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DH Department of Health

Dangerousness of Drugs

A Guide To The Risks And Harms Associated With Substance Misuse

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Introduction

This publication has been prepared for the Department of Health by the National Addiction Centre. The authors are David Best, Samantha Gross, Louisa Vingoe, John Witton and John Strang, (special thanks to Nick Hope and Joanne Bell of the National Drug Prevention Development Team for their help in preparing the document for publication). This document supersedes the original version of the report published by the Department of Health in September 2001. A number of revisions have been made following a consultation exercise undertaken by the Department, the most prominent of which are the introduction of glossary and contents sections, the addition of tables on khat, nitrites and dissociative anaesthetics, as well as a significantly revised overview and discussion section. The paper has also been internally reviewed by Dr. Francis Keaney and Dr. Michael Kelleher of the Maudsley Hospital to complete the process of amendment and updating.

Rationale & aims

The purpose of this report is to provide a basic reference document, targeting non-medical practitioners and others who work with drug issues, with a core set of risk factors associated with a range of licit and illicit substances commonly used in the UK. The document revolves around a set of tables which outline the chronic and acute problems associated with each of these substances, and factors that mediate or moderate the risk; while the remaining text attempts to provide a brief overview of how to make sense of the information contained in the tables and what other issues are worthy of further consideration in examining drug-related risk.

It is generally acknowledged that there are dangers associated with drug use; however, that may be about as far as it is possible to go without encountering disagreement and courting controversy. The questions that generate this dissension are based on the reader's priorities (e.g. death rates versus costs to society), the availability of appropriate evidence, the interpretation of that evidence where it does exist and in the way that secondary outcomes (crime, employment, blood-borne disease and so on) are attributed to any drug.

Therefore, depending on the criterion selected, the evidence used to measure danger and the interpretation of that evidence, a 'league table' of dangers may look radically different from one in which different but equally plausible criteria are selected. What we will attempt to do in this report is to provide a context for this question by examining some definitional and

methodological issues before undertaking the task of assessing the dangers associated with particular drugs. We will then attempt to provide a structured, tabular analysis of the dangers associated with individual drugs, followed by a commentary on the strengths and limitations of this approach.

However, this tells only part of the story as drug effects relate not only to the chemical properties of the substances themselves, but also to the pattern and context of their use. Although some consideration of the ways in which drugs are used, such as route of administration, will be included in the tables, the next section will focus more specifically on the context of drug use. The context will be defined in terms of prevalence and using populations to facilitate subsequent recommendations and conclusions.

Definitions

The definition of danger to be used in this report is the actual or potential exposure to harm, or the risk that certain drug-related activities will increase the possibility of harm. While it is important to recognise the dynamic nature of danger, it is possible to establish predisposing factors that increase risk.

Hall (1999) has argued that an appraisal of the personal and public health impact of drug use must account for the prevalence of use, the relative risk of harm and the base rate of the adverse effect. In other words, the danger of the drug is related to both the prevalence of its use and the likelihood of any harm – this is an issue we will return to when examining the 'capture rates' for different drugs.

Jaffe (1985) has provided an initial taxonomy for assessing the dangers associated with drugs and the key factors related to this. He has argued that the variability in hazard is a consequence of the drug, the dose, the route of administration, and the setting as well as the expectations and experiences of the user. He argues that, while certain risks may be limited to more intensive use patterns, others can occur during experimental or recreational use, depending on the drug and the context of use.

The European Monitoring Centre for Drugs & Drug Addiction (EMCDDA) published guidelines for the risk assessment of new synthetic drugs in 1999, which included the following taxonomies of drug-related risk:

Sources of hazard emanating from:

- Properties of the substance (pharmacology & toxicity)
- Measures of social control (regulatory policies & informal norms)
- Modalities of drug use (patterns & context of use)
- Individual characteristics of user (age, gender, genetics & personality)

Hazardous effects of drugs:

- On the user:
  Biological (toxicity, dependence)
  Psychological (functional impairment, effects on personality)
  Behavioural (neglect of social roles, violence etc)
- On the social environment:
  Family – micro level (disruption, neglect, violence)
  Neighbourhood & community – meso level (public disorder & insecurity)
  Society at large – macro level (effects on the economy, public health & judicial systems)

English (1995) also emphasised the distinction between drug associated effects and drug caused effects. Here the distinction is between things associated with use of the drug (social ostracism, criminal involvement) and those directly caused by the drug (intoxication or withdrawal). While this approach is useful, it may often be a question of attribution whether a particular outcome is explained in terms of preceding substance use. This is one of a number of critical methodological questions that has shaped the development of the investigation.

Single et al (2000) used a different approach to examining risk on the basis of the number of deaths and hospital admissions that could be attributed to alcohol, tobacco and illicit drug use in Canada in 1995. They calculated that 6,507 deaths and 82,014 hospital admissions were attributed to alcohol, 34,728 deaths and 194,072 hospital admissions to tobacco, and 805 deaths and 6,940 hospital admissions to illicit drugs. They concluded that substance abuse accounted for 20.0% of total deaths, 22.2% of total potential years of life lost and 9.4% of all hospital admissions, although the authors acknowledged that these estimates were low compared to those made in previous studies. Such studies offer a useful starting point for assessing the costs associated with substance use, but also indicate the problems in delineating the areas for investigation and their relative weightings.

Methodological issues

To start with the question of attribution of causality, it is important to note that this applies to both 'drug-associated' effects and 'drug-caused' effects. One particularly good example of this, as a 'drug-associated' effect, is the relationship between drugs and crime, in which the complexity of the association precludes a simplistic assertion that criminal involvement is a consequence of using drugs. The problems are twofold, the first relates to the number of potential mediating variables (such as poverty or concurrent alcohol use), while the second is about our confidence in asserting causal status to factors that may be separated by both time and circumstances (ie the drug use does not always follow the crime, nor does most of the research on this topic suggest that all of the money raised is spent on funding drug use).

One of the most illuminating examples of this comes from the 'death data' associated with different drugs. A person who dies from heart disease may well have had their heart weakened by prolonged excessive drinking, but may also have had a poor diet, little exercise and a stressful lifestyle. In this way, alcohol may well be an enabling condition rather than the single causal determinant, complicating the question of 'cause'. The recording of this death and its inclusion in the statistics of alcohol deaths is therefore not simply a question of monitoring, but of political decision-making, custom and practice and the dominant belief models about the relationships between events.

Attributing cause is further complicated by the way in which data are recorded and information gathered. Jaffe (1985), for example, emphasises the importance of frequency and prevalence of behaviour, yet this is something around which we have limited information for drug use, relying on relatively weak prevalence indicators for the baseline against which to measure dangers. The problem this creates is that, if the prevalence of an outcome, like treatment-seeking or mortality is known for all drugs, yet prevalence of use is not known for certain substances, then it is not possible to calculate the incidence rate of the problem comparatively across drugs. This is, in part, a result of the legal situation in which many drugs are acquired illicitly and so neither the total population of users nor the total amount consumed can be readily or reliably estimated.

Even for a legal substance like alcohol, quantity and prevalence questions cannot be readily calculated. Although it is possible to record the total amount of alcohol sold legally, this excludes legally and illegally imported alcohol, that consumed out of the

country by UK citizens and tells us little about patterns and prevalence of alcohol consumption. For this reason, we frequently have to rely on research evidence – either from national surveys or from specific population investigations. The problem with these surveys is partly about representativeness (i.e. is the sample obtained an accurate reflection of the total population) and partly about the type of information obtained. People may not accurately report their drug use because of inadequate memory, the desire to create a good impression or concerns about how the information may be used, while questions about use may not pick up the kinds of problems that are associated with substance use.

Thus, a fundamental problem for research relates to the accuracy and comparability of the measures used. The difficulty of interpretation of risk or prevalence data are confounded by issues of confidence – if there is limited evidence available, or the evidence available is out of date or based on atypical populations, then comparability becomes especially problematic.

Comparability is not only a question of quality of information (how reliable, representative, up-to-date, etc), but of the type of indicators measured and by sources with different objectives. Thus, two of the major reference sources utilised in the literature analysis for the project are Home Office statistics on drug misuse (from which the mortality data have been drawn) and the British Crime Survey, a national household survey.

The Home Office data are based on reported cases, so they reflect the system of recording and reporting used (changes in these methods will alter the results obtained), as well as the decision-making of those who present the original information (is this a drug death? Does this person qualify as an addict?).In contrast, the BCS is a voluntary participation survey in which the data are compiled with the participants' consent and so is prey to the limitations inherent in self-report. This means that questions of confidence are not the same across sources of information as they reflect the differing objectives of those for whom the data are prepared. For this reason, we have attempted to analyse our data in the context of a qualitative study in which a literature trawl has been supplemented by expert interviews.

Methods

A small number of initial interviews were conducted with addiction specialists (3 senior academics at the National Addiction Centre – Professor John Strang, Professor Michael

Gossop and Dr Michael Farrell) to discuss the key components of the project, identify target substances and isolate key sources of information. These interviews informed both the subsequent literature search and the design of the interview schedule.

The list of drugs identified are listed in Box 1 below:

Box 1: Target substances identified for consideration

- **Alcohol**
- **Amphetamines** (amphetamine sulphate, dexamphetamine, methamphetamine)
- **Amphetamine type stimulants & novel synthetic drugs** (MDMA & analogues, GHB)
- **Anabolic-androgenic steroids**
- **Benzodiazepines** (temazepam, diazepam, nitrazepam)
- **Cannabis**
- **Cocaine hydrochloride** (cocaine powder) **& Freebase cocaine** (crack/rock cocaine)
- **Dissociative anaesthetics** (ketamine, PCP)
- **Hallucinogens** (LSD, psilocybe mushrooms)
- **Khat**
- **Nitrites** (amyl, butyl, isobutyl)
- **Opiates** (heroin, methadone)
- **Tobacco**
- **Volatile substances**

Literature search

The list of substances targeted became the focus for the first wave of the literature search in which review articles considering key effects, risks and dangers were sought, along with basic information concerning the pharmacology of each of the target substances. Key journal articles and books were abstracted from one of the following information sources:

- Psychlit, Medline and BIDS (social science citation index) computerised databases
- National Addiction Centre archives
- Addiction Abstracts
- Institute for the Study of Drug Dependence (ISDD), now Drugscope, library

The literature on dangers associated with drug use is large and it has therefore been necessary to be selective in the texts chosen to inform this project. Following the initial survey of overview articles and texts, more detailed literature searches were carried out to complement the suggestions and recommendations of the interviewees.

