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A Pipeline Analysis of Healthcare Technologies in Development for Addiction

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This horizon scan was requested by the Addiction Healthcare Goals programme (AHG) led by the OLS, to establish a comprehensive overview of emerging global MedTech, pharmaceutical and psychedelic innovations for the treatment and recovery from drug and alcohol addictions undergoing research studies and clinical trials. The OLS team were closely involved in designing the scope and eligibility criteria for the scan.

The results of the scan will be used to:

- Identify trends in emerging technologies that could be attracted to the UK for further research and deployment to address drug and alcohol addiction treatment and recovery needs.
- Highlight gaps in UK specific, and global R&D portfolios, for development of new technologies for addressing unmet needs in drug and alcohol addiction treatment and recovery.
- Build understanding of countries/regions which are current global leaders in attracting drug and alcohol addiction studies to use as international comparators for improving the attractiveness of the UK's research environment through AHG and wider government initiatives.

The AHG programme is aiming to make the UK a place where researchers and industry in addiction healthcare can thrive and partner effectively with NHS and Third Sector treatment providers to design, research and deploy innovative treatments and technologies which effectively tackle the challenges of drug and alcohol addictions, saving and improving the lives of those affected, and reducing the harms to the individual, their family and friends, and wider society.

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Abstract

Substance addiction is a disorder that causes loss of control over substance use or causes the compulsive seeking and taking of substances despite adverse consequences. The United Nations Office on Drugs and Crime estimated that in 2021, 39.5 million people worldwide were suffering from substance addiction, but only 1 in 5 people received drug treatment. As addiction is still stigmatised, and treatment options limited, meaning the identification of innovative treatments is important.

The aim of this project was to give an overview of the emerging global healthcare technologies perceived to treat or promote recovery from addiction to opioids, opiates, stimulants, cannabis, cannabinoids, alcohol, gabapentin, pregabalin, benzodiazepines, gamma-hydroxybutyrate (GHB), ketamine and/or novel psychoactive substances. In November 2023 three comprehensive and systematic searches, one each for pharmaceuticals, regulated medical devices and psychedelics were run, searching global trial registries, the Innovation Observatory's 'Medicines INnovation Database' (MInD) and BiomedTracker. Search results were included across all trial phases, all trial locations, and all trial statuses. Results were excluded if they were for the prevention of disease, the treatment of overdose or were in pre-clinical research.

The overall number of trials for the treatment of addiction have increased over time. The United States was consistently listed as a location of conduct across all three searches; the United Kingdom listed for 30 trials. There were no trials identified that were held in Africa and no trials held in Asia for psychedelics. Across all healthcare technologies, 88% were in development to treat or support recovery from addiction to alcohol, stimulants, and opioids/opiates; less than 1% for addiction to benzodiazepines, ketamine and GHB and there were no trials for addiction to gabapentin, pregabalin, or novel psychoactive substances. Of the healthcare technologies identified, 84% were in development as stand-alone treatments and 16% were in development for use alongside other pharmaceuticals and/or psychological interventions e.g., group or cognitive behavioural therapy. There were few registrations of complex intervention trials for substance addiction, such as co-occurring health conditions or poly-substance addiction.

There is real opportunity to stimulate innovation within the gaps that correlate with unmet need. Future innovation could focus on increasingly prevalent addiction to newer substance types, addressing poly-substance addiction, addiction amongst those with co-occurring mental health conditions, positioning across the addiction pathway.

Overall Trends

- The United States is listed as a location of conduct for the largest number of clinical trials irrespective of the healthcare technology type in development or under evaluation.
- Across all healthcare technology types, Germany was listed as a trial location of conduct the second greatest number of times and Canada third.
- Of the 1636 trials identified, 30 listed the United Kingdom (UK) as a location of conduct. Of the trials conducted in the UK, 25 were evaluating pharmaceuticals, 3 devices and 2 psychedelics for treatment of or supported recovery from addiction.
- Across all healthcare technology types there were no clinical trials identified being conducted in Africa.
- Of the healthcare technologies identified, 88% were in development to treat or support recovery from addiction to: alcohol, stimulants, and opioids/opiates.
- Less than 1% of all healthcare technologies identified were in development to treat addiction to benzodiazepines, ketamine and gamma-hydroxybutyrate (GHB).
- There were no trials identified of healthcare technologies to treat addiction to gabapentin, pregabalin, or novel psychoactive substances.
- The overall number of trials evaluating healthcare technologies to treat and support recovery from substance addiction have increased over time. This trend is seen across trials of health care technologies for each substance addiction (for which trials were identified) except for addiction to stimulants.
- There has been little change in the relative proportion of all trials evaluating healthcare technologies for addiction to different substances over time.
- Of the healthcare technologies identified, 84% were in development as stand-alone treatments and 16% were in development for use alongside other pharmaceuticals and/or psychological interventions e.g., group or cognitive behavioural therapy. There were few registrations of complex intervention trials for substance addiction.

Pharmaceutical trends

- The search identified 1,369 clinical trial registrations for pharmaceuticals in development for the treatment of or supported recovery from substance addictions
- There were 1,096 trials that listed any North American country as a location of conduct, 215 that listed any European country, 51 that listed any Asian country, 7 that listed any Australasian country and 5 that listed any South American country. There were no trials identified that listed Africa as a trial location of conduct.
- The US was listed as a trial location the greatest number of times (n = 1,078) followed by Germany (n = 35), Iran (n = 27), Sweden (n = 19) and the UK (n = 5). A total of 1,259 trials had a single location of conduct; 29 had multiple locations of conduct. 81 trials did not list any trial locations.
- 79% (n = 1077) of trials of pharmaceuticals were being delivered as monotherapies and 21% (n = 292) were for trials of pharmaceuticals being delivered in combination with additional interventions.

- Of the combination interventions, more than a third (43%, n = 127/292) were evaluating pharmaceuticals in combination with psychological interventions and more than half (57%, n = 165/292) were evaluating pharmaceuticals in combination with an additional pharmaceutical. Less than ten percent (9%, 26/292) were evaluating pharmaceuticals in combination with both psychological and additional pharmaceutical therapies.
- Approximately third of pharmaceuticals were evaluating treatment for and recovery from alcohol addiction (33%, n = 456), opioid/opiate addiction (29%, n = 396) or stimulant addiction (27%, n = 376).
- There were no registered clinical trials identified that were evaluating treatments for addictions to gabapentin, pregabalin, or novel psychoactive substances.
- Oral administration was the most common administration method (56%, n= 761), followed by sublingual (6%, n = 85), subcutaneous (5%, n = 75), intravenous (5%, n = 66) and intramuscular (5%, n = 62). A fifth (20%, n = 272) did not report the administration method.
- Nearly half of pharmaceuticals were intended to manage substance withdrawal (46%, n = 630), a quarter to prevent relapse (25%, n = 343) and 1% (n = 19) to act as a substitute. More than a quarter did not report the intended place in the treatment stage (27%, n = 375).
- Less than 5% (4%, n = 55) were targeting poly-substance addiction in a single trial i.e. patients with poly-substance addictions or patients with different substance addictions.
- A total of 137 trials of pharmaceuticals were targeting co-occurring mental health conditions such as post-traumatic stress disorder (n = 40), bipolar disorder (n = 28), depression/depressive symptoms (n = 23), schizophrenia/schizoaffective disorder (n = 23), major depressive disorder (n = 12), and anxiety/anxiety disorder (n = 11).
- There were 23 trials of pharmaceuticals were targeting co-occurring attention-deficit/hyperactivity disorder (ADHD).

Device trends

- The search identified 234 clinical trial registrations for devices in development for the treatment of or supported recovery from substance addictions
- There were 151 trials that listed any North American country as a location of conduct, 30 that listed any Asian country, 25 that listed any European country. There were no trials identified that listed Africa as a trial location of conduct.
- The US was listed as a trial location the greatest number of times (n = 142) followed by China (n = 13) and France (n = 9). The UK was listed as a trial location of conduct for three trials. All trials listed a single trial location of conduct.
- There were 34 clinical trials registrations detailing studies of repetitive transcranial magnetic stimulation (rTMS) and 30 of transcranial direct current stimulation (tCDS).
- The majority (91%, n = 213) of clinical trials registrations were evaluating single devices in development and 6% (n = 14) were evaluating combination devices.
- Less than a fifth (19%, n = 44) of clinical trials registrations for studies evaluating devices in combination with psychological interventions, 72% (n = 168) were in development

without psychological interventions and for 9% (n = 22) of registrations this could not be determined.

- Less than a fifth (18%, n = 43) of clinical trials registrations for studies evaluating devices in combination with pharmaceuticals, 74% (n = 173) were in development without pharmaceuticals and for 8% of registrations this could not be determined.
- 40% (n = 90) of studies were evaluating the device's ability to treat opioids and opiate addiction, 35% (n = 81) alcohol addiction, 15% (n = 36) stimulant addiction and 6% (n = 15) cannabis/cannabinoid addiction.
- There was one clinical trial registration for a study evaluating device ability to treat benzodiazepine addiction and 11 clinical trial registrations for studies evaluating device ability to treat more than one substance (poly-substance) addiction.
- There were no clinical trial registrations for studies of devices relating to GHB, gabapentin, pregabalin, ketamine or novel psychoactive substance addiction.
- Of the 234 trials for devices, 10% (n = 24) mentioned the device had an AI component. Devices with an AI component were in trials initiated from 2016 onwards; 2021 was the most common year of initiation.
- Nearly half (47%, n = 109) of clinical trial registrations listed the individual with an addiction as the user of the device, 33% (n = 77) listed a clinician, 20% (n = 47) listed a health care professional and for 12% (n = 28) of registrations it was unclear or unknown.
- More than a third (42%, n = 97) of clinical trial registrations specified use of the device as within a clinical setting or at home (37%, n = 86) and for 16% (n = 38) of registrations it was unclear where the setting of use would be.

Psychedelic trends

- The search identified 33 clinical trial registrations for psychedelics in development for the treatment of or supported recovery from substance addictions
- There were 18 trials that listed any North American country as a location of conduct, 12 that listed any European country, 1 that listed Australasia and 1 that listed South America. There were no trials identified that listed Asia or Africa as a trial location of conduct.
- The US was listed as a trial location the greatest number of times (n = 13) followed by Canada (n = 4) and Denmark (n = 3). The UK was listed as a trial location of conduct for two trials. 27 trials had a single location of conduct; 2 trials had more than one location of conduct.
- Within the 33 unique clinical trial registrations there were 6 unique psychedelics being evaluated. There were 24 trials for psilocybin, 5 for ibogaine, and 1 each for BPL-003, CMND-100, Dimethyltryptamine and LSD.
- More than half (55%, n = 18) of psychedelics were being evaluated for use in combination with pharmacological interventions and 45% (n = 15) of psychedelics were being evaluated as monotherapies.
- Oral administration was the most common administration method (64%, n = 21) followed by intravenous and nasal (both 3%, n = 1). Nearly a third (30%, n = 10) of clinical trial registrations did not specify the administration method.

- The small majority (55%, n = 18) of pharmaceuticals were in development to manage relapse prevention and withdrawal (24%, n = 8). There were no pharmaceuticals that would act as a substitute and the treatment stage was not known for nearly a quarter (21%, n = 7) of trials.

Executive Summary

We identified clinical research relevant to healthcare technologies in development for the treatment of or supported recovery from addictions to alcohol, opioids/opiates, stimulants, cannabis, gabapentin, pregabalin, benzodiazepines, GHB (gamma-hydroxybutyrate), ketamine and novel psychoactive substances. Healthcare technologies of interest were pharmaceuticals, regulated medical devices, or psychedelics.

In November 2023 we comprehensively and systematically searched secondary data sources then consistently filtered the information found. We identified 1,369 clinical trial registrations of studies of pharmaceuticals, 234 clinical trial registrations of studies of regulated medical devices and 33 clinical trial registrations of studies of psychedelics. Studies identified were initiated between 1980 and 2024 and were not excluded on the basis of status, year, or location. The trials for pharmaceuticals were largely inactive (e.g., completed, suspended, or terminated) potentially due to the trial start date, as 78% were initiated before the 2020s. For devices and psychedelics, 57% and 81% respectively of identified trials were active (e.g., recruiting, ongoing, or enrolling) and more recently initiated. The earliest trial identified for devices was initiated in 2010 and the earliest trial identified for psychedelics was initiated in 2012.

The median enrolment across all technology types was 52 and the interquartile range was 102. These participants were recruited globally, with trials held in countries across Europe, North and South America, Asia, and Australasia. No relevant trials were identified in Africa for any health technology type; there were no trials identified for psychedelics in Asia. North America, and the United States were consistently the continental and country leaders respectively for trials of treatments across substance addictions and across technology types. Across all healthcare technology types, Germany was listed as a trial location of conduct the second greatest number of times and Canada third.

