Department of Health

A summary of the health harms of drugs

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About the research team
The research team are based at the Centre for Public Health and School of Pharmacy and Biomolecular Sciences, Liverpool John Moores University. Lisa Jones led the production of the updated tables and this report, with support from Geoff Bates and Ellie McCoy. The update of the tables was guided by a lead expert for each licit and illicit drug, comprising Mark Bellis (alcohol), Caryl Beynon (illicit opioids, tobacco), Paul Duffy (cocaine powder and freebase cocaine), Michael Evans-Brown (anabolic agents), Adam Mackridge (prescription opioids, prescription drugs and over-the-counter products) and Harry Sumnall (amphetamines and amphetamine-type stimulants, cannabis, dissociative anaesthetics, serotinergic hallucinogens, GHB and GBL, nitrites, novel synthetic drugs, khat and Salvia divinorum). Jim McVeigh had overall management responsibility for the delivery of the updated tables and this report.

Declaration of interest
No member of the research team has any financial, professional or other interests to disclose that are relevant to the subject of this report, or any interests that could be significantly affected by the outcome of this work.

Table of tables

Glossary

1,4-butanediol (1,4-BD)	See gamma-hydroxybutrate
2C series phenylamines	Derivatives of the phenethylamine class of drugs with hallucinogenic properties
abstinence	Refraining from licit and/or illicit drug use
acute effect	Effects that develops rapidly following ingestion of a drug or substance as a result of short term exposure
alcoholic cardiomyopathy	A diffuse disorder of the heart muscle seen in individuals with a history of hazardous alcohol use. Common symptoms include shortness of breath on exertion and on lying down, palpitations, swollen ankles (oedema), and abdominal distention
alcoholic cerebellar degeneration	Neurological complication characterised by unsteadiness and lack of coordination (cerebellar ataxia) predominantly affecting the lower extremities
alcoholic gastritis	Inflammation of the mucosal lining of the stomach caused by alcohol
alcoholic hepatitis	A disorder of the liver characterised by liver cell death and inflammation following chronic consumption of hazardous levels of alcohol
alcoholic pancreatitis	A disorder characterised by inflammation and destruction of the pancreas, and associated with long-term heavy alcohol consumption
amotivational syndrome	A constellation of features thought to be associated with substance use, principally cannabis use. Features include apathy, loss of effectiveness, diminished capacity to carry out complex or long-term plans, low tolerance for frustration, impaired concentration and difficulty in following routines
amphetamine	One of a class of sympathomimetic amines with powerful stimulant action on the central nervous system. The class includes amphetamine, dexamphetamine and methamphetamine
amphetamine psychosis	A disorder characterised by paranoid delusions, frequently accompanied by hallucinations, hyperactivity and mood swings. Develops during or shortly after repeated use of moderate or high doses of amphetamine
amyl nitrite	See nitrites
anabolic agents	Drugs that are used for their purported muscle-building (anabolic) effects, including anabolic-androgenic steroids and other agents with similar anabolic effects
anabolic-androgenic steroids (AAS)	A class of drugs with both muscle-building (anabolic) and masculinising (androgenic) effects
analgesic	A substance that reduces pain. Analgesics may or may not have psychoactive properties
anorectic	Causing loss of appetite
anxiolytics	Anti-anxiety drugs
arrhythmias	A disorder of the heart rate or rhythm, such as beating too fast (tachycardia), too slow (bradycardia), or irregularly. There are various types of arrhythmias depending on where problems occur along the heart's electrical conduction system
barbiturate	A group of central nervous system depressant drugs
benzodiazepine	A group of structurally related drugs used mainly as sedatives/hypnotics
blackout	A period of memory loss during which there is little recall of activities; not associated with loss of consciousness
blood alcohol level	The concentration of alcohol present in blood
butyl nitrite	See nitrites
caffeine	A mild central nervous system stimulant, vasodilator and diuretic
cannabis	Denotes psychoactive preparations of the marijuana (hemp) plant, Cannabis sativa
chronic effect	Effects arising as a consequence of repeated or long term exposure to a drug or substance
clenbuterol	An adrenergic stimulant with short-term effects similar to amphetamine. May be used alone or in combination with other substances to promote the growth of skeletal muscle (anabolic effects) and to reduce body fat (catabolic effects)
clonazepam	See benzodiazepines

CNS stimulants	A loosely defined group of drugs that tend to increase behavioural alertness, agitation, or excitation
cocaine	An alkaloid obtained from coca leaves or synthesised from ecgonine or its derivatives. A powerful central nervous system stimulant
cocaine powder	Cocaine hydrochloride, a water soluble salt
codeine containing products	Widely available as analgesic products containing codeine with aspirin, paracetamol or ibuprofen. These products may contain other ingredients such as caffeine. Cough medicines containing codeine and other ingredients are also available
convulsion	A seizure-like event characterised by loss of consciousness and muscular rigidity, followed by jerking of the limbs and trunk
crack/rock cocaine	A highly pure form of the freebase of cocaine
cross-tolerance	The development of tolerance to a substance, to which the individual has not previously been exposed, as result of acute or chronic intake of another substance
delirium	An acute organic cerebral syndrome characterised by concurrent disturbances of consciousness, attention, perception, orientation, thinking, memory, psychomotor behaviour, emotion and the sleep-wake cycle. An alcohol-induced withdrawal syndrome with delirium is known as delirium tremens
delirium tremens	Withdrawal syndrome with delirium; an acute psychotic state occurring during the withdrawal phase in people with alcohol dependence. Characterised by confusion, disorientation, paranoid ideation, delusions, illusions, hallucinations, restlessness, distractibility, tremor, sweating, tachycardia and hypertension
dependence	A cluster of symptoms that indicate a person has impaired control over their psychoactive substance use, e.g continuing use despite adverse consequences
dependence potential	The propensity of a substance to give rise to dependence
dependence syndrome	A cluster of behavioural, cognitive and physiological phenomena that may develop after repeated substance use
depressant	Any drug that suppresses, inhibits, or decreases some aspect of central nervous system activity
dexamphetamine	A central nervous system stimulant and sympathomimetic. Has been used in the treatment of narcolepsy and attention-deficit disorders and hyperactivity in children
dextromethorphan	Developed as a non-opioid cough suppressant. The main metabolite of the drug, dextrorphan, is thought to be largely responsible for the abuse potential of the drug. At high doses exerts similar actions to phencyclidine
diazepam	See benzodiazepines
disinhibition	A state of release from internal constraints on an individual's behaviour
dissociative anaesthetic	Compound, such as phencyclidine or ketamine, which produces an anaesthetic effect characterised by a feeling of being detached from the physical self
ecstasy	See MDMA
fatty liver disease	Accumulation of fat in the liver following exposure to hazardous levels of alcohol
flashbacks	A spontaneous recurrence of visual distortions, physical symptoms, loss of ego boundaries, or intense emotions that occurred during past use of hallucinogens and dissociative drugs
foetal alcohol spectrum disorder	A combination of mental and physical disabilities present at birth caused by maternal alcohol consumption during pregnancy
gamma-butyrolactone (GBL)	See GHB
gamma-hydroxybutyrate (GHB)	A naturally occurring endogenous compound. Originally synthesised for use as an anaesthetic it is used recreationally for its sedative and anaesthetic effects. The precursors of GHB, gamma-butyrolactone (GBL) and 1,4-butanediol (1,4-BD) are rapidly broken down in vivo to GHB and may also be used recreationally
growth hormone	May be used alone or in combination with other substances to induce muscle-building (anabolic) effects, reduce muscle cell breakdown and reduce body fat
hallucinations	Hallucinations involve sensing things while awake that appear to be real, but instead have been created by the mind
hallucinogen	A chemical agent that induces alterations in perception, thinking and feeling

heroin	A simple derivative of morphine. Heroin is the most widely used illicit opioid because of its potency, availability, solubility in water and speed with which it crosses the blood-brain barrier
human (and non-human) chorionic gonadotropin	Used to complement a cycle of anabolic-androgenic steroids. Their primary use is as part of the post-cycle recovery, to 'kickstart' natural testosterone production following a long cycle of AAS
illicit drug	A psychoactive substance, the production, sale, possession or use of which is prohibited
isobutyl nitrite	See nitrites
ketamine	A dissociative anaesthetic with central nervous system depressant, stimulant, analgesic, and hallucinogenic effects similar to phencyclidine, but less potent and of a shorter duration. Used in human anaesthesia and veterinary medicine. Some ketamine users may experience a terrifying feeling of almost complete sensory detachment that is likened to a near-death experience; known as the 'K-hole'
khat	The leaves of the plant, Catha edulis, which are chewed or brewed as a drink
legal highs	A term used to describe unregulated psychoactive substances. The term encompasses a wide range of synthetic and plant-derived substances and products, including 'research chemicals', 'party pills' and 'herbal highs', which are usually sold via the Internet or in head shops
licit drug	A drug that is legally available with or without a medical prescription
liver cirrhosis	Scarring of the liver and poor liver function
lysergic acid diethylamide (LSD)	A semi-synthetic product of lysergic acid, a natural substance from the parasitic rye fungus Claviceps purpurea. See serotonergic hallucinogens
MDMA	3,4-methylenedioxymethamphetamine, a synthetic derivative of amphetamine, exhibiting both stimulant and mild hallucinogenic properties. Entactogenic effects include feelings of euphoria and solidarity, heightened sensory awareness and ease of contact with others. Commonly known as ecstasy, a wide range of substances, including MDMA analogues or 4-MTA, may appear in varying concentrations in ecstasy tablets. Most ecstasy tablets now available in the UK no longer contain MDMA
mescaline	A hallucinogenic substance found in the peyote cactus in South-Western USA and North Mexico. See serotonergic hallucinogens
methadone	A synthetic opioid drug
methamphetamine	A derivative of amphetamine. The pure crystalline hydrochloride form of methamphetamine known as 'ice' may be smoked, achieving as rapid or even more rapid onset of effects than injection of methamphetamine powder (the hydrochloride salt form). Methamphetamine freebase is a colourless volatile oil insoluble in water
methylphenidate	A mild central nervous system stimulant. Commonly used in the treatment of attention-deficit disorders in children
modafinil	A wake-promoting medication used in the treatment of narcolepsy and other sleep disorders. Misused with the expectation that it will improve cognitive performance
N,N-dimethyltryptamine (DMT)	A plant hallucinogen. See serotonergic hallucinogens
nicotine	An alkaloid and the major psychoactive substance in tobacco. Nicotine has both stimulant and relaxing properties
nitrazepam	See benzodiazepines
nitrites	Volatile inhalants
non-benzodiazepine hypnotics	A class of drugs, which although chemically unrelated to the benzodiazepines, exert similar actions
novel synthetic drugs	New drugs and drug classes that have emerged since 2003. These drugs may or may not be scheduled as controlled substances and in some cases may be sold as legal highs
opioid	The generic term applied to alkaloids from the opium poppy (Papaver somniferum), their synthetic analogues, and compounds synthesised within the body
overdose	The use of any drug in such an amount that acute adverse physical or mental effects are produced
over-the-counter products	Medicines that are available without prescription

peripheral neuropathy	Disorder and functional disturbance of the peripheral nerves. Symptoms include numbness of the extremities, 'pins and needles', weakness of the limbs, or wasting of the muscles and loss of deep tendon reflexes
phencyclidine (PCP)	A psychoactive drug with central nervous system depressant, stimulant, analgesic, and hallucinogenic effects. Introduced into clinical medicine as a dissociative anaesthetic
piperazines	Initially developed as veterinary anthelmintic agents. Piperazines have a chemical structure similar to amphetamine. They have been identified in tablets sold as ecstasy. See novel synthetic drugs
polysubstance use	The use of more than one drug or type of drug by an individual, often concurrently or sequentially
psilocybin	A naturally occurring hallucinogen found in certain species of mushroom. See serotonergic hallucinogens
psychoactive drug or substance	A substance that when ingested affects mental processes, e.g. cognition or effect
psychosis	A loss of contact with reality, usually including delusions and hallucinations
psychotic	Experiencing psychosis
relapse	A return to drinking or other substance use after a period of abstinence
rhabdomyolysis	A condition caused by the breakdown of skeletal muscle fibres resulting in the release of muscle fibre content (myoglobin) into the bloodstream
route of administration	The way in which a substance is introduced into the body
Salvia divinorum	A hallucinogenic plant, the leaves of which can be chewed or smoked to release a psychoactive compound, salvinorin A
serotonergic hallucinogens	A class of hallucinogens with a method of action strongly tied to the serotonin neurotransmitter
serotonin syndrome	A potentially life threatening drug reaction that causes the body to have too much serotonin
speedball	Refers to the combined use of a stimulant and an opioid, most commonly simultaneous injection of cocaine and heroin
stimulant	Any agent that activates, enhances, or increases neural activity
substituted cathinones	Synthetic drugs with stimulant properties related to a plant product, cathinone. See novel synthetic drugs
sympathomimetic	Producing physiological effects resembling those caused by the action of the sympathetic nervous system
synthetic cannabinoids	Products typically containing synthetic cannabinoid receptor agonists sprayed onto a mixture of 'smokeable herbs'. The class of products is commonly known as 'Spice'. See novel synthetic drugs
temazepam	See benzodiazepines
THC	Δ9-tetrahydrocannabinol, the most active constituent in cannabis
tolerance	A decrease in response to a drug dose that occurs with continued use
tryptamine derivatives	Synthetic drugs with hallucinogenic properties. Chemically related to the hallucinogen DMT. See novel synthetic drugs
volatile substances	Substances that vaporise at ambient temperatures
Wernicke–Korsakoff syndrome	A spectrum of disease resulting from vitamin B1 (thiamine) deficiency
withdrawal syndrome	A group of symptoms of variable clustering and degree of severity which occur on cessation, or reduction of use of a psychoactive substances that has been taken repeatedly, usually for a prolonged period and/or in high doses
zaleplon	See non-benzodiazepine hypnotics
zolpidem	See non-benzodiazepine hypnotics
zopiclone	See non-benzodiazepine hypnotics

PART ONE
INTRODUCTION

A summary of the health harms of drugs

1. Introduction

The health harms arising from licit and illicit substance use and misuse are wide-ranging and vary depending on the substance used and the pattern and context of their use, but it is well established that their use represents a major public health burden. This report summarises the health-related harms of emerging and established licit and illicit drugs[a], providing an update to *Dangerousness of drugs: a guide to the risks and harms associated with substance misuse*[1].

1.1 Influence of drug, set and setting

The health harms arising from licit and illicit substance use are diverse and need to be considered within the culture and context of drug use among specific populations. That is, drug-related harms do not only vary according to the different types of drug or drugs being used; alongside this, it is the way a drug is used, the way it is used in combination with other substances, and the social context in which it is used that contribute to risk.

Researchers often consider the influence of the drug (referring to the pharmacological properties of a drug), set (the characteristics of the person using the drug) and setting (the social and physical environment in which the drug is used) on drug-related harms. For example, studies have identified specific characteristics associated with alcohol-related harm in drinking environments, including crowding, low levels of comfort, cheap drink promotions, and poorly trained staff[2]. These factors may also interact, as in the case of MDMA, the acute effects of which are intensified by taking it in stimulating conditions such as nightclubs[3]. In particular, the harms associated with illicit substance use, or use of other unregulated psychoactive substances, are further confounded by lack of suitable quality control in their manufacture and distribution. People who use these substances can therefore only make inadequate assessments of the quality, purity, and chemical composition of any drugs they use[4]. The route or mode of administration of a drug plays a particular role in escalating risk. Injection drug use poses the greatest risk to users, putting them at a very high risk of acquiring blood borne viral infections, and at an increased risk of overdose and dependence. Injecting drug users also frequently face discrimination and stigmatisation, which may discourage users away from accessing treatment and other health services[5].

1.2 Assessing health-related harms

There are major challenges to the assessment of health-related harms of drugs. There may be difficulties in interpreting evidence of harm due to uncertainties whether the substance used is a direct or indirect cause of the acute and chronic adverse effects that have been attributed to its use. In addition, it may be difficult to quantify the magnitude of the risk of experiencing these health harms among users.

The methods used to develop the updated tables were based on the systematic retrieval and collection of relevant peer reviewed literature. For further details on the methodology please see the

[a]The list of licit and illicit drugs to be included in the updated tables was agreed between the research team, NTA and DH. For further details see the Technical Document that accompanies this report

Technical Report that accompanies this report. Evidence from systematic reviews and well designed observational studies was prioritised for inclusion, providing, where available, the strongest evidence available of an association between the substance use in question and a particular health outcome. However, it was beyond the scope of the work to provide an estimation of the magnitude of the health risks associated with each of the substances presented. Research is ongoing to develop systematic and transparent approaches for the assessment of drug-related harms[6,7].