The following key search terms were used, but the search strategy focused primarily on substance specific review articles.

The selection criteria were:

- *The material concerned dangers associated with use of the target drugs.*
- *The material either took the form of books by acknowledged experts in the field or was published in peer-reviewed journals.*
- *The material was recent (published within the last 10 years).*

We have also tried to be flexible in our approach. For instance, older material was included when a topic was poorly served by the literature published in the last 10 years.

Expert interviews

The initial round of interviews were almost unstructured to allow the interviewees to describe and prioritise what they felt were the key elements of the study and how we should go about conducting the project. This also enabled us to establish a more structured pro forma for each of the interviewees who were approached about the dangers associated with specific drugs.

For each of the target drugs, one or two experts were identified in this initial phase and recruited to participate. Interviews were tape-recorded and subsequently transcribed. None of the individuals approached refused to participate. Similarly, none of the interviewees objected to being tape-recorded. Interviews were approximately 45 minutes in length.

Results

Typology

Dangers associated with use of the target substances were initially categorised as chronic or acute, and further classified under the main domains of physical dangers (morbidity and mortality), psychological / psychiatric dangers and social / contextual negative effects.

When exploring chronic effects, additional questions about the 'addictiveness' of each substance were included. Participants were asked to describe this in terms of how addictive the substance is, the likelihood and circumstances of physical dependence, as well as evidence of tolerance and withdrawal in chronic users.

To reduce abstraction, participants were also asked to consider the factors that would mediate or moderate the main effects of the substance. This was an attempt to account for individual or group vulnerabilities and dangers associated with the ways in which drugs were used (such as the route of administration and popular combinations). However, it is important to note that there are also factors which may reduce the risk associated with particular drugs and these were included as moderating variables. The main framework for this analysis is outlined in Box 2 below:

Box 2: Framework for typology of dangerousness of drugs

Acute adverse effects – dangers regardless of frequency of use

Physical

- **Mortality** (factors or conditions which may lead to death)
- **Morbidity** (a diseased or damaged state)

Psychological / Psychiatric

Social

Chronic adverse effects – dangers that are cumulative with increased use

Physical

- **Mortality** (factors or conditions which may lead to death)
- **Morbidity** (a diseased or damaged state)

Psychological / Psychiatric

Dependence, Tolerance, Withdrawal

Social

Factors that may mediate or moderate dangers

Aspects of ingestion (route of administration, dose and purity)
Combination use (use with other drugs either concurrently or consecutively)
Availability (how easily accessible is the substance and how this impacts upon use)
Legal situation (both the law and its implementation around use of the substance)
Social context (consequences of set, setting & social milieu on dangerousness)
Age & developmental issues (the likely impact of age of onset and use on danger)
Individual vulnerability (particular individuals or groups susceptible to specific harms)
Incapacitation (the effect of imprisonment or treatment on patterns of use - including the substitution of other drugs)

The consideration of target drugs was then completed by an estimation of the adequacy of the information and the severity or likelihood of each risk factor for each drug.

Substance specific dangers

When evaluating and assessing the possible dangers of drugs, due to the vast amount of information obtained from expert interviews and literature searches, we decided to present the results in the form of tables. Three basic tables were designed (acute dangers, chronic dangers, mediating and moderating factors) and completed for each of the 14 target substances. A glossary has been included (see Appendix 1) to clarify the medical and technical terminology for lay readers.

Alcohol Consumption Tables

Table 1a: Acute adverse effects of alcohol consumption

ALCOHOL			
ACUTE ADVERSE EFFECTS DANGERS OF ALCOHOL REGARDLESS OF FREQUENCY OF USE			
PHYSICAL		**PSYCHOLOGICAL PSYCHIATRIC**	**SOCIAL**
MORTALITY	**MORBIDITY**		
• non drinkers – large dose may lead to coma and death • death by asphyxiation • death by depressing respiratory centre in medulla oblongata • acute pancreatitis • cardiovascular deaths • increased mortality associated with accidents (road traffic, swim, fire, falls)	• reduced audiovisual acuity • ataxia, decreased coordination & loss of balance • drowsiness, loss of consciousness • gastritis, diarrhoea, nausea, vomiting, oesophageal reflux, dehydration • sleep disturbance • hypoglycaemia • arrhythmia • Mallory-Weiss tear • flushing • hypothermia • diuresis • increased morbidity associated with accidents	<u>Organic/neurological</u> • psychomotor & cognitive impairment (memory, planning, judgement) • anterograde amnesia, blackout <u>Personality/mood</u> • reduced inhibitions • argumentative, aggressive • suicidal ideation intensified with alcohol	• accident (road traffic, swim, fire, falls) • disinhibition, engaging in high risk behaviour (dangerous driving, unsafe sexual practices, use of other substances of abuse), victim of crime • acute intoxication possibly resulting in aggressive & violent behaviour, disorderly conduct, criminal acts • job loss due to intoxication • relationship problems • increased risk of involvement in violent crime

Table 1b: Chronic adverse effects of alcohol consumption

ALCOHOL

CHRONIC ADVERSE EFFECTS
DANGERS OF ALCOHOL THAT ARE CUMULATIVE WITH INCREASED USE

PHYSICAL		PSYCHIATRIC PSYCHOLOGICAL	DEPENDENCE TOLERANCE WITHDRAWAL	SOCIAL
MORTALITY	**MORBIDITY**			
• liver cirrhosis • increased risk of premature mortality from accidents, suicide or violence <u>Cardiovascular disease</u> • cardiomyopathy • coronary heart disease • cardiac arrhythmia <u>Cerebrovascular disease</u> • stroke <u>Cancers</u> • oropharynx • larynx • oesophagus • liver • breast	• toxic/nutritional disorders, vitamin deficiency • gastritis, gastric ulcer • peripheral neuropathy • poly neuropathy • hypertension • pancreatitis • cirrhosis of the liver • alcoholic hepatitis • enlarged and damaged veins in the lower oesophagus • alcoholic cardiomyopathy • myopathy, muscle weakness & pain <u>Complications in pregnancy and delivery</u> • spontaneous abortion • still birth • foetal alcohol syndrome	<u>Organic/neurological</u> • brain injury • anterior lobe cerebellar degenerative disease • Wernicke encephalopathy (vitamin B1 thiamine deficiency – reversible) • Korsakoffs psychosis (may produce irreversible cognitive impairment) • memory loss, blackouts <u>Personality/mood</u> • psychotic symptoms during intoxication or withdrawal (depression, paranoia, anxiety) • loss of self esteem	<u>Dependence syndrome</u> • moderate dependence potential <u>Withdrawal syndrome</u> • can be fatal • seizures / fits • tremors • anxiety • Delirium Tremens • paranoia • hallucinations <u>Tolerance</u> • tolerance to toxic effects may not develop in parallel with tolerance to CNS depression – increase the likelihood of drug induced organ damage • increased capacity to metabolise alcohol (declines after several weeks abstinence)	<u>Alcohol and performance</u> • impaired occupational performance in adults – absenteeism, poor performance, workplace accidents, financial hardship) • impaired educational achievements in adolescents <u>Alcohol related crime</u> • while intoxicated or during withdrawal period • acquisitive crime including prostitution • domestic violence, abuse, marital separation, divorce <u>Children of parents with alcohol problems</u> • more often taken into care • more prone to anxiety & low self esteem • girls - higher incidence of depression in childhood & adolescence • boys - raised incidence of anti social behaviour • perform poorly at school • more likely to get into trouble with the law • at greater risk of developing a drinking problem in adulthood • child abuse (emotional, physical, sexual) associated with heavy drinking parents

Table 1c: Factors that mediate & moderate dangers associated with alcohol consumption.

ALCOHOL						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH ALCOHOL USE						
ROUTE OF ADMINISTRATION PURITY DOSE	**COMBINATION USE (concurrent use, consecutive use)**	**AVAILABILITY**	**CONTEXT SETTING**	**AGE DEVELOPMENTAL ISSUES**	**INDIVIDUAL VULNERABILITY**	**INCAPACITATION LEGAL SITUATION**
• coma & death in inexperienced drinker • rare examples of intravenous use • consuming designer drinks (alco-pops) leads to rapid intoxication	Concurrent use • link between cigarette smoking & alcohol use • used in combination with sedatives, opiates, cannabis, amphetamines • used in combination with opiates = risk factor for overdose by respiratory depression	• cross-tolerance with benzodiazepines • alcohol may be used when other drug of choice is not available	• alcohol use perceived differently by different societies (wet vs. dry cultures)	• alcohol use in early adolescence is a risk factor for drug use • some evidence of heavy drinking as a risk factor for persistence of delinquent career up to age 32	• a low activity variant of enzyme (ALDH2) causes the relatively high frequency of flushing in oriental populations (a protective factor against alcohol abuse) • genetic factors may create predisposition to problem alcohol use • diabetic may become hypoglycaemic as a result of alcohol use	NOT controlled under Misuse of Drugs Act 1971

Amphetamine Consumption Tables

Table 2a: Acute adverse effects of amphetamine consumption.