Trials were evaluating a range of products as stand-alone treatments or as combinations with pharmaceutical or psychological interventions. The majority of pharmaceuticals (79%) and devices (91%) were in development as stand-alone therapies. Just over half of psychedelics (55%) were in development as combination therapies, with psychological interventions such as group therapy or cognitive behavioural therapy.

There were 1,369 trials for pharmaceuticals consisting of 246 unique products being evaluated. Four products, naltrexone, buprenorphine, buprenorphine-naloxone, and oxytocin in particular,

had a multitude of trials evaluating their potential. For medical devices there were 234 trials and 151 unique devices being evaluated. Together, repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tCDS) were included in 27% of all medical device trials. Further, of the 33 trials investigating psychedelics identified, 73% were evaluating psilocybin. The proportion of trials evaluating unique products was higher for medical devices than for pharmaceuticals or psychedelics.

Of all the healthcare technologies identified, 88% were in development to treat addictions to alcohol, stimulants, opioids/opiates. Less than 1% of all healthcare technologies were in development to treat addiction to benzodiazepines, GHB and ketamine. There were no trials of healthcare technologies to treat addiction to gabapentin, pregabalin, or novel psychoactive substances. There were 65 trials evaluating either pharmaceuticals or devices as treatments for more than one substance addiction. Trials for psychedelics were evaluating their ability to treat alcohol, opioid/opiate, and stimulant addictions.

Trials for pharmaceuticals and psychedelics were most often listed as being in phase 2, and for devices were most often listed as "not available". Medical devices tend to go through distinct stages such as traditional feasibility studies, pivotal studies, and post marketing studies and are therefore often identified as "not available" on clinical trial registrations.

Oral administration was the most often listed administration method for both psychedelics and pharmaceuticals. Nearly half (47%) of devices being trialled were for use by the individual with an addiction and 37% were intended for use at home. Examples of home-based devices include wearable sensors. Devices to be used by the individual with an addiction included apps, virtual reality and therapies delivered electronically.

Whether a device, pharmaceutical or psychedelic, the healthcare technologies identified in this horizon scan aim to offer new treatment options to people with substance addictions. These treatments may be used at different stages of the addiction treatment pathway, where possible this information has been inferred from the records identified. Most pharmaceuticals were in development to either manage substance withdrawal (46%) or to prevent relapse (25%). Less than two percent of pharmaceutical records specified the treatment was a substitute and approximately a third did not report the positioning of the intervention. The trials evaluating substitute pharmaceuticals were for the treatment of opioids/opiates, stimulants, and poly-substance addictions.

Background

Addiction is a disorder that can be defined as a loss of control over drug or alcohol use, or the compulsive seeking and taking of drugs despite adverse consequences. This drug or alcohol seeking behaviour is associated with cravings and loss of control and is a result of drug or alcohol abuse and/or repeated drug or alcohol exposure. There are strong genetic, psychological, environmental, and social factors that can contribute to drug and alcohol addiction.[1] For example, childhood trauma, attention deficit hyperactivity disorder (ADHD) and depression.[2]

Often the terms 'addiction' and 'dependence' have been used somewhat inter-changeably by those working in the field, though 'addiction' has not been a diagnostic category for some time. DSM-IV and ICD-10 / ICD-11 both used 'dependence' when referring to the most severe form of drug/alcohol use with less severe use referred to as 'abuse' (DSM-III) or 'harmful use' (ICD-10/11). Currently in DSM-5, the term alcohol / substance use disorder' (AUD/SUD) is used, with mild, moderate, and severe categories; mild AUD/SUD is equivalent to 'harmful use' in ICD and severe AUD/SUD with 'dependence'. As the DSM is the most widely used diagnostic framework for research, it is important to be aware of these changes in terms used when comparing trials and also of the differences between DSM-5 and ICD.[3] It should also be noted that 'misuse' or 'problematic use' are not diagnostic terms but can be used when it is unclear which diagnostic category is met. In this report, we use the terminology "addiction" throughout.

Drug and alcohol addictions are considered substance addictions, however, it is also possible to have non-substance addictions, for example gambling. Numerous substances have been associated with addiction. According to the DSM-5, the most common addictive substances include alcohol, caffeine, cannabis, opioids (e.g., heroin), sedatives (e.g., barbiturates), stimulants (e.g., cocaine, amphetamine), tobacco/nicotine as well as those less commonly used, including hallucinogens (e.g., Lysergic acid diethylamide (LSD)), inhalants (e.g., nitrous oxide), hypnotics (e.g., zolpidem), anxiolytics (e.g., diazepam), and amphetamine-type substances (e.g., methylphenidate). [1]

Data from the 2018 National Survey on Drug Use and Health suggest that, in the United States (US) in 2017, 20.3 million people aged 12 or older had substance addictions, including 14.8 million cases of alcohol addiction, 4.4 million cases of marijuana addiction and 2.0 million cases of opiate addiction. Such substance addictions often co-occur with other psychiatric illnesses,

with 9.2 million adults being estimated to have a 1-year prevalence of at least one substance addiction and a mental illness.[4]

In the England, between April 2023 and March 2024 there were 310,863 adults in contact with drug and alcohol services (a seven percent rise on the previous year). Opiate addiction is the most common substance addiction that individuals seek drug and alcohol services for, with nearly half of all adults in contact with drug and alcohol services seeking treatment for opiate addiction (44%, n = 137,965) and nearly a third seeking treatment for alcohol addiction (30%, n = 94,173). Individuals starting treatment for powder cocaine addiction has increased by 2% on the previous year and cannabis addiction by 0.5% (n = 28,263). Adults in contact with drug and alcohol services for ketamine addiction is eight times higher than it was in 2014-2015 (n = 3,609). The number of individuals seeking treatment for benzodiazepine addiction (n = 3,872) has increased compared to the previous year, and has increased every year from 2018 to 2021.[5]

Substance addiction has a significant impact, across the rest of the world. The United Nations Office on Drugs and Crime estimated that in 2021, 39.5 million people worldwide were suffering from substance addiction, but only 1 in 5 people received drug treatment.[6] Addiction has a high burden, particularly in high and upper-middle-income countries, which has increased in recent decades. However, addiction is still stigmatised, and treatment options limited.[7] The identification of new treatments is therefore imperative for individuals suffering from substance addictions.

Aims

The aim of this project was to give an overview of the emerging global innovations (medical devices, digital health technologies and pharmaceuticals) perceived to treat or promote recovery from addiction to a prespecified set of substances and alcohol.

Based on this aim, the objectives were to:

1. Identify and describe pharmaceutical products for treatment of and supported recovery from addiction to specific substances and alcohol in early-stage trials
    1.1. Identify and describe any medicinal products designed to target poly-substance use and/or drug use amongst those with co-occurring mental health conditions.
2. Identify and describe forthcoming regulated medical devices for treatment of and supported recovery from addiction to specific substances and alcohol.
    2.1. Identify any which exploit emerging technologies such as Artificial Intelligence/Machine Learning, Augmented Reality/Virtual Reality, etc.
3. Identify and describe psychedelic drugs and substances being developed for use as a medicinal product for treatment of and supported recovery from addiction to specific substances and alcohol in early-stage trial.

Methods

We used horizon scanning methods as follows:

Clinical landscape

In November 2023 a comprehensive and systematic search for relevant information (within the Innovation Observatory's 'Medicines INnovation Database' (MInD), ScanMedicine (a clinical trial database), global trial registries (e.g., ClinicalTrials.Gov, European Union Drug Regulating Authorities Clinical Trials Database (EudraCT), International Clinical Trials Registry Platform (ICTRP)), BiomedTracker (a site that provides pharmaceutical intelligence) was run.

MInD is a comprehensive database that captures innovative medicinal products. Records are created on MInD based on clinical trial records listed by ClinicalTrials.gov and EudraCT. Records contain an innovative intervention, the target indication and trial information and therefore can contain multiple trial records if the trial sponsor, indication and intervention all match.

The search strategies for the three horizon scans are outlined in Tables 1 through 11 in the appendix.

Selection criteria

Identified records were filtered using pre-specified selection criteria until only those records relevant to the aim and objectives remained. The prespecified selection criteria were carefully designed in consultation with the Office for Life Sciences Addiction Healthcare Goals team to ensure that the records included remained focused to the three project objectives.

Pharmaceuticals products in development for treatment of and supported recovery from specific substance addictions

Inclusion criteria:

- Medicinal products in development for the treatment of or supported recovery from addiction to any of the following specific substances:
  - Opioids/opiates - including synthetic e.g., nitazines and fentanyl
  - Stimulants - cocaine and crack cocaine, amphetamines, and methamphetamines
  - Cannabis and novel cannabinoids
  - Alcohol
  - Gabapentin
  - Pregabalin
  - Benzodiazepines
  - Gamma-hydroxybutyrate (GHB)
  - Ketamine

    - Novel psychoactive substances (e.g. nitrous oxide)
- Phase I trials and onwards
- All trial locations
- All trial statuses (including withdrawn and terminated)

Exclusion criteria:

- Medicinal products in development for prevention of addiction disease or treatment of overdose.
- Medicinal products in development for other addictions e.g., nicotine, gambling
- Interventions which include psilocybin, Lysergic Acid Diethylamide (LSD), methcathinone, inhalants, anabolic steroids, supplements
- Pre-clinical data

Devices in development for treatment of and supported recovery from specific substance addictions

Inclusion criteria:

- Medical devices in development for the treatment of or supported recovery from addiction to specific substances (as listed for scan 1)
- Phase I trials and onwards.
- All trial locations
- All trial statuses (including withdrawn and terminated)

Exclusion criteria:

- Medical devices in development for prevention of addiction disease or treatment of overdose.
- Medical devices in development for other addictions e.g., nicotine, gambling
- Pre-clinical data

Psychedelics in development for treatment of and supported recovery from substance addictions

Inclusion criteria:

- Psychedelic drugs or substances in development for the treatment or supported recovery for addiction to specific substances (as listed for scan 1)
- Phase I trials and onwards.
- All trial locations
- All trial statuses (including withdrawn and terminated)

Exclusion criteria:

- Psychedelic drugs or substances in development for prevention of disease or treatment of overdose
- Psychedelic drugs or substances in development for other addictions e.g., nicotine and gambling
- Pre-clinical data

Some trial records were identified through a search of MInD. As some MInD records contain more than one trial, a primary trial was identified according to a descending preference for

1. Description of the trials with a higher phase (e.g., phase 3 over phase 2)
2. Description of the trials with the most advanced active status (e.g., active not recruiting over recruiting)
3. Trials taking place in the most relevant geography (i.e., trials with a United Kingdom (UK) location were preferred)

Where a single primary record could not be identified according to the criteria above, records were then assessed manually with a single record selected based on a preference for a newer trial ID.

Data supplementation

Once the records for inclusion had been finalised, any missing data for variables which had been agreed in advance were supplemented using free text or categorical data available within other data sources.

Results

Searches identified 6,756 clinical research records.

Pharmaceuticals in development for the treatment of substance addictions

The search for pharmaceuticals returned 4,241 records, 2,872 of which were excluded. These records detailed 1,376 clinical trial registrations with unique trial IDs of which 1,369 were included for analysis.

Characteristics of clinical trial registrations

Of the 1,369 clinical trial registrations, there were approximately a third (n= 434/1,369, 32%) with an active status: active not recruiting (n = 19/1,369, 1%), enrolling by invitation (n = 2/1,369, 0.2%), not recruiting (n = 228/1,369, 17%), recruiting (n = 164/1,369, 12%) and ongoing (n=21/1,369, 2%). There were approximately two thirds (n = 935/1,369, 68%) with an inactive status: completed (n = 782/1,369, 57%), other (n = 2/1,369, 0.2%), prematurely ended (n = 10/1,369, 1%), suspended (n = 3/1,369, 0.2%), terminated (n = 67/1,369, 5%), unknown (n = 31, 2%) and withdrawn (n = 40/1,369, 3%). Of the 1,369 clinical trial registrations, 1,067 (78%) had published results on the trial website and 302 (22%) did not.

Trials were identified from early phase 1 through to post marketing surveillance studies. Phase 2 trial were the most common (n = 526/1,369, 38%), followed by phase 4 (n = 192/1,369, 14%), phase 1 (n = 174/1,369, 13%) and phase 3 (n = 140/1,369, 10%). Studies identified were mostly interventional (n = 1,282/1,369, 94%) rather than observational (n = 19/1,369, 1%); some records did not report the type of study (n = 68/1,369, 5%).