1.3 Patterns of substance use

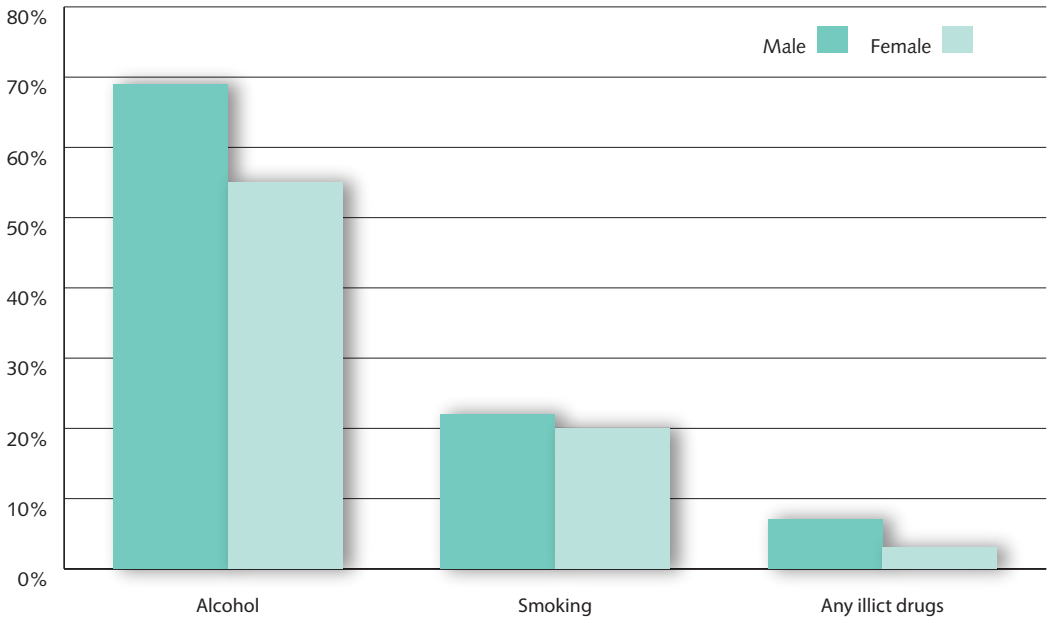
Patterns of licit and illicit substance use in the general population underlie the nature and prevalence of the health harms associated with their use. The following section considers patterns of substance use reported by adults and young people in England and Wales.

Patterns of substance use among adults

Among 32.3 million adults aged 16 to 59 in England and Wales there are an estimated:
- 20 million weekly alcohol drinkers
- 6.8 million current smokers
- 1.6 million regular users of illicit drugs

The use and misuse of licit and illicit substances is common among the British population. The majority of adults consume alcohol: 69% and 55% of men and women in England and Wales, respectively, are weekly drinkers[8]; 26% of British men and 18% of British women exceed the recommended limits for weekly alcohol drinking; and 7% of men and 4% of women may be classified as higher risk drinkers[b]. Smoking prevalence has fallen considerably over the past three decades: 22% of men and 20% of women in England and Wales over the age of 16 currently

Figure 1. Percentage of adults reporting substance use, 2009



Source: General Lifestyle Survey, Office for National Statistics; British Crime Survey

Alcohol: 16-65+ year olds who drank last week. *Smoking*: 16-60+ year olds who smoke cigarettes. *Any illicit drug*: 16-59 year olds reporting last month use of illicit drugs

[b]Consumption of over 50 units of alcohol per week for males, and over 35 units per week for females

smoke. In addition, the proportion of heavy adult smokers (an average of 20 or more cigarettes a day) has also fallen over this period; currently 7% and 5% of men and women in England and Wales, respectively, are heavy smokers.

An estimated 36% of the adult population in England and Wales have ever used an illicit drug and 5% have used illicit drugs in the last month. Class A drug use is less common: 15% have ever used a Class A drug, with 1% having used a Class A drug in the last month[9]. After cigarettes and alcohol, cannabis is by far the most commonly used substance among the general population; 4% of 16 to 59-year olds have used the drug in the last month.

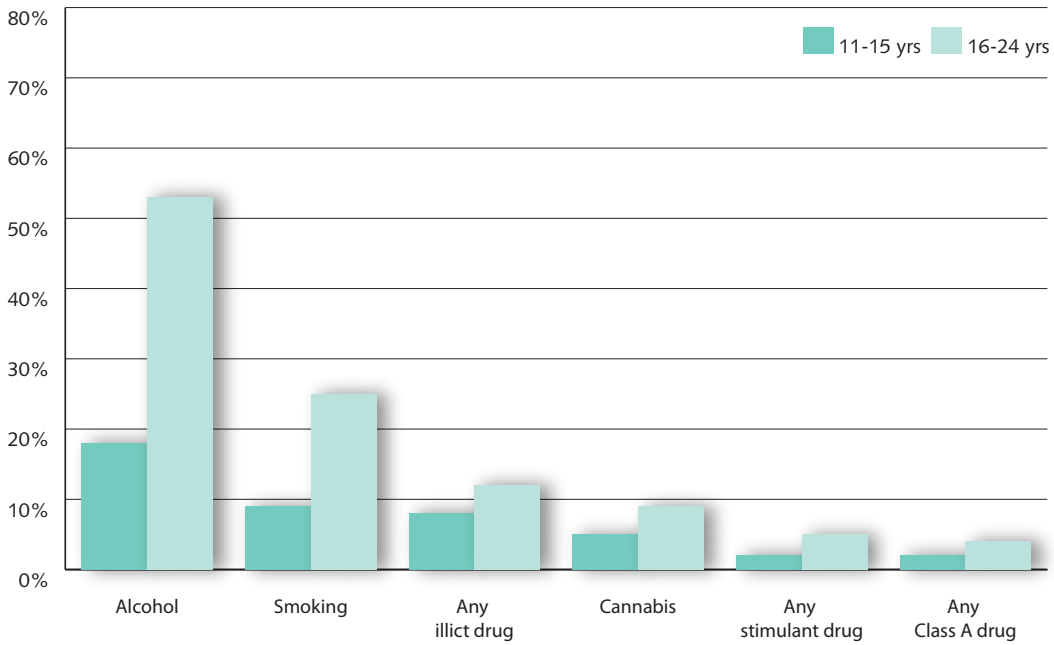
Patterns of substance use among young people

Among 6.6 million young people aged 16 to 24 in England and Wales there are an estimated:

- 3.5 million weekly alcohol drinkers
- 1.7 million current smokers
- 0.8 million regular users of illicit drugs

Young adults aged 16 to 24 years are more likely to use illicit drugs than older age groups; 41% have ever used an illicit drug and 20% have used illicit drugs in the last year. Among younger age groups, 22% of 11 to 15-year olds have ever used an illicit drug and 15% have used an illicit drug in the past year. After cigarettes and alcohol, cannabis is the most commonly used substance by young people; 9% of 16 to 24-year olds and 5% of 11 to 15-year olds have used cannabis in the last month. Among 16 to 24-year olds, 5% reported using 'skunk'.

Figure 2. Percentage of young people reporting substance use, 2009



Alcohol: drinking during the past week. *Smoking*: current smokers (16-24yrs) and those who smoked in the past week (11-15yrs). *Any illicit drug*: those reporting use in the past month. *Cannabis*: those reporting use in the past month. *Any stimulant drug*: reported use in the past month, includes powder cocaine, crack cocaine, ecstasy. amphetamines, amyl nitrate and methamphetamine. *Any Class A drug*: reported use in the past month, includes powder cocaine, crack cocaine, ecstasy, LSD, magic mushrooms, heroin, methadone and methampethamine

Source: General Lifestyle Survey, Office for National Statistics; Smoking, drinking and drug use among young people in England in 2009, Health and Social Care Information Centre

The British Crime Survey 2009-10 examined use of khat and recently classified drugs finding that in the last year among 16 to 24-year olds, 1% had used Spice or a synthetic cannabinoid, 1% had used BZP, 0.5% had used GBL/GHB and 0.5% had used khat.

1.4 Dependence

There are also problems of dependence among the general population. Dependence is currently defined by the World Health Organisation International Classification of Diseases (ICD-10) as a cluster of behavioural, cognitive, and physiological phenomena which typically includes a strong desire to take the substance, difficulties in controlling its use despite harmful consequences, a higher priority given to drug use than other activities, increased tolerance, and sometimes a physical withdrawal state. The general principles of dependence do not apply equally to all psychoactive substances[10] and the characteristics and severity of symptoms and signs of the dependence syndrome vary by drug. In addition, harmful use may occur without a substance causing physical or psychological dependence. Ghodse notes that "dependence is not just a manifestation of a specific drug effect, but is a behaviour profoundly influenced by the individual personality and the environment, as well as by the specific drugs that are available"[11]. The main concepts associated with drug dependence are described below.

Drug dependence

Psychological dependence

A core component of the definition of drug dependence. Described by Ghodse (2010) as "an overriding compulsion to take the drug even in the certain knowledge that it is harmful, and whatever the consequences of the method of obtaining it" (page 7).

Physical dependence

Not all drugs cause physical dependence, but for those that do, sudden drug withdrawal is followed by a withdrawal syndrome, characteristic of the psychoactive substance taken. Whether an individual develops physical dependence varies from person to person and depends on regular administration of the drug (e.g. daily), in sufficient dosage over a period of time (e.g. a number of years).

Withdrawal syndrome

A specific array of symptoms and signs that follow sudden withdrawal of a drug that causes physical dependence.

Tolerance

Following repeated administration of some drugs, users may become less sensitive to the effects of the drug and over time require larger doses to achieve the same effects previously produced at lower doses. Therefore, they may be able to tolerate much higher doses than individuals who have not previously been exposed to the drug. Tolerance does not necessarily develop equally or at the same rate for all the effects of a drug.

Among 33.7 million adults aged 16 to 64 in England there are:
- 2.4 million adults who show signs of dependence on alcohol
- 1.4 million adults who show signs of dependence on illicit drugs

Among the general population, alcohol dependence affects 9% of men and 3% of women in England and 24% of adults drink alcohol in a way that puts them at risk of physical and psychological harm[12]. There is a continuing debate about how best to characterise nicotine dependence among tobacco smokers[13]. One indicator of dependence is how soon after waking smokers smoke their first cigarette. Among the general population, 15% of smokers have their first cigarette within the first five minutes of waking[14].

General population surveys estimate that around 3% of adults in England show signs of dependence on illicit drugs, most frequently cannabis (4% of men and 2% of women)[12]. For other illicit drugs, 0.4% show signs of dependence on cocaine and 0.1% each show signs of dependence on crack, ecstasy and heroin/methadone. However, general population surveys significantly underestimate the numbers of dependent drug users; based on estimates of opiate and crack cocaine use, there are over 320,000 opiate and/or crack cocaine users in England (equivalent to approximately 0.9% of the population).

1.5 Substance-related deaths

Alcohol

Alcohol use has been linked to the development of a number of chronic conditions and acute consequences, ranging from cancer to road traffic accidents. There were 7,075 alcohol-related deaths in England and Wales in 2009, if only the causes of death regarded as being most directly due to alcohol consumption are included[c]. There were more alcohol-related deaths among men than women; 4,649 deaths among men and 2,426 deaths among women.

Using a broader definition of alcohol-related deaths, the North West Public Health Observatory estimated that in 2005 there were 14,982 deaths attributable to alcohol consumption[15], representing 3% of all deaths in England for that year. Alcohol-related deaths varied by age, and young people were disproportionally affected by their alcohol use. For example, among males it was estimated that 27% of deaths among 16-24 year olds were attributable to alcohol consumption.

Smoking

Smoking-related deaths have been attributed to a range of diseases including cardiovascular disease, respiratory disease (including chronic obstructive pulmonary disorder) and lung cancer. Nineteen per cent of all deaths in the UK were estimated to be directly attributable to smoking in 2005[16]. In 2009, an estimated 81,400 deaths among adults aged 35 and over were attributable to smoking, representing 18% of all deaths for that year[17].

Illicit drugs

The majority of recorded drug-related deaths are related to opioid use and mostly occur among injecting drug users[18]. In 2009[19], there were 2,878 deaths in England and Wales related to drug poisoning and 1,876 drug misuse deaths[d]. Of deaths from drug-related poisoning, 880 involved

[c] Based on the current Office for National Statistics definition of alcohol-related deaths

[d] Defined as deaths where the underlying cause is drug abuse or drug dependence or deaths where the underlying cause is drug poisoning and where any of the substances controlled under the Misuse of Drugs Act (1971) are involved

heroin or morphine, 378 deaths involved methadone, 261 involved benzodiazepines and 202 involved cocaine. An alternative source of data on drug-related deaths is published by the National Programme on Substance Abuse Deaths (np-SAD). In 2009, there were 1,524 drug-related deaths in England reported to the programme[20]. The main cause of death was accidental poisoning and heroin/morphine were the principle substances implicated in deaths.

However, neither of these sources take into account other deaths related to illicit drug use such as those from blood borne infections, violent assaults, and suicides. For example, deaths from AIDS among injecting drug users accounted for 8% of all AIDS deaths in England and Wales in 2009[21].

1.6 The economic costs of substance use

Health care

Studies of the health-related costs of substance use indicate an annual spend of nearly £3bn on alcohol misuse in England[22], in the region of £5 billion on smoking-related ill health in the UK[16], and just under £500m on Class A drug use in England and Wales[23]. Hospital admissions arising from diseases or conditions directly and indirectly related to substance use make a large contribution to the costs to the NHS. The most recent data available indicates that each year there are over one million admissions related to alcohol consumption[24], and over 45,000 admissions attributable to smoking among people over 35[17]. In relation to illicit drug use, there are around 5,800 admissions for drug-related mental health and behavioural disorders[e] each year and over 11,500 admissions for drug poisoning[25]. These statistics, however, do not take into account other types of drug-related hospital admissions, for example, those related to respiratory disease, HIV-related illness, chronic liver disease associated with hepatitis C infection and injection site infections. In addition, older people who continue to use drugs and require the support of health services are emerging as an important but relatively under-researched population.[26]

Substance-related crime

Although it is difficult to estimate the number of offences that are related to alcohol or illicit drug use, it is well established that there is a link between substance use and acquisitive crime. The 2005 Offending Crime and Justice Survey[27] included questions on offending among young people aged 10 to 25 years related to alcohol and illicit drug use. For 18% of all violent offences and 10% of all property offences, offenders were under the influence of alcohol only. For 3% and 2% of all violent offences and all property offences, respectively, offenders were under the influence of illicit drugs only.

In 2008, the Home Office calculated that the costs associated with alcohol-related crime were between £8.75bn and £14.78bn[28]. These costs were mainly incurred as a result of less serious wounding, criminal damage, sexual offences and causing death by dangerous driving. The costs associated with drug-related crime were last updated in 2003-04 and estimated at £13.32bn[23]. The estimation of these costs included the following offence categories: fraud, burglary, robbery and shoplifting.

[e]Including admissions for acute intoxication, harmful use, dependence syndrome, withdrawal state, psychotic disorder, amnesic syndrome and other disorders

1.7 The updated tables

The basic layout of the updated tables follows the 'framework for typology of dangerousness of drugs' as outlined in the 2003 report, focusing on the acute and chronic adverse effects associated with each substance and factors that mediate or moderate the risk.

Following the format of the 2003 report, evidence on specific harms associated with different contextual factors related to drug use (different routes of administration, polypharmacy, and age and gender-related factors) have been included in the updated tables for each specific drug, and as a set of new tables addressing these as cross-cutting themes across the included substances. Two additional tables also consider the potential health risks arising from adulterants.