AMPHETAMINES
(amphetamine sulphate, dexamphetamine, methamphetamine)

ACUTE ADVERSE EFFECTS
DANGERS OF AMPHETAMINES REGARDLESS OF FREQUENCY OF USE

PHYSICAL		PSYCHOLOGICAL PSYCHIATRIC	SOCIAL
MORTALITY	**MORBIDITY**		
Excitation syndrome • hyperthermia • tachycardia followed by circulatory collapse with fatal outcome Vascular accidents • increase in blood pressure • cerebral haemorrhage or myocardial infarction with increased risk of mortality Cerebral convulsions & coma • cardiovascular shock & fatal outcome Methamphetamine • mortality associated with methamphetamine use is greater than that with amphetamine	Acute intoxication • pupil dilation • headache • dyskinesia • nausea, abdominal cramps • dry mouth • sweating • decreased appetite • dose related increase in body temperature • increased breathing rate, blood pressure, heart rate (possible arrhythmia) • naive user - dizziness, tremor, irritability, confusion, hallucinations	Organic/neurological • drowsiness • reduced ability to concentrate • judgement & learning impaired • toxic delirium with amnesia Personality/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) • toxic syndrome may develop after ingestion of a single dose in sensitive individuals, risk not dose related and a substantial number of cases are reversible	• driving impaired (increased risk of road traffic accident) • paranoid & psychotic behaviour may be accompanied by violent behaviour, aggressiveness, hostility, physical assault, homicide • relationship problems

Table 2b: Chronic adverse effects of amphetamine consumption

AMPHETAMINES
(amphetamine sulphate, dexamphetamine, methamphetamine)

CHRONIC ADVERSE EFFECTS
DANGERS OF AMPHETAMINES THAT ARE CUMULATIVE WITH INCREASED USE

PHYSICAL		PSYCHIATRIC PSYCHOLOGICAL	DEPENDENCE TOLERANCE WITHDRAWAL	SOCIAL
MORTALITY	MORBIDITY			
Excitation syndrome • hyperthermia • tachycardia followed by circulatory collapse Vascular accidents • increased blood pressure, cerebral haemorrhage or myocardial infarction Cerebral convulsions & coma • cardiovascular shock & fatal outcome • depression leading to suicide	• negative health effects from lack of food & sleep such as lower resistance to disease • possible neurotoxic damage	Organic/neurological • impairment of memory & ability to concentrate • 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 Personality/mood • irritability • suspiciousness • dysphoria • anxiety • paranoid psychosis • depression • restlessness • delirium • depersonalisation • feelings of persecution • lethargy	High abuse potential due to mood elevating properties Dependence syndrome • moderate dependence potential Withdrawal syndrome • rarely life threatening • symptoms - depression (risk of suicide), seclusiveness, craving, fatigue/exhaustion, weakness, lack of energy, sleep disturbance Tolerance • to euphorigenic, anorectic, hyperthermic and cardiovascular effects	• driving impaired (increased risk of road traffic accidents) • paranoid & psychotic behaviour may be accompanied by violent behaviour, aggressiveness, hostility, physical assault, homicide • relationship problems • impairs occupational performance in adults & educational achievements in adolescents Involvement in crime • property crime - shoplifting, burglary, fraud • motivator / facilitator role in violent/organised crime e.g. football hooliganism

Table 2c: Factors that mediate & moderate dangers associated with amphetamine consumption.

AMPHETAMINES (amphetamine sulphate, dexamphetamine, methamphetamine)						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH AMPHETAMINE USE						
ROUTE OF ADMINISTRATION PURITY DOSE	**COMBINATION USE (concurrent use, consecutive use)**	**AVAILABILITY**	**SOCIAL CONTEXT SETTING**	**AGE DEVELOPMENTAL ISSUES**	**INDIVIDUAL VULNERABILITY**	**INCAPACITATION LEGAL SITUATION**
• amphetamine purity low in UK 4-9% • increased mortality associated with methamphetamine use Route specific dangers • use by injection - see table 15 • smoking - see table 17	Concurrent use • increased risk of withdrawal fits when amphetamines are used in combination with benzodiazepines &/or alcohol	Not documented, limited evidence base	• use combined with hot, crowded settings may result in overheating, exhaustion	• use is primarily short-term BUT there are small pockets of 'career' amphetamine use in the UK	Chronic paranoid psychosis • genetic predisposition to psychotic reaction	Misuse of Drugs Act 1971 Class A amphetamines prepared for injection Class B oral amphetamines, methamphetamine

Amphetamine Type Stimulants & Novel Synthetic Drug Consumption Tables

Table 3a: Acute adverse effects associated with use of amphetamine type stimulants & novel synthetic drugs (MDMA & analogues, GHB).

AMPHETAMINE TYPE STIMULANTS & NOVEL SYNTHETIC DRUGS
(MDMA (ecstasy) & analogues, GHB)

ACUTE ADVERSE EFFECTS
DANGERS OF AMPHETAMINE TYPE STIMULANTS & NOVEL SYNTHETIC DRUGS REGARDLESS OF FREQUENCY OF USE

PHYSICAL		PSYCHOLOGICAL PSYCHIATRIC	SOCIAL
MORTALITY	**MORBIDITY**		
GHB • lose consciousness as difficult to get dose right & varies in strength MDMA & analogues • main cause of death is hyperthermia • causes surge in antidiuretic hormone so unable to pass excess water through kidneys; consequently the brain may swell and cause illness, liver damage, stroke	• nausea, vomiting • fainting • overheating, dehydration • headache • dry mouth & throat • increased blood pressure • loss of appetite • difficulty with bodily coordination GHB • confusion • muscle tremors • coma • breathing difficulties MDMA • inhibits orgasm in men & women • inhibits male erection	Personality/mood • anxiety, panic attacks • confusion • depression • insomnia • restlessness • fatigue • anorexia • paranoia • visual & auditory hallucinations are rare MDMA • suggestions that MDMA mildly interferes with cognition after acute administration • idiosyncratic psychotic episodes may occur but are not dose related 4 MTA • 4 MTA has a greater propensity to cause visual hallucinations than MDMA	• no evidence of major harmful social consequences such as family or other social relations, problems concerning education, employment or marginalisation • no evidence linked to disorderly conduct, acquisitive crime or violence • arrest for possession or dealing (buying for friends) Class A drug • disinhibition increases risk of unsafe sexual practices • driving impaired (difficulty with bodily coordination) • accidents may result from sleep deprivation • GHB reportedly used as a ‘date rape’ drug

Table 3b: Chronic adverse effects associated with the use of amphetamine type stimulants & novel synthetic Drugs (MDMA & analogues, GHB).

AMPHETAMINE TYPE STIMULANTS & NOVEL SYNTHETIC DRUGS (MDMA (ecstasy) & analogues, GHB)				
CHRONIC ADVERSE EFFECTS DANGERS OF AMPHETAMINE TYPE STIMULANTS & NOVEL SYNTHETIC DRUGS THAT ARE CUMULATIVE WITH INCREASED USE				
PHYSICAL		**PSYCHIATRIC PSYCHOLOGICAL**	**DEPENDENCE TOLERANCE WITHDRAWAL**	**SOCIAL**
MORTALITY	**MORBIDITY**			
Not documented, limited evidence base	• some reports of increased susceptibility to minor ailments - colds, flu, sore throats • possible liver damage	Organic/neurological • long term use of MDMA may be associated with mild memory impairment. Personality/mood • repeated use of MDMA may have long lasting effects on mood and personality characteristics such as depression and impulsivity Animal studies • MDMA is toxic to serotonin terminals in brain (in humans may increase risk of depression or other mental illness later in life) • dose related neurotoxicity	No dependence syndrome • group of binge users who may consume large quantities of tablets over 2-3 day period may fulfill criteria for dependence • low dependence potential Tolerance • tolerance potential	Not documented, limited evidence base

Table 3c: Factors that mediate & moderate dangers associated with the use of amphetamine type stimulants & novel synthetic drugs (MDMA & analogues, GHB).

AMPHETAMINE TYPE STIMULANTS & NOVEL SYNTHETIC DRUGS (MDMA (ecstasy) & analogues, GHB)						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH AMPHETAMINE TYPE STIMULANTS & NOVEL SYNTHETIC DRUG USE						
ROUTE OF ADMINISTRATION PURITY DOSE	**COMBINATION USE (concurrent use, consecutive use)**	**AVAILABILITY**	**SOCIAL CONTEXT SETTING**	**AGE DEVELOPMENTAL ISSUES**	**INDIVIDUAL VULNERABILITY**	**INCAPACITATION LEGAL SITUATION**
• influence of set & setting has greater impact at a lower dose. As dose increases, pharmacological properties of the drug override the effect of set & setting Route specific • use by injection- see table 15 • intranasal -see table 16 (rare for ecstasy)	• use of ecstasy may increase individual's social network to include drug scene, peer networking, other drugs more available (route to polydrug use) Concurrent use • ecstasy in combination with other stimulant drugs - increase the possible cardiotoxicity & hyperthermic effects of ecstasy • ecstasy in combination with cocaine - increased risk neurotoxicity • ecstasy in combination with alcohol – reduce perceived level of intoxication - might think ok to drive (impair task performance) Consecutive use • anecdotal reports of ecstasy users using benzodiazepines or heroin to self medicate adverse effects (especially crash period)	market well informed & shift patterns of use depending on: • rumours regarding pill content • media campaigns adverse publicity regarding neurotoxicity • subjective effects of lower dose MDMA • changes in price of ecstasy & other drugs - possibly substitute with drugs like amphetamine & cocaine	• overcrowding & overheating at unregulated dance events may increase risk of hyperthermia or dehydration	• no clear evidence on relationship between uptake of ecstasy and use of other drugs or drug careers	• individual vulnerability for acute physical problems - previous history of epilepsy, cardiovascular or cerebrovascular disease • poor metaboliser status - 2 phenotypes in population of the enzyme that metabolises ecstasy – however influence of metaboliser status unknown • psychological vulnerability increased with previous or current history of psychiatric illness, or family history.	Misuse of Drugs Act 1971 Class A MDMA & MDA family (MDMA, MDA, MDEA, MBDB, MMDA) Class C GHB

Anabolic-androgenic Steroid Consumption Tables

Table 4a: Acute adverse effects associated with the use of anabolic-androgenic steroids.

