmes, however, it is recommended by:

- NICE, National institute for Health and Care Excellence

- https://www.nice.org.uk/guidance/ta114/chapter/4-Evidence-and-interpretation
- https://www.gov.uk/government/publications/opioid-substitution-treatment-guide-for-keyworkers/part-1-introducing-opioid-substitution-treatment-ost

They give evidence like:

- **Higher doses of OST**, within guideline-recommended margins (60 to 120mg for methadone and 12 to 16mg (up to 32mg for some) for buprenorphine), are associated with less illicit drug use and **better treatment outcomes**.
- **The longer** individuals stay in an OST program, **the lower** their risk of relapse tends to be.
- Methadone Maintenance Treatment (MMT) and buprenorphine maintenance therapy (BMT). Some research suggests that, on average, MMT can reduce the risk of relapse by around 60-90%.
- The results from the **meta-analyses** showed that fixed-dose MMT/BMT has higher levels of **retention** on treatment and lower rates of **self-reported illicit opioid use** compared with placebo or no treatment.

However, **different factors** play a role on relapsing after OST programme: psychosocial Support, type of treatment, **individual factors**.

Question 2

In 2020, approximately 61 million individuals, equivalent to 1.2% of the global population, used opioids. Opioids remained the deadliest category of drugs, contributing to two-thirds of drug-related deaths, primarily from overdoses. In addition, about 40% of people in drug treatment named opioids as their primary drug of use in 2020. A significant portion, around half, lived in South Asia and South-West Asia, with an estimated 31 million primarily using heroin. This figure had doubled from 2010, primarily due to better data collection in large population countries [18].

Starting from 2008, opiates and opioids have consistently been the primary substances involved in drug misuse-related deaths in Scotland. There has been a notable rise in these fatalities since 2013 as it can be seen in figure 1, with opiates/opioids contributing to 867 deaths in 2022 [16].

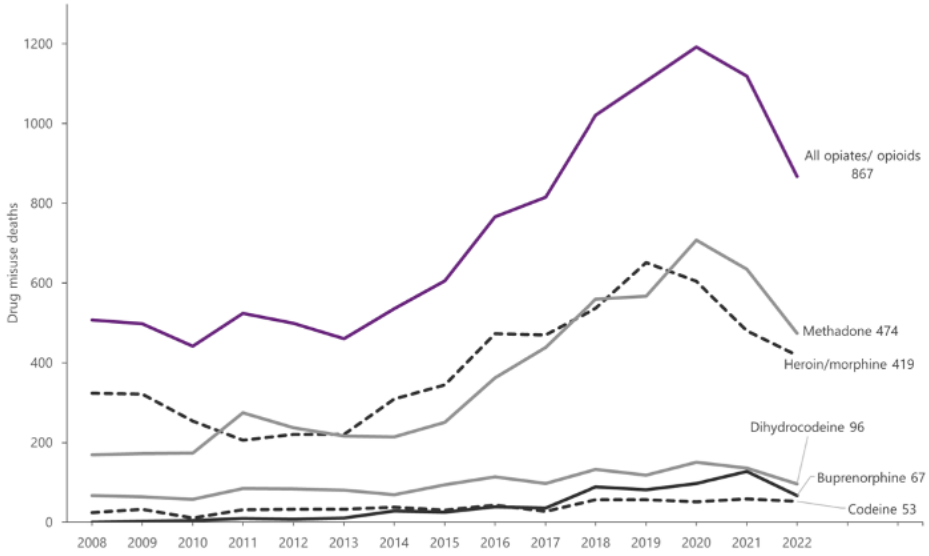


Figure 1: Drug misuse deaths in Scotland by drugs implicated, opiates and opioids [17].

Looking at figure 2, the prevalence of OUD shows the dual epidemics of opioid misuse, one involving fentanyls in North America and the other centered on tramadol misuse in North Africa, West Africa, the Near and Middle East, and South-West Asia, persisting as significant health threats [18].