PART TWO
THE UPDATED TABLES

1. Alcohol

1.1 Acute adverse effects associated with the use of alcohol

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Large doses (blood alcohol concentrations greater than 3-4 g/L) may lead to: • coma and death • asphyxiation • respiratory depression Heavy drinking episodes associated with: • acute pancreatitis • cardiovascular deaths Increased mortality associated with accidents including: • road traffic accidents • drowning • deaths from fire • workplace accidents • falls	Violence and injuries • increased morbidity associated with violence (e.g. assaults) and accidents Physiological responses • low blood sugar (hypoglycaemia) • raised blood pressure, irregular heartbeat (arrhythmia) • sleep disturbance • decrease in sharpness of vision, hearing, and other senses • decreased coordination and loss of balance (ataxia) • drowsiness, loss of consciousness • facial flushing • hypothermia • increased rate of urination (diuresis), dehydration Gastrointestinal complications • gastritis, vomiting and acid reflux from acute intake of large amounts of alcohol • diarrhoea, nausea • rupture of the oesophageal mucosa; associated with vomiting after drinking (Mallory-Weiss tears)	Organic/neurological • impairment in memory, planning and judgement (psychomotor and cognitive impairment) • temporary loss of the ability to form new memories (anterograde amnesia) • memory blackout Personality/mood • reduced inhibitions • argumentative and aggressive behaviour • thoughts about suicide (suicidal ideation) may be intensified with alcohol use

1. Alcohol

1.2 Chronic adverse effects associated with the use of alcohol

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
Violence and injuries • increased risk of premature mortality from accidents, suicide and violence Liver disease • alcoholic hepatitis • liver cirrhosis Cardiovascular complications • disease of the heart muscles (cardiomyopathy) • coronary heart disease • abnormal heart rhythm (arrhythmia) Neurological complications • haemorrhagic stroke Cancers • mouth and throat (lip, oral cavity, pharynx and larynx) • digestive system (oesophagus, colon and rectum) • liver • breast Gastrointestinal complications • gastrointestinal bleeding • pancreatitis • gastritis • peptic ulcer disease, evidence is inconclusive but higher prevalence in patients with liver cirrhosis • enlarged and damaged veins in the lower oesophagus	Neurological complications • risk factor for first epileptic seizure Infectious diseases • risk factor for incidence and re-infection of tuberculosis Muscle, joint and bone • damage to the peripheral nervous system (peripheral neuropathy/polyneuropathy) • muscle weakness and pain (myopathy) Cardiovascular complications • high blood pressure (hypertension) • alcohol-related heart failure (alcoholic cardiomyopathy) Gastrointestinal complications • pancreatitis • gastritis • peptic ulcer disease, evidence is inconclusive but higher prevalence in patients with liver cirrhosis • enlarged and damaged veins in the lower oesophagus Liver disease • fatty liver disease • alcoholic hepatitis • cirrhosis of the liver Reproductive disorders • disrupts the menstrual cycle and ovulation • can reduce chances of conception • long-term alcohol abuse has been linked to sexual dysfunction and impairment of sperm production in men Complications in pregnancy • spontaneous abortion • still birth • preterm delivery and decrease in length of gestation • decreased foetal growth and birth weight • fetal alcohol syndrome – a clearly-defined disorder particularly seen in heavy drinkers • fetal alcohol spectrum disorder – a more recent categorisation that acknowledges the likely wider impacts of varying levels of alcohol consumption on the developing foetus	Organic/neurological • neurobiological brain injury • alcoholic cerebellar degeneration • deficiency of vitamin B1 (Wernicke–Korsakoff syndrome) • memory loss, memory blackouts Personality/mood • psychotic symptoms during intoxication or withdrawal (including depression, paranoia and anxiety) • loss of self esteem	Dependence • a range of dependence issues, from mild through to moderate to severe: *moderate dependence* – characterised by raised level of tolerance, symptoms of alcohol withdrawal and impaired control over drinking; *severe dependence* – characterised by severe alcohol withdrawal and high tolerance; individuals may have experienced withdrawal fits or delirium tremens, and they may drink to avoid symptoms of withdrawal Withdrawal • withdrawal can be fatal • convulsions • tremors • anxiety • paranoia • hallucinations • sudden and severe mental or neurological changes (delirium tremens) Tolerance • tolerance to the toxic effects may not develop in parallel with tolerance to the central nervous system depressant effects – increases the likelihood of drug induced organ damage • increased capacity to metabolise alcohol (declines after several weeks of abstinence)

1. Alcohol

1.3 Factors that mediate and moderate harms associated with the use of alcohol

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE / DEVELOPMENTAL ISSUES*	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Route of administration • rare reports of intravenous use among polysubstance users Dose • risk of coma and death associated with bouts of heavy drinking	Concurrent use • link between cigarettesmoking and alcohol use • commonly used in combination with sedatives, opioid drugs, cannabis and amphetamines • alcohol used in combination with opioid drugs is a significant risk factor for overdose by respiratory depression • a metabolite (cocaethylene) is formed following concurrent use of alcohol and cocaine – toxic effects of this combination are commonly seen in cocaine related deaths	Availability • age limit of 18 on purchase • readily available from on and off-licensed premises • alcohol has become more affordable over the last two decades	Social context • alcohol use is perceived differently by different societies ('wet' versus 'dry' cultures or subcultures)	Developmental issues • alcohol use in early adolescence is a risk factor for later drug use • heavy drinking during adolescence is associated with cognitive deficits, with implications for learning and other cognitive abilities, that may worsen as drinking continues into late adolescence and young adulthood • early age of drinking onset is associated with an increased likelihood of developing alcohol abuse or dependence in adolescence and adulthood • heavy drinking in adolescence may have an adverse effect on reproductive development; suggestion that continued use into adulthood may affect reproductive functions	• inherited deficiency of a particular enzyme (ALDH2) causes the relatively high frequency of flushing in East Asian populations (a protective factor against alcohol use disorders) • genetic factors may influence the risk of individuals experiencing problems with alcohol use • people who are diabetic may become hypoglycaemic as a result of alcohol use	Not controlled under the Misuse of Drugs Act 1971

*For further duscussion on the effects of alcohol use from a developmental perspective, see Brown *et al* (2008).

2. Amphetamines*

2.1 Acute adverse effects associated with the use of amphetamines

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Excitation syndrome • abnormal heart rhythms (arrhythmias) associated with collapse/cardiac arrest leading to sudden death Vascular accidents • increase in blood pressure (hypertension) • stroke • heart attack (myocardial infarction) • cardiovascular shock	Acute intoxication • agitation/aggression • pupil dilation • headache • tremors and writhing movements of the body and limbs (dyskinesia) • nausea, abdominal cramps • dry mouth • sweating • anorectic effects, decreased appetite • increase in body temperature (hyperthermia) • increased breathing rate, blood pressure and heart rate (possible arrhythmia) • dizziness, tremor, irritability and confusion • hallucinations • convulsions Methamphetamine Acute intoxication • more pronounced central nervous system stimulant effects and longer duration of effect than amphetamine sulphate Lifestyle factors • use strongly associated with risky sexual practices	Organic/neurological • toxic delirium with amnesia • as stimulant effects dissipate users may experience drowsiness, reduced ability to concentrate, and/or judgement and learning impaired Personality/mood • low mood (dysphoria) • anxiety, depression • irritability, aggression Acute paranoid psychosis • psychotic reaction similar to acute paranoid schizophrenia (vivid visual, auditory, or tactile hallucinations, paranoid ideation possibly resulting in aggressive behaviour) • may develop after single or repeated ingestion of amphetamines • people with underlying mental health problems are at greatest risk

*Including amphetamine sulphate and methamphetamine.
For MDMA and related analogues, see table 3

2. Amphetamines

2.2 Chronic adverse effects associated with the use of amphetamines

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
Excitation syndrome • abnormal heart rhythms (arrhythmias) associated with collapse/cardiac arrest leading to sudden death Cardiovascular complications • inflammation of the blood vessels (vasculitis) • aortic dissection • cardiovascular shock Other complications • depression leading to suicide	Cardiovascular complications • cumulative risk of cardiac and coronary artery disease • abnormally high blood pressure in the arteries of the lungs (pulmonary hypertension) • inflammation of the blood vessels (vasculitis) • bleeding into and along the wall of the aorta, the major artery carrying blood from the heart (aortic dissection) Lifestyle factors • negative health effects from lack of food and sleep, such as lower resistance to disease Complications in pregnancy • use in pregnancy has been associated with low birth weight, prematurity and increased foetal morbidity • confounded by the impact of other situational, health and lifestyle factors, and polysubstance use	Organic/neurological • cognitive deficits associated with damage to the nervous system and brain (e.g. impairment of memory, learning and monitoring of complex goal-directed behaviour [executive function]) • behaviour stereotypes – mechanical hyperactivities, repetitive actions, stereotype motor phenomena (e.g. teeth grinding) Chronic paranoid psychosis • psychotic reaction similar to paranoid schizophrenia – hallucinations, paranoid ideation possibly resulting in aggressive behaviour, potentially reversible • incidence and severity of methamphetamine psychosis related to frequency of use and injection or smoking as the route of administration • symptoms usually resolve with abstinence, but case reports suggest some methamphetamine users may experience prolonged or recurrent psychosis, even after stopping use Personality/mood • irritability • suspiciousness • dysphoria • anxiety • paranoid psychosis • depression • restlessness • delirium • depersonalisation • feelings of persecution • lethargy Methamphetamine Personality/mood • user reports of physical aggression	Dependence • high abuse potential due to mood elevating properties • good evidence for an amphetamine dependence syndrome • typically occurs after a period of sustained regular use Withdrawal • rarely life threatening • symptoms may include depression (increasing risk of suicide), seclusiveness, craving, fatigue/exhaustion, weakness, lack of energy and sleep disturbance • psychotic symptoms may also be a feature of the methamphetamine withdrawal syndrome Tolerance • users may become tolerant to the euphorigenic, anorectic, hyperthermic and cardiovascular effects

2. Amphetamines

2.3 Factors that mediate and moderate harms associated with the use of amphetamines

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE / DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Route of administration • use by injection • smoking • crystalline hydrochloride form of methampheta-mine ('ice') is potentially more harmful than other forms due to relatively high purity and ease with which it can be smoked	Concurrent use • in combination with alcohol – increase in perceived total intoxication • in combination with cocaine – limited evidence but may have harmful cardiovascular effects (e.g. one case of vasospasm reported in the literature)	Availability • amphetamine use has declined since the mid-1990s • no evidence of increasing use of methampheta-mine in the UK, use remains low Purity • amphetamine purity low in UK at a mean of 8% (2009 data) • generally low methampheta-mine purity in the UK at a mean of 9% (2001–04 data)	Social context/ setting • amphetamine use combined with hot, crowded settings may result in overheating and/ or exhaustion	Age • most amphetamine users are young adults who primarily use the drug for a relatively short period of time	• chronic paranoid • psychosis • genetic predisposition to psychotic reaction	Misuse of Drugs Act 1971 Class A amphetamines prepared for injection, methamphetamine Class B oral amphetamines

3. MDMA and related substances*

3.1 Acute adverse effects associated with the use of MDMA and related substances

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Overheating/heat stroke (hyperthermia) • major acute symptom of MDMA-related toxicity that can lead to death • associated with serotonin syndrome, and complications including rhabdomyolysis, abnormal blood clotting (disseminated intravascular coagulation), kidney failure and liver failure Swelling of the brain (cerebral oedema) • caused by low sodium levels (hyponatraemia) secondary to water intoxication • propensity for women to be disproportionately affected Other complications • fatal cases of liver damage are rare • small number of case reports have linked the use of ecstasy with cerebrovascular accidents (e.g. stroke) • a few fatalities have been reported in the literature associated with the use of 'counterfeit ecstasy' containing paramethoxymethamphetamine (PMMA) and/or paramethoxyamphetamine (PMA) • many MDMA-related fatalities are attributable to polysubstance use (multiple drug toxicity)	Acute intoxication • elevated blood pressure and increased heart rate (palpitations) • nausea, vomiting • fatigue, dizziness and/or vertigo • overheating, dehydration • headache • dry mouth and throat • loss of appetite • difficulty with bodily coordination, muscle aches or tightness • agitation/aggression • convulsions Other complications • may inhibit orgasm in men and women, and male erection • examples of acute liver injury reported in the literature – may be secondary to hyperthermia or caused by direct drug toxicity • associated with risk taking in general, and sexual risk taking in particular • teeth grinding and clenching (bruxism)/teeth problems	Personality/mood • anxiety, panic attacks • confusion • depressive symptomatology • insomnia • restlessness • fatigue • anorexia • paranoia • visual and auditory hallucinations are rare – tend to be associated with high doses • suggestions that may have mild and transient effects on cognition after acute administration • individual or unpredictable psychotic episodes may occur • incorrect interpretation of emotions and other social cues 4-Methylthioamphetamine (4-MTA) Personality/mood • has a greater propensity to cause visual hallucinations than MDMA

*3,4-Methylenedioxymethamphetamine (MDMA) and related analogues, including 3,4-methylenedioxyamphetamine (MDA), 3,4-methylenedioxyethylamphetamine (MDEA), methylbenzodioxolylbutanamine (MBDB), 3-methoxy-4,5-methylenedioxyamphetamine (MMDA), 4-methylthioamphetamine (4-MTA)

3. MDMA and related substances

3.2 Chronic adverse effects associated with the use of MDMA and related substances

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
• not documented, limited evidence base	Immune function • emerging evidence that MDMA may have immunosuppressive properties – users report increased susceptibility to minor ailments including colds, flu, sore throats Other complications • possible liver damage	Organic/neurological • unclear whether long term use is associated with memory and learning (cognitive) impairment • growing evidence that chronic, heavy use is most strongly associated with subtle cognitive effects • unclear whether deficits reflect the use of MDMA or the combination of MDMA and other substances Personality/mood • repeated use may have long-lasting effects on mood and personality characteristics such as depression and anxiety, but evidence is inconsistent Animal studies • an excess of serotonin in the central nervous system (serotonergic toxicity) has been demonstrated in experimental animal studies of MDMA • inconsistent effects in humans – may result in increased risk of depression or other mental illness later in life but the equivalence is uncertain	Dependence • evidence for a dependence syndrome is limited • in cases of dependence, the psychological aspects of dependence appear to predominate Withdrawal • features of a withdrawal syndrome are not clearly defined and mainly based on user reports Tolerance • tolerance potential, but evidence is based on self-report

3. MDMA and related substances

3.3 Factors that mediate and moderate harms associated with the use of MDMA and related substances

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE / DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Route of administration • use by injection (rare) • MDMA powder may be snorted (insufflated) influence of set and setting has greater impact at a lower dose compared with hallucinogens Dose • as dose increases, pharmacological properties of the drug override the effect of set and setting • 'ecstasy' tablets may contain a combination of MDMA and related substances – others may not actually contain any MDMA	Concurrent use • in combination with cocaine – evidence from animal studies suggests an increased risk of neurotoxicity • in combination with alcohol – reduce perceived levels of intoxication but not associated impairments • in combination with cannabis – may potentially experience cumulative CNS impairment and may increase susceptibility to colds and flu Consecutive use • reports of using benzodiazepines or heroin to self medicate adverse effects (especially during the 'crash period')	Availability • poor availability of MDMA in the UK; most 'ecstasy' tablets don't contain MDMA • market is generally well informed and may shift patterns of use depending on: rumours or evidence regarding pill content; media campaigns (including reports on inconsistencies in research findings and potential uses of MDMA in psychotherapy); or availability of drugs likely to act as MDMA/ ecstasy substitutes (e.g. mephedrone) Purity • MDMA powder has become increasingly popular due to perceived higher levels of purity, but little forensic evidence to support this conclusion	Social context/ setting • overcrowding and overheating at unregulated dance events may increase risk of hyperthermia or dehydration	Age • no clear evidence on relationship between uptake of ecstasy and use of other drugs or drug careers	• individual vulnerability for acute physical problems include previous history of epilepsy, and cardiovascular or cerebrovascular disease • 'poor metaboliser' status – two phenotypes in the population of the enzyme that metabolises ecstasy – influence of metaboliser status is not known • psychological vulnerability increased with previous or current history of psychiatric illness, or family history	Misuse of Drugs Act 1971 Class A MDMA and MDA family (MDMA, MDA, MDEA, MBDB, MMDA, 4-MTA)

4. Anabolic agents*

4.1 Acute adverse effects associated with the use of anabolic agents

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
• few recorded cases in the UK of mortality directly linked to AAS use	Injecting complications • users may have additional risks from injecting, including damage to the injection site and surrounding structures Clenbuterol Acute effects • anxiety • palpitations • shortness of breath • abnormal heart rhythm (atrial fibrillation) • increased heart rate • heart attack	Personality/mood • anti-social behaviour • aggression • hypomania • mania • paranoia • psychosis • violence

*Anabolic-androgenic steroids (AAS), growth hormone, clenbuterol and (human and non-human) chorionic gonadotropin (hCG)