ANABOLIC-ANDROGENIC STEROIDS			
ACUTE ADVERSE EFFECTS DANGERS OF ANABOLIC-ANDROGENIC STEROIDS REGARDLESS OF FREQUENCY OF USE			
PHYSICAL		**PSYCHOLOGICAL PSYCHIATRIC**	**SOCIAL**
MORTALITY	**MORBIDITY**		
• few recorded cases in UK of mortality directly linked to AAS use • several use cases of HIV fatalities related to AAS use (shared injecting equipment)	steroid users may have additional risks regarding injection: • intramuscular injection is administered in the buttocks out of sight of the user therefore their technique may be more clumsy & increase chances of infection • chance of sharing injecting equipment may be increased as larger bore needles are needed for intramuscular injection & these may not be as easily available as the narrower gauge intravenous varieties	<u>Personality/mood</u> • aggression, violence • confusion • distractibility • mood swings • forgetfulness	• deviant social behaviours as a result of increased aggression and violence

Note: Almost all of the side effects of anabolic steroids are dose dependent and are more likely when prolonged administration occurs.

Table 4b: Chronic adverse effects associated with the use of anabolic-androgenic steroids.

ANABOLIC-ANDROGENIC STEROIDS

CHRONIC ADVERSE EFFECTS

DANGERS OF ANABOLIC STEROIDS THAT ARE CUMULATIVE WITH INCREASED USE

PHYSICAL		PSYCHIATRIC PSYCHOLOGICAL	DEPENDENCE TOLERANCE WITHDRAWAL	SOCIAL
MORTALITY	**MORBIDITY**			
• premature accumulation of fats in arteries, death due to effect on heart & blood vessels • HIV deaths from injection equipment sharing	• hypertension • liver damage (tumours, cysts, internal bleeding) • Increased risk of stroke or myocardial infarction (from blood clots and build up of fatty deposits inside arteries blocking blood flow) • growth stunting in adolescence • cancer rare but liver, prostate & kidney been reported • acne • hair loss • increased risk of tendon damage through exercise • suggested link between steroid use and immunosuppression – but no clear evidence • sleep disorders <u>Males</u> Effects which may be reversible if discontinue use • inhibiting effect on normal testicular function - reduced testosterone production & sperm production, testicular atrophy (shrinking) • enlargement of prostate gland or prostate cancer • impotence, excessive odour production Potentially irreversible effects • excessive testosterone levels leading to gynaecomastia <u>Females</u> Effects in women are potentially irreversible • masculinising / virilisation effects (increased growth of hair on body & face, deepening of voice, enlargement of clitoris, increased libido, reduced breast size) • menstruation irregularities or amenorrhoea • reduced fertility	<u>Personality/mood</u> • argumentative • impetuous • moody • suspicious • antisocial behaviour • paranoia • aggression • violence • depression	<u>Dependence syndrome</u> • some evidence to suggest dependence potential <u>Withdrawal syndrome</u> • unclear, but depression has been noted as common and may persist for many months	• limited evidence suggests increased access to stimulants • sharing of injecting equipment with training partners

Table 4c: Factors that mediate & moderate dangers associated with the use of anabolic-androgenic steroids.

ANABOLIC-ANDROGENIC STEROIDS						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH ANABOLIC-ANDROGENIC STEROID USE						
ROUTE OF ADMINISTRATION PURITY DOSE	**COMBINATION USE (concurrent use, consecutive use)**	**AVAILABILITY**	**SOCIAL CONTEXT SETTING**	**AGE DEVELOPMENTAL ISSUES**	**INDIVIDUAL VULNERABILITY**	**INCAPACITATION LEGAL SITUATION**
• users often consume 10-100 times the medical dose • users often "pyramid" their dose over 6-12 week cycles, beginning with a lower dose which is raised slowly and then decreased slowly over this period • heavy users tend to reduce 'off periods' leading to continuous use Route specific • use by injection - see table 15 • oral use – see table 17	Concurrent use • most typically use two or more types of steroids ("stacking") believing that this will cause greater effects on muscle growth range of other drugs (prescribed, illicit) are used to counteract the side effects or augment the desired effects of steroids. Examples include: • diuretics - counteract fluid retention caused by steroids & sharpen definition of skeletal muscle contours • tamoxifen - helps to reduce gynaecomastia • humanchorionic gonadotrophin –increases secretion of testosterone • some evidence of cross-over to stimulant use	• variability in quality of imports • widely available in both legal and illegal gym facilities	• gyms • used primarily by men in a variety of professions (firemen, policemen etc) but most common use by bodybuilders	• use is currently on the rise in adolescents which poses particular concern as significant reproductive problems and growth stunting can occur with adolescent use	• dispositional tendency towards aggression	Misuse of Drugs Act 1971 Class C • anabolic-androgenic steroids But exempt from the prohibition on possession when in the form of a medicinal product

Benzodiazepine Consumption Tables

Table 5a: Acute adverse effects associated with the use of benzodiazepines.

BENZODIAZEPINES (temazepam, diazepam, nitrazepam)			
ACUTE ADVERSE EFFECTS DANGERS OF BENZODIAZEPINES REGARDLESS OF FREQUENCY OF USE			
PHYSICAL		**PSYCHOLOGICAL PSYCHIATRIC**	**SOCIAL**
MORTALITY	**MORBIDITY**		
Overdose • prolonged sleep, coma, impairment of breathing, death • especially when used in combination with alcohol or heroin	no evidence to suggest acute risk from drug itself – risk associated with route of use (injection)	Organic/neurological • depress mental activity & alertness • memory loss Personality/mood • drowsiness • lethargy • disinhibition • chaotic paranoid behaviour • aggression, violent behaviour	• engaging in high risk behaviour, unsafe sexual practices • aggressive & violent behaviour • criminal activity

Note – 2 different aspects to benzodiazepine abuse:

- over-prescribing &/or inappropriate prescribing of benzodiazepines has resulted in large numbers of patients becoming dependent on them
- abuse of benzodiazepines occurs on the street often by intravenous injection of formulations designed for oral administration – purchased on black market or from legitimate receivers of prescriptions, theft from health centres or pharmacies, obtaining prescriptions by deception false names etc

Table 5b: Chronic adverse effects associated with the use of benzodiazepines.

BENZODIAZEPINES (temazepam, diazepam, nitrazepam)				
CHRONIC ADVERSE EFFECTS DANGERS OF BENZODIAZEPINES THAT ARE CUMULATIVE WITH INCREASED USE				
PHYSICAL		**PSYCHIATRIC PSYCHOLOGICAL**	**DEPENDENCE TOLERANCE WITHDRAWAL**	**SOCIAL**
MORTALITY	**MORBIDITY**			
• low rates of mortality BUT implicated in a significant proportion of opiate overdose fatalities and in combination with alcohol	• no evidence to suggest chronic risk from drug itself – risk associated with route of use (injection)	Organic/neurological • loss of volitional control Personality/mood • depression • anxiety • attention deficit • loss of sleep	Dependence syndrome • moderate dependence potential • tolerance present Withdrawal syndrome • convulsions – possibly fatal • insomnia • dysphoria, anxiety, irritability, depression, malaise • decreased concentration • muscle twitching, tremors • depersonalisation • nausea & vomiting • perceptual hypersensitivity / distortions • headaches	• use among poly-substance users, adolescent users and street population increases their engagement with "grey markets" (markets of prescribed drugs)

Table 5c: Factors that mediate & moderate dangers associated with the use of benzodiazepines.

BENZODIAZEPINES (temazepam, diazepam, nitrazepam)						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH BENZODIAZEPINE USE						
ROUTE OF ADMINISTRATION PURITY DOSE	**COMBINATION USE (concurrent use, consecutive use)**	**AVAILABILITY**	**SOCIAL CONTEXT SETTING**	**AGE DEVELOPMENTAL ISSUES**	**INDIVIDUAL VULNERABILITY**	**INCAPACITATION LEGAL SITUATION**
Route specific • use by injection- see table 15 Temazepam gel capsules, injecting complications • blocking peripheral veins in arms, legs, skin abscesses, deep vein thrombosis	Concurrent use • benzodiazepines used in combination with opiates – increased risk of drug use • benzodiazepines used in combination with alcohol - increases risk of withdrawal fits - can be fatal • opiate users take benzodiazepines to augment the effects of weak illicit heroin	• prescribing practices • dose related factors • effectiveness of importation policies	• social use rare among long-term prescription users	• early use of benzodiazepines has been noted in some adolescent groups, but this has tended to be localised	• overdose risk may be enhanced by pre-existing depressant drug use	Misuse of Drugs Act 1971 Class C benzodiazepines

Cannabis Consumption Tables

Table 6a: Acute adverse effects of cannabis consumption.

CANNABIS			
ACUTE ADVERSE EFFECTS DANGERS OF CANNABIS REGARDLESS OF FREQUENCY OF USE			
PHYSICAL		**PSYCHOLOGICAL PSYCHIATRIC**	**SOCIAL**
MORTALITY	**MORBIDITY**		
• no danger of fatal overdose • no confirmed cases of human deaths	• irritant effects of smoke on respiratory system (coughing, sore throat, bronchospasm in asthmatic people) • facial flushing • abdominal pain, nausea, vomiting • cannabis use can cause tachycardia & in some cases increased blood pressure • difficulty in motor co-ordination and performance	<u>Organic/neurological</u> • perceptual distortion (hallucinations) • amnesia / forgetfulness • confusion of thought processes, impaired judgement <u>Personality/mood</u> The effects of cannabis upon mental state vary considerably between individuals & are determined by dose, route of administration, expectations, concomitant use of other drugs, emotional state, and psychiatric illness. • temporary psychological distress (especially naive users) • dysphoria • anxiety • confusion • drowsiness • depression • panic attacks • agitation • hypomanic symptoms • short-lived & reversible psychotic reaction	• driving impaired but evidence that drivers aware of impairment and more cautious • impaired decision making, take unnecessary risks

Table 6b: Chronic adverse effects of cannabis consumption.