As there were 935 trials with an inactive status and pharmaceuticals in these trials may already be licensed or their development discontinued, to better reflect the potential market, the trial phases of the active trials were compared (Figure 1). Figure 1 illustrates that most active trials were phase 2.

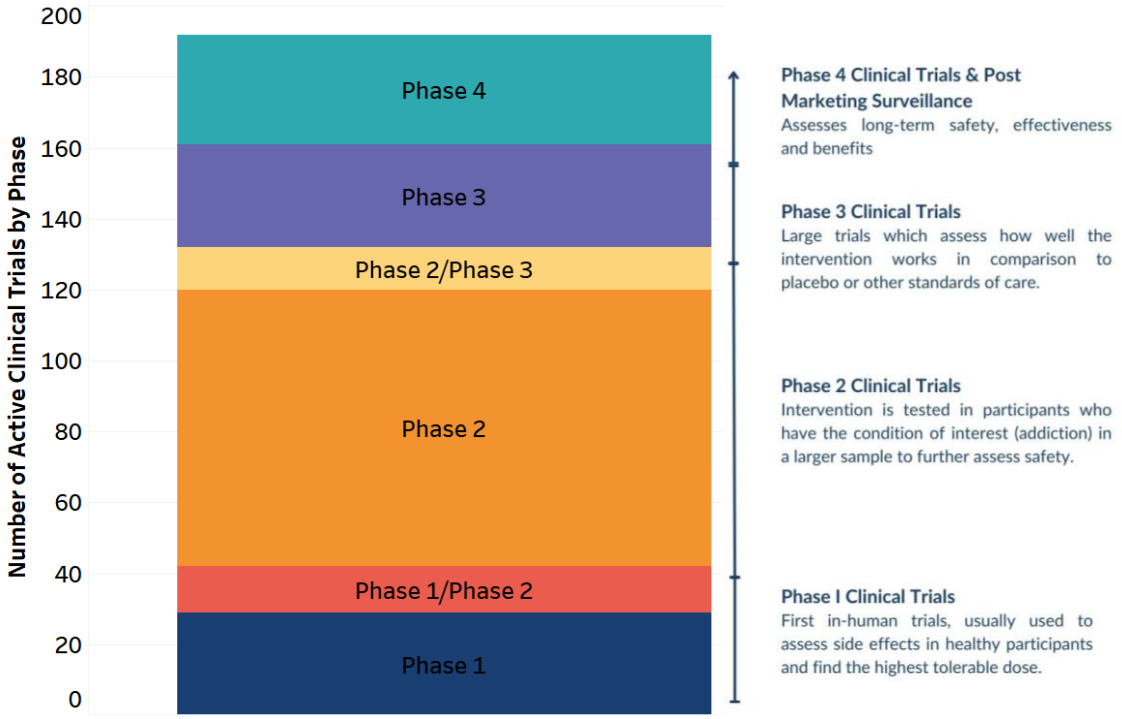

Figure 1. Active trials and post marketing studies evaluating pharmaceuticals for treatment of and to support recovery from addiction grouped by phase

The searches were run across global trial registries and identified no relevant clinical trials that were registered as being conducted in Africa. There were 81 trial records which did not list a location of conduct at the time of analysis. Trial records could list a single trial location, trial locations across a single continent or trial locations across multiple continents. There were 1,096 trials that listed any North American country as a location of conduct, 215 that listed any European country, 51 that listed any Asian country, seven that listed any Australasian country and five that listed any South American country.

The US was listed as a trial location the greatest number of times (n = 1,078) followed by Germany (n = 35), Iran (n = 27), the UK (n = 25) and Sweden (n = 19). A total of 1,259 trials had a single location of conduct; 29 had multiple locations of conduct. 81 trials did not list any trial locations.

The median number of participants enrolled in the studies was 55, interquartile range 101.

In the US, most trials were of pharmaceuticals to treat or facilitate recovery from alcohol addiction (n = 353/1078, 26%), stimulant addiction (n = 318/1078, 23%) and opioid/opiate addiction (n = 298/1078, 22%). In Germany, the greatest number of trials were of

pharmaceuticals to treat or promote recovery from alcohol addiction (n = 26/35, 74%), opioid/opiate addiction (n = 6/35, 17%) and cannabis addiction (n = 3/35, 9%). In the UK there were trials evaluating pharmaceuticals to treat or promote recovery from alcohol addiction (n =12/25, 48%) and opioid/opiate addiction (n = 13/25, 52%). In Iran, the greatest number of trials (n = 13/27, 48%) were of pharmaceuticals to treat or promote recovery from stimulant addiction, followed by opioid/opiate addiction (n = 8/27, 30%) and poly- substance (n = 3/27, 11%); these Iranian trials were all initiated between 2013 and 2023. For Sweden, treatments for alcohol addiction also had the greatest number of trials (n = 8/19, 42%) followed by opioid/opiate (n = 6/19, 32%), and stimulant (n = 4/19, 21%) addiction.

Addiction trials over time

Trials identified and included in this scan were initiated between 1980 and 2024. Start dates were gathered, where possible, from the trial registry alongside a primary completion date and an actual completion date. To gain a snapshot of the trajectory of innovation for those with addiction to different substances trial start dates were categorised by decade (from the 1980s to the 2020s) and compared between addictive substances. In order to reflect the fact that we are only part way through the 2020s, the data was standardised to an average number of trials per year for each decade (figure 2).

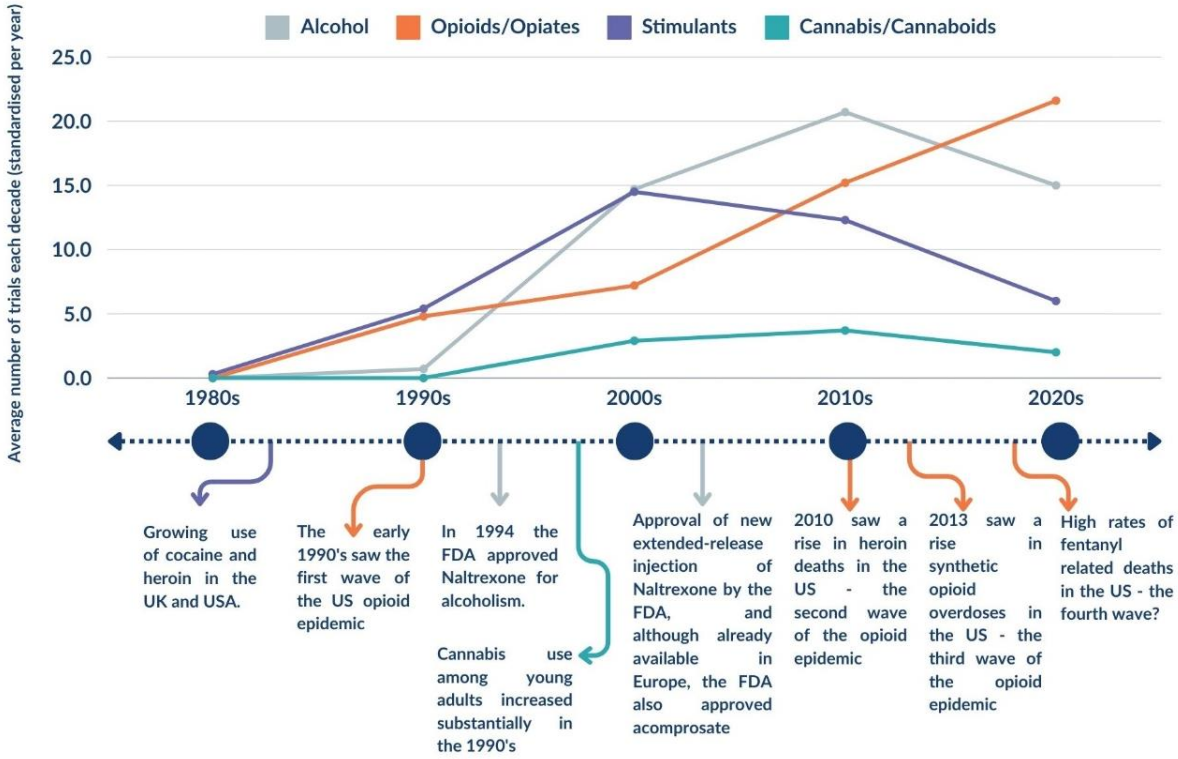

Figure 2. Standardised average number per year for each decade (based on the trial start date) of trials evaluating treatment for and recovery from substance addictions plotted alongside real-world events relevant to addiction *The standardised average number of trials per year for each decade was plotted by dividing the total number of phase 1 to phase 4 trials in the decade by the number of years that had passed in that decade.*

Trials started in the 1980s were for stimulant addictions only. Then, since the 1990s, the average number of trials in addictions to opioids/opiates have been increasing. For alcohol, the average number of trials were increasing until a peak in the 2010s, which has decreased slightly in the 2020s. For stimulant addictions, the average number of trials per decade has decreased since a peak in the 2000s. The average number of trials in cannabis have increased from the 2000s, however, have decreased slightly in the 2020s.

Interventions

Of the pharmaceutical interventions within the trials identified, 1,194 were already licensed in the US and 1,068 were already licensed in the UK and EU. The licensed pharmaceuticals in the identified trials include repurposed pharmaceuticals that are already licensed as interventions for other indications as well as, given the date range of trials included, pharmaceuticals that have been licensed post-trial.

After deduplication, we identified 246 unique pharmaceuticals in development. The top ten unique pharmaceuticals being evaluated in trials initiated within the last five years are displayed in Figure 3 reflecting the potential pharmaceutical pipeline over the next five years.

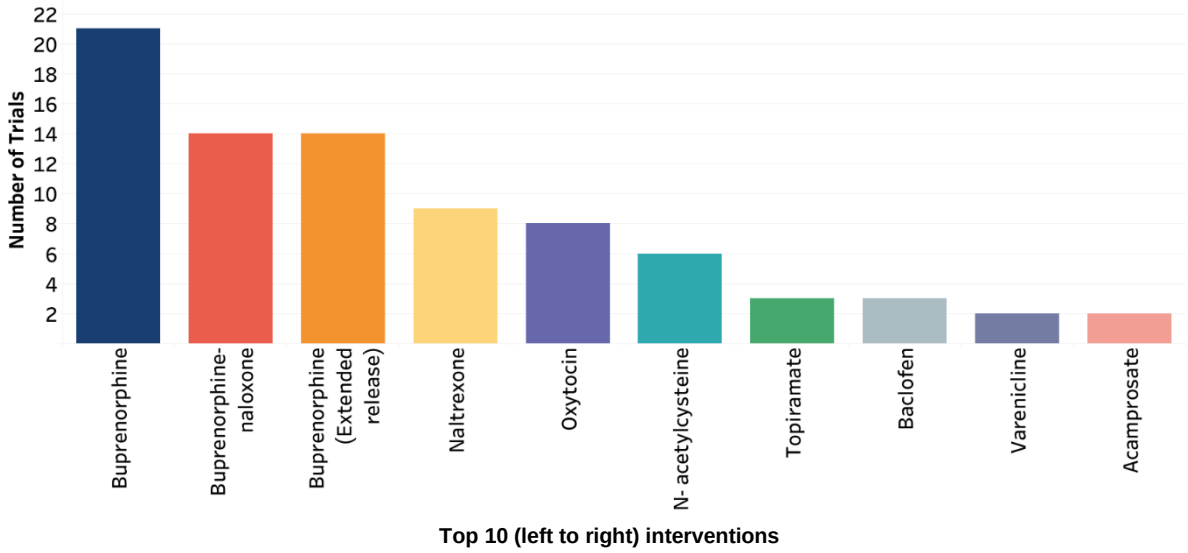

Figure 3. Ten most common interventions being evaluated, in clinical trials initiated from 2019 onwards, for treatment of and recovery from addictions.

Of the 1,369 clinical trial registrations included in analysis, 1,077 (79%) were for trials of pharmaceuticals being delivered as monotherapies and 292 (21%) were for trials of pharmaceuticals being delivered in combination with additional interventions. Of these 291 trials of combination interventions, over a third (n = 127/292, 43%) were evaluating pharmaceuticals in combination with psychological interventions (such as cognitive behavioural therapy), and more than half (n = 165/292, 57%) were evaluating pharmaceuticals in combination with an additional pharmaceutical and less than ten percent (n = 26/292, 9%) were evaluating pharmaceuticals in combination with both psychological and additional pharmaceutical therapies.