4. Anabolic agents

4.2 Chronic adverse effects associated with the use of anabolic agents

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
Vascular complications • heart attack • sudden cardiac death • stroke Liver damage • a small number of deaths have been attributed to liver injury from AAS use	Vascular complications • high blood pressure (hypertension) • altered lipid metabolism • heart attack (myocardial infarction) • stroke • blood clot formation (thrombosis) • thickening of the heart muscle (cardiac hypertrophy) Liver damage • acute liver injury associated with particular type of anabolic steroid (17α-alkylated oral steroids) • chronic liver damage (a few cases reported of benign liver tumours, blood-filled cavities in the liver [peliosis hepatis] and liver cancer) Other complications • acne (occasionally a severe form) • disruption of the normal pattern of growth and behavioural maturation in adolescence (e.g. stunting of height, virilization) • tendon/ligament damage thought to be due to disproportionate growth of muscle • scalp hair loss/growth of body hair • disordered sleep • bacterial and fungal infections as a result of poor injecting technique or contaminated drugs • growth hormone users may develop some of the clinical features of a chronic metabolic disorder, acromegaly Males Potentially reversible effects: • inhibiting effect on normal testicular function – reduced testosterone and sperm production, shrinking of the testicles (testicular atrophy) • prostate cancer (based on a few case reports) • erectile dysfunction Potentially irreversible effects: • growth of the glandular breast tissue (gynaecomastia) • scalp hair loss Females Effects are potentially irreversible: • masculinising/virilization – growth of body and facial hair, deepening of voice, clitoris enlargement, increased libido, reduced breasts • scalp hair loss • menstruation irregularities or amenorrhoea • reduced fertility • AAS are teratogenic – use of these and other anabolic agents are contraindicated in pregnancy	Personality/mood • anti-social behaviour • aggression • depression • hypomania • mania • paranoia • psychosis • suicide • violence	Dependence • some evidence to suggest dependence potential • positive psychological effects experienced may reinforce the continuing use of steroids for some users Withdrawal • unclear, but depression has been noted as common when on an 'off cycle' or ceasing use • may persist for many months and similar to that seen in clinical populations with decreased functional activity of the sex glands (hypogonadism)

4. Anabolic agents

4.3 Factors that mediate and moderate harms associated with the use of anabolic agents

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE / DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Route of administration • majority of users inject AAS and use oral AAS Dose • AAS users often consume 10-100 times the therapeutic dose • cycling is where AAS are taken for a period of time (e.g. 6–12 weeks) known as an 'on cycle', followed by a similar period of steroid-free training known as an 'off cycle' • cycling is practised to prevent tolerance to the AAS, reduce the risk of side effects from prolonged use, and allow the hypothalamic-pituitary-gonadal axis time to resume normal function • a minority (such as some competitive bodybuilders) may use the drugs on an almost continuous basis; anecdotal reports suggest that some individuals continue to use various drugs during the 'off cycle'	Concurrent use • users will typically take two or more different AAS at the same time in a practice known as 'stacking' which, based on the different effects AAS can exert, users believe will have specific, additional or synergistic effects • users may also take a combination of ancillary drugs Examples include: • tamoxifen – to prevent or reduce gynaecomastia • human chorionic gonadotrophin – to stimulate secretion of testosterone • diuretics – to counteract fluid retention caused by AAS and sharpen definition of skeletal muscle contours • some evidence of crossover to stimulant use	Availability • majority of products obtained from the illicit market • available in some gyms but internet sites are increasingly important for the distribution of anabolic agents and related drugs Purity • concerns over quality and safety of drugs from the illicit market – suggestion that falsified, substandard and counterfeit products are common (including microbial contamination of injectable drugs)	Social context/ setting • gyms • used primarily by males • may use due to their participation in sport (including bodybuilding); for occupational reasons (e.g. door supervisors, first responders); to enhance body image: to get 'bigger', 'look better'; or to prevent or treat disease (such as anti-ageing or HIV-related wasting)	Developmental issues • disruption of the normal pattern of growth and behavioural maturation in adolescence (e.g. stunting of height and virilization in case of AAS) • AAS are teratogenic; use of these and other anabolic agents are contraindicated in pregnancy	• tendency towards aggression and violence in some users with aggressive personalities	Misuse of Drugs Act 1971 Class C AAS (named compounds and generic definition*), human growth hormone, recombinant human growth hormone, clenbuterol and human chorionic gonadotropin (hCG), non-human chorionic gonadotropin, Zeranol, Zilpaterol

*Exempt from the prohibition on possession for personal use (including import and export) when in the form of a medicinal product

5. Cannabis*

5.1 Acute adverse effects associated with the use of cannabis

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
• no cases of fatal overdose have been reported • no confirmed cases of human deaths	Acute intoxication • irritant effects of smoke on the respiratory system (coughing, sore throat and bronchospasm among people with asthma) • facial flushing • abdominal pain, nausea, vomiting • can cause an increase in heart rate (tachycardia) and in some cases increased blood pressure (hypertension) • difficulty in motor co-ordination and performance Synthetic cannabinoids • not documented, limited evidence base	Organic/neurological • perceptual distortion (hallucinations) • amnesia/forgetfulness • confusion of thought processes, impaired judgement Personality/mood • the effects of cannabis upon mental state vary considerably between individuals; determined by dose, route of administration, expectations, concomitant use of other drugs, emotional state, and psychiatric illness: – temporary psychological distress (especially naive users) – low mood (dysphoria) – anxiety – confusion – drowsiness – depression – panic attacks – agitation – symptoms indicative of a persistent and pervasive elevated (euphoric) or irritable mood (hypomanic symptoms) – short-lived and reversible psychotic reaction Synthetic cannabinoids Organic/neurological • suggestion that overdose could include significant alterations in mental state with paranoia and perceptual distortions

*Cannabis (*cannabis sativa*) and synthetic cannabinoids

5. Cannabis

5.2 Chronic adverse effects associated with the use of cannabis

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
Cancers • no conclusive evidence that cannabis causes cancer • cannabis use may be an important risk factor for the development of respiratory cancers but the relationship is unclear* Chronic respiratory disease* • chronic bronchitis • lung damage • number of reports in the literature of an association between cannabis use and bullous lung disease in relatively young users	Cancers • no conclusive evidence that cannabis causes cancer Immune function • evidence for the effects of cannabis on human immune function is limited Complications in pregnancy • like tobacco, cannabis use in pregnancy may be harmful to foetal development; studies show a consistent association between cannabis use in pregnancy and reduced birth weight – though less so than as a result of tobacco smoking during pregnancy • some reports that children born to women who have used cannabis in pregnancy may face mild developmental problems; however, the evidence is mixed and confounded by the other situational, health and lifestyle factors and polysubstance use in this population e.g. cannabis users are more likely to use tobacco, alcohol and other illicit drugs during pregnancy Reproductive disorders • use can inhibit reproductive functions and disrupt ovulation, sperm production and sperm function Other complications • persistent sore throat	Organic/neurological • no evidence of structural change in brains of heavy long term cannabis users • no severe or grossly debilitating impairment in cognitive function (subtle impairment in higher cognitive functions of memory, learning processes, attention and organization and the integration of complex information – may or may not be reversible after abstinence) Personality/mood • evidence that early initiation and regular, heavy cannabis use is associated with a small but significantly increased risk of psychotic symptoms and disorders in later life • complex association between cannabis use and schizophrenia – some evidence that use may exacerbate psychotic symptoms and is linked with relapse but it is unknown whether this is a universal risk or due to differences in individual vulnerability • insomnia, depression, aggression, anxiety • inconsistent and mixed evidence for whether heavy, chronic cannabis use is associated with a persistent 'amotivational syndrome' characterised by social withdrawal and apathy	Dependence • good evidence for a cannabis dependence syndrome • frequent, heavy users are at the greatest risk of dependence Withdrawal • irritability • anxious mood • physical changes (tremor, perspiration and nausea) • sleep disturbance Tolerance • tolerance to psychoactive and physical effects unlikely to occur unless there is sustained heavy exposure Synthetic cannabinoids Withdrawal • some evidence of a withdrawal syndrome among heavy users Tolerance • suggestion that users may develop tolerance quickly

*Studies of the harms associated with cannabis use are limited by confounding as many users smoke tobacco as well as cannabis, or use tobacco as vehicle for smoking cannabis resin. Although tobacco smoke and cannabis smoke are known to contain a similar range of mutagens and carcinogens, actual exposure to these compounds may differ between tobacco and cannabis users in terms of the frequency and duration of use, and because of factors such as the depth of inhalation

5. Cannabis

5.3 Factors that mediate and moderate harms associated with the use of cannabis

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE / DEVELOPMENTAL ISSUES*	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Route of administration • smoking • oral consumption – makes dosage difficult to regulate and unpleasant reactions more difficult to avoid • overall benefits and harms of the use of alternative delivery systems for inhalation, such as through vaporisation, have not been well studied Dose • health effects of increases in the potency of cannabis products are not clear; may depend on the impact on routine use, however there is evidence of binge use among some users increasing the risk of dependence and psychotic symptoms	Concurrent use • smoking with tobacco	Availability • three products commonly available – cannabis resin (hash), traditional imported herbal cannabis (marijuana) and typically higher potency forms of herbal cannabis (e.g. sinsemilla, 'skunk', homegrown) • increase in market share of sinsemilla, 'skunk', and homegrown forms of herbal cannabis suggests that cannabis users are now exposed to higher potency products • widely available in the UK and internationally	Social context • use has declined over the last decade • used across wide range of social and age contexts • perceived therapeutic use (pain relief, anti-nausea) • possible self-medication among psychiatric patients; e.g. people with schizophrenia, or its symptoms, may use cannabis to cope with the negative symptoms associated with schizophrenia, or to suppress the side-effects of antipsychotic medication • widely used by opiate and crack cocaine users • sole illicit drug used by a proportion of the population	Developmental issues • suggestion that regular use may encourage users to progress to other forms of drug abuse; the likelihood of this occurring is more related to the lifestyle and personality of the individual and access to sources of other illicit drugs than the effect of cannabis itself	• increased risk of experiencing psychotic symptoms in vulnerable individuals e.g. those with a personal or family history of schizophrenia • use may precipitate relapse of schizophrenia • use may adversely affect the course of schizophrenia • stimulating effects on the cardiovascular system of the major psychoactive compound in cannabis (THC) can be detrimental to individuals with cardiovascular or respiratory disease	Misuse of Drugs Act 1971 Class B cannabis, cannabis resin, synthetic cannabinoids

6. Cocaine*

6.1 Acute adverse effects associated with the use of cocaine

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Acute complications • toxic reactions (e.g. cardiovascular complications) are not predicable from the route of administration, quantity taken, an individual's pattern of drug use, or blood concentrations of cocaine (or its metabolites) • injection of cocaine powder or crack cocaine is associated with a greater risk of death than infrequent, intranasal use of cocaine powder alone; appears to be linked to factors associated with injecting (such as more frequent use and higher levels of cocaine dependence) rather than the route of administration per se Vascular complications • abnormal heart rhythms (arrhythmias) • heart attack • inflammation and injury to the intestines (mesenteric ischaemia) • stroke Allergic reaction from intravenous use of cocaine • based on anecdotal citations – possibly caused by additives in street cocaine Excited delirium syndrome • characterised by hyperthermia, delirium and agitation • associated with cardiac/respiratory arrest and subsequent death	Cardiovascular complications • increase in blood pressure • accelerated heart rate • abnormal heart rhythms (supraventricular/ventricular tachycardia, torsade de pointes) • increased risk of heart attack, particularly in the first hour after use Respiratory complications • chest pain • shortness of breath • rapid breathing Neurological complications • stroke • convulsions Other complications • hyperthermia • muscle spasms, tremor • abdominal pain, nausea, vomiting • insufficient blood flow (ischaemia) • bleeding (haemorrhage) • liver damage Genitourinary • increased sexual appetite and desire	Personality/mood • sleep disturbance • anxiety • paranoia • grandiosity • transient psychotic reactions • hallucinations (visual, auditory and tactile) after large doses • aggression and possible violence (especially associated with crack cocaine use)

*Cocaine hydrochloride (e.g. cocaine powder) and cocaine base (e.g. crack cocaine and freebase cocaine)

6. Cocaine

6.2 Chronic adverse effects associated with the use of cocaine

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
Cardiovascular complications • increased risk of cardiovascular disease through toxic effects on cardiovascular system (including premature atherosclerosis, vasospasm and thrombus formation) • heart attack • heart failure • abnormal heart rhythms (arrhythmias) • aortic dissection • inflammation and injury of the heart muscle (endocarditis, cardiomyopathy) • sudden death	Vascular complications • increased risk of cardiovascular disease through toxic effects on cardiovascular system • abnormally high blood pressure in the arteries of the lungs (pulmonary hypertension) • inflammation and injury of blood vessels (vasculitis) Neurological complications • stroke • inflammation and injury of the blood vessels of the brain (cerebral vasculitis) Renal complications • kidney failure – commonly associated with rhabdomyolysis Lifestyle factors • anorectic effect – may contribute to malnutrition and weight loss • chronic use diminishes sexual appetite and ability – reversible on stopping use Localised effects • dental erosions • perforation of the nasal septum • chronic rhinitis • loss of sense of smell • nosebleeds Complications in pregnancy • premature rupture of the membranes and placental abruption associated with use during pregnancy • effects of cocaine exposure may persist into childhood; suggestion that may impact on behaviour problems, attention, language and cognition • situational, health and lifestyle factors and polysubstance use in this population may also affect pregnancy outcomes	Personality/mood • anxiety, depression • obsessional rituals/preoccupation, repetitive behaviours • sleep disturbance (decrease in quantity and quality of sleep) • irritability, restlessness • auditory hallucinations • paranoid delusions and psychosis • hyperexcitability • exhaustion • aggression and possible violence (especially associated with crack cocaine use) Toxic syndrome • psychotic reaction similar to acute paranoid schizophrenia and psychoses with vivid auditory and tactile hallucinations, picking and excoriation of skin, delusions of infection from parasites, paranoid ideation Neurological • studies have shown that chronic cocaine use may contribute to cognitive impairments in the group of processes involved in the learning, control and monitoring of complex goal-directed behaviour (executive function) • may include deficits in memory function and inhibitory control	Dependence • good evidence for a cocaine dependence syndrome • a minority of users may exhibit cocaine dependence soon after onset of cocaine use (in the first 1-2 years of use) – risk is greater among those who smoke crack cocaine and those who begin use at an earlier age Withdrawal • symptoms may be mild to moderate but type and severity vary from person to person: – craving – exhaustion/lack of energy, fatigue – over-eating – depression – low (dysphoric) mood – unpleasant dreams – insomnia or hypersomnia, psychomotor retardation – agitation, irritability – anxiety, restlessness, – aggression Substance specific Withdrawal • craving – possibly of a greater magnitude for crack cocaine as compared to that for cocaine powder

6. Cocaine

6.3 Factors that mediate and moderate harms associated with the use of cocaine

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE / DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Route of administration • higher acute risk of death associated with injection of cocaine or smoking crack cocaine than intranasal use of cocaine powder – due to rapid increase in brain levels of the drug and route specific factors • injection of crack cocaine or cocaine powder – linked to risky injecting practices (such as frequent injection), which increase the risk of acquiring HIV, hepatitis C virus and bacterial infections	Concurrent use • a metabolite (cocaethylene) is formed following concurrent use of alcohol and cocaine – toxic effects of this combination are commonly seen in cocaine related deaths • concurrent use of cocaine and heroin (speedball) frequently mentioned in fatal emergency room admissions Consecutive use • reports of use of heroin after cocaine to manage negative effects after prolonged use • chronic use of cocaine may be a risk factor for use of heroin	Availability • last few years have seen the emergence of cheaper, more heavily adulterated, cocaine powder • when adjusted for purity, the price of cocaine powder has almost doubled since 2003 Purity • relatively low street level purity of cocaine powder and crack cocaine – mean 20% and 27% respectively (2009 data)	Social context/ setting • cocaine powder and crack cocaine likely to be used in very different social settings • crack cocaine use most commonly associated with existing opiate and crack cocaine users • cocaine powder more widespread and used functionally in both employment and social settings	Age • evidence that early onset (before age 18) of other illicit drug use (e.g. cannabis) increases likelihood of progression to cocaine use	• for individuals with pre-existing ischaemic heart disease, cocaine can have an apparently sympathomimetic effect on the heart – increasing myocardial oxygen demands to the extent that angina pains occur and sometimes heart attack • snorting or smoking can exacerbate asthma • significant exacerbating effect on individuals with pre-existing mental health problems	Misuse of Drugs Act 1971 Class A cocaine