CANNABIS

CHRONIC ADVERSE EFFECTS
DANGERS OF CANNABIS THAT ARE CUMULATIVE WITH INCREASED USE

PHYSICAL		PSYCHIATRIC PSYCHOLOGICAL	DEPENDENCE TOLERANCE WITHDRAWAL	SOCIAL
MORTALITY	MORBIDITY			
Contributory cause of cancers of the aero-digestive tract • mouth • tongue • throat • oesophagus • lung Chronic respiratory disease • chronic bronchitis • lung damage	• persistent sore throat • use can inhibit reproductive functions & disrupt ovulation, sperm production & sperm function • no evidence of structural change in brains of heavy long term cannabis users • effects of cannabis on human immune function not known (possible suppression of immune system) • no conclusive evidence that cannabis causes cancer in humans but may be an important risk factor for the development of respiratory cancer (confounders - smoke tobacco as well or use of tobacco as vehicle for smoking cannabis resin) Complications in pregnancy Like tobacco, cannabis smoke is highly likely to be harmful to foetal development & should be avoided by pregnant women: • Babies may weigh less and children of cannabis smoking mothers may face developmental problems • However, the research thus far has been unable to untangle the effects of smoking & other factors from that of cannabis use per se	Organic/neurological • no severe or grossly debilitating impairment in cognitive function (subtle cognitive impairment in higher cognitive functions of memory, learning processes, attention & organization & the integration of complex information - may or may not be reversible after abstinence) Personality/mood • evidence of an association between cannabis use & schizophrenia, but significance is unclear • can exacerbate the symptoms of schizophrenia in affected individuals & is linked with relapse in schizophrenia • insomnia, depression, aggression anxiety • controversial evidence for social withdrawal, apathy, amotivational syndrome	Dependence syndrome • generally considered to be a drug of very low dependence potential Withdrawal syndrome • mild symptoms may include: • irritability • anxious mood • physical changes - tremor, perspiration, nausea • sleep disturbance Tolerance • to psychoactive & physical effects unlikely to occur unless there is sustained heavy exposure	• chronic heavy use may cause subtle impairments in occupational & educational performance of adults (poor performance due to apathy, impaired motivation, lack of energy BUT confounding factors) • financial difficulties

Table 6c: Factors that mediate & moderate dangers associated with cannabis consumption.

CANNABIS						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH CANNABIS USE						
ROUTE OF ADMINISTRATION PURITY DOSE	COMBINATION USE (concurrent use, consecutive use)	AVAILABILITY	SOCIAL CONTEXT SETTING	AGE DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	INCAPACITATION LEGAL SITUATION
Route specific dangers • Smoke – see table 17 Oral consumption • makes dosage difficult to regulate • unpleasant reaction more difficult to avoid	Concurrent use • smoking with tobacco	• widely available across the UK and internationally – no clear evidence of impact of police or custom interventions on supply • also difficult to police as a result of the increased popularity of home-grown cannabis	• used across wide range of social and age contexts • perceived therapeutic use (pain relief, anti-nausea) • possible self-medication among psychiatric patients • widely used by problem drug users	• regular use of cannabis may encourage users to progress to other forms of drug abuse, although the likelihood of this occurring is more related to the lifestyle & personality of the individual than the effect of cannabis itself	• increased risk of experiencing psychotic reactions in vulnerable individuals • precipitate relapse schizophrenia • adversely affect course of schizophrenia • stimulating effects of THC on cardiovascular system can be detrimental to individuals with cardiovascular or respiratory disease	Misuse of Drugs Act 1971 Currently proposed to move from Class B to Class C with reclassification anticipated in early 2004 Cannabis, Cannabis resin

Table 7a: Acute adverse effects associated with the use of cocaine hydrochloride or freebase cocaine.

COCAINE HYDROCHLORIDE (cocaine powder)
FREEBASE COCAINE (crack/rock cocaine)

ACUTE ADVERSE EFFECTS
DANGERS OF COCAINE HYDROCHLORIDE (cocaine powder) & FREEBASE COCAINE (crack/ rock cocaine) REGARDLESS OF FREQUENCY OF USE

PHYSICAL		PSYCHOLOGICAL PSYCHIATRIC	SOCIAL
MORTALITY	**MORBIDITY**		
Cardiovascular crisis • death from respiratory or heart failure – rare Allergic reaction from intravenous use of cocaine • anecdotal citations - possibly caused by additives in street cocaine Substance Specific • mortality rare from cocaine hydrochloride use alone - adverse effects are unlikely to lead to death • toxic reactions (e.g. cardiovascular crisis) are dose related and are therefore more likely to occur from smoking crack cocaine than intranasal use of cocaine hydrochloride • excited delirium – possible restraint related death among cocaine users in custody	Cardiovascular • dose dependent increase in blood pressure & body temperature, accelerated heart rate & breathing • disturbed heart rhythm - ventricular fibrillation • chest pain • shortness of breath • respiratory arrest • heart attack Neurological • stroke • seizure • headaches Musculo-skeletal • muscle spasms, tremor Gastrointestinal • abdominal pain, nausea, vomiting Genital-Urinary • increased sexual appetite & desire	Organic/neurological • impaired mental functioning Personality/mood • sleep disturbance • anxiety • paranoia • grandiosity • transient psychotic reactions • hallucinations (visual, auditory, tactile) after large doses • aggression & possible violence (especially associated with crack cocaine use)	• disinhibition & increased sexual desire - possibility of high risk sexual behaviour • women exchange sex for crack, engage in high risk sex when using the drug • aggression & possible violence (especially associated with crack cocaine use)

Table 7b: Chronic adverse effects associated with the use of cocaine hydrochloride or freebase cocaine.

COCAINE HYDROCHLORIDE (cocaine powder)
FREEBASE COCAINE (crack/rock cocaine)

CHRONIC ADVERSE EFFECTS
DANGERS OF COCAINE HYDROCHLORIDE & FREEBASE COCAINE THAT ARE CUMULATIVE WITH INCREASED USE

PHYSICAL		PSYCHIATRIC PSYCHOLOGICAL	DEPENDENCE TOLERANCE WITHDRAWAL	SOCIAL
MORTALITY	MORBIDITY			
Freebase cocaine • coronary arteries fur with fatty deposits leading to premature heart attacks	• malnutrition & weight loss • chronic use diminishes sexual appetite & ability - reversible after abstinence Complications in Pregnancy • increased risk of birth defects in child	Personality/mood • anxiety, depression • obsessional rituals / preoccupation, repetitive behaviours • sleep disturbance (decrease quantity & quality of sleep) • irritability, restlessness • auditory hallucinations • paranoid delusions & psychosis • hyperexcitability • exhaustion Toxic syndrome • psychotic reaction similar to acute paranoid schizophrenia and psychoses with vivid auditory and tactile hallucinations, picking & excoriation of skin, delusions of infection from parasites, paranoid ideation Organic/neurological • blood flow deficit in brain leading to cognitive problems	Dependence syndrome dependence potential may vary according to mode of administration • intranasal powder – high/moderate • smoked crack – very high Withdrawal syndrome Can be mild to moderate with intra & inter individual variation in type & severity of problems. Symptoms may include: • craving • exhaustion/lack of energy, fatigue • over-eating • depression • dysphoric mood • unpleasant dreams • insomnia or hypersomnia, psychomotor retardation • agitation, irritability • anxiety, restlessness, • aggression Substance Specific • craving – possibly greater magnitude for freebase/crack cocaine as compared to that for cocaine hydrochloride	• financial difficulties • context of purchasing drug on the street associated with danger around street culture, increased probability of violence • women exchange sex for crack, engage in high risk sex when using the drug

Note: Generally binge cycle of use of crack cocaine therefore unlikely to sustain chronic pattern of use for lengthy period.

Table 7c: Factors that mediate & moderate dangers associated with the use of cocaine hydrochloride or freebase cocaine.

COCAINE HYDROCHLORIDE (cocaine powder) **FREEBASE COCAINE** (crack/rock cocaine)						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH COCAINE HYDROCHLORIDE & FREEBASE COCAINE USE						
ROUTE OF ADMINISTRATION PURITY DOSE	**COMBINATION USE (concurrent use, consecutive use)**	**AVAILABILITY**	**SOCIAL CONTEXT SETTING**	**AGE DEVELOPMENTAL ISSUES**	**INDIVIDUAL VULNERABILITY**	**INCAPACITATION LEGAL SITUATION**
Route specific dangers use by injection - see Table 15 • effects of cocaine by injection are relatively brief and therefore users may inject frequently increasing likelihood of sharing & viral exposure intranasal use- see Table 16 smoking –see Table 17 Substance Specific • risk of acute death higher for crack cocaine than cocaine hydrochloride due to rapidity of onset and route specific (smoking) factors	• chronic use of cocaine may be a risk factor for use of heroin Concurrent use • alcohol & cocaine used in combination potentiate one another by production of enzyme - this combination is most commonly seen in cocaine related deaths • mixture of cocaine & 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	• cocaine is now more available, cheaper & of greater purity - possibly accounting for increases in prevalence of use	• cocaine and crack likely to be used in very different social settings • crack most commonly associated with existing problem drug users • cocaine powder more widespread and used functionally in both employment and social settings	• evidence of cocaine use resulting from early onset of other forms of drug use	• for individuals with pre- existing ischemic heart disease, cocaine can have an apparently sympatho-mimetic effect on the heart - increasing myocardial oxygen demands to the extent that angina pains occur and sometimes myocardial infarction • 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

Dissociative Anaesthetic Consumption Tables

Table 8a: Acute adverse effects associated with the use of dissociative anaesthetics (Ketamine, PCP).