Approximately a third of the 1,369 clinical trial registrations included for analysis, were evaluating treatment for and recovery from alcohol addiction (n = 456/1,369, 33%), opioid/opiate addiction (n = 396/1,369, 29%) or stimulant addiction (n =376/1,369, 27%). There were 55 of the 1,369 clinical trial registrations (4%) investigating treatments for more than one substance addiction (poly-substance). There were no clinical trials registered looking at addictions to gabapentin, pregabalin, or novel psychoactive substances. Data were plotted for the sub-group of trials initiated from 2019 onwards (figure 4). Trials initiated from 2019 onwards were most commonly evaluating treatments for opioid/opiate (n = 134/298, 45%), followed by

alcohol (n = 102,/298 34%) and stimulant (n = 35/298, 12%) addiction. Less than five percent of trials initiated from 2019 onwards were evaluating treatments for cannabis (n = 13/298, 4%), poly-substance (n = 11/298, 4%), and benzodiazepine (n = 2/298, 1%) addiction.

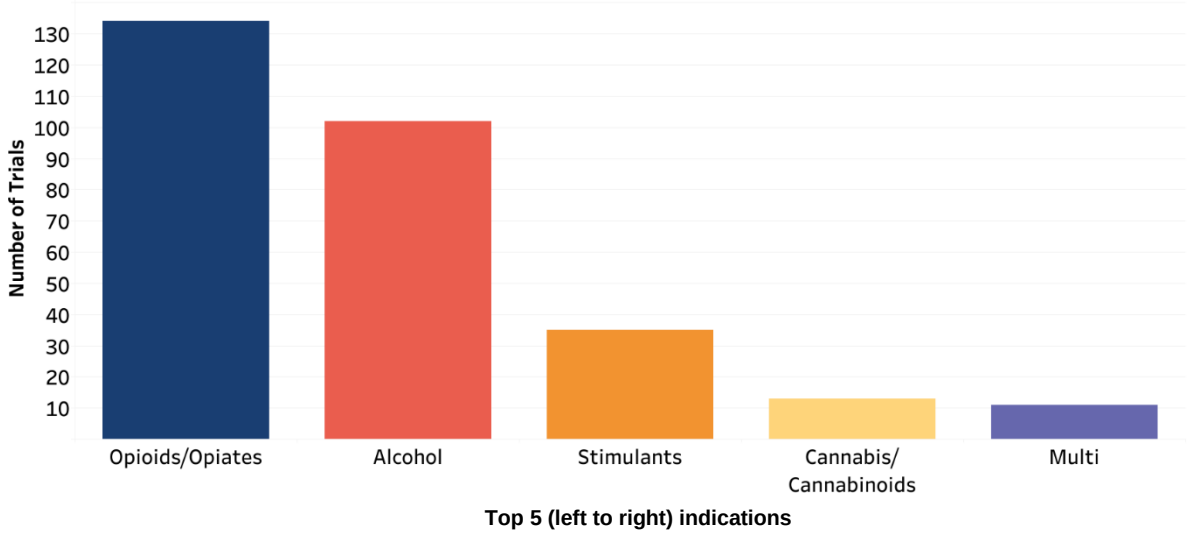

Figure 4. Five most common substance addictions for which pharmaceuticals were in development between 2019 and 2024.

Route of administration

When available, information was gathered from records regarding the administration method for pharmaceuticals in trials. Oral administration was the most common administration method (n = 762/1,369, 56%) (figure 5) followed by sublingual (n = 85/1,369, 6%), subcutaneous (n = 75/1,369, 5%), intravenous (n = 66/1,369, 5%) intramuscular (n = 63/1,369, 5%) and nasal (n = 41/1,369, 3%). and There were no trials listed as administering pharmaceuticals via inhalation, intradermal, intrathecal, parental, or rectal methods, however, a fifth of records (n = 272/1,369, 20%) did not specify the administration method for pharmaceuticals in their associated trial.

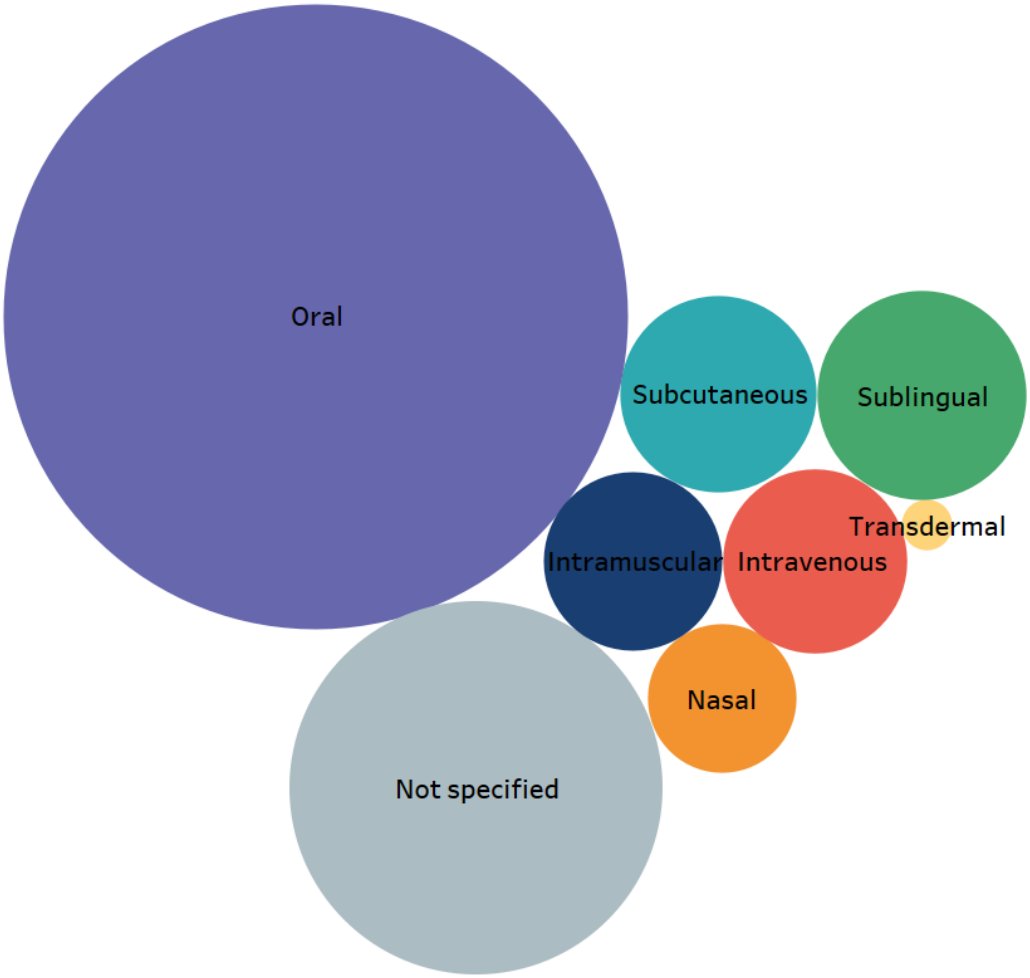

Figure 5. Administration methods for interventions in clinical development for substance addiction.
"Not specified" indicates when a trial record did not disclose the administration method for the intervention in trial.

The most common administration method for pharmaceuticals irrespective of the substance addictions they were intending to treat was oral administration (n = 761). Sublingual administration of pharmaceuticals was common in trials for opioid/opiate addictions (n = 80) but not trials for other substance addictions (n ≤ 3). The most common administration methods were independent of the geography of trial conduct.

Treatment stage

Individuals treated for substance addictions may be offered pharmaceuticals which could offer a substitute to the addictive substance, pharmaceuticals that help to manage withdrawal symptoms or pharmaceuticals which help to prevent relapse. Where possible, for each pharmaceutical the positioning of the intervention was determined using the purpose of study description on a clinical trial registration. Nearly half of pharmaceuticals within trial were

intended to manage substance withdrawal (n = 630/1,369, 46%) and a quarter to prevent relapse (n = 343/1,369, 25%). There were 19 (1%) trials which specified the pharmaceutical as a substitute and nearly a third (n = 375/1,369, 27%) trial records did not report the treatment stage. Trials for treatment of and recovery from addiction to opioids/opiates, stimulants or poly-substance addiction were evaluating substitute pharmaceuticals.

Trials within the UK

There were 25 trials identified that listed the UK as a trial location; 22 of which had a single location of conduct. These trials were in early phase 1 through to phase 4 and were initiated between 2005 and 2022. The median enrolment was 96 and the interquartile range was 274. There were 13 trials evaluating treatment for or recovery from opioid/opiate addiction and 12 for alcohol. There were 10 orally administered pharmaceuticals, 5 subcutaneous, 4 intravenous, 2 sublingual, 2 nasal, 1 intramuscular and 1 trial did not specify. The pharmaceuticals under evaluation in the UK included acamprosate, baclofen, buprenorphine (and variants), buprenorphine-naloxone, diamorphine hydrochloride, exenatide (with deacyl ghrelin), INDV-6,200 (with buprenorphine and naltrexone), ketamine, MDMA, methadone, mifepristone, nalmefene, naltrexone and oxytocin. Of these, three were evaluated in combination with psychological interventions and two were evaluated in combination with additional pharmaceutical. There were 20 pharmaceuticals which held a UK licence and five that did not.

National Institute on Drug Abuse funded trials

The search identified 158 registrations of trials of pharmaceuticals funded by the National Institute on Drug Abuse (NIDA). These trials ranged from phase 1 to phase 4. The earliest trial identified was initiated in 1987 and the latest trial identified was initiated in 2023. The median enrolment was 12 and the interquartile range was 60. There were 87 trials for stimulants, 56 trials for opioids/opiates, 6 for poly-substance, 4 for cannabis/cannabinoids and 3 for alcohol. There were 66 orally administered pharmaceuticals, 11 sublingual, 3 nasal, 2 intramuscular, 2 transdermal, 1 intravenous and 1 subcutaneous. There were 72 trials that did not specify an administration method. Two were evaluated in combination with psychological interventions and 16 were evaluated in combination with additional pharmaceutical. There were 140 pharmaceuticals which held a US licence and 129 that held a UK licence.

There were six trials identified that have been initiated by the NIDA since 2019. There were two phase 1 trials, one phase 1/2 trials and three phase 2 trials. The median enrolment was 48 and the interquartile range was 32. There were three trials for alcohol, two trials for opioids/opiates

and one trial for stimulants; all trials were for managing withdrawal from substance addictions. There were two trials for orally administered pharmaceuticals, one for nasal, one for transdermal, one for subcutaneous and one that did not specify. None were in development as combinations with either other pharmaceutical or psychological interventions. Four were pharmaceuticals that are already licensed in both the US and UK and two were not licensed in either the US or the UK.

Pharmaceuticals in development for those with poly-substance addictions and for those with co-occurring mental health conditions and neurodivergence

Within the trials identified, 55 were of pharmaceuticals listed as intending to act upon more than one substance addiction. These pharmaceuticals, for example, could be used to treat individuals with addiction to substance one, individuals with addiction to substance two or individuals with addiction to substances one and two etc (poly-substance addiction).

There were 137 trials of pharmaceuticals intending to act upon substance addiction amongst those with mental health conditions co-occurring with addiction. The populations enrolled with mental health conditions co-occurring with addiction included those with post-traumatic stress disorder (n = 40), bipolar disorder (n = 28), depression/depressive symptoms (n = 23), schizophrenia/schizoaffective disorder (n = 23), major depressive disorder (n = 12), and anxiety/anxiety disorder (n = 11). Of the pharmaceuticals in trial for those with co-occurring mental health conditions, 91 were for alcohol addiction, 15 stimulant addiction, 12 cannabis and cannabinoid addiction, 11 opioid/opiate addiction and 8 poly-substance addiction. There were 109 trials of pharmaceuticals as a monotherapy and 28 trials of pharmaceuticals as combination therapy, 12 of which were with psychological interventions. The most common administration route was oral (n = 94), followed by intravenous (n =9), intramuscular (n = 4), nasal (n = 4), sublingual (n = 3) and subcutaneous (n = 1). There were 22 trials that did not specify the administration method. Where possible, the intended stage in the addiction treatment stage for each pharmaceutical is described. This was determined using information on the trial registrations and website. There were 51 trials of pharmaceuticals to manage withdrawal, 43 for relapse prevention and one as a substitute. There were 42 trials with records that did not report this information.

There were 23 trials for addiction co-occurring with ADHD; 9 were for stimulant addiction, 5 alcohol addiction, 4 cannabis and cannabinoid addiction, 4 poly-substance addiction and 1 opioid and opiate addiction. There were 21 trials of pharmaceuticals as a monotherapy and 2 trials of

pharmaceuticals as combination therapy, both of which were with psychological interventions. The most common administration route was oral (n = 19), and 1 trial for intramuscular. There were 3 trials that did not specify the administration method. Where possible, the intended stage in the addiction treatment stage for each pharmaceutical is described. There were 9 trials of pharmaceuticals for relapse prevention, 2 for managing withdrawal and 12 trials that did not report this information.