7. The dissociative anaesthetics, ketamine and phencyclidine*

7.1 Acute adverse effects associated with the use of dissociative anaesthetics

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Acute complications • death is more often a result of accidents due to loss of coordination/control, disassociation and analgesia (e.g. jumping from heights, road traffic accidents, drowning) • risk of respiratory depression Ketamine Acute complications • limited evidence base, but low risk of mortality associated with the medicinal use of ketamine • rare reports of overdose deaths from heart attack or respiratory problems • majority of fatalities have been attributed to polysubstance use (multiple drug toxicity) PCP Acute complications • substantially more toxic than ketamine • death as a result of hyperthermia, convulsions	Acute intoxication • increased heart rate and respiration • loss of consciousness, coma • muscle jerking, repetitive movements, outbursts (automatic behaviour) • gastric/stomach pain • many effects are polarised among users (i.e. reports of opposing responses in different individuals) Ketamine Injury • increased risk of injury from jumping from heights, road traffic accidents and drowning; associated with loss of coordination/ temporary paralysis and/or dissociative effects (e.g. depersonalisation, derealisation and reduced perception of pain) PCP Acute intoxication • increase in body temperature (hyperthermia) • stroke • respiratory arrest • nausea, vomiting • loss of coordination (ataxia) • hypersalivation	Organic/neurological • hallucinations, distorted sensory perception • impaired attention, memory and learning • altered body perception • impairments of cognitive function and verbal fluency Personality/mood • confusion • depersonalisation • derealisation • panic attacks, agitation, paranoia • delirium • depression • night terrors • behavioural effects resembling certain symptoms of schizophrenia • extreme loss of motor skills (catatonia) PCP Organic/neurological • toxic psychosis (catatonia or paranoia)

*Ketamine and phencyclidine (PCP)

7. The dissociative anaesthetics, ketamine and phencyclidine*

7.2 Chronic adverse effects associated with the use of dissociative anaesthetics

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
• very low risk of mortality	Ketamine Chronic complications • ketamine-induced ulcerative cystitis (marked thickening of the bladder wall and severe inflammation) has been described in clinical case reports; only following heavy use • vague abdominal pains (gastritis) PCP Chronic complications • no human evidence to suggest long term physical damage • evidence from animal studies of congenital malformations and reproductive disorders	Organic/neurological • memory impairment • prolonged hallucinations, flashbacks, persistent perceptual changes Personality/mood • night terrors • evidence of triggering depression post traumatic stress disorder, mania in susceptible individuals • may aggravate psychotic symptomatology Ketamine Organic/neurological • evidence from animal studies suggests that ketamine may accelerate nerve cell death in the brain – no evidence that such an effect occurs in humans • some evidence of cognitive impairments among regular, heavy users PCP Personality/mood • anorexia • insomnia • auditory hallucinations • disorientation • paranoid delusions	Ketamine Dependence • there have been few published reports of ketamine dependence, however, cases have been noted among regular, heavy users Withdrawal • no evidence to suggest withdrawal symptoms or syndrome Tolerance • evidence to support the rapid development of tolerance over regular repeated dosing PCP Dependence • evidence to suggest a dependence syndrome for PCP Withdrawal • some evidence to suggest withdrawal syndrome • craving • increased appetite • hypersomnia • depression

7. The dissociative anaesthetics, ketamine and phencyclidine*

7.3 Factors that mediate and moderate harms associated with the use of dissociative anaesthetics

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE / DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Ketamine Route of administration • intranasal use is most popular • by injection, among long-term users Dose • street dose is approximately 10-25% of the general anaesthetic dose (1 to 2 mg/kg racemic ketamine) • influence of set and setting has greater impact at a lower (street) dose • as dose increases pharmacological properties of the drug override the effect of set and setting • ketamine has a short half life and thus regular, sequential dosing occurs, thereby increasing related risks PCP Route of administration • smoked	Concurrent use • ketamine may commonly be used with other stimulants or alcohol • suggestion that the dissociative effects of ketamine may make users less aware of the effects of respiratory depression caused by other drug use (e.g. alcohol or opioids)	Ketamine Availability • majority found on the illicit market is diverted from legitimate sources • may be sold as MDMA in clubs PCP Availability • often taken unknowingly when sold in other illicit drugs • abuse not considered to have ever been a major problem in the UK	Ketamine Social context • has emerged as a mainstream club drug in recent years • has been marketed in clubs as a 'quick, fun high' but dissociative effects may prove disturbing for the inexperienced user • distinct subculture of older ketamine users has been identified – tendency for injecting use and use to achieve "greater understanding of the self or universe" PCP Setting • overcrowding and heat in dance environment may increase risk for hyperthermia	• Not documented, limited evidence base	• individual vulnerability for acute physical problems – previous history of epilepsy, cardiovascular or cerebrovascular disease • psychological vulnerability increased with previous or current history of psychiatric illness, or family history	Misuse of Drugs Act 1971 Class A PCP Class C ketamine

8. Gamma-hydroxybutyrate and gamma-butyrolactone*

8.1 Acute adverse effects associated with the use of GHB, GBL or 1,4-BD

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Acute complications • loss of consciousness – difficult to get dose right and solutions of GHB often vary in concentration • deaths solely caused by GHB appear to be rare – fatalities appear to be mostly in combination with alcohol or other central nervous system depressants	Acute intoxication • loss of consciousness • coma • respiratory and cardiac depression, bradycardia • hypothermia • nausea, vomiting • seizures • confusion • involuntary muscle twitching or spasm (myoclonus, dystonia) • breathing difficulties • agitation	• Limited evidence for the psychological/ psychiatric effects of GHB, GBL and 1,4-BD Personality/mood • agitation • combativeness

*Gamma-hydroxybutyrate (GHB), gamma-butyrolactone (GBL) and 1,4 butanediol (1,4-BD)

8. Gamma-hydroxybutyrate and gamma-butyrolactone

8.2 Chronic adverse effects associated with the use of GHB, GBL or 1,4-BD

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
Withdrawal • severe cases of withdrawal, including fatalities have been reported	• not documented	• not documented	Dependence • evidence of a dependence syndrome associated with heavy, frequent use • no dependence syndrome has been observed at low doses of GHB Withdrawal • examples in the literature of physical dependence evidenced by a withdrawal syndrome • anxiety • insomnia • increased heart rate (tachycardia) • hallucinations, delirium and psychosis • sweating • aches • abdominal pain • impotence • severe depression • reports of severe withdrawal symptoms (e.g. rapid onset of delirium) associated with unplanned detoxification

8. Gamma-hydroxybutyrate and gamma-butyrolactone

8.3 Factors that mediate and moderate harms associated with the use of GHB, GBL or 1,4-BD

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE / DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Route of administration • prepared as a liquid • small alterations in the manufacture of illicit GHB can result in the synthesis of GBL Dose • toxicity is dose dependent – small increase in dose can cause severe harms • GBL is absorbed more rapidly than GHB and has a faster onset of action	Concurrent use • use often involves concurrent use of other drugs such as alcohol or MDMA • in combination with alcohol – associated with increased agitation and aggressive behaviour • overdose in combination with stimulants has been associated with deeper, more prolonged coma, and longer recovery times	Availability • suggestion that GBL may be more easily acquired than GHB – use of GHB precursor chemicals is still allowed in products in the chemical industry	Social context/ setting • evidence of use among body-builders for proposed anabolic effects, although this category of users has decreased in recent years • emergence as a recreational drug is a relatively recent phenomenon; earliest reports of use date back to the 1990's • the use of GHB precursor chemicals, GBL and to a lesser extent 1,4-BD has increased over the last few years	• not documented	• not documented	Misuse of Drugs Act 1971 Class C GHB, GBL and 1,4-BD

9. Serotonergic hallucinogens*

9.1 Acute adverse effects associated with the use of serotonergic hallucinogens

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Acute complications • risk of injury and accidental death due to perceptual distortions and impaired decision making LSD Acute complications • one case of fatal overdose has been reported in the literature; associated with a high dose of LSD Psilocybin Acute complications • fatal poisoning due to mistaken identity of mushrooms	Violence and injuries • self harm, accidents or violence while intoxicated LSD Common effects • adrenergic `fight or flight` effects • tachycardia • flushing • dry mouth • sweating • exhaustion, tiredness, weakness Rare effects • ataxia • convulsions • hyperpyrexia Psilocybin Acute intoxication • nausea, vomiting, stomach pains – commonly due to mistaken identity of mushrooms • dizziness DMT Acute intoxication • nausea and vomiting	Personality/mood • dysphoria • unpleasant distortions in shapes and colours • frightening illusions, delusions; 'true hallucinations' in psychiatric terms (i.e. indicative of psychiatric morbidity) are very rare • anxiety, panic, depression • dizziness, disorientation • impaired concentration • frequent mood changes (emotional lability) • recall of psychologically troubling memories • depersonalisation and derealisation at high doses • short lived psychotic episode (hallucinations, paranoia) • precipitates relapses in schizophrenia

*Lysergic acid diethylamide (LSD), psilocybin, mescaline and N,N-dimethyltryptamine (DMT)

9. Serotonergic hallucinogens

9.2 Chronic adverse effects associated with the use of serotonergic hallucinogens

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
• limited evidence base	• no known physical dangers associated with long-term LSD use	Personality/mood* • persistence of low-level hallucinations, known as hallucinogen persisting perception disorder – rare • brief flashbacks or recollection of previous hallucinatory experience may occur days or months after use • depression • feelings of isolation • delirium Psychosis • uncertain whether drug induced condition or unmasking of a latent mental illness	Dependence • evidence suggests that few users of hallucinogens experience signs or symptoms of dependence Withdrawal • a withdrawal syndrome has not been identified Tolerance • tolerance develops rapidly to behavioural effects and sensitivity returns after comparable drug free interval, tolerance to cardiovascular effects less pronounced • cross tolerance between serotonergic hallucinogens

*Post-exposure

9. Serotonergic hallucinogens

9.3 Factors that mediate and moderate harms associated with the use of serotonergic hallucinogens

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE/ DEVELOPMENTAL ISSUES*	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Psilocybin Route of administration • poisoning due to mistaken identity of mushrooms	Concurrent use • may be combined with MDMA to heighten physical sensations • oral DMT may be combined with a variety of natural and synthetic monoamine oxidase inhibitors to simulate ayahuasca (an Amazonian 'plant medicine')	Availability • seasonal and localised availability of mushrooms • LSD generally available; use has declined over last few years • mescaline and DMT rarely available Purity • purity data not commonly available	Setting • risk of injury when consumed alone in potentially dangerous locations – e.g. near water (risk of drowning), on a high building (risk of falls)	Age • noted as a drug of early experimentation, but not of long-term use	• psychosis as a result of chronic use – uncertain whether drug induced condition or unmasking of a latent mental illness	Misuse of Drugs Act 1971 Class A LSD, psilocybin, DMT, mescaline

10. Nitrites*

10.1 Acute adverse effects associated with the use of nitrites

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Acute complications • death may be caused by a lack of oxygen (hypoxia) resulting in severe injury to red blood cells and reduction in the supply of oxygen to vital organs • may lose consciousness and die through choking on own vomit • 'sudden sniffing death syndrome' fatality caused by abnormal heart rhythms (cardiac arrhythmia) • some cases of death reported from direct oral consumption of nitrites	Acute intoxication • nausea • headache • loss of consciousness, sedation, anaesthesia • loss of coordination (ataxia), weakness (less common) Lifestyle factors • associated with high risk sexual practices Cardiovascular complications • profound hypotension (low blood pressure) • rebound tachycardia • flushed skin followed by vasoconstriction Other complications • rash around nose and mouth and contact dermatitis • irritation of the nose and throat • increased ocular pressure, blurred vision	Personality/mood • disorientation • distorted perceptions • delirium

*Amyl nitrite, butyl nitrite and isobutyl nitrite

10. Nitrites

10.2 Chronic adverse effects associated with the use of nitrites

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
Carcinogenic properties • use produces nitrosamine which is carcinogenic – however still to be determined whether formed in sufficient quantities to make the risk clinically significant Lifestyle factors • by facilitating unsafe sexual practices some evidence that use indirectly increases susceptibility to Kaposi's sarcoma in people who are HIV positive Immune function • limited evidence that immunologic function may be suppressed – use of nitrites has been associated with facilitating the transmission of HIV	Chronic medical problems • rash and irritation around the nose, mouth or other exposed areas • sinusitis Blood-related (haematological) complications • anaemia • difficulty circulating oxygen through the blood stream (methaemoglobinaemia)	Organic/neurological some evidence to suggest impairment to: • cognition • movement • vision • hearing	Dependence • no evidence for a dependence syndrome Withdrawal • no withdrawal syndrome documented Tolerance • evidence to suggest chronic, regular users may develop tolerance

10. Nitrites

10.3 Factors that mediate and moderate harms associated with the use of nitrites

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE/ DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Route of administration • inhaled – substance is an irritant	Concurrent use • use with alcohol and other central nervous system depressants may increase the risk of asphyxiation and death • anecdotal evidence to suggest may be used to increase the effects of other drugs, such as cannabis or MDMA • in combination with drugs used to treat erectile dysfunction (e.g. Viagra) – causes abnormally low blood pressure	Availability • amyl nitrite available on grey market • also available in shops and on mail order; may be sold as room odouriser	Social context • associated with risky sexual behaviour leading to increased risk of exposure to sexually transmitted infections Setting • risk of injury when consumed alone in potentially dangerous locations – e.g. near water (risk of drowning), on a high building (risk of falls)	Age • used mainly by older adolescents and adults, to enhance sexual function or the effects of other drugs	• people with HIV • people with poor general physical health • people with ocular conditions, particularly glaucoma	Not controlled under the Misuse of Drugs Act 1971 Amyl nitrite is regulated under the Medicines Act 1968

11. Novel synthetic drugs*

11.1 Acute adverse effects associated with the use of novel synthetic drugs

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Acute complications • substituted cathinones (primarily mephedrone) have been implicated in deaths in England and Scotland – however, with a limited evidence base the exact role of cathinones in causing or contributing to death is still to be determined • one case of fatal overdose reported in the international literature relating to the use of 2C series phenethylamines • one case of fatal overdose reported in the international literature relating to the use of tryptamine derivatives	Acute intoxication • few clinical data available for novel synthetic drugs, most data regarding harms are self-reported • chest pain is common feature of acute intoxication Substituted cathinones and piperazines Acute intoxication • consistent with sympathomimetic toxicity – agitation – palpitations – seizure – vomiting – sweating – headache – reduced appetite – severe vasoconstriction of extremities, leading to bluing of fingers or hands (cathinone users) 2C series phenethylamines Neurological complications • one case of damage to the blood vessels in the brain associated with persistent neurologic deficits reported in the international literature Tryptamine derivatives • not documented, limited evidence base	Substituted cathinones and piperazines Personality/mood • consistent with sympathomimetic toxicity – mood swings – anxiety – strange thoughts – irritability, confusion Substituted cathinones Organic/neurological • high doses may be associated with hallucinations and psychosis 2C series phenethylamines Organic/neurological • one case of acute intoxication associated with psychosis reported in the international literature Tryptamine derivatives Organic/neurological • hallucinations

*Substituted cathinones, piperazines, 2C series phenethylamines and tryptamine derivatives

11. Novel synthetic drugs

11.2 Chronic adverse effects associated with the use of novel synthetic drugs

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
• not documented	• not documented	• not documented	Substituted cathinones and piperazines Dependence • suggestion that similar to amphetamine in terms of abuse and dependence potential Tolerance • some evidence to suggest that substituted cathinone users may develop tolerance quickly

11. Novel synthetic drugs

11.3 Factors that mediate and moderate harms associated with the use of novel synthetic drugs

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE/ DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Substituted cathinones Route of administration • may be snorted or swallowed (often after wrapping in tissue paper) • rare cases of substituted cathinones being injected Tryptamines Route of administration • majority taken non-orally i.e. injected, snorted, or smoked) • 5-MeO-DIPT may be taken orally	Concurrent use • suggestion that novel synthetics are sometimes used in conjunction with alcohol or other drugs, including cocaine, cannabis, ketamine and MDMA • suggestion that novel synthetics are sometimes used as substitutes for cocaine, hallucinogens, ketamine and MDMA; particularly when drug is legal	Availability/purity • limited evidence base • suggestion that piperazines (e.g. BZP) and synthetic cathinones are being used as substitutes for MDMA in ecstasy tablets	• not documented	• not documented	• not documented	Misuse of Drugs Act 1971 Class A tryptamines, 2C series phenethylamines Class B cathinone derivatives Class C piperazines