DISSOCIATIVE ANAESTHETICS
(Ketamine & phencyclidine (PCP))

ACUTE ADVERSE EFFECTS
DANGERS OF DISSOCIATIVE ANAESTHETICS (Ketamine, phencyclidine) REGARDLESS OF FREQUENCY OF USE

PHYSICAL		PSYCHOLOGICAL PSYCHIATRIC	SOCIAL
MORTALITY	**MORBIDITY**		
• limited evidence base at below surgical doses BUT low risk of mortality at surgical doses associated with drug itself • death more often a result of accidents, due to loss of coordination / control, disassociation and analgesia (car accident, injury, fire) • respiratory shut down Ketamine • rare reports of overdose death from heart attack or respiration problems. PCP substantially more toxic death as a result of: • hyperthermia • convulsions	• acts as a stimulant at low doses • increase heart rate • increase respiration • loss of consciousness, coma • automatic behaviour (muscle jerking, repetitive movements, outbursts) • gastric/stomach pain • many effects are polarised (reports of opposing responses in different individuals) Ketamine • many effects are brand specific • some lead to faster loss of consciousness and difficulty breathing • injury often a result of automatic physical activity (ie: repeatedly walking into a wall) PCP • hyperthermia • intercranial hemorrhage • respiratory arrest • nausea, vomiting • ataxia • hypersalivation	Organic/neurological • hallucinations, distorted sensory • perception • impaired attention, memory, learning • altered body perception • blank stare • impairments of frontal cortical function and verbal fluency Personality/mood • confusion • depersonalisation • derealisation • panic attacks, agitation, paranoia • delirium • depression • night terrors • schitzotypal states, catatonia PCP • toxic psychosis (catatonia or paranoia)	• adverse social interactions including aggression and violence may result from the user's perceived inappropriate behaviour (involuntary movements, bumping into others, blank stare) • some recorded cases of 'sedate rape' using Ketamine • driving impaired • social withdrawal

Note: Users of dissociative anaesthetics outside of the medical setting usually involves the administration of a substantially reduced dose of the drug (eg: 10-15% of surgical dose) thus tables are based primarily upon this level of consumption.

Table 8b: Chronic adverse effects associated with the use of dissociative anaesthetics (Ketamine, PCP).

DISSOCIATIVE ANAESTHETICS
(Ketamine & phencyclidine (PCP))

CHRONIC ADVERSE EFFECTS
DANGERS OF DISSOCIATIVE ANAESTHETICS THAT ARE CUMULATIVE WITH INCREASED USE

PHYSICAL		PSYCHIATRIC PSYCHOLOGICAL	DEPENDENCE TOLERANCE WITHDRAWAL	SOCIAL
MORTALITY	MORBIDITY			
• very low risk of mortality	• no human evidence to suggest long term physical damage PCP • animal evidence 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 schizophrenic symptoms Ketamine • some evidence to suggest may damage neurotransmission PCP • anorexia • insomnia • auditory hallucinations • disorientation • paranoid delusions	Tolerance • evidence to support the rapid development of tolerance over regular repeated dosing Dependence Syndrome • evidence to suggest a dependence syndrome for PCP Withdrawal Syndrome Ketamine • no evidence to suggest withdrawal symptoms or syndrome PCP • some evidence to suggest withdrawal syndrome, including: • craving • increased appetite • hypersomnia • depression	• anecdotal cases of long term isolation and social withdrawal

Table 8c: Factors that mediate & moderate dangers associated with the use of dissociative anaesthetics (Ketamine, PCP).

DISSOCIATIVE ANAESTHETICS (Ketamine & phencyclidine (PCP))						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH DISSOCIATIVE ANAESTHETIC USE ROUTE OF						
ROUTE OF ADMINISTRATION PURITY DOSE	**COMBINATION USE (concurrent use, consecutive use)**	**AVAILABILITY**	**SOCIAL CONTEXT SETTING**	**AGE DEVELOPMENTAL ISSUES**	**INDIVIDUAL VULNERABILITY**	**INCAPACITATION LEGAL SITUATION**
• street dose is approximately 10-15% of the surgical dose. • influence of set & setting has greater impact at a lower (street) dose. As dose increases pharmacological properties of the drug override the effect of set & setting • Ketamine has a short half life and thus regular, sequential dosing occurs, thereby increasing related risks Route specific • use by injection-see table 15 • intranasal -see table 16 PCP: • smoke – see table 17	Concurrent use • Ketamine may be used with other stimulants to reduce dissociation. • Ketamine when used with alcohol may increase confusion and decrease motor control, less respect of social mores	Ketamine • often first taken unknowingly when sold as MDMA in clubs PCP • often taken unknowingly when sold in other illicit drugs.	• dissociation in dance environment may lead to inappropriate behaviour, social incidents and accidents. PCP • 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.	Ketamine • NOT included in Misuse of Drugs Act, but sale is restricted by the Medicines Act PCP Misuse of Drugs Act – Class A - phencyclidine

Hallucinogen Consumption Tables

Table 9a: Acute adverse effects associated with the use of hallucinogens (LSD, psilocybe mushrooms).

HALLUCINOGENS (LSD, psilocybe mushrooms)			
ACUTE ADVERSE EFFECTS DANGERS OF HALLUCINOGENS REGARDLESS OF FREQUENCY OF USE			
PHYSICAL		**PSYCHOLOGICAL PSYCHIATRIC**	**SOCIAL**
MORTALITY	**MORBIDITY**		
• risk of injury & accidental death LSD • one case of fatal overdose has been reported Mushrooms • fatal poisoning due to mistaken identity	• 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 Mushrooms • nausea, vomiting, stomach pains • dizziness	Personality/mood • dysphoria • unpleasant distortions in shapes & colours • frightening illusions, delusions or hallucinations • anxiety, panic, depression • dizziness, disorientation • impaired concentration • short lived psychotic episode (hallucinations, paranoia) • precipitates relapses in schizophrenia	• self harm, accidents or violence while intoxicated • driving impaired

Table 9b: Chronic adverse effects associated with the use of hallucinogens (LSD, psilocybe mushrooms).

HALLUCINOGENS (LSD, psilocybe mushrooms)				
CHRONIC ADVERSE EFFECTS DANGERS OF HALLUCINOGENS THAT ARE CUMULATIVE WITH INCREASED USE				
PHYSICAL		**PSYCHIATRIC PSYCHOLOGICAL**	**DEPENDENCE TOLERANCE WITHDRAWAL**	**SOCIAL**
MORTALITY	**MORBIDITY**			
Limited evidence base	• no known physical dangers associated with long term LSD use	Personality/mood post exposure • post hallucinogen perceptual disorder (flashbacks – unwanted recurrence of previous hallucinatory experience days or months after use) • depression • feelings of isolation • tiredness • delirium Psychosis • uncertain whether drug induced condition or unmasking of a latent mental illness	Dependence Syndrome • very low dependence potential • no withdrawal symptoms Tolerance • develops rapidly to behavioural effects & sensitivity returns after comparable drug free interval, tolerance to cardiovascular effects less pronounced	Not documented, limited evidence base

Table 9c: Factors that mediate & moderate dangers associated with the use of hallucinogens (LSD, psilocybe mushrooms).

HALLUCINOGENS (LSD, psilocybe mushrooms)						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH HALLUCINOGEN USE						
ROUTE OF ADMINISTRATION PURITY DOSE	**COMBINATION USE (concurrent use, consecutive use)**	**AVAILABILITY**	**SOCIAL CONTEXT SETTING**	**AGE DEVELOPMENTAL ISSUES**	**INDIVIDUAL VULNERABILITY**	**INCAPACITATION LEGAL SITUATION**
Mushrooms • poisoning due to mistaken identity	• anecdotal evidence of combining hallucinogens with MDMA to heighten physical sensations.	• seasonal and localised availability of mushrooms • LSD widely available	• risk of injury, accident if intoxicated in dangerous surroundings e.g. river, high building	• 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 Lysergide (LSD)

Khat Consumption Tables

10a: Acute adverse effects associated with the use of Khat.

KHAT (Catha edulis Forsk)			
ACUTE ADVERSE EFFECTS DANGERS OF KHAT REGARDLESS OF FREQUENCY OF USE			
PHYSICAL		**PSYCHOLOGICAL PSYCHIATRIC**	**SOCIAL**
MORTALITY	**MORBIDITY**		
Not documented, limited evidence base	• staring gaze • dry mouth • hyperthermia • sweating • aching Cardiovascular • transient facial and conjunctival congestion, tachycardia, raised blood pressure, extra-systoles, myocardial insufficiency and cerebral hemorrhage through stimulation of adrenergic pathways Gastrointestinal • constipation Genito-urinary • increased libido	Personality/mood • euphoria • alertness • excitement • insomnia • increased self-esteem and sociability • loquacity (talkativeness) • decreased fatigue. Cognitive • transient confusional states	• used to facilitate social events such as weddings, naming ceremonies and Islamic religious festivals. Literature on 'khat parties' records khat-enhanced good-humoured discussions, loquacity, euphoria, and less frequent irritability and aggressiveness. • disinhibition & increased sexual desire.

Table 10b: Chronic adverse effects associated with the use of Khat

KHAT (Catha edulis Forsk)				
CHRONIC ADVERSE EFFECTS DANGERS OF KHAT THAT ARE CUMULATIVE WITH INCREASED USE				
PHYSICAL		**PSYCHIATRIC PSYCHOLOGICAL**	**DEPENDENCE TOLERANCE WITHDRAWAL**	**SOCIAL**
MORTALITY	**MORBIDITY**			
Not documented, limited evidence base	Cardiovascular • transient facial and conjunctival congestion • tachycardia • raised blood pressure • extra-systoles • myocardial insufficiency and cerebral hemorrhage through stimulation of adrenergic pathways Gastrointestinal • brown staining of the teeth periodontal disease • stomatitis, oesophagitis and gastritis • anorexic effect and delayed intestinal absorption may contribute to malnutrition • constipation- leading to laxative abuse • liver cirrhosis Respiratory • increased prevalence of respiratory diseases including tuberculosis may be related to secondary malnutrition and heavy tobacco smoking. Genito-urinary • frequent, involuntary ejaculation and impotence • inhibition of lactation	Personality/mood • anxiety • lability of mood • nightmares • irritability, aggressive behaviour • psychotic phenomena • Khat psychosis cases reported in the literature had recorded family histories of psychotic disorders Cognitive • cognitive dysfunction including disturbed perceptual-visual memory function	Dependence Syndrome Specific Khat dependence syndrome not investigated BUT elements of ICD 10 stimulant dependence described: • compulsive consumption • tolerance • borderline withdrawal syndrome of tiredness, fine tremors and nightmares • craving and the urge to seek out khat are well known	• criticisms by spouse or family about use itself and money spent on khat • psychosexual complications resulting from khat use reported in divorce cases • extra pressure -financial hardship

Table 10c: Factors that mediate & moderate dangers associated with Khat consumption.