Characteristics of registrations for inactive clinical trials

Of the trials that were prematurely ended, all were phase 2 or 3 conducted in Europe between 2009 and 2018. The median enrolment was 95 and the interquartile range was 123. There was a range of pharmaceuticals being evaluated, nine as monotherapies and one in combination with a psychological intervention. Six of the pharmaceutical interventions were orally administered, two intramuscularly, one via nasal spray and one subcutaneously. Eight of the pharmaceuticals in prematurely ended trials were already licensed in the US and seven were already licensed in the UK/European Union (EU). Three were studies of pharmaceuticals for treatment of substance addictions to alcohol (n = 4), opioids/opiates (n = 2), stimulants (n = 2) and cannabis and cannabinoids (n = 2) amongst individuals with ADHD.

Suspended trials were all phase 1/2 or 2; they were undertaken between 2005 and 2021; and conducted in the US or UK. The median enrolment was 40 and the interquartile range was 20. There were no consistent interventions being evaluated in these suspended trials; all three interventions were monotherapies. Two of the pharmaceuticals were orally administered and one was subcutaneously administered. All three pharmaceuticals being evaluated in suspended trials are licensed in both the US and UK/EU. The substance addiction participants were to alcohol (n = 1) and opioids/opiates (n = 2).

The terminated trials were early phase 1 through to phase 4, the majority being phase 2 (n = 27) and phase 1 (n = 14). These trials were run between 1994 and 2022, the median enrolment was 16 and the interquartile range was 37. There were 45 different interventions including four trials each for buprenorphine, buprenorphine-naloxone, and lorcaserin. The majority (n=36) were monotherapies or pharmaceuticals in combination with psychological interventions (n=9). Most of the terminated trials were for orally administered interventions (n = 45) followed by intramuscular (n = 4) and sublingual (n = 3); the trial did not specify the administration method on ten occasions. When the search was run, 60 of the pharmaceuticals in terminated trials were already licensed in the US and 52 were already licensed in the UK/EU. The substance addictions

being treated included alcohol (n = 29), stimulants (n = 16), opioids/opiates (n =13), poly-substance (n = 7), benzodiazepines (n = 1) and cannabis or cannabinoids (n = 1).

The withdrawn trials were phase 1 thorough to phase 4, with most in phase 2 (n = 13). The trials were run between 1993 and 2023 and all had an enrolment number of 0. There were 28 different interventions being evaluated including eight for buprenorphine-naloxone, and four for buprenorphine. 27 were monotherapies and 13 were in combination including two with psychological interventions. Most of the withdrawn trials were for orally administered interventions (n = 23) followed by sublingual (n = 5) and intravenous (n = 3) pharmaceuticals; the trial did not specify the administration method on seven occasions. When the search was run, 34 of the pharmaceuticals held a US licence and 31 had a UK/EU licence. The substance addictions included alcohol (n = 13), opioids/opiates (n =18), stimulants (n = 7), poly-substance (n = 1) and GHB (n = 1).

Devices in development for the treatment of substance addictions

The search returned 2,412 clinical trial registrations, 2,178 of which were excluded and 234 of which were included for analysis. Trials were not excluded on the basis of trial status or year.

Characteristics of clinical trial registrations

There were 125 clinical trial registrations with an active status: active not recruiting (n = 14/234, 6%), enrolling by invitation (n = 2/234, 1%), not yet recruiting (n = 36/234, 15%), recruiting (n = 73/234, 31%). There were 108 with an inactive status: completed (n = 73/234, 31%), suspended (n = 2/234, 1%), terminated (n = 6/234, 3%), unknown (n = 21/234, 9%) and withdrawn (n = 6/234, 3%). One trial had a status of 'not available'. Of all the clinical trial registrations, 32 (14%) had published results on the trial website, and 201 (86%) did not have results; it was unclear if there were results for 14 trials.

The most commonly reported trial phase was "Not available" (n = 189/234, 81%), followed by phase 2 (n = 14/234, 6%). Studies were mostly interventional (n = 229/234, 98%), rather than observational (n =5/234, 2%). This likely reflects that, whilst pharmaceuticals follow the phase 1-4 development outline, medical devices go through the following distinct stages: traditional feasibility studies, pivotal studies, and post marketing studies. Trial phases for devices are therefore often identified as "not available" on clinical trial registrations as they are not categorised as phases.

The median enrolment was 115 and the interquartile range was 69. One trial which was recruiting 1840 participants was an online assessment tool used to measure outcomes.

The searches were run across global trial registries, and identified no relevant clinical trials that were registered as being conducted in Africa. North America was listed as a conduct location in the greatest number of clinical trial registrations (n = 151), there were 30 that listed any country in Asia and 25 that listed any country in Europe. Location of conduct could not be determined for 22 trials, as the information was missing from the trial records. The US was the listed country of conduct for the greatest number of trials (n = 142) followed by China (n = 13) and France (n = 9). The UK was listed as trial location of conduct for three trials. All trials listed a single trial location of conduct.

Device characteristics

After deduplication, 151 unique medical devices were identified.

There were 34 clinical trials registrations detailing studies of repetitive transcranial magnetic stimulation (rTMS) and 30 of transcranial direct current stimulation (tCDS). There were 213 (91%) clinical trials registrations for studies evaluating single devices in development and 14 (6%) evaluating combination devices. There were 44 (19%) clinical trials registrations for studies evaluating devices in combination with psychological interventions, 168 (72%) without psychological interventions and 22 (9%) where this could not be determined. There were 43 (18%) clinical trials registrations for studies evaluating devices in combination with pharmaceuticals, 173 (74%) without pharmaceuticals and 18 (8%) where this could not be determined.

Of the 234 unique clinical trials registrations, 90 (40%) were of studies evaluating device ability to treat for opioid/opiate addiction, 81 (35%) alcohol, 36 (15%) stimulant and 15 (6%) cannabis and cannabinoid addiction. There was one clinical trial registration for a study evaluating device ability to treat benzodiazepine addiction and 11 clinical trial registrations for studies evaluating device ability to treat more than one substance (poly-substance) addiction. There were no clinical trial registrations for studies of devices relating to GHB, gabapentin, pregabalin, ketamine or novel psychoactive substance addiction.

Mode of use

Based on the available information in their clinical trial registration, devices were categorised on their mode of use which included “implantable” “wearable” or “other”, with “other” including devices not placed on or in the body. The majority (n = 157/234, 67%) were ‘other’ which included devices such as electronic training programmes, and compliance monitoring programmes. The second most common mode of use was wearables (n = 32/234, 14%) then implantable devices (n = 9/234, 4%) (figure 6). The mode of use could not be determined for 35 devices.

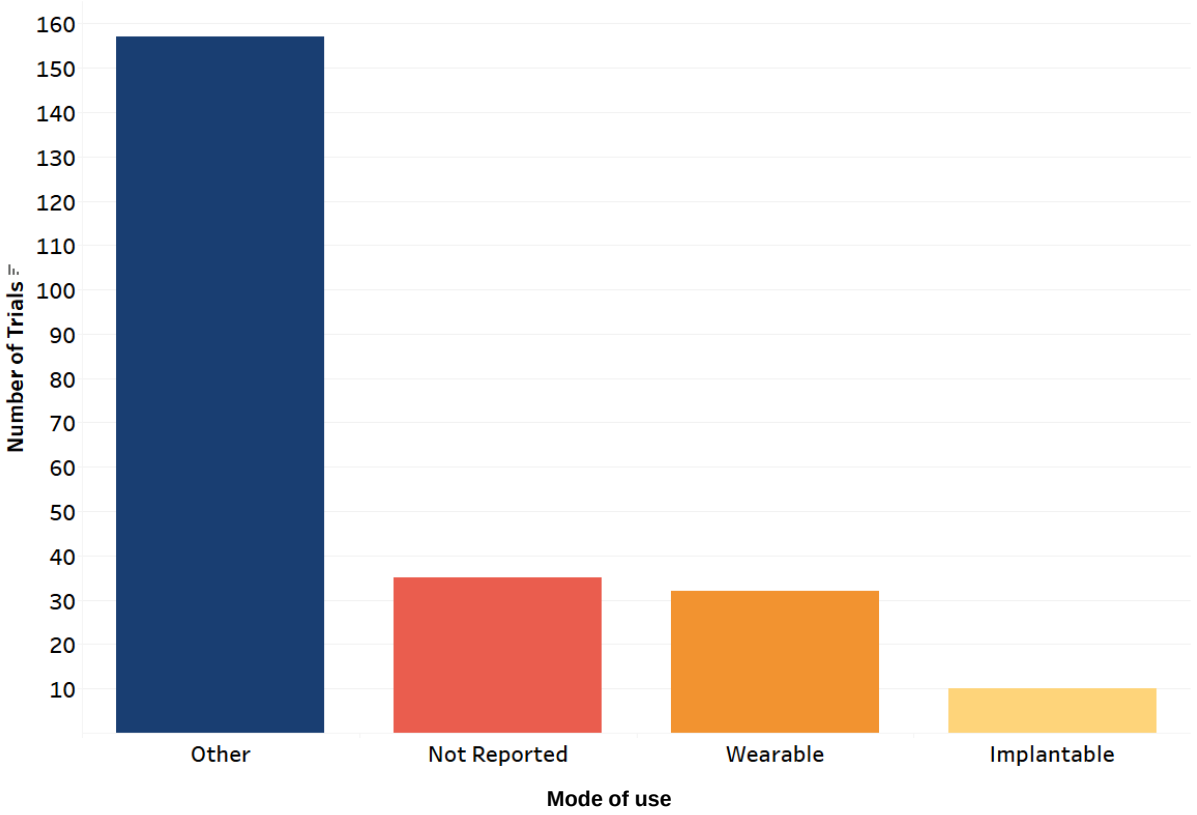

Figure 6. Mode of use of devices intended to treat and support recovery from substance addiction

AI component

Devices can include an AI component, whereby the device can perform tasks that would normally requiring human intelligence, such as decision-making. Of the 234 clinical trial registrations, 10% (n = 24) mentioned a device which had an AI component; 77% (n = 181) did not have an AI component (figure 7). There were 22 (9%) devices where it could not be determined whether or not there was an AI component (as it could not be identified from the available information).

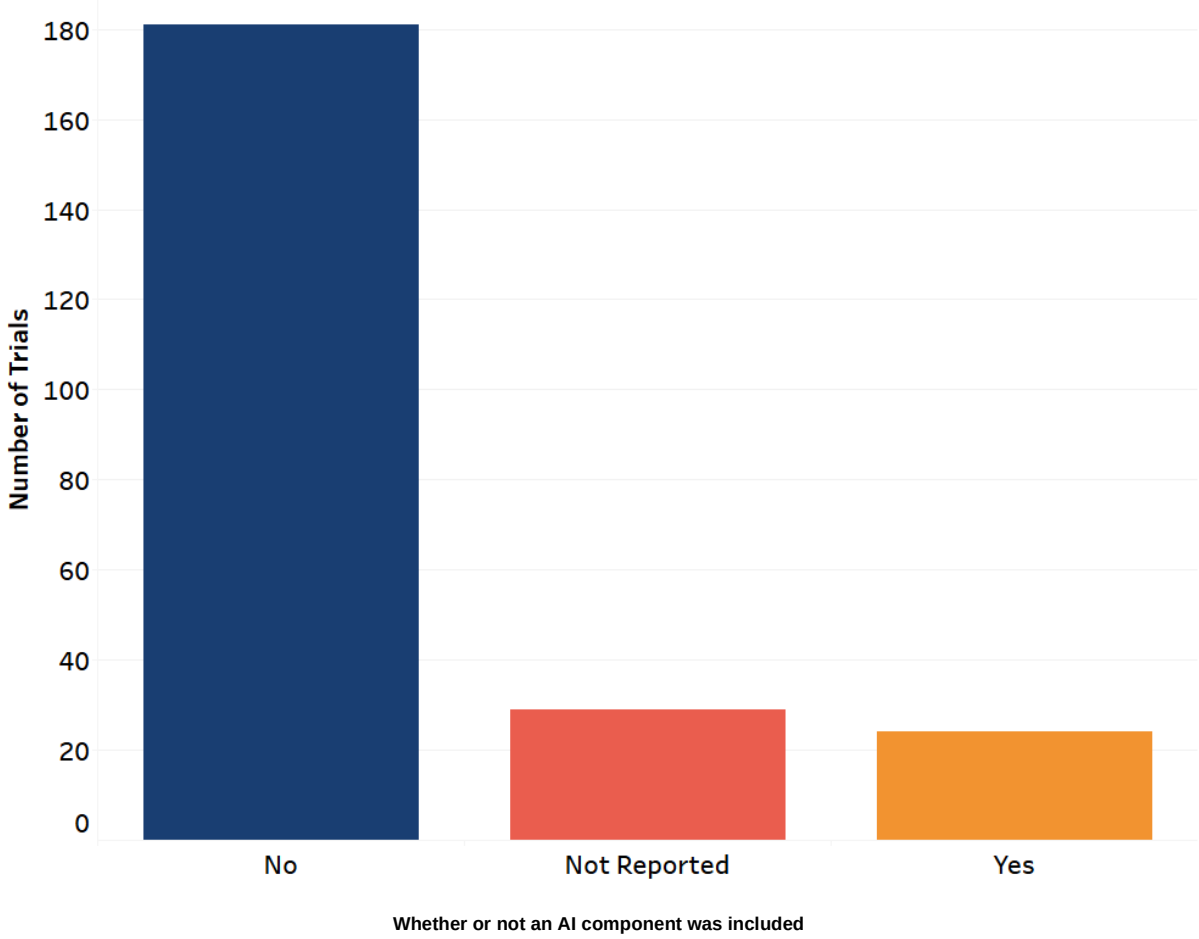

Figure 7. Number of devices with an AI component for the treatment of and supported recovery from addiction by clinical trial registrations