12. Opioids*

12.1 Acute adverse effects associated with the use of illicit opioids and abuse of prescription opioids

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Overdose • respiratory depression and drop in blood pressure resulting in respiratory arrest • illicit opioid use is associated with the majority of illicit drug-related deaths in the UK, primarily from overdose Common correlates of overdose fatality • long history of opioid dependence • high level of opioid dependence • recent abstinence (e.g. prison, detoxification release) • polydrug use (particularly with alcohol and benzodiazepines) • being male • increasing age (most fatalities occur among those in their 30's) • social isolation • neurocognitive deficits • while drug treatment generally provides a protective effect, there is a significantly enhanced risk in the first two weeks of methadone treatment, following detoxification treatment and on cessation of naltrexone treatment • recent abstinence on release from prison	Common features of acute intoxication • nausea, vomiting • depressed nervous system activity • constipation • drowsiness, decreased consciousness • sedation, mental confusion Infrequent features of acute intoxication • sweating • facial flushing • itching (pruritus) • dry mouth • hallucinations • dysphoria • difficulty in passing urine (urinary retention) Rare features of acute intoxication • complications associated with non fatal overdose e.g. hypoxia causing brain damage • disease of the white matter of the brain (leukoencephalopathy) resulting from inhalation of heroin vapours that does not seem to occur with injection; sporadic reports of cases in the literature Prescription drugs Serotonin syndrome • few cases of tramadol use associated with serotonin syndrome, a potentially life threatening condition, have been reported in the literature	• no acute psychological adverse effects • cause little psychomotor or cognitive impairment in tolerant user

*Including illicit (i.e. heroin) and prescription (e.g. methadone, buprenorphine, tramadol, dihydrocodeine and oxycodone) opioids

12. Opioids

12.2 Chronic adverse effects associated with the use of illicit opioids and abuse of prescription opioids

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
Overdose • increased mortality risk from overdose and route specific hazards Suicide • suicide rate higher than general population; associated with situational, health and lifestyle factors	Chronic complications • non-injected opioids carry little risk of chronic adverse health effects • chronic constipation • dry mouth • menstrual irregularity • malnutrition, anorexia; associated with situational, health and lifestyle factors • tooth decay • decreased sexual desire and performance Respiratory complications • respiratory diseases (asthma, chronic obstructive pulmonary disease) Hormones and immune function • modest suppression of hormone levels • suppression of immune system, social deprivation and malnutrition may also be factors Complications in pregnancy • intrauterine growth of the foetus may be inhibited • newborns exposed to illicit opioids may have low birth weight compared to non-exposed children, be born prematurely, and experience respiratory depression and withdrawal symptoms – these symptoms may contribute to the increased risk of perinatal mortality associated with use of illicit opioids in pregnancy • evidence for a direct effect of illicit opioids is confounded by other situational, health and lifestyle factors (e.g. use of other drugs, mother's nutritional status, lifestyle, infections and exposure to trauma) that may be at least as decisive for the outcome of the pregnancy • suggestion that a deprived social environment may also contribute to problems with neurological developments	Personality/mood • depressive disorder is common among those dependent on opioids but difficult to attribute causality • instability of mood • lethargy • opiates are not causally linked to chronic psychiatric disorders	Dependence • characterised by profound psychological and physical dependence • develops after repeated administration over a period of time, which varies according to the quantity, frequency and route of administration – factors of individual vulnerability and the context of drug use also play a role Withdrawal • rarely life threatening • dependent on opioid used, dose, route of administration, the interval between doses, duration of use, and users' physical and psychological health • symptoms include watery eyes, nasal discharge, yawning, sweating, sleep disturbance, dilated pupils, anorexia, gooseflesh, restlessness, irritability, tremor, sneezing, weakness, depression, nausea, vomiting, abdominal cramps, muscle spasms and diarrhoea Tolerance • characterised by shortened duration and decreased intensity of drug's depressant effects, marked elevation in average lethal dose

12. Opioids

12.3 Factors that mediate and moderate harms associated with the use of illicit opioids and abuse of prescription opioids

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE/ DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Route of administration • opioids in various formulations may be prepared for injection – particular problems may arise from injection of non-parenteral preparations (e.g. liquid preparations or tablets) • heroin may be smoked – increases risk of respiratory diseases including asthma and chronic obstructive pulmonary disorder	Concurrent use • increased risk of overdose if used in combination with alcohol, benzodiazepines or other CNS depressants • cyclizine (an antiemetic) used in combination with methadone and other opioids causes disorientation, gross intoxication	Availability • heroin has decreased in price in the UK since 2003 • methadone is widely available on prescription and as a result may be sold illicitly in the UK; the size of the illicit market is unknown Purity • mean purity of heroin has remained relatively stable since 2003 – mean 44% (2009 data) • limited evidence for fatal anaphylactoid shock, but may arise from an acute allergic response to illicit heroin (either to the drug itself or to adulterants)	Setting • injection of opioids when alone increases the risk of fatal overdose as no one is present to resuscitate or get help • slow onset of methadone may induce naive users and those new to drug treatment to increase dose leading to overdose (particularly related to polysubstance use) • increased risk of overdose on induction into methadone treatment due to pharmacokinetics of methadone • tolerance decreases after abstinence and individuals are at increased risk of overdose following cessation of treatment or on release from prison	Age • increase in heroin use among young people in England and Wales in the mid 1990s; however, use remains rare among this age group	• some people may have a genetic vulnerability that increases the likelihood of dependence on opioids	Misuse of Drugs Act 1971 Class A fentanyl, heroin, methadone, morphine, oxycodone Class B dihydrocodeine, codeine Class C buprenorphine Not controlled but regulated under Medicines Act 1968 tramadol

13. Over-the-counter products*

13.1 Acute adverse effects associated with the use of over-the-counter (OTC) products

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Dextromethorphan Acute complications • ingestion of large amounts has been associated with death through respiratory depression Codeine-containing products Acute complications • risk of death as a consequence of paracetamol, aspirin or ibuprofen overdose	Dextromethorphan Acute intoxication • increased heart rate • elevated blood pressure • increased body temperature (hyperthermia) • loss of coordination (ataxia), dizziness • nausea and vomiting • restlessness • slurred speech • tremor • involuntary eye movements (nystagmus), blurred vision Codeine-containing products Acute complications • adverse effects are similar to the those seen with other opioids (see Table 12.1), but may vary in intensity • complications relating to toxicity of paracetamol, aspirin or ibuprofen; including liver damage, renal failure and gastric bleeds	Dextromethorphan Organic/neurological • psychosis and mania associated with high doses Personality/mood • lethargy, sleepiness or insomnia • confusion

*Including dextromethorphan and codeine-containing products

13. Over-the-counter products

13.2 Chronic adverse effects associated with the use of OTC products

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
Dextromethorphan • rare case of death following overdose associated with choking on own vomit Codeine-containing products • risk of death as a consequence of paracetamol, aspirin or ibuprofen overdose	Dextromethorphan Respiratory complications • respiratory depression Codeine-containing products Toxicity related to paracetamol, aspirin or ibuprofen overdose • several cases of low blood potassium (hypokalaemia) secondary to an ibuprofen-induced kidney disorder (renal tubule acidosis) • cases of perforated gastric ulcers associated with combination ibuprofen-codeine preparations	Dextromethorphan Organic/neurological • cases of psychosis and mania associated with high doses of dextromethorphan reported in the international literature	Dextromethorphan Withdrawal • withdrawal symptoms described include craving for the drug, insomnia, somnambulism, lethargy, dysphoria, depression and ataxia Codeine-containing products Dependence • effects of combination product in addition to codeine are likely to be a contributory factor in dependence

13. Over-the-counter products

13.3 Factors that mediate and moderate harms associated with the use of OTC products

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE/ DEVELOPMENTAL ISSUES*	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Dextromethorphan Route of administration • taken orally Dose • at high doses converted to the active metabolite, dextrophan; similar effects to those associated with ketamine and PCP • 'plateaus' of effect have been described by recreational users • full dissociative phase occurs at doses 40-100 times greater than the cough suppressant dose (10 to 20 mg up to 4 times per day) Codeine-containing products Route of administration • taken orally • reports of products being reformulated by users to extract codeine part	Concurrent use • toxicity arising from combination products e.g. aspirin, paracetamol and ibuprofen	Dextromethorphan Availability • over-the-counter cough medicine Codeine-containing products Availability • over-the-counter analgesic and cough suppressant • pack sizes recently limited to 32 tablets in the UK	Social context • abuse of OTC products may be associated with intentional misuse, or it may develop secondary to dependence that has developed as a result of legitimate use; the size of the problem is unknown	• not documented	Dextromethorphan • limited data suggest that 'poor metabolisers' experience greater dysphoric effects	Both products available for sale only from pharmacies under the supervision of a pharmacist

14. Khat and Salvia divinorum

14.1 Acute adverse effects associated with the use of khat and Salvia divinorum

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
• not documented, limited evidence base	Khat Acute complications • dry mouth • hyperthermia • sweating • aching Cardiovascular complications • transient facial and conjunctival congestion • increased heart rate (tachycardia) • raised blood pressure • heart palpitations (extra-systoles) • myocardial insufficiency and cerebral haemorrhage through stimulation of adrenergic pathways Gastrointestinal complications • constipation Genitourinary complications • increased libido Salvia divinorum Acute complications • some users report experiencing physical and mental tiredness • flushed sensation • tachycardia	Khat Personality/mood • insomnia • transient confusional states Salvia divinorum Organic/neurological • hallucinations • giddiness/dizziness • confusion/disorientation

14. Khat and Salvia divinorum

14.2 Chronic adverse effects associated with the use of khat and Salvia divinorum

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
• not documented, limited evidence base	Khat Cardiovascular complications • transient facial and conjunctival congestion • increased heart rate and raised blood pressure • heart palpitations (extra-systoles) • myocardial insufficiency and cerebral haemorrhage through stimulation of adrenergic pathways Gastrointestinal complications • brown staining of the teeth, periodontal disease • inflammation of the mouth and digestive system • anorectic effect and delayed intestinal absorption; may contribute to malnutrition • constipation – may lead to laxative abuse • liver cirrhosis Respiratory complications • increased prevalence of respiratory diseases including tuberculosis may be related to secondary malnutrition and heavy tobacco smoking Reproductive disorders • limited evidence suggests that khat chewing during pregnancy may have an impact on foetal growth and development; low mean birth weights have been reported in some studies • no published evidence that khat causes teratogenic effects in humans • limited evidence base for effects on male reproductive health but suggestion that use may be associated with decreased fertility Salvia divinorum • not documented	Khat Personality/mood • anxiety • 'mood swings' (lability of mood) • nightmares • irritability, aggressive behaviour • psychotic phenomena • khat psychosis cases reported in the literature; individuals had recorded family histories of psychotic disorders Organic/neurological • cognitive dysfunction including disturbed perceptual-visual memory function Salvia divinorum • not documented	Khat Dependence • limited evidence for a khat dependence syndrome • elements of ICD 10 stimulant dependence have been described among users including: – compulsive consumption – tolerance – borderline withdrawal syndrome of tiredness, fine tremors and nightmares – craving and the urge to seek out khat are well known Salvia divinorum Dependence • limited evidence base but one survey found little evidence of dependence among users

14. Khat and Salvia divinorum

14.3 Factors that mediate and moderate harms associated with the use of khat and Salvia divinorum

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE/ DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Khat Route of administration • chewed Salvia divinorum Route of administration • user surveys suggest smoking is preferred route of administration • may also be eaten fresh or chewed and vaporised, and administered as a tincture	Khat Concurrent use • nicotine may be commonly used at the same time Salvia divinorum • limited evidence base	Khat Availability • supplies largely limited to areas of high levels of migrant populations from East Africa – Somali, Yemen and Ethiopian communities Salvia divinorum Availability • perceived to be easy to access through internet and head shops	Khat Social context • tends to be used in groups by men • suggestion that social stigma surrounding khat use by women means they may be more likely to use on their own or in small groups, or to keep their use a secret	• not documented	Khat • may contribute to psychiatric morbidity in vulnerable individuals	Khat plant and Salvia divinorum are not controlled under the Misuse of Drugs Act Active ingredients of khat (cathinone and cathine) are Class C drugs

15. Prescription drugs*

15.1 Acute adverse effects associated with the use of prescription drugs

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Benzodiazepines and non-benzodiazepine hypnotics Overdose • risk of coma, respiratory depression and death associated with use in combination with alcohol or other central nervous system depressants (e.g. heroin) CNS stimulants Overdose • reports of fatal overdoses involving the use of these drugs alone are rare	Benzodiazepines and non-benzodiazepine hypnotics Acute complications • no evidence to suggest acute risk from drug itself – risk historically associated with route of use (e.g. injection of temazepam) • risk of injury arising from sedative properties of these drugs CNS stimulants Acute complications • toxicity arising from methylphenidate and dexamphetamine overdose similar to other amphetamine-like drugs • minor effects commonly described following cases of modafinil overdose include agitation, anxiety and headache, and increased heart rate • reported complications of intravenous abuse of methylphenidate include retinopathy, emphysema, medial medullary syndrome (a rare type of stroke), hepatic dysfunction and multiple organ system failure	Benzodiazepines and non-benzodiazepine hypnotics Organic/neurological • depress mental activity and altertness • memory loss/amnesia Personality/mood • drowsiness • lethargy • disinhibition • chaotic paranoid behaviour • aggression, violent behaviour CNS stimulants Personality/mood • toxicity arising from methylphenidate and dexamphetamine overdose similar to other amphetamine-like drugs (e.g. agitation, panic) • concerns that modafinil use may be associated with suicidal thoughts, mania and symptoms of psychosis such as delusion

*Including benzodiazepines (temazepam, diazepam, nitrazepam and clonazepam), non-benzodiazepine hypnotics (zaleplon, zolpidem and zopiclone) and central nervous system (CNS) stimulants (dexamphetamine, methylphenidate and modafinil)
For prescription opioids see Table 12

15. Prescription drugs

15.2 Chronic adverse effects associated with the use of prescription drugs

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
Benzodiazepines Overdose • low rates of mortality but implicated in a significant proportion of opioid overdose fatalities and in combination with alcohol Non-benzodiazepine hypnotics and CNS stimulants • not documented	Benzodiazepines and non-benzodiazepine hypnotics Chronic complications • no evidence to suggest chronic risk from drug itself – risk historically associated with route of use (e.g. injection of temazepam) • limited evidence that exposure to benzodiazepines in early pregnancy is associated with an increased risk of major malformations and oral cleft CNS stimulants • not documented	Benzodiazepines and non-benzodiazepine hypnotics Organic/neurological • loss of control over own behaviour (loss of volitional control) Personality/mood • depression • anxiety • attention deficit CNS stimulants Personality/mood • not documented, but effects likely to be similar to other amphetamine-like drugs (e.g. psychosis, repetitive behaviours, paranoia)	Benzodiazepines Dependence • good evidence for a benzodiazepine dependence syndrome • can induce psychological dependence without tolerance Withdrawal • convulsions – possibly fatal • rebound insomnia • dysphoria, anxiety, irritability, depression, malaise • decreased concentration • muscle twitching, tremors • depersonalisation • nausea and vomiting • perceptual hypersensitivity/ distortions • headaches Non-benzodiazepine hypnotics Dependence • rarely reported in the international literature Withdrawal • symptoms described following long-term use include craving, anxiety, and insomnia CNS stimulants Dependence • indication that methylphenidate has a high abuse potential • abuse potential of modafinil may be greater than thought

15. Prescription drugs

15.3 Factors that mediate and moderate harms associated with the use of prescription drugs

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE/ DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Benzodiazepines Route of administration • risk historically associated with use by injection – blocking of peripheral veins in arms, legs, skin abscesses, deep vein thrombosis Non-benzodiazepine hypnotics Route of administration • orally, intravenously or by crushing or snorting it CNS stimulants Route of administration • methylphenidate and dexamphetamine used orally, by injection, or by snorting • injecting complications related to insoluble excipients in tablets	Benzodiazepines Concurrent use • in combination with opioids – increased risk of drug use • use in combination with alcohol increases the risk of withdrawal fits, which can be fatal • opioid users may use benzodiazepines for their pharmacological effects and to augment the effects of weak heroin Non-benzodiazepine hypnotics • suggestion that may be used by drug users as a replacement for benzodiazepines CNS stimulants Concurrent use • US college settings – reports of combined use of methylphenidate with alcohol and/or cannabis	Benzodiazepines and non-benzodiazepine hypnotics Availability • long term prescribing increases risk of dependence • dose related factors • effective importation policies have reduced availability of illegal imports	Benzodiazepines and non-benzodiazepine hypnotics Social context • social use rare among long-term prescription users CNS stimulants Social context/ setting • methylphenidate use has been reported in US college settings to enhance study, as well as recreationally	Benzodiazepines and non-benzodiazepine hypnotics Age • early use has been noted in some adolescent groups, but this has tended to be localised CNS stimulants Age • risk of serious life-threatening skin reactions with modafinil in children	Benzodiazepines • overdose risk may be enhanced by concurrent depressant drug use CNS stimulants • higher risk of abuse among people with a history of substance abuse or psychiatric problems	Misuse of Drugs Act 1971 Class B dexamphetamine, methylphenidate Class C benzodiazepines, zolpidem Not controlled zopiclone, zaleplon, modafinil