KHAT						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH KHAT USE						
ROUTE OF ADMINISTRATION PURITY DOSE	COMBINATION USE (concurrent use, consecutive use)	AVAILABILITY	SOCIAL CONTEXT SETTING	AGE DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	INCAPACITATION LEGAL SITUATION
Not documented, limited evidence base	Not documented, limited evidence base	• supplies largely limited to areas of high levels of migrant populations from East Africa	Not documented, limited evidence base	Not documented, limited evidence base	Not documented, limited evidence base	Khat plant is NOT controlled under the Misuse of Drugs Act but the active ingredients, cathinone and cathine are Class C drugs.

Nitrites Consumption Tables

Table 11a: Acute adverse effects associated with the use of Nitrites.

NITRITES
(amyl nitrite, butyl nitrite, isobutyl nitrite)

ACUTE ADVERSE EFFECTS
DANGERS OF NITRITES REGARDLESS OF FREQUENCY OF USE

PHYSICAL		PSYCHOLOGICAL PSYCHIATRIC	SOCIAL
MORTALITY	**MORBIDITY**		
• death may be caused by hypoxia resulting in severe injury to red blood cells and reducing supply of oxygen to vital organs • individuals may lose consciousness & die through choking on vomit • "sudden sniffing death syndrome" fatality caused by cardiac arrhythmia • some cases of death reported from direct oral consumption of nitrites	• ataxia • weakness • nausea • headache • loss of consciousness, sedation, anaesthesia • rash around nose and mouth & contact dermatitis • irritation of the nose and throat • increased ocular pressure Cardiovascular • profound hypotension (low blood pressure) • rebound tachycardia • flushed skin followed by vasoconstriction Genito-Urinary • heightened sexual arousal • relaxed anal sphincter • prolonged orgasm	Personality/mood • disorientation • distorted perceptions • delirium	• accident (road traffic, swimming, fire, falls) • disinhibition, engaging in high risk behaviour, particularly sexual practices

Table 11b: Chronic adverse effects associated with the use of Nitrites.

NITRITES (amyl nitrite, butyl nitrite, isobutyl nitrite)				
CHRONIC ADVERSE EFFECTS DANGERS OF NITRITES THAT ARE CUMULATIVE WITH INCREASED USE				
PHYSICAL		**PSYCHIATRIC PSYCHOLOGICAL**	**DEPENDENCE TOLERANCE WITHDRAWAL**	**SOCIAL**
MORTALITY	**MORBIDITY**			
• use produces nitrosamine which is carcinogenic • some evidence suggests use increases susceptibility to Kaposi's sarcoma in HIV positive people • suppressed immunologic function which has been associated with potentiation of AIDS Butyl Nitrite • some evidence to suggest that Butyl Nitrite use accelerates the growth of tumours and potentiates the advancement of disease by impairing the immune system	Chronic medical problems • rash and irritation around the nose, mouth or other exposed areas may cause a variety of haematological (blood related) complications, including: • anaemia • methemoglobinemia (difficulty circulating oxygen through the blood stream) • suppressed immunologic function	Organic/Neurological some evidence to suggest impairment to: • cognition • movement • vision • hearing	Dependence • dependence potential Withdrawal syndrome • no withdrawal syndrome documented Tolerance • evidence to suggest tolerance	• accident (road traffic, swimming, fire, falls) • disinhibition, engaging in high risk behaviour dangerous driving, unsafe sexual practices thereby increasing risk to sexually transmitted infections

Table 11c: Factors that mediate & moderate dangers associated with the use of Nitrites.

NITRITES (akyl nitrites (amyl nitrite, butyl nitrite, isobutyl nitrite))						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH NITRITE USE						
ROUTE OF ADMINISTRATION PURITY DOSE	**COMBINATION USE (concurrent use, consecutive use)**	**AVAILABILITY**	**SOCIAL CONTEXT SETTING**	**AGE DEVELOPMENTAL ISSUES**	**INDIVIDUAL VULNERABILITY**	**INCAPACITATION LEGAL SITUATION**
Route specific dangers oral (smoking, inhalation) - see table 17	• use with alcohol and other central nervous system depressants may bring increased risk of asphyxiation and death • anecdotal evidence to suggest may be used to increase the effects of other drugs, for example dipping cannabis cigarettes in nitrites or inhaling to bring up the effects of MDMA more quickly.	• amyl nitrite available on grey market • also available in shops (sex shops/ porn stores, mailorder, pubs) sold as room odouriser	• 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 exposure to sexually transmitted infections	• used mainly by older adolescents and adults, to enhance sexual function or the effects of other drugs	• HIV positive • poor general physical health	NOT controlled under Misuse of Drugs Act 1971

Opiate Consumption Tables

Table 12a: Acute adverse effects associated with the use of opiates (heroin, methadone).

OPIATES (Heroin, methadone)			
ACUTE ADVERSE EFFECTS DANGERS OF OPIATES REGARDLESS OF FREQUENCY OF USE			
PHYSICAL		**PSYCHOLOGICAL PSYCHIATRIC**	**SOCIAL**
MORTALITY	**MORBIDITY**		
<u>Overdose</u> • depression of breathing rate & blood pressure resulting in respiratory arrest makes opiates the illicit drug group resulting in the most deaths in the UK, primarily from overdose Common correlates of overdose fatality are: • long history of opiate dependence • high level of opiate dependence • recent abstinence (eg prison, detoxification release) • poydrug use (particularly with alcohol and benzodiazepines) • being male • being older (most fatalities occur in those in their 30's) • social isolation • neuro-cognitive deficits • little evidence that opiate overdose fatality is strongly linked with drug purity • while drug treatment generally provides a protective effect, there is a significantly enhanced risk in the first two weeks of methadone treatment	• cause little psychomotor or cognitive impairment in tolerant user <u>Common</u> • depressed nervous system activity • constipation • nausea, vomiting • drowsiness, • sedation • decreased consciousness • mental confusion <u>Infrequent</u> • sweating • facial flushing • pruritus • dry mouth • hallucinations • dysphoria • urinary retention • headache <u>Rare</u> complications associated with non fatal overdose eg hypoxia causing brain damage • spongiform encephalopathy - major neurological problems in heroin smokers / chasers that does not seem to occur in injectors	• no acute psychological adverse effects	• few acute social adverse effects in contrast to other drugs • intoxication may increase risk of causing or being exposed to accidents • disinhibition & subjectively enhanced sexual performance can result in increased sexual activity & increased risk of viral infection, sexually transmitted diseases, unwanted pregnancies

Table 12b: Chronic adverse effects associated with the use of opiates (heroin, methadone).

OPIATES
(Heroin, methadone)

CHRONIC ADVERSE EFFECTS
DANGERS OF OPIATES THAT ARE CUMULATIVE WITH INCREASED USE

PHYSICAL		PSYCHIATRIC PSYCHOLOGICAL	DEPENDENCE TOLERANCE WITHDRAWAL	SOCIAL
MORTALITY	MORBIDITY			
• increased mortality risk from overdose & route specific hazards • suicide rate higher than general population	• non- injected opiates carry little risk of chronic adverse health effects • modest suppression of hormone levels • suppression of immune system, social deprivation and malnutrition may also be factors • chronic constipation • respiratory complaints • menstrual irregularity • malnutrition • tooth decay • decreased sexual desire & performance Complications in Pregnancy • uncertainty over possible increased risk of miscarriage, foetal death, low birth weight, withdrawal symptoms in newborn, developmental consequences	Personality/mood • depressive disorder is common among opiate addicts but difficult to attribute causality • instability of mood • anorexia • lethargy • opiates are NOT causally linked to chronic psychiatric disorders	Dependence syndrome • very high dependence potential Tolerance • characterised by shortened duration & decreased intensity of CNS depressant effects, marked elevation in average lethal dose Withdrawal syndrome • rarely life threatening • dependent on dose, interval between doses, duration of use, physical & 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, pains in bones, muscles, muscle spasms and diarrhoea • methadone withdrawal qualitatively similar to withdrawal from heroin but develops more slowly, is more prolonged & less intense	• poor living conditions • poor health & diet • disrupted relationships • involvement in crime • high percentage of violent deaths at the hands of others • risk of methadone patients becoming “stuck” in treatment with concomitant risks of prolonging addiction

Table 12c: Factors that mediate & moderate dangers associated with the use of opiates (heroin, methadone).

OPIATES (Heroin, methadone)						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH OPIATE USE						
ROUTE OF ADMINISTRATION PURITY DOSE	**COMBINATION USE (concurrent use, consecutive use)**	**AVAILABILITY**	**SOCIAL CONTEXT SETTING**	**AGE DEVELOPMENTAL ISSUES**	**INDIVIDUAL VULNERABILITY**	**INCAPACITATION LEGAL SITUATION**
Overdose • Most overdose deaths associated with IV use • Increased risk of fatal & nonfatal overdose due to fluctuations in purity of illicit heroin, adulterated illicit methadone Fatal anaphylactoid (hypersensitive) reaction • Rare - results from intravenous injection of heroin containing impurities Route specific dangers Injecting – see table 15 Local problems resulting from injection of methadone linctus or tablets Smoking – see table 17 • Respiratory complaints e.g. asthma in heroin chasers / smokers • Inadequate calculation of dose – either between formulation (e.g. blue vs. green) or from heroin	Concurrent use • increased risk of overdose if used in combination with alcohol or other CNS depressants • cyclizine (an antiemetic present in diconal) used in combination with methadone causes disorientation, gross intoxication • interaction between opiate use & use of prescribed drugs – anti-epileptic/ anticonvulsant & anti-tuberculosis medications decrease the methadone levels in the body - higher dose of methadone required. Conversely, protease inhibitors used in the treatment of HIV/ AIDS increase methadone levels in the body - lower dose of methadone required	• heroin has decreased in price in the UK • methadone is now more readily available on prescription & illicitly in Britain	• injection of opiates when alone increases the risk of fatal overdose as no one is present to resuscitate or get help • methadone's slow onset may induce naive users to increase dose leading to overdose (particularly for polydrug use) • increased risk of overdose on induction into methadone treatment due to pharmacokinetics of methadone • tolerance decreases after abstinence & individuals are at increased risk of overdose post treatment or incarceration	• recent increase in heroin use among young people • in settings with limited heroin use or high stigma, methadone can be route to opiate use & injection	• possible individual molecular genetic vulnerability to effects of opiates, the risk of dependence, the risk of overdose & sensitivity to harms	Misuse of Drugs Act 1971 Class A heroin, methadone

Tobacco Consumption Tables

Table 13a: Acute adverse effects of tobacco consumption.