Actor

The 'actor' is the person using the device for the benefit of a particular 'target', sometimes the actor and the target are one and the same i.e. the individual uses a device for their own benefit. There may be more than one listed actor per device, for example an individual with an addiction and/or clinician. There were 109 (47%) clinical trial registrations that listed the individual with an addiction as the actor, 77 (33%) that listed a clinician, 47 (20%) that listed a health care professional and 28 (12%) where it was unclear or unknown. The researcher would not be the intended user of a medical device once out of development, however it is sometimes unclear who the final intended actor is.

Intended setting

The intended setting of use is the place in which the device will be used if approved. This could include more than one location, for example a clinic and at home. There were 97 (42%) clinical trial registrations that specified use of the device as within a clinical setting, 86 (37%) at home

and 38 (16%) where it was unclear where the setting of use would be once no longer a research facility, the setting of use was entirely unclear or unknown for 10 trials (4%).

UK Data

There were three clinical trial registrations that listed the UK as a trial conduct location which were initiated from 2012 onwards. These devices were called: Drinksmeter, fMRI-based neurofeedback and Transdermal alcohol sensor. The median participant enrolment was 31 and the interquartile range was 21. All three studies were of devices for alcohol addiction. Drinksmeter and the transdermal alcohol sensor were intended to be used by the individual with an addiction at home whereas the fMRI with neurofeedback was intended to be used by a healthcare professional in a clinical setting. Drinksmeter was the only device that mentioned having an AI component; the AI component of the Drinksmeter provides instant personalised feedback on the user's drinking and normative feedback on how their drinking compares with other Drinksmeter users. None of the devices were intended to be used alongside a pharmaceutical. Both the Drinksmeter and transdermal alcohol sensor were intended to be used alongside a psychological intervention.

National Institute on Drug Abuse funded trials

There was one trial identified for regulated medical devices that was funded by the NIDA. The trial was a phase 1 trial initiated in 2009. As the study was withdrawn, the enrolment number is zero. The trial was for rTMS to reduce cannabis craving. It was not aimed to be administered alongside either a psychological, pharmaceutical or device combination. It did not have an AI component.

Psychedelics in development for the treatment of substance addictions

Psychedelics (also known as hallucinogens) are a class of psychoactive substances that produce changes in perception, mood, and cognitive processes. Psychedelics affect all the senses, altering a person's thinking, sense of time and emotions. They can also cause a person to hallucinate—seeing or hearing things that do not exist or are distorted.[8] For the purpose of this report, both synthetic psychedelics and plant derivatives were included, such as LSD, psilocybin, and ibogaine, whereas other drugs which are not classed as psychedelics but that have hallucinogenic effects, such as ketamine, were not included.

The search returned 105 clinical trial registrations, 72 of which were excluded and 33 of which were included for analysis. Trials were not excluded on the basis of trials status or year.

Characteristics of clinical trial registrations

The search identified 33 unique clinical trial registrations for studies of psychedelics in development for substance addictions initiated between 2012 and 2024.

There were 27 clinical trial registrations for studies with an active status: active not recruiting (n = 3/33, 9%), not recruiting (n = 12/33, 36%), recruiting (n = 12/33, 36%). There were 3 clinical trials registrations for studies with an inactive status: completed (n = 1/33, 3%) and authorised (n = 2/33, 6%). Of these, 2 (6%) had published results on the trial website, and 29 (88%) had not published their results.

Studies were included from early phase 1 through to post marketing surveillance. Phase 2 was the most common trial phase (n = 23/33, 70%), followed by phase 1 (n = 6/33, 18%), phase 1/2 (n = 3/33, 9%), and phase 3 (n = 1/33, 3%). All studies were interventional (n = 32/33, 97%), although one did not specify. The median enrolment was 34 and the interquartile range was 78.

The searches were run across global trial registries, and identified relevant clinical trials were registered as being conducted in: North America (n = 18), Europe (n = 12), Oceania (n = 1) and South America (n = 1). No clinical trial registrations listed Africa, or Asia. Conduct locations were not listed on 4 clinical trial registrations.

Two trials were listed as being conducted in more than one country, 27 were listed in a single country and 4 did not report a country of conduct. The US was listed most often on clinical trial registrations as the country of conduct (n = 13) followed by Canada (n = 4), Denmark (n = 3), then Finland (n =2), Switzerland (n =2), the UK (n =2) and lastly Australia (n = 1), Brazil (n = 1),

Bulgaria (n = 1), Mexico (n = 1), Netherlands (n = 1), Spain (n =1) and those with no country of conduct listed (n = 4).

Studies of psychedelics over time

Trials identified and included in the search were initiated between 2012 and 2024. Start dates were gathered, where possible, from the trial registration (figure 8). There were 6 trials initiated in the 2010s and 25 in the 2020s. The start date was not specified for 2 trials.

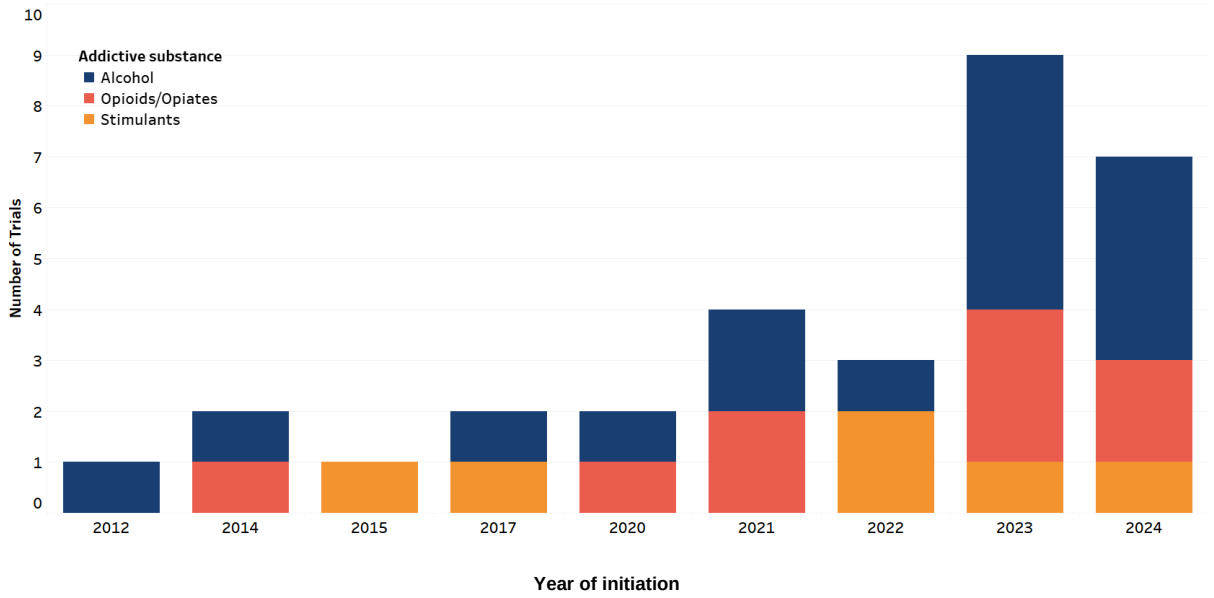

Figure 8. Trials evaluating psychedelics for the treatment of substance addiction between 2012 and 2024.

Interventions

Within the 33 unique clinical trial registrations there were 6 unique psychedelics being evaluated. There were 24 trials for psilocybin, 5 for ibogaine, and 1 each for BPL-003, CMND-100, Dimethyltryptamine and LSD.

There were 15 (45%) psychedelics being evaluated as monotherapies and 18 (55%) being evaluated for use in combination with pharmacological or psychological interventions. Of these, 16 were being evaluated for use in combination with psychological interventions such as CBT, and four were being evaluated for use in combination with other pharmaceuticals. Two were being evaluated for use in combination with both psychological and pharmaceutical interventions.

None of the clinical trial registrations were for psychedelics that are currently licensed for the treatment of addiction by the FDA, European Medicines Agency (EMA) or MHRA. In the UK, psychedelics are schedule 1 drugs, and include drugs not used medicinally such as hallucinogenic

drugs, ecstasy-type substances, raw opium, and cannabis. A Home Office licence is generally required for their production, possession, or supply.[9]

Of the 33 clinical trial registrations, 18 (55%) were for studies evaluating psychedelics for treatment of alcohol addiction, nine (27%) for opioids/opiates addiction and six (18%) for stimulant addiction (figure 9). There were no studies evaluating psychedelics as treatment for addiction to any other substances.

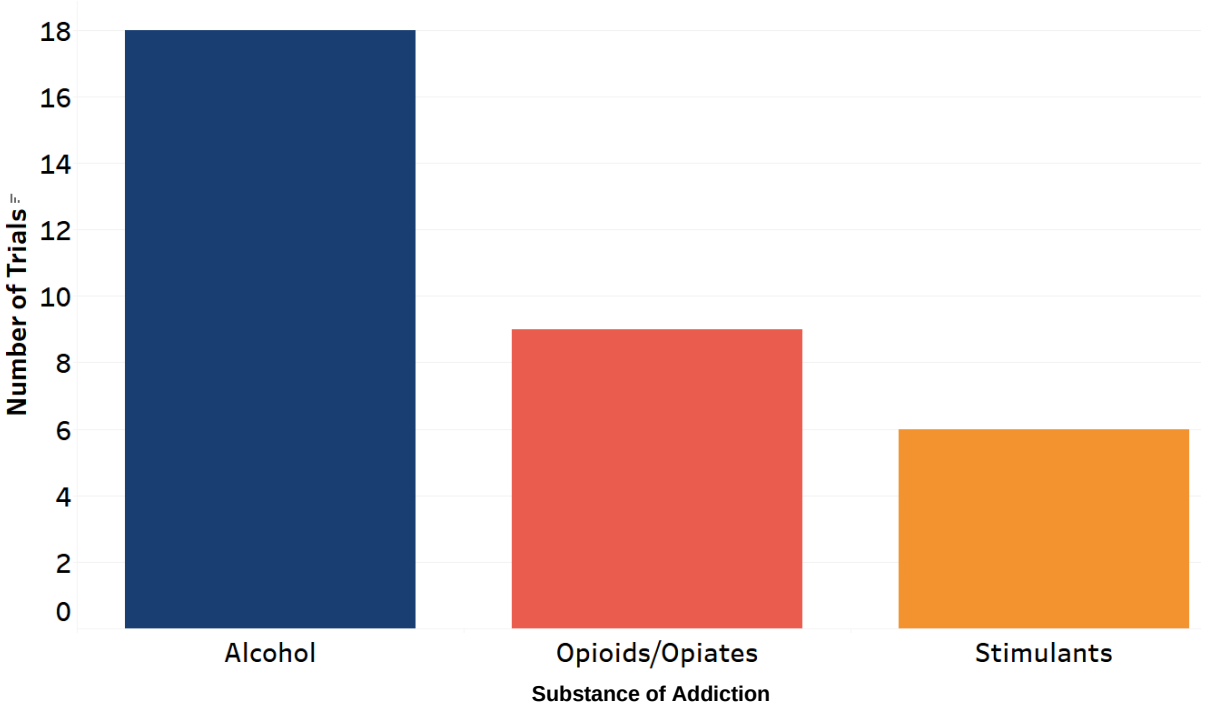

Figure 9. Trials for psychedelics for the treatment of substance addiction.
Three most common substance addictions for which psychedelics were in development to treat or support recovery from

Route of administration

Where available, information was gathered from the clinical trial registrations regarding the administration method. Oral administration was the most common administration method (n = 21/33, 64%) followed by intravenous and nasal (both n = 1/33, 3%). There were 10 (30%) clinical trial registrations that did not specify the administration method.