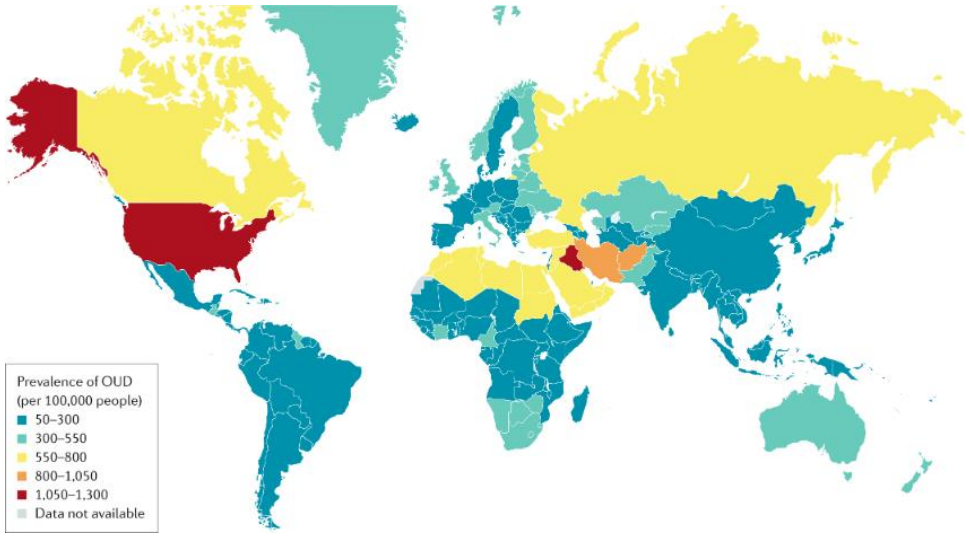


Figure 2: Age-standardized prevalence of opioid use disorder per 100,000 people [7].

Communities at higher risk for opioid use often face increased exposure to social and contextual risks, including drug availability, peer drug use, societal norms, adverse childhood experiences, family history of drug use, and individual factors like being male, childhood disorders, and lower education and economic opportunities. While opioid dependence has a partial hereditary component, it appears to be a genetic predisposition to substance use disorders in general, rather than specifically to opioids[6].

Opioid misuse has a profound impact on vulnerable communities. People who inject drugs (PWID) are at high risk of contracting HIV and HCV. Opioid injection prevalence varies by region and the type of opioid used. For instance, in South Asian countries, non-injecting methods of administration have been more prevalent. Furthermore, opioid dependence is linked to a range of adverse outcomes, including a reduced quality of life, mental health issues, increased involvement in criminal activities, and interactions with the criminal justice system. Consequently, opioid misuse presents a substantial challenge for society, particularly impacting vulnerable communities [6].

Fortunately, solutions for opioid misuse, like opioid agonist treatment (OAT) with medications such as methadone or buprenorphine, exist. Additional interventions, including sterile injecting equipment, naloxone, or condoms, may be provided alongside OAT. However, there's limited research on these interventions, with weak or unclear evidence of their impact on outcomes, often based on just a couple of trials. Understanding the effects of interventions beyond OAT on overdose and health outcomes is essential for shaping a comprehensive approach to treating those with opioid dependence [6].

The ideal opioid policy should reduce health and social harms from non-medical use while ensuring access to prescribed opioids. More research is needed to determine the best policy frameworks. There's an urgent need for national and global drug policies, clinical guidelines, and research to address opioid-related harm. Shifting focus from criminal justice to public health is vital. Clinical strategies should prioritize harm prevention through a combination of pharmacological, psychological, and harm reduction interventions, guided by research [6].

Who is missed in the SDMD?

How does mark recapture work in this context?

How does data from deaths differ from service use and do we miss different sub groups with each data source?

Does the UK have good systems or could we learn from other place?

Do we incorporate drug related crime rates?

Question 3

The Scottish Drug Misuse Database (SDMD) is key for tracking drug misuse in Scotland, gathering data on client demographics and behaviours in various services. However, it's voluntary and may not cover everyone. In addition, Public Health Scotland uses capture/recapture methods to estimate broader Problem Drug Use, relying on data from treatment services, hospital admissions, and criminal justice reports in each Council Area. These estimates depend on overlaps across data sources, requiring certain modelling assumptions that may not hold if there's population heterogeneity with varying group probabilities of appearing in a source [11]. The UK Office for National Statistics publishes an annual report on drug poisoning deaths in England and Wales. This report covers deaths from 1993 to 2021, detailing causes, gender, age, and the substances involved. The Advisory Council on the Misuse of Drugs (ACMD) suggests government funding for independent research to gain a deeper understanding of factors influencing trends in opioid-related and other drug-related deaths [12].