16. Tobacco

16.1 Acute adverse effects associated with the use of tobacco

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Death by nicotine poisoning • rare, occurs in children or non-smokers Accidental death • can be caused by fires that may result from smoking	Sympathetic over-activation • especially among novice users • palpitations • sweating • tremor • nausea • dizziness Respiratory complications • irritant effects of smoke on respiratory system Injury • injury resulting from fires Oral tobacco use Acute complications • irritant effects on site of absorption	Personality/mood • increased anxiety • mood disturbance • increased irritability during periods of enforced abstinence

16. Tobacco

16.2 Chronic adverse effects associated with the use of tobacco

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
Cardiovascular disease • coronary heart disease • peripheral vascular disease • blood clots may form in the arteries supplying the heart (coronary thrombosis) or the brain (cerebral thrombosis) leading to a heart attack or stroke Cancers • lung • digestive tract (mouth, tongue, throat and oesophagus) Respiratory disease • chronic obstructive pulmonary disease, defined by a long-term cough with mucus (chronic bronchitis) and/or destruction of the lungs over time (emphysema) • death from slow and progressive breathlessness Accidents • fires are an important cause of accidental death that may result from smoking Exposure to second hand smoke • coronary heart disease and lung cancer among adults	Cancers strongly linked to smoking • cancer of lung, mouth, pharynx, larynx • cancer of oesophagus, bladder, kidney, pancreas • cancer of stomach, liver, cervix, nose, lip Vascular complications • chronic obstructive pulmonary disease • heart attack • abdominal aortic aneurysm • coronary artery disease • peripheral vascular disease • stroke Other diseases/conditions • pneumonia • peptic ulcer • periodontal disease • osteoporosis • macular degeneration, cataracts Minor ailments • decreased exercise tolerance • weight loss • bad breath (halitosis) • increased susceptibility to coughs and colds • increased signs of ageing Reproductive disorders • decreased fertility in males and females • smoking in pregnancy associated with increased risk of miscarriage, perinatal mortality and low birth weight Exposure to second hand smoke Among adults: • lung cancer • coronary heart disease Among infants and children: • infections of the lower respiratory tract • middle ear disease • major respiratory symptoms (cough, phlegm, wheeze and breathlessness) • asthma • reduced lung function	Association with mental health disorders • strong association between mental health disorders, including schizophrenia and mood disorders, and tobacco smoking Significant risk factor for dementia • Alzheimer's disease • other types of dementias • evidence of cognitive decline among elderly smokers	Dependence • good evidence for a nicotine dependence syndrome • nicotine is comparatively more likely to cause dependence among users than other psychoactive substances including alcohol, heroin, cocaine and cannabis Withdrawal • craving for nicotine • anxiety • irritability • frequent changes in mood (emotional lability) • inability to concentrate • insomnia • increased appetite Tolerance • rapid development of tolerance to adverse effects e.g. nausea • acute tolerance to effects on heart rate • no tolerance to peripheral vasoconstriction • acute tolerance to the subjective sensations of nicotine (i.e. the 'pleasurable' effects of smoking)

16. Tobacco

16.3 Factors that mediate and moderate harms associated with the use of tobacco

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE/ DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Route of administration • smoked • use of filters in some cigarettes • increased tobacco use in pipes and roll-ups • varies as a function of intensity of inhalation	Consecutive use • cigarette smoking is a relapse risk in drinkers	Availability • age limit of 18 on purchase • increased availability and reduced price associated with illegal importation of illicit tobacco	Social context/ setting • smoking is common among opioid users • frequent use among drinkers	Age • early onset of smoking and drinking clearly linked to earlier onset and more regular use of illicit drugs in adolescents and more difficulty in quitting as an adult	• the stimulating effects of nicotine on cardiovascular system can be detrimental to people with cardiovascular or respiratory disease	Not controlled under Misuse of Drugs Act 1971

17. Volatile substances*

17.1 Acute adverse effects associated with the use of volatile substances

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC
MORTALITY	MORBIDITY	
Acute complications • toxicity varies greatly with the specific substance and causes of fatalities are unclear • most fatalities involve physiological depression of the central nervous system, accidents (falls, drowning, fire) or sudden death related to abnormal heart rhythms (cardiac arrhythmia) • may lose consciousness and die through choking on own vomit • danger from suffocation if plastic bag placed over head to inhale • intense cooling in mouth caused by squirting lighter fuel down throat may result in laryngeal spasm blocking airways and causing death by asphyxiation, or by profound slowing of the heart via vagal action	Acute intoxication • adverse effects vary greatly with the specific substance and mode of administration – flushed face and neck – cold sweats – loss of balance, unsteadiness and lack of coordination – fainting – headache – nausea, vomiting – confusion, dizziness, disorientation – tachycardia, palpitations – drowsiness, sedation, unconsciousness – risk of accidental injury while intoxicated	Personality/mood • confusional states, disorientation • distorted perceptions, delusions, hallucinations, pseudo hallucinations • aggression, agitation and fear

*Glues, thinners, aerosols, paints and lighter fuel

17. Volatile substances

17.2 Chronic adverse effects associated with the use of volatile substances

PHYSICAL		PSYCHOLOGICAL/PSYCHIATRIC	DEPENDENCE/ WITHDRAWAL/ TOLERANCE
MORTALITY	MORBIDITY		
• not documented, limited evidence base	Chronic complications • no consistent pattern – unclear why some users are affected and others are not • peripheral and central neurological damage • kidney failure • liver toxicity • severe gastrointestinal upset • muscle damage • very long term (e.g. 10 years) solvent misuse may result in lasting impairment of brain function (especially affecting control of movement) Pregnancy • use during pregnancy may increase the risk of adverse outcomes • suggestion that use may be associated with a neonatal withdrawal syndrome Substance specific – petrol Chronic complications • lead poisoning	Organic/neurological • decreased ability to concentrate Personality/mood • insomnia • nightmares	Dependence • evidence that volatile substance users experience signs and symptoms of a dependence syndrome is limited Withdrawal • reports in the literature of a withdrawal syndrome similar to alcohol withdrawal • irritability, headaches Tolerance • develops within 2 to 3 weeks of persistent use but is lost after a few days of abstinence

17. Volatile substances

17.3 Factors that mediate and moderate harms associated with the use of volatile substances

ROUTE OF ADMINISTRATION/ DOSE	COMBINATION USE (CONCURRENT USE, CONSECUTIVE USE)	AVAILABILITY/ PURITY	SOCIAL CONTEXT/ SETTING	AGE/ DEVELOPMENTAL ISSUES*	INDIVIDUAL VULNERABILITY	LEGAL SITUATION
Route of administration • inhaled • method of placing plastic bags completely over the heads increases risk of suffocation • some substances (e.g. butane) may be sprayed directly down the throat – practice has been associated with cases of sudden death	Concurrent use • use with alcohol and other central nervous system depressants will bring increased risk of asphyxiation and death	Availability • widely available in the household and shops (newsagents, chemists, supermarkets) • commercially available cans of lighter fuel are the most common cause of volatile substance abuse deaths	Setting • risk of injury when consumed alone in potentially dangerous locations – e.g. near water (risk of drowning), on a high building (risk of falls) • risk of death when consumed alone – e.g. from the consequences of an abnormal heart rhythm (arrhythmia)	Age • volatile substances are unique among substances of abuse as the main abusers are children and adolescents (aged 10 to 18 years)	• behavioural problems, learning difficulties • poor general physical health • increased risk of involvement with problem alcohol and tobacco use	Not controlled under Misuse of Drugs Act 1971

PART THREE
CROSS-CUTTING THEMES

18. Adulterants in illict drugs*

18.1 Adulterants commonly identified in illicit drugs

ADULTERANT(S)/ LICIT USE	POTENTIAL REASON FOR PRESENCE AS ADULTERANT	POTENTIAL PUBLIC HEATH RISKS	HEALTH EFFECTS ASSOCIATED WITH USE OF ADULTERATED ILLICIT DRUGS IDENTIFIED IN CASE REPORTS
Sucrose, lactose, dextrose and mannitol • sugars	• commonly used to dilute/add bulk to heroin and cocaine • legally and readily available	• inactive adulterants	• none reported
Lead • soft, malleable metal	Heroin • potentially a by-product of the use of lead pots in illicit heroin manufacture Methamphetamine • sometimes used in methamphetamine manufacture; poor manufacturing can result in lead residue in the drug product	• in low dosages lead poisoning can have mild effects • injecting illicit drugs adulterated with lead causes severe adverse health effects	Lead poisoning Symptoms may include: • abdominal pain and cramping • headaches • anaemia • dizziness • nausea/vomiting • muscle weakness • convulsions • coma • kidney damage • damage to the central nervous system
Caffeine • psychoactive stimulant drug	Caffeine is legal, cheap and more readily available than illicit drugs. Heroin • vaporizes heroin at lower temperature when smoked – slightly increases efficiency Cocaine, amphetamine, methamphetamine and ecstasy • stimulant properties of caffeine can create similar, although usually milder, effects to stimulant drugs	• in small doses there are few serious health repercussions • moderate to large doses can cause considerable harms (e.g. mood disturbances, anxiety, sleep disturbance)	• none reported
Procaine • local anaesthetic	Heroin • facilitates smoking of heroin • may relieve the pain of intravenous injection due to anaesthetic properties Cocaine • similar anaesthetic and subjective effects as cocaine	• risk of toxicity at high doses (e.g. nausea, vomiting, dizziness, tremors, convulsions, anxiety)	• none reported
Paracetamol • over-the-counter analgesic	Paracetamol is legal, easily available and relatively cheap Heroin • analgesic effects and bitter taste of paracetamol may disguise poor quality heroin • may be used because it has similar melting point to heroin	• low dosages should have minimal impact • risk of liver toxicity at high doses	• none reported
Strychnine • pesticide	Fine motor stimulant; at low doses acts as a muscle stimulant Heroin • enables greater retention of heroin when volatized (the process of smoking heroin) • has only been found at non-life threatening quantities. Cocaine • reason for inclusion unknown – may have been unintentional	• has only been reported in non-life-threatening quantities • small increases could potentially be fatal	Strychnine poisoning Symptoms may include: • muscle spasm • a form of spasm in which the head, neck and spine are arched backwards (opisthotonus)

*Tables 18.1 and 18.2 summarise the findings of an evidence-based overview of adulterants in illicit drugs (Cole et al., 2010), and their associated adverse health effects. It should be noted that adulterants in illicit drugs are predominantly substances which are legal, readily available, and likely to have minimal impact on users' health at low dosages. However, the methods currently used to analyse illicit drug samples mean that it is not possible to determine how commonly adulterants are present in illicit drugs at doses likely to cause harm.

18. Adulterants in illict drugs

18.2 Adulterants identified in particular illicit drugs

ADULTERANT(S)/ LICIT USE	POTENTIAL REASON FOR PRESENCE AS ADULTERANT	POTENTIAL PUBLIC HEATH RISKS	HEALTH EFFECTS ASSOCIATED WITH USE OF ADULTERATED ILLICIT DRUGS IDENTIFIED IN CASE REPORTS
Heroin			
Phenobarbital • barbiturate	• psychoactive drug • facilitates smoking of heroin	• risk of adverse effects and death from large doses (e.g. disorders of the liver, respiratory depression, mood disturbances) • may be life-threatening in injecting drug users who are hypersensitive to phenobarbital	• none reported
Quinine • antimalarial medication	• bitter taste similar to heroin and may be used as a diluents • mimics the respiratory 'rush' felt by injecting heroin users shortly after administration	• adverse effects from large doses are serious and may be life-threatening (e.g. acute renal failure; cinchonism including tinnitus, hearing impairment, vertigo, vomiting, diarrhoea, visual disturbances, confusion; muscle weakness) • can also cause a host of other adverse health reactions including acute kidney failure, gastric disturbances and cardiovascular complications	• none reported
Clenbuterol • asthma decongestant and bronchodilator drug	• reason for inclusion unknown • may be related to unintentional contamination	• can cause poisoning at moderate to high dosages • low doses typically cause adverse cardiovascular effects (e.g. increase in heart rate, blood pressure)	• cardiovascular effects • novel neuromuscular syndrome characterised by muscle spasm and overactive or overresponsive reflexes (hyperreflexia)
Scopolamine • anticholinergic alkaloid	• colourless, odourless and tasteless • not easily detectable	• low doses cause sleepiness and drowsiness • high doses can cause euphoria	Anticholinergic toxicity Complications include: • blurred vision • agitation • fever • urinary retention • flushed skin • dilated pupils
Cocaine			
Local anaesthetics • e.g. lidocaine, benzocaine and procaine	• similar (stronger) anaesthetic effects as cocaine • gives the impression of higher quality cocaine	• adverse cardiovascular and central nervous system reactions can occur at low doses • adverse effects from a large dose(s) are serious and may be life-threatening • increases the toxicity of cocaine	• difficulty circulating oxygen through the blood stream (methaemoglobinaemia)
Phenacetin • analgesic	• pain relieving properties • similar physical properties to cocaine	• banned in many countries due to links with kidney failure and suspected carcinogenicity	• difficulty circulating oxygen through the blood stream (methemoglobinaemia)
Levamisole • medication to expel parasitic worms (anthelmintic)	• unknown – may give a more intense high	• generally no longer used in human treatment, but still available as a veterinary medicine • highly toxic	• levamisole poisoning • fever • lowered white blood cell count (agranulocytosis)

18. Adulterants in illict drugs

18.2 Adulterants identified in particular illicit drugs (continued)

MDMA			
Amphetamine, methamphetamine • illicit stimulant drugs	• have similar properties to the stimulant effects of MDMA/'ecstasy' • amphetamine substances are often sold as, or in combination with, MDMA	• moderate doses can cause a range of adverse health effects • adverse effects from a large dose(s) are serious and may be life-threatening	• none reported
PMMA, PMA • synthetic drugs, chemically analogous to MDMA	• unknown • potentially to improve apparent quality and increase weight	• lack of evidence on the health consequences, but suggestion that may be more toxic than MDMA • high doses have caused death	• none reported
Cannabis			
Aluminium • soft, malleable metal	• unknown • aluminium contamination may result from impure water supply	• contribute to smoking related diseases	• none reported
Glass	• unknown • potentially to improve apparent quality and increase weight	• health risks associated with the inhalation of hot glass fumes	• none reported

19. Age-related factors

19.1 Age-related harm associated with substance use

CHILDREN AND ADOLESCENTS	OTHER ADULTS
Harms associated with substance use at an early age • onset of drug use in adolescent has been shown to be associated with an excess risk of drug dependence soon after onset of drug use, compared to onset in adulthood Harms associated with early use of specific substances Alcohol • a significant proportion of deaths among young people are related to the acute consequences of alcohol consumption (e.g. road traffic accidents) • use in early adolescence is a risk factor for drug use in later life • heavy drinking during adolescence may affect normal brain functioning during adulthood • early age of drinking onset is associated with an increased likelihood of developing alcohol abuse or dependence in adolescence and adulthood Tobacco • early onset of smoking and drinking clearly linked to earlier onset and more regular use of illicit drugs Anabolic agents • disruption of the normal pattern of growth and behavioural maturation in adolescence (e.g. stunting of height; virilization) Risk factors associated with substance use at an early age • having a parent or other family members who uses psychoactive substances or alcohol – may be associated with problems in family functioning or the effects of maternal substance use during pregnancy on child development • early school leaving, school truancy, poor school performance and expulsion or exclusion from school • involvement in crime • being in care • psychological problems	Alcohol • the majority of alcohol-related deaths occur among older age groups, mostly from liver disease and cancers • evidence suggests that older adults are at a relatively high risk of experiencing drinking problems • metabolic and physiological changes associated with ageing may lead to harmful effects at lower levels of consumption than for younger drinkers; may aggravate existing medical problems • risks of interaction between alcohol use and prescription drugs and over-the-counter products Prescription drugs and OTC products • frequent users of prescription drugs and OTC products • older women are more likely to be prescribed, and to misuse, psychoactive medications than men • older women are at a higher risk of prescription drug misuse compared to any other age group • misuse may be intentional or unintentional Illicit drugs • prevalence of illicit drug use is increasing among older age groups as current cohorts of drug users age • little is known about the longer term effects of recreational drug use