Treatment stage

Where possible, the place in treatment stage for each psychedelic was described. This was determined based on the clinical trial registration or on supplementary material. Most psychedelics were in development to manage relapse prevention (n = 18/33, 55%) and

withdrawal (n = 8/33, 24%). There were no psychedelics that would act as a substitute. The treatment stage was not known for seven trials (21%).

UK Data

There were two trials that listed the UK as a trial location. One is a phase 2 trial for nasally administered BPL-003 for alcohol addiction that is aiming to prevent relapse and is administered alongside a psychological intervention. It is currently recruiting and aims to enrol 12 participants. The second trial is a phase 1/2 trial for orally administered ibogaine that is aiming to manage withdrawal from opioid/opiate addiction. It is currently recruiting and aims to enrol 116 participants.

National Institute on Drug Abuse funded trials

There were no relevant clinical trials identified in this scan that are being run by NIDA.

Discussion

In November 2023, a comprehensive and sensitive systematic search was run to identify clinical trial registrations of healthcare technologies (pharmaceuticals, regulated medical devices, and psychedelics) in development for addictions to alcohol, opioids/opiates, stimulants, cannabis, gabapentin, pregabalin, benzodiazepines, GHB, ketamine and novel psychoactive substances. The search returned 1,369 trials for pharmaceuticals, 234 trials for regulated medical devices and 33 trials for psychedelics.

Across all healthcare technology types, the US was listed as a location of conduct for the largest number of clinical trials. There were 30 trials that listed the UK as a location of conduct - 25 evaluating pharmaceuticals, 3 evaluating devices and 2 evaluating psychedelics. Across all healthcare technology types there were no clinical trials being conducted in Africa and there were no trials for psychedelics in Asia.

The lack of clinical trials in Africa for substance addictions can be attributed to a number of factors. For example, limited infrastructure - including healthcare facilities and research centres - lack of clear regulatory and ethical guidelines, misconceptions and cultural dispositions to clinical trial participation and operational challenges contribute to the paucity of trials in this region.[10]

Beyond trials, there are both structural and non-structural barriers for individuals in Africa wishing to access rehabilitative services, such as stigma and discrimination.[11] Women are particularly likely to experience stigma but also social and economic disadvantages on account of substance addiction; women make up approximately 7% of individuals seeking treatment in Africa from 2016 to 2021. 70% of individuals seeking treatment were aged 15-34 years and 5% were 10 to 14 years. The African Union therefore convened a regional session to address substance use and related mental health disorders in the region in order to secure and address these challenges.[12]

Africa has seen an increase in the use of cocaine and heroin over the past few years.[12] But compared to North America, there is great inequality in the availability of prescription opioids; in 2020, there were 7,500 more doses per 1 million inhabitants of controlled pain medication in North America than in West and Central Africa.[13] However, for the US and UK, controlled pain medication, such as opioids or opiates, are the substance of addiction for many individuals. In England, from 2023-2024, nearly half of adults in contact with drug and alcohol services were

seeking treatment for opiate addiction.[5] In the US, in 2017, there were 2.0 million reported cases of opiate addiction and in the US and Canada, overdose deaths, predominantly driven by an epidemic of the non-medical use of fentanyl, are estimated to have caused 107,000 drug overdose deaths in 2021.[13]

Across all healthcare technologies identified, 88% were in development to treat or support recovery from addiction to opioids/opiates, alcohol, and stimulants. Less than 1% of all healthcare technologies were in development to treat addiction to benzodiazepines, ketamine and GHB. There were no trials of healthcare technologies to treat addiction to gabapentin, pregabalin, or novel psychoactive substances.

In England, from 2023-2024, a third of adults in contact with drug and alcohol services were seeking treatment for alcohol addiction. Less than ten percent were seeking treatment for powder cocaine or cannabis addiction.[5] In the US, in 2017 there were 14.8 million reported cases of alcohol addiction and 4.4 million cases of marijuana addiction. [4] In 2019, The WHO estimated that globally 609 million people live with alcohol addiction.[14]The geographical and substance trends observed in this scan largely mimic reported cases in the US and in England, although there is more disparity between cases of cannabis addiction and the number of trials for cannabis addiction. Cannabis legalisation in North America appears to have increased daily cannabis use, particularly among young adults [13]; this may therefore account for the increase in cannabis addiction but does not account for the number of trials.

In 2022, the United Nations Office on Drugs and Crime published a report on the trends in illicit drug use and cannabis legalisation. Across Africa, South and Central America, the largest proportion of people in treatment for substance addictions were for cannabis addiction. In Eastern and South-Eastern Europe and in Central Asia, individuals were most often in treatment for opioid addiction. Globally, seizures of methamphetamine increased – by 7% in North America, 30% in South-East Asia and 50% in South-West Asia. [13] However, these needs are not being mirrored in clinical trial data, as limited trials were identified across all technology types in South America and Asia, and no trials were identified in Africa.

Many individuals may need treatment for more than one substance addiction. Less than 5% of clinical trial registrations were investigating treatments for more than one substance addiction. These pharmaceuticals, for example, could be used to treat individuals with addiction to substance one, individuals with addiction to substance two or individuals with addiction to

substances one and two etc. (poly-substance addiction). This suggests most trials are focussed on treating one addiction at a time, or at least do not account for the impact of other substance use. If the treatment aimed to act as a substitute for a substance addiction (for example alternative opioids to heroin), this would suggest that the substitute would only target the addiction which it was being substituted. Beyond substitute treatments however, it may be useful to develop non-specific or repurposed treatment options for all types of substance addiction, rather than following the traditional route of targeting a single substance addiction.

The 1369 trials in this report were investigating numerous pharmaceuticals, including 246 unique technologies. Many trials were for naltrexone, buprenorphine, buprenorphine-naloxone, and oxytocin. This will be in part due to the nature of the inclusion criteria, as trials were included with any start date; therefore, trials will have been included in this report for pharmaceuticals that were in clinical trial for specific substance addictions, that have now been licensed for those indications. However, this will also include trials for licensed technologies which are in new clinical trials for new substance addictions, i.e. repurposed technologies.

Of the pharmaceutical interventions within the trials identified, 1,194 were already licensed in the US and 1,068 were already licensed in the UK and EU. The licensed pharmaceuticals in the identified trials include repurposed pharmaceuticals that are already licensed as interventions for other indications as well as, given the date range of trials included, pharmaceuticals that have been licensed post-trial.

Beyond repurposed technologies, there is a need for technologies with new innovative mechanisms of action. Some examples include viral vectors (e.g., AAV8-hCocH) monoclonal antibodies (e.g., devextinetug), microtubule stabilisers (e.g., MAP4343) and vaccines (e.g., OXY vaccine, TA-CD). Some repurposed technologies were also being developed as combinations, such as memantine and naltrexone or perampanel and disulfiram.

A fifth of trials for pharmaceuticals were being evaluated in combination with other pharmacological or psychological interventions; nearly 80% of pharmaceutical interventions were in development as monotherapies. Psychological interventions such as CBT, contingency management, couples and family therapy have been shown to be effective interventions for various substance addictions[15] and combined psychological and pharmacological interventions are considered best practices for addiction [16] in order to target both the psychological and physiological aspects of addiction.

Administering psychedelics alongside psychological interventions such as CBT may augment the therapeutic effects of psychological treatments, as the acute effects of classic psychedelics such as psilocybin include psychological flexibility (a capacity to respond effectively to the challenges of life in an ongoing way) and outcomes explicitly targeted by CBT (e.g., depression and anxiety).[17] This was reflected in the results of this scan which found psychological intervention combinations in more than half of trials for psychedelics.

In 2023, Australia became the first country to allow the use of psilocybin and MDMA for the treatment of depression and post-traumatic stress disorder (PTSD). A phase II trial, published in 2022 showed that a 25mg dose of psilocybin was twice as effective as a 1mg dose in combating treatment-resistant depression; a phase III trial of MDMA was described in a report as a "potential breakthrough treatment" for PTSD. Both psychedelics have also shown potential in treating anxiety, anorexia, and substance addiction.

However, treatment with psychedelics have been reported to cause significant side effects including "bad trips" and increased psychological issues if used improperly. As there is currently limited data on their efficacy and long-term effects, more evidence is needed to support their use with a focus on patient safety. There are also significant implementation requirements; even in Australia, where it is now approved, it is unclear how their administration will be regulated.[18]

In 2020, the first ketamine-assisted clinic was opened in the UK which offered treatment for patients with treatment resistant depression, anxiety, PTSD, and substance addiction. However, despite the centre's reported success rates, in 2024 the first clinic was closed due a lack of patients. A contribution to the closure was that the NHS was not willing to fund the clinic, meaning treatments were not subsidised and would cost patients £6000, limiting the number of individuals who would be able to afford the treatment costs.[19]

Psychological interventions were listed in combination with less than a fifth of regulated medical devices. The devices that aimed to be delivered alongside psychological interventions were largely non-invasive stimulatory devices such as transcranial direct current stimulation but also included electronic training programmes, and compliance monitoring programmes.

Nearly half of trials for devices were for devices intended to be used by the patient and nearly a third were intended for use at home – potentially offering more convenient treatment options for those with substance addictions. Examples of these home-based devices include implantable deep brain stimulatory devices and wearable sensors. Examples of devices used by the patient

included virtual reality and therapies delivered electronically. This may increase ease of use and patient compliance.

Ease of use is also important for pharmaceutical interventions in order to increase compliance. One factor that can increase compliance is the administration method, which can impact whether the patient can administer the medication themselves as well as potential side effects. Oral administration was the most common administration method for both psychedelics and pharmaceuticals. Oral administration is a convenient, cost-effective, and commonly used administration route [20] but in some cases may have to be delivered in a clinical setting [21] therefore would have more significant implementation requirements.

Whether a device, pharmaceutical or psychedelic, the healthcare technologies in this scan aim to offer additional treatment options to people with substance addictions. These treatments may fall into different parts of an addiction treatment stage. For example, they may offer a safer substitute to the addictive substance (e.g., in place of heroin), they may help manage withdrawal symptoms or aid in long term recovery through relapse prevention.

Where possible, the place in treatment stage for each pharmaceutical and psychedelic was inferred from the trial database. Most pharmaceuticals were in development to manage substance withdrawal and relapse prevention. Less than two percent of trials specified the pharmaceutical was a substitute and approximately a third of trials did not describe the purpose of the intervention. Trials developing substitute pharmaceuticals were for opioids and opiates, stimulants and poly-substance addictions.

In the last year, two pharmaceuticals have been approved by the FDA for substance addictions - subcutaneous buprenorphine (Brixadi) and intranasal nalmefene (OPNT003).[22,23] Both these products are already licensed by the FDA, MHRA and EMA in different formulations but have not been approved by the MHRA or EMA in these formulations.

There have been no new devices for substance addictions approved by the FDA, MHRA and EMA in the last five years. There is therefore a need for new medical devices to be developed for the treatment of substance addictions.

The results of this scan suggest that there is a need for more for clinical research into innovative treatments for substances addictions. Trials for pharmaceuticals were largely in an inactive status (such as completed or terminated) rather than in active status. This may be due to the start date

of the trials, with the majority of trials being initiated before the 2020s and may also be due to the number of unique interventions (n = 246). A large number of these unique pharmaceuticals were in development for now licensed products – such as buprenorphine-naloxone and naltrexone – therefore trials may have ceased since their approval.

Trials for devices identified in this scan were all initiated from the 2010s onwards. Trials are only required for devices if they are considered "high risk" although they are always tested for mechanical and/or electrical safety before use in patients. [24] UK regulations for devices have only been in place since 2002[25] and globally could account for the later trial dates.

The oldest psychedelic trial identified and included in this scan was initiated in 2012. Psychedelics have been used in medical research in the West since the late nineteenth century. They were increasingly researched from the 1940s after the development of LSD, and later in the 1950s and 1960s after the development of biological psychiatry. In the late 1960s, the use of LSD was made illegal in the US, but other drugs, such as MDMA, emerged and were then similarly made illegal in the mid-1980s. However, in the last two decades there has been a resurgence of psychedelic research.[26] The results of this scan found that there has been an almost two-fold increase in clinical trial registrations with psychedelics over the last two years.