Opioid misuse isn't the sole concern; over 20 opioid medicines are authorized for pain treatment in the UK which can lead to addiction. Government agencies, such as the Medicines & Healthcare products Regulatory Agency and the National Institute for Health and Care Excellence, collaborate to decide on licensing and variations based on safety, quality, and effectiveness data[12]. However, death registration accuracy is critical. Hospital inpatient data quality is generally high, but it may miss some Accident and Emergency cases. Although the current UK-wide opioid-related death definition is consistent, data collection has weaknesses, making long-term trends unclear. Improving data collection processes is crucial for informed policymaking and reducing deaths [12].

Monitoring drug-induced deaths is one part of the drug-related death indicator. Many countries, including the UK, use good-quality sources like mortality registries to measure health risks from opioids and other drugs. However, there are limitations due to differences in how countries identify, certify, and report these deaths, as well as variations in forensic capacities and procedures. Therefore, interpreting and comparing this data over time and between countries should be done cautiously. Despite these limitations, reviewing the available information is informative. It shows that opioids, often combined with other substances, remain the leading causes of drug-induced deaths [1].

Are these other opioids more a problem than heroine?

Treatment for overdose - does this include supplying naloxone to those at risk? If we are making possessing drugs illegal, how are people supposed to legally access treatment? Are there ways around this problem.

You mentioned 'The Commission' -which one?

Are people in prison becoming addicted there or are they going in because they have been caught in a drug-related offence? Which comes first?

Any places where there is less focus on criminalisation?

What might happen/ will happen if opium availability changes radically?

Question 4

The Misuse of Drugs Act 1971 regulates dangerous substances in Great Britain, classifying them as A, B, or C based on their harm potential, with A being the most harmful. Once a substance is included, its possession becomes illegal, and intent to supply can lead to life imprisonment and/or an unlimited fine. Following the ACMD's 2022 report on nitazene and brorphine, the government announced that 11 synthetic opioids would be classified as Class A drugs and placed under Schedule 1 of the Misuse of Drugs Regulations 2001[9]. In addition to law enforcement, UK is implementing six policies and responses to decrease opioid-related deaths. These include supply reduction, opioid substitution therapy (OST), support for recovery and abstinence from dependence, social and integrated responses, research and prevention and treatment for overdose [13].

Drug policies can sometimes lead to harmful consequences. Laws prohibiting drug paraphernalia possession, such as equipment for injecting, make people who inject drugs (PWID) scared to carry syringes, forcing them to dispose or share of them unsafely, significantly raising the risk of HIV transmission through injection. Hard consequences can also block access to vital services like opioid substitution therapy (OST) and needle and syringe programs (NSP) for those who inject opioids [8].

The Commission's mathematical modeling highlights the substantial impact of incarceration and the elevated post-release HCV risk on HCV national incidence among PWID in various countries. For instance, in Thailand, PWID stay a large portion of their injection careers in prison, around 63% of new HCV infections could be attributed to correctional facilities. In Scotland, with shorter sentences for drug users and relatively high OST coverage, around 54% of new HCV infections occur in prison, and up to 21% in the post-release period. These findings highlight the need for different prison sentences for minor drug offenses, access to OST within correctional facilities, and smooth transitions from prison services to community-based OST [8].

A solution to address this problem is shifting the focus and resources from legal enforcement to health advancements. Redirect funding towards providing uncomplicated access to comprehensive harm reduction services for those who need it. These critical services, such as NSP, OST, access to injection equipment, and naloxone, must be expanded to adequately meet the demand and involve active participation from people involved with drugs in their planning and execution. Expanding these services is vital in both pretrial detention and prison environments. Moreover, guaranteeing access to regulated medicines and establishing national authorities to assess their necessity is essential.[8]

Another case of problematic drug policies involves concerns about reduced opium poppy production in Afghanistan, critical for heroin production. Afghanistan supplies up to 80% of the world's opium and 95% of Europe's heroin. In April 2022, the Taliban leader, Haibatullah Akhundzada, banned opium production. Now, the ban has taken effect, leading to a reported 99% reduction in this year's production in Helmand province and an anticipated 20% decrease in the

2023 harvest compared to 2022 levels. The UNODC has suggested that a lasting reduction in opium production in Afghanistan could result in opium production moving to other countries, or substitution of opium or heroin with other drugs at the user level, including potentially more harmful substances like fentanyl and its analogues. This dynamic has played a role in the ongoing opioid crisis in North America [10].