20. Gender-related factors

20.1 Gender-specific harms associated with substance use

ACROSS LICIT AND ILLICIT SUBSTANCES	LICIT SUBSTANCES	ILLICIT SUBSTANCES
• in general, drug use is considerably more common among men than women • women generally report shorter progressions from first drug use to dependence than men • women appear to be more sensitive to the adverse effects of drugs than men • older women are at a higher risk of prescription drug misuse compared to any other age group • women with drug problems may suffer disproportionately from a range of problems and experience particularly high levels of mental health problems	Alcohol • women are more sensitive to the physiological effects of alcohol than men – achieve higher blood concentrations, report feeling more intoxicated and show higher vulnerability to alcohol dependence • women may have a greater sensitivity to the neurotoxic effects of alcohol Tobacco • women are more likely than men to develop a dependence on nicotine • women report shorter intervals between cigarettes, and find it more difficult to quit tobacco smoking than men	Amphetamines and cocaine • women may have a faster progression to dependence than men • some differences in the use and effects of cocaine have been reported between men and women; evidence is limited MDMA • women are more likely than men to experience low sodium levels in the blood caused by excessive ingestion of water (hyponatraemia) • physical and/or psychological adverse effects may be more frequent among women than men (similar effects with cocaine) • men may experience greater acute physiological effects (e.g. effects on blood pressure, heart rate and body temperature) compared with females Cannabis • compared to men, women may experience quicker progression to cannabis dependence and treatment entry Opioids • some studies of heroin users indicate that women tend to escalate their use of heroin more rapidly, become addicted in a shorter period of time, and seek treatment earlier than men do • excess mortality among female opioid users in comparison with the general female population is higher than the corresponding figure for males

20. Gender-related factors

20.2 Complications and harms associated with substance use in pregnancy

LICIT DRUGS	ILLICIT DRUGS
Alcohol • spontaneous abortion • still birth • preterm delivery and decrease in length of gestation • decreased foetal growth and birth weight • Fetal Alcohol Spectrum Disorder Tobacco • marginally increased risk for spontaneous abortion • contributes to a condition where the placenta remains in the lower portion of the uterus in later stages of pregnancy (placenta praevia) and placental abruption • low birth weight • premature birth • perinatal mortality is increased as a result of these effects Licit opioids • animal studies have shown adverse effects of tramadol on the foetus	Cannabis • like tobacco, cannabis use in pregnancy may be harmful to foetal development; studies show a consistent association between cannabis use in pregnancy and reduced birth weight – though less so than as a result of tobacco smoking during pregnancy • some reports that children born to women who have used cannabis in pregnancy may face mild developmental problems; however, the evidence is mixed and confounded by the other situational, health and lifestyle factors and polysubstance use in this population e.g. cannabis users are more likely to use tobacco, alcohol and other illicit drugs during pregnancy Cocaine • premature rupture of the membranes and placental abruption associated with cocaine use in pregnancy • other adverse effects attributed to cocaine may be caused by the other confounding situational, health and lifestyle factors and polysubstance use in this population Amphetamines • use in pregnancy has been associated with low birth weight, prematurity and increased foetal morbidity – confounded by the other situational, health and lifestyle factors and polydrug use in this population Anabolic agents • anabolic-androgenic steroids are teratogenic – use of these and other anabolic agents are contraindicated in pregnancy Illicit opioids • intrauterine growth of the foetus may be inhibited • newborns exposed to illicit opioids may have low birth weight compared to non-exposed children, be born prematurely, and experience respiratory depression and withdrawal symptoms – these symptoms may contribute to the increased risk of perinatal mortality associated with use of illicit opioids in pregnancy • evidence for a direct effect of illicit opioids is confounded by other situational, health and lifestyle factors (e.g. use of other drugs, mother's nutritional status, lifestyle, infections and exposure to trauma) are at least as decisive for the outcome of the pregnancy • problems with neurological developments may also arise as a consequence of a deprived social environment Plants • limited evidence suggests that khat chewing during pregnancy may have an impact on foetal growth and development; low mean birth weights have been reported in some studies • no published evidence that khat causes teratogenic effects in humans Volatile substances • use during pregnancy may increase the risk of adverse outcomes • suggestion that use may be associated with a neonatal withdrawal syndrome

21. Route of administration

21.1 Harms associated with injecting drug use

INFECTIOUS COMPLICATIONS	EMBOLI, BLOOD VESSEL OCCLUSION AND THROMBOSIS	OTHER HARMS	SUBSTANCE-SPECIFIC HARMS
Systemic infections • Viral infections • HIV • hepatitis B • hepatitis C *Bacterial and fungal infections* • bacteria in the bloodstream (bacterial septicaemia) • infection of the heart valves and/or endocardium (endocarditis) • inflammation of a joint (septic arthritis) • infection of the bones (osteomyelitis) Skin and injection site infections Common presentations: • collection of pus with associated swelling and inflammation (abscesses) • skin infection caused by bacteria (cellulitis) More severe local infections may include: • cervical abscesses • advanced soft tissue infection (necrotising fasciitis) • bacterial infections causing death of muscle tissue (myonecrosis) • infected ulcers as a consequence of impaired blood flow *Bacterial and fungal infections* • *staphylococcus aureus* is the most commonly identified cause of skin infections • serious harms including life-threatening soft tissue infection and death have resulted from outbreaks of infection with *clostridium novyi*, other *clostridium* species (including *clostridium botulinum*) and *bacillus anthracis* • use of lemon juice to prepare heroin for injection has been implicated as the cause of outbreaks of fungal infections related to the Candida species, including serious eye infections (endophthalmitis) Increased risk of infection arises from: • injecting in areas of skin with high populations of commensal bacteria • subcutaneous and intramuscular injections	Impurities and non-soluble excipients may become microemboli in blood causing: • small clumps of dead cells to form (granulomas) in the lung leading to breathing difficulties (dyspnoea), lack of oxygen (hypoxia), pulmonary hypertension or emphysema • damage to the retina – cases associated with the injection of methylphenidate have been described Certain risk factors increase the chance of venous blockage: • inflammation of the vein (phlebitis) • injecting into the groin • lack of exercise • smoking • taking oral contraceptives	Overdose risk • injecting drug use poses particular risks for overdose • allows for the almost instant absorption of large quantities of the drug from the bloodstream Irritant effects • irritant reactions at injecting sites (e.g. phlebitis) can be attributed to: – some drugs e.g. temazepam – may directly cause abscesses, tissue necrosis, venous fibrosis, inflammation of veins (phlebitis) – adulterants e.g. quinine – poor injection technique – acidic substances used to aid dilution – more likely to occur with subcutaneous injection or via the accidental administration of drugs to the surrounding tissues on intravenous injection (extravasation) Intra-arterial injection irritant substances or those containing solid particles • swelling distal to the injection site • pain • discolouration • sensory and/or motor deficit Air embolus • potential hazard associated with the intravenous injection of large volumes of drugs	Anabolic agents • intramuscular injection may result in damage to the injection site and surrounding structures Cocaine • has local anaesthetic properties which may mask the pain of impending damage • effects of cocaine by injection are relatively brief and therefore users may inject frequently increasing likelihood of sharing and blood borne virus exposure Crack cocaine • is not soluble without the addition of a weak acid (e.g. citric acid) • increased risk of infection associated with the use of lemon juice as an acidifier • increased risk of tissue damage and possibly anaerobic infections is associated with the excess use of acidifiers Prescription drugs • injecting complications related to insoluble excipients in tablets; including blockage of blood vessels, formation of blood clots, and arterial inflammation

21. Route of administration

21.2 Harms associated with drug use orally, intranasally or by inhalation

ORAL USE (SWALLOWING)	INTRANASAL USE (SNORTING)	INHALATION USE (INHALATION/SMOKING)	SUBSTANCE-SPECIFIC HARMS
• oral route may be preferred for convenience (e.g. MDMA, LSD and alcohol) • nearly all drugs can be taken orally, but many drugs are absorbed unpredictably via this route • tends to be the route least associated with harmful consequences as psychoactive effects can take longer to develop and/or may be less intense	• impaired breathing • minor nosebleeds • irritation and possible perforation of nasal septum • ulceration of nasal mucosa • vasoconstriction of mucous membranes and subsequent vasodilation sometimes causing chronic inflammation of the mucous membrane of the nose (rhinitis) • dental erosion if substance is snorted through the nose and then enters the mouth; associated with cocaine and methamphetamine use	Inhalation • irritation and rash around nose and mouth from directly inhaled substances Smoking • respiratory complaints e.g. coughing, wheezing, chest pain, black sputum, lung damage • may exacerbate existing respiratory illnesses such as asthma • increased risk of respiratory cancers associated with tobacco use	Anabolic agents • acute liver injury associated with use of 17α-alkylated oral AAS Cocaine • local anaesthetic effect resulting in difficulty swallowing Cannabis • differences in the administration (i.e. compared to tobacco smoking) mean smoking cannabis may result in greater harm to the respiratory system • oral consumption makes dosage difficult to regulate – unpleasant reactions more difficult to avoid Heroin • rare reports of a disease of the white matter of the brain (leukoencephalopathy) associated with smoking heroin Volatile substances • intense cooling in mouth/throat may cause laryngeal spasm blocking airways and causing subsequent death by asphyxiation

22. Polysubstance use

22.1 Harms associated with the concurrent use of specific substances

	EFFECTS ASSOCIATED WITH CONCURRENT USE OF:	
	ALCOHOL	ILLICIT DRUGS
Amphetamines	• increases perceived total intoxication • increases adverse cardiovascular effects	Cocaine • limited evidence; may have adverse consequences on the central nervous system
MDMA and related analogues	• reduces subjective sedation associated with alcohol, but not alcohol-induced impairments • increase in plasma levels of MDMA • decrease in blood alcohol levels • may enhance the temporary impairment of immune cells associated with MDMA use (transient immune dysfunction)	Cannabis • users may potentially experience cumulative CNS impairment • may increase susceptibility to infection Cocaine • evidence from animal studies suggests an increased risk of neurotoxicity
Anabolic agents	• none documented	Cocaine • potential for clenbuterol and AAS to exacerbate the adverse cardiovascular effects of cocaine
Cannabis	• reduction in driving performance	
Cocaine	• increases blood levels of cocaine and the active metabolite cocaethylene; users may perceive a more intense feeling of intoxication • users may perceive a reduction in the sedating effects of alcohol • combination potentially increases adverse cardiovascular effects • patients with coronary artery disease or alcohol dependence may be particularly vulnerable to the combined toxic effects of alcohol and cocaine	Ketamine • potential to exacerbate the cardiovascular risks of cocaine (crack) Methadone • increases adverse cardiovascular effects (e.g. increased blood pressure and heart rate)
GHB	• increases the risk of respiratory depression	• none documented
Nitrites	• none documented	Misuse of drugs for treating erectile dysfunction (e.g. viagra) • increases the hypotensive effects (abnormally low blood pressure)
Opioids	• increases the depressant effects of alcohol on the central nervous system; can be fatal • acute use of alcohol and methadone appears to result in lower blood-alcohol levels – clinical significance unclear	Benzodiazepines • increase the depressant effects of opioids on the central nervous system
Prescription drug misuse	Benzodiazepines • increase the depressant effects of alcohol on the central nervous system • diazepam increases plasma levels of alcohol • may increase aggression and/or amnesia • may reduce the anxiety reducing (anxiolytic) effects of benzodiazepines CNS stimulants • increases methylphenidate levels and exacerbates effects on the central nervous system	

References

1. Best D., Gross S., Vingoe L., Witton J., Strang J. Dangerousness of drugs. A guide to the risks and harms associated with substance misuse. London: Department of Health; 2003.
2. Graham K., Homel R. Raising the bar: preventing aggression in and around bars, pubs and clubs. Portland: Wilan Publishing; 2008.
3. Parrott A. C. Drug-related harm: a complex and difficult concept to scale. Human Psychopharmacology: Clinical and Experimental 2007; 22: 423-5.
4. Cole C., Jones L., McVeigh J., Kicman A., Syed Q., Bellis M. A. Adulterants in illicit drugs: a review of empirical evidence. Drug Testing and Analysis 2010; 3: 89-96.
5. Lloyd C. Sinning and sinned against: the stigmatisation of problem drug users. London: The UK Drug Policy Commission; 2010.
6. Nutt D., King L. A., Saulsbury W., Blakemore C. Development of a rational scale to assess the harm of drugs of potential misuse. Lancet 2007; 369: 1047-53.
7. Nutt D. J., King L. A., Phillips L. D., on behalf of the Independent Scientifi c Committee on Drugs. Drug harms in the UK: a multicriteria decision analysis. Lancet 2010; 376: 1558-65.
8. Hoare J., Moon D. Drug misuse declared: findings fromthe 2009/10 British Crime Survey. London: Home Office; 2010.
9. Robinson S., Bugler C. Smoking and drinking among adults, 2008 Newport: Office for National Statistics; 2010.
10. Babor T., Caulkins J., Edwards G., Fischer B., Foxcroft D., Humphreys K. et al. Drug policy and the public good. Oxford: Oxford University Press; 2010.
11. Ghodse H. Ghodse's drugs and addictive behaviour: a guide to treatment. Cambridge: Cambridge University Press; 2010.
12. McManus S., Meltzer H., Brugha T., Bebbington P., Jenkins R. Adult psychiatric morbidity in England, 2007. London: The Health & Social Care Information Centre; 2009.
13. Fidler J. A., Shahab L., West R. Strength of urges to smoke as a measure of severity of cigarette dependence: comparison with the Fagerström Test for Nicotine Dependence and its components. Addiction 2010; 106: 631-8.
14. Robinson S., Harris H. Smoking and drinking among adults, 2009. Newport: Office for National Statistics; 2011.
15. Jones L., Bellis M. A., Dedman D., Sumnall H., Tocque K. Alcohol attributable fractions for England. Liverpool: North West Public Health Observatory; 2008.
16. Allender S., Balakrishnan R., Scarborough P., Webster P., Rayner M. The burden of smoking-related ill health in the UK. Tobacco Control 2009; 18: 262-7.
17. The Health and Social Care Information Centre. Statistics on Smoking: England, 2010. London: The Health and Social Care Information Centre; 2010.
18. Bird S. M., Hutchinson S. J., Hay G., King R. Missing targets on drugs-related deaths, and a Scottish paradox. International Journal of Drug Policy 2010; 21: 155-9.
19. Office for National Statistics. Deaths related to drug poisoning in England and Wales, 2009 Newport: Office for National Statistics; 2010.
20. Ghodse A. H., Corkery J., Ahmed K., Naidoo V., Oyefeso A., Schifano F. Drug-related deaths in the UK. London: International Centre for Drug Policy, St George's, University of London; 2010.
21. Davies C., English L., Lodwick A., McVeigh J., Bellis M. A. United Kingdom drug situation: annual report to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) 2010. Liverpool: UK Focal Point on Drugs; 2010.
22. Health Improvement Analytical Team. The cost of alcohol harm to the NHS in England London: Department of Health; 2008.
23. Singleton N., Murray R., Tinsley L. Measuring different aspects of problem drug use: methodological developments. London: Home Office; 2006.
24. North West Public Health Observatory. Local alcohol profiles for England. Liverpool: North West Public Health Observatory; 2011; Available at: www.nwph.net/alcohol/lape.
25. The Health and Social Care Information Centre. Statistics on Drug Misuse: England, 2010. London: Health and Social Care Information Centre; 2011.
26. Roe B., Beynon C., Pickering L., Duffy P. Experiences of drug use and ageing: health, quality of life, relationship and service implications. Journal of Advanced Nursing 2010; 66: 1968-79.
27. Wilson D., Sharp C., Patterson A. Young People and Crime: Findings from the 2005 Offending, Crime and Justice Survey. London: Home Office; 2006.
28. Department of Health. Safe, Sensible, Social – Consultation on further action. Impact Assessments. London: Department of Health; 2008.
29. Brown S. A., McGue M., Maggs J., Schulenberg J., Hingson R., Swartzwelder S. et al. A developmental perspective on alcohol and youths 16 to 20 years of age. Pediatrics 2008; 121: S290–S310.

www.dh.gov.uk/publications