The potential of cannabis, psychedelics and other drugs as therapeutics have been a target of research by NIDA. NIDA have also identified other aforementioned unmet needs in addiction research, such as sensitive and accessible tools for detection of new compounds. In 2024 NIDA published a description of plans to evolve their research with the changing landscape of substance use, including research into new synthetic drugs and state-level legalised medicinal and recreational drugs such as cannabis. [27]

There is real opportunity to stimulate innovation within the gaps that correlate with unmet need. Future innovation could focus on increasingly prevalent addiction to newer substance types, addressing poly-substance addiction, addiction amongst those with co-occurring mental health conditions, positioning across the addiction pathway.

Appendix

Searches

Pharmaceuticals in development for substance addictions

Table 1. Scan 1 Search Strategy for the Medicines Innovation Database (MInD)

#	String
1	opioid use disorders (OUD) OR opioid dependence
2	cocaine addiction
3	alcohol addiction OR alcohol withdrawal syndrome OR alcohol use disorder
4	cannabis use disorder OR cannabis use disorder (CUD) OR cannabis withdrawal symptoms
5	methamphetamine use disorder OR methamphetamine-dependence
6	cannabis use disorder OR cannabis use disorder (CUD) OR cannabis withdrawal symptoms

Table 2. Scan 1 Search Strategy for CT.gov

#	String
1	((opioid OR cocaine OR amphetamine OR methamphetamine OR ketamine OR cannabis OR cannabinoid OR "spice" OR "synthetic marijuana" OR K2 OR benzodiazepine OR GHB OR alcohol OR nitrous oxide OR methadone) AND
2	("harmful use" OR disorder OR dependence OR addiction OR abuse OR withdrawal OR detox OR detoxification))

Table 3. Scan 1 Search Strategy for EudraCT

#	String
1	("opioid use disorder" OR "opioid dependence" OR "opioid addiction" OR "opioid abuse" OR "OUD" OR "opioid withdrawal" OR "cocaine abuse" OR "cocaine dependence" OR "cocaine addiction" OR "cocaine use disorder" OR "CUD" OR "cocaine withdrawal" OR "amphetamine abuse" OR "amphetamine dependence" OR "amphetamine addiction" OR "amphetamine use disorder" OR "amphetamine withdrawal" OR "methamphetamine abuse" OR "methamphetamine dependence" OR "methamphetamine addiction" OR "methamphetamine use disorder" OR "amphetamine withdrawal" OR "ketamine abuse" OR "ketamine dependence" OR "ketamine addiction" OR "ketamine use disorder" OR "ketamine withdrawal" OR "cannabis abuse" OR "cannabis dependence" OR "cannabis addiction" OR "cannabis use disorder" OR "cannabis withdrawal" OR "cannabinoid abuse" OR "cannabinoid dependence" OR "cannabinoid misuse" OR "cannabinoid addiction" OR "cannabinoid use disorder" OR "cannabinoid withdrawal" OR "benzodiazepine abuse" OR "benzodiazepine dependence" OR "benzodiazepine addiction" OR "benzodiazepine use disorder" OR "benzodiazepine withdrawal" OR "GHB abuse" OR "GHB dependence" OR "GHB addiction" OR "GHB use disorder" OR "GHB withdrawal" OR "alcohol addiction"

	OR "alcohol withdrawal" OR "alcohol use disorder" OR "alcohol related disorder" OR "alcoholism" OR "AUD" OR "methadone use disorder" OR "methadone dependence" OR "methadone addiction" OR "methadone abuse" OR "methadone withdrawal" OR "nitrous oxide use disorder" OR "nitrous oxide dependence" OR "nitrous oxide addiction" OR "nitrous oxide abuse" OR "nitrous oxide withdrawal" OR "detox" or "detoxification")

Table 4. Scan 1 Search Strategy for ICTRP

#	String
1	((opioid OR cocaine OR amphetamine OR methamphetamine OR ketamine OR cannabis OR cannabinoid OR "spice" OR "synthetic marijuana" OR K2 OR benzodiazepine OR GHB OR alcohol OR nitrous oxide OR methadone) AND
2	("harmful use" OR disorder OR dependence OR addiction OR abuse OR withdrawal OR detox OR detoxification)

Table 5. Scan 1 Search Strategy for BiomedTracker

#	String
1	Opioid use disorder
2	Cocaine use disorder
3	amphetamine use disorder
4	methamphetamine use disorder
5	ketamine use disorder
6	cannabis use disorder
7	cannabinoid use disorder
8	Benzodiazepine abuse
9	GHB abuse
10	alcohol use disorder
11	Nitrous oxide use disorder
12	Methadone use disorder

NB: BiomedTracker has basic search functionality only

Devices in development for substance addictions

For scan 2, it is important to note that some types of medical devices are not required to undergo clinical trials, only those that are considered "high-risk". Class I medical devices are considered to be low risk. Class II medical devices are considered to be moderate risk, and Class III medical devices are considered to be high risk. Given this, all Class III medical devices undergo clinical trial. Most Class I medical devices are not subject to clinical trials; however, some may require what is known as a “safety and effectiveness study” as will some Class II medical devices. Safety and effectiveness studies are intended to determine whether a medical device is safe and effective for its intended use. Class II medical devices usually require clinical trials only if they are new or if they are significantly different from other medical devices on

the market. If our searching purely relied on trial databases, we would miss some relevant devices. To address this issue, information was manually retrieved about recently approved technologies from various databases, including the Recently-Approved Devices | Food and Drug Administration (FDA), humanitarian device exemption (HDE) database - FDA, the MHRA public access registration database (PARD), the Japanese's Pharmaceuticals and Medical Devices Agency (PMDA) database, and the European Medicines Agency (EMA).

The search strategies for devices are outlined in Table 6 to 8.

Table 6 Scan 2 Search Strategy for CT.gov*

#	String
1	((opioid OR cocaine OR amphetamine OR methamphetamine OR ketamine OR cannabis OR cannabinoid OR "spice" OR "synthetic marijuana" OR K2 OR benzodiazepine OR GHB OR alcohol OR nitrous oxide OR methadone) AND
2	("harmful use" OR disorder OR dependence OR addiction OR abuse OR withdrawal OR detox OR detoxification))

Table 7 Scan 2 Search Strategy for Scanmedicine search 1

#	String
1	("opioid use disorder" | "opioid addiction" | "opioid dependence" | "opioid abuse" | "opioid withdrawal" | "cocaine use disorder" | "cocaine addiction" | "cocaine dependence" | "cocaine abuse" | "cocaine withdrawal" | "amphetamine use disorder" | "amphetamine addiction" | "amphetamine dependence" | "amphetamine abuse" | "amphetamine withdrawal" | "methamphetamine use disorder" | "methamphetamine addiction" | "methamphetamine dependence" | "methamphetamine abuse" | " methamphetamine withdrawal"| "ketamine use disorder" | "ketamine addiction" | "ketamine dependence" | "ketamine abuse" | "ketamine withdrawal" | "cannabis use disorder" | "cannabis addiction" | "cannabis dependence" | "cannabis abuse" | "cannabis withdrawal" | "cannabinoid use disorder" | "cannabinoid addiction" | "cannabinoid dependence" | "cannabinoid abuse" | "cannabinoid withdrawal" | "synthetic cannabinoid use disorder"| "synthetic cannabinoid use disorder" | "synthetic cannabinoid addiction" | "synthetic cannabinoid dependence" | "synthetic cannabinoid abuse" | "synthetic cannabinoid withdrawal"| "Benzodiazepine use disorder" | "Benzodiazepine addiction" | "Benzodiazepine dependence" | "Benzodiazepine abuse" | "Benzodiazepine withdrawal" | "GHB use disorder" | "GHB addiction" | "GHB dependence" | "GHB abuse" | "GHB withdrawal" | "methadone use disorder" | "methadone addiction" | "methadone dependence" | "methadone abuse" | "methadone withdrawal" | "nitrous oxide use disorder" | "nitrous oxide addiction" | "nitrous oxide dependence" | "nitrous oxide abuse" | "nitrous oxide withdrawal" | "harmful use" | detox | detoxification) +
2	Device

Table 8 Scan 2 Search Strategy for Scanmedicine search 2

#	String
1	("alcohol use disorder" | "alcohol addiction" | "harmful use" | detox | detoxification) +
2	Device

Table 9 Scan 2 Search Strategy for Scanmedicine search 3

#	String
1	("alcohol dependence" | "alcohol withdrawal" | "harmful use" | detox | detoxification) +
2	Device

Table 10 Scan 2 Search Strategy for Scanmedicine search 4

#	String
1	("alcohol abuse" | "harmful use" | detox | detoxification) +
2	"medical device"

Table 11. Scan 2 Search Strategy for ICTRP

#	String
1	((opioid OR cocaine OR amphetamine OR methamphetamine OR ketamine OR cannabis OR cannabinoid OR "spice" OR "synthetic marijuana" OR K2 OR benzodiazepine OR GHB OR alcohol OR nitrous oxide OR methadone) AND
2	("harmful use" OR disorder OR dependence OR addiction OR abuse OR withdrawal OR detox OR detoxification) AND
3	(device OR machine learning OR artificial intelligence))

Psychedelics in development for substance addictions

Table 12. Scan 3 Search Strategy for CT.gov

#	String
1	((opioid OR cocaine OR amphetamine OR methamphetamine OR ketamine OR cannabis OR cannabinoid OR "spice" OR "synthetic marijuana" OR K2 OR benzodiazepine OR GHB OR alcohol OR nitrous oxide OR methadone) AND
2	("harmful use" OR disorder OR dependence OR addiction OR abuse OR withdrawal OR detox OR detoxification)) AND
3	(psychedelic OR psychoactive OR LSD OR Psilocybin OR Mescaline OR DMT OR Diemethyltryptamine OR "2C-B" OR Peyote OR "25[-x]-NBOMe"))

Table 13. Scan 3 Search Strategy for Scanmedicine

#	String
	("opioid use disorder" | "opioid addiction" | "opioid dependence" | "opioid abuse" | "opioid withdrawal" | "cocaine use disorder" | "cocaine addiction" | "cocaine dependence" | "cocaine abuse" | "cocaine withdrawal" | "amphetamine use disorder" | "amphetamine addiction" | "amphetamine dependence" | "amphetamine abuse" | "amphetamine withdrawal" | "methamphetamine use

	disorder" | "methamphetamine addiction" | "methamphetamine dependence" | "methamphetamine abuse" | " methamphetamine withdrawal"| "ketamine use disorder" | "ketamine addiction" | "ketamine dependence" | "ketamine abuse" | "ketamine withdrawal" | "cannabis use disorder" | "cannabis addiction" | "cannabis dependence" | "cannabis abuse" | "cannabis withdrawal" | "cannabinoid use disorder" | "cannabinoid addiction" | "cannabinoid dependence" | "cannabinoid abuse" | "cannabinoid withdrawal" | "synthetic cannabinoid use disorder"| "synthetic cannabinoid use disorder" | "synthetic cannabinoid addiction" | "synthetic cannabinoid dependence" | "synthetic cannabinoid abuse" | "synthetic cannabinoid withdrawal" | "Benzodiazepine use disorder" | "Benzodiazepine addiction" | "Benzodiazepine dependence" | "Benzodiazepine abuse" | "Benzodiazepine withdrawal" | "GHB use disorder" | "GHB addiction" | "GHB dependence" | "GHB abuse" | "GHB withdrawal" | "methadone use disorder" | "methadone addiction" | "methadone dependence" | "methadone abuse" | "methadone withdrawal" | "nitrous oxide use disorder" | "nitrous oxide addiction" | "nitrous oxide dependence" | "nitrous oxide abuse" | "nitrous oxide withdrawal" | "alcohol use disorder" | "alcohol addiction" | "alcohol dependence" | "alcohol withdrawal" | "alcohol abuse" | "harmful use" | detox | detoxification) +
	Psychedelic

Table 14. Scan 3 Search Strategy for ICTRP

#	String
1	((opioid OR cocaine OR amphetamine OR methamphetamine OR ketamine OR cannabis OR cannabinoid OR "spice" OR "synthetic marijuana" OR K2 OR benzodiazepine OR GHB OR alcohol OR nitrous oxide OR methadone) AND
2	("harmful use" OR disorder OR dependence OR addiction OR abuse OR withdrawal OR detox OR detoxification)) AND
3	(psychedelic OR psychoactive OR LSD OR Psilocybin OR Mescaline OR DMT OR Diemethyltryptamine OR "2C-B" OR Peyote OR "25[-x]-NBOMe"))

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