Furthermore, the international community should address the root of the problem by providing essential services to vulnerable regions, like Afghanistan, to reduce illicit drug production. These programs should involve meaningful consultation and development with affected communities living in unstable conditions. This approach could shift illicit demand towards regulated medical production. Over time, society can transition to regulated drug markets, guided by scientific evaluation. Although immediate legal drug markets may not be politically feasible in some areas, the negative consequences of criminal markets and prohibition could prompt more countries like US to gradually move in that direction. As these decisions are made, researchers and governments should follow the scientific method, ensuring independent, comprehensive evaluation of controlled markets to learn and improve controlled practices continually

Detailed and a good global perspective but is there some data on the effectiveness (or lack of) these programmes?

What is our evidence that interventions work (or not) based on?

Is it good enough to focus on what to do if someone overdoses?

Are there issues that lead to addiction that we should be tackling?

Any particular data gaps that you think should be addressed?

Question 5

The MHRA provides a safety leaflet for safe opioid medicine use for the public to use and recommended including addiction warnings for all opioid medicines in the UK. In addition, GPs

and clinical pharmacists in the corresponding UK healthcare system conduct personalized medication reviews and jointly decide if treatment changes are necessary, like moving patients from potentially addictive prescribed drugs. Aiming to combat drug misuse, the NHS and PHE collaborate with charities, support groups, and private drug treatment organizations, raising awareness and offering assistance for addressing drug misuse [14].

Numerous overdose awareness campaigns seek early intervention and prevention. Governments like the USA, Spain, and the UK have dedicated websites offering advice. International Overdose Awareness Day, observed on August 31 annually, is a global initiative with broad international participation. In 2021, the Scottish Government funded the How to Save A Life (HTSAL) campaign, aiming to increase awareness of drug-related deaths, overdose signs, and recommended responses. These efforts align with research suggesting that familiarity with affected groups reduces stigma and boosts support. Effective nationwide media campaigns can target high-risk groups while also promoting general awareness [15].

Countries' opioid addiction early prevention policies vary due to cultural, regulatory, and healthcare system disparities. Some emphasize law enforcement, while others prioritize healthcare and harm reduction. High-income countries have greater resources to address opioid use issues, with more funding for treatments and awareness campaigns. In contrast, low-income nations face limited access to treatment for opioid use disorders, particularly in low- to middle-income countries. This limitation often results from a lack of understanding about opioid use disorders and inadequate access due to financial constraints. Even if low- to middle-income campaigns similar to HTSAL exist, there is a lack of evaluation regarding their effectiveness. It remains unknown whether these campaigns work or if their components can be improved based on intervention development frameworks [15].

A clear final paragraph emphasising the importance of health care infrastructure and combating stigma.

Are there any ways in which the UK's approach to drug offences could itself be a barrier?

Are there places we can compare this to for advice and help in dealing with drug misuse more sympathetically?

Question 6

Individuals with substance use disorders often encounter societal mistreatment, stereotypes, and biases, including in healthcare settings, discouraging them from seeking medical help. In 2021,

approximately 10.4% of those who needed substance use treatment but didn't seek it mentioned fear of community stigma as a reason. A 2019 national survey of primary care providers revealed that despite recognizing opioid use disorder as treatable, many held stigmatizing attitudes that affected their care. The criminal stigma associated with drug addiction often discourages users from seeking treatment and medical assistance, as they are seen as criminals rather than recognizing it as a medical condition. People with substance use disorders may already experience self-blame and guilt, leading to self-stigma and negative self-attitudes. These emotions of shame and isolation can further reinforce drug-seeking behaviour [16].

The UK has a robust and unique medical regulation for opioids, supporting safe and effective prescribing. Effective opioid prescribing should follow general prescription principles. A well-established national health system aids awareness and coordinated policies against opioid addiction [19]. This is crucial because restrictions on healthcare can worsen opioid addiction. In the US, the decentralized physician network allows "doctor shopping" for multiple opioid prescriptions. Direct-to-consumer pharmaceutical marketing in the US boosts demand and awareness of opioids as a "quick fix" for pain [6]. In the battle against opioid addiction, the significance of a resilient healthcare community cannot be overstated. Coordinating healthcare efforts is vital to raise awareness, implement effective policies, and offer comprehensive responses aimed at reducing opioid-related fatalities.