TOBACCO			
ACUTE ADVERSE EFFECTS DANGERS OF TOBACCO REGARDLESS OF FREQUENCY OF USE			
PHYSICAL		**PSYCHOLOGICAL PSYCHIATRIC**	**SOCIAL**
MORTALITY	**MORBIDITY**		
Fatal nicotine toxicity • rare, occurs in children or non-smokers Accidental death • fires are an important cause of accidental death that may result from careless smoking	Sympathetic over-activation Especially novice users: • palpitations • sweating • tremor • nausea • dizziness • irritant effects of smoke on respiratory system • oral tobacco use – irritant effects on site of absorption • injury resulting from fires	Personality/mood • increased anxiety • mood disturbance • increased irritability during periods of enforced abstinence	• social stigma • financial difficulties

Table 13b: Chronic adverse effects of tobacco consumption.

TOBACCO				
CHRONIC ADVERSE EFFECTS DANGERS OF TOBACCO THAT ARE CUMULATIVE WITH INCREASED USE				
PHYSICAL		**PSYCHIATRIC PSYCHOLOGICAL**	**DEPENDENCE TOLERANCE WITHDRAWAL**	**SOCIAL**
MORTALITY	**MORBIDITY**			
Cardiovascular disease • coronary heart disease Cerebrovascular disease • blood clots • stroke Peripheral vascular disease Cancers • aerodigestive tract -mouth, tongue, throat, oesophagus, lungs Chronic respiratory disease • chronic bronchitis • chronic obstructive lung disease • emphysema Accident • fires are an important cause of accidental death that may result from careless smoking	Cancers strongly linked to smoking • cancer of lung, mouth, pharynx, larynx • cancer of oesophagus, bladder, kidney, pancreas • cancer of stomach, liver, cervix, nose, lip Other diseases linked to smoking • chronic obstructive airways disease • pneumonia • myocardial infarction • aortic aneurysm • ischaemic heart disease • peripheral vascular disease • cerebrovascular accidents • peptic ulcer • periodontal disease • osteoporosis • cataracts Minor ailments • decreased exercise tolerance, weight loss, halitosis, increased susceptibility to coughs & colds, increased signs of aging Reproductive disorders • decreased fertility in males & females • smoking in pregnancy – increased risk miscarriage, perinatal mortality, low birth weight	• mood disorders	Dependence syndrome • high/moderate dependence potential Withdrawal syndrome Symptoms include: • craving for nicotine • anxiety • irritability • 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 subjective sensations	• limited evidence-some evidence of stigmatisation leading to loss of esteem and confidence

Table 13c: Factors that mediate & moderate dangers associated with tobacco consumption.

TOBACCO						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH TOBACCO USE						
ROUTE OF ADMINISTRATION PURITY DOSE	**COMBINATION USE (concurrent use, consecutive use)**	**AVAILABILITY**	**SOCIAL CONTEXT SETTING**	**AGE DEVELOPMENTAL ISSUES**	**INDIVIDUAL VULNERABILITY**	**INCAPACITATION LEGAL SITUATION**
<u>Route specific dangers</u> oral (smoking) - see table 17 • variation in contents of cigarette • use of filters in some cigarettes • increased tobacco use in pipes and roll-ups • varies as a function of intensity of inhalation	• cigarette smoking is a relapse risk in drinkers • cigarette smoking may have facilitatory effects in opiate addicts	• age limit of 16 on purchase • increased availability and reduced price associated with illegal importation of duty-free tobacco	• widespread smoking among opiate users – 93% among methadone patients and frequent use among drinkers	• early onset of smoking and drinking clearly linked to earlier onset and more regular use of illicit drugs in adolescents	• stimulating effects of nicotine on cardiovascular system can be detrimental to persons with cardiovascular or respiratory disease	NOT controlled under Misuse of Drugs Act 1971

Volatile Substances Consumption Tables

Table 14a: Acute adverse effects associated with the use of volatile substances.

VOLATILE SUBSTANCES			
ACUTE ADVERSE EFFECTS DANGERS OF VOLATILE SUBSTANCES REGARDLESS OF FREQUENCY OF USE			
PHYSICAL		**PSYCHOLOGICAL PSYCHIATRIC**	**SOCIAL**
MORTALITY	**MORBIDITY**		
Toxicity varies greatly with the specific substance & causes of fatalities are unclear • most fatalities involve cardiac arrhythmia or accident (falls, drowning, fire) • individuals may lose consciousness & die through choking on 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 & causing death by asphyxiation	Adverse effects vary greatly with the specific substance & mode of administration • flushed face & neck • cold sweats • loss of balance, unsteadiness, lack of co-ordination • fainting • headache • nausea, vomiting • confusion, dizziness, disorientation • tachycardia, palpitations • drowsiness, sedation, unconsciousness • risk of accidental injury while intoxicated	<u>Personality/mood</u> • confusional states, disorientation • distorted perceptions, delusions, hallucinations, pseudo-hallucinations • aggression, agitation, fear	• accident (road traffic, swim, fire, falls) • disinhibition, engaging in high risk behaviour (dangerous driving, unsafe sexual practices), victim of crime • acute intoxication possibly resulting in aggressive & violent behaviour, disorderly conduct • relationship problems • impairment of educational achievements in adolescents

Notes:

The most widely used volatile substances are glues, thinners, aerosols, paints & lighter fuel.

Volatile substances are unique amongst substances of abuse as the main users are children & adolescents (10 - 18 years of age). The exception to this is the nitrites, which tend to be used by a different population (gay men aged 18+, although recent reports of use by wider populations, in club settings or as sex aid). Nitrites are therefore assigned in their own table.

Table 14b: Chronic adverse effects associated with the use of volatile substances.

VOLATILE SUBSTANCES

CHRONIC ADVERSE EFFECTS
DANGERS OF VOLATILE SUBSTANCES THAT ARE CUMULATIVE WITH INCREASED USE

PHYSICAL		PSYCHIATRIC PSYCHOLOGICAL	DEPENDENCE TOLERANCE WITHDRAWAL	SOCIAL
MORTALITY	MORBIDITY			
Not documented, limited evidence base	<u>Chronic medical problems</u> • no consistent pattern - unclear why some suffer and others not <u>Adverse effects reported</u> • peripheral and central neurological damage • renal failure • hepatotoxicity • severe gastrointestinal upset • muscle damage • very long term (e.g. 10 years) solvent misuse might result in lasting impairment of brain function affecting especially control of movement <u>Substance specific - Petrol</u> • lead poisoning	<u>Organic/neurological</u> • decreased ability to concentrate <u>Personality/mood</u> • insomnia • nightmares	<u>Dependence</u> • low dependence potential <u>Withdrawal syndrome</u> • irritability, headaches <u>Tolerance</u> • develops within 2-3 weeks of continual use but is lost after a few days of abstinence	• theft of volatile substances or money to buy volatile substances • accident (road traffic, swim, fire, falls) • disinhibition, engaging in high risk behaviour (dangerous driving, unsafe sexual practices), victim of crime • acute intoxication possibly resulting in aggressive & violent behaviour, disorderly conduct • relationship problems • impairment of educational achievements in adolescents

Table 14c: Factors that mediate & moderate dangers associated with the use of volatile substances.

VOLATILE SUBSTANCES						
FACTORS THAT MEDIATE (INCREASE) OR MODERATE (REDUCE) DANGERS ASSOCIATED WITH VOLATILE SUBSTANCE USE						
ROUTE OF ADMINISTRATION PURITY DOSE	COMBINATION USE (concurrent use, consecutive use)	AVAILABILITY	SOCIAL CONTEXT SETTING	AGE DEVELOPMENTAL ISSUES	INDIVIDUAL VULNERABILITY	INCAPACITATION LEGAL SITUATION
Route specific dangers oral (inhalation, swallowing) - see table 17	• use with alcohol and other central nervous system depressants will bring increased risk of asphyxiation and death	• widely available in the household & shops (newsagents, chemists, supermarkets).	• risk of injury when consumed alone in potentially dangerous locations - e.g. near water (risk of drowning), on a high building (risk of falls) • if an individual suffers an arrhythmia whilst alone may result in fatality as no one is present to perform resuscitation	• volatile substances are unique amongst substances of abuse as the main abusers are children and adolescents (10 - 18 years of age)	• comorbidity • neurocognitive deficits • poor general physical health • increased risk of involvement with problem alcohol and tobacco use	NOT controlled under Misuse of Drugs Act 1971

Strengths & limitations of tabular approach

The preceding tables provide a comprehensive assessment of the main categories of danger that apply to the selected target drugs. This permits a certain amount of comparability between drugs, as the probability of the main classes of danger are indicated for each of the drugs listed. For example, while there is a high dependence risk and mortality danger among opiate users, there is little evidence to suggest chronic psychiatric problems in this population. However, variation in the quantity of information available has limited the comparisons, and there are very limited evidence bases for a number of the substances examined.

In contrast, no attempt has been made to rank order the target substances, even within each of the domains specified. This is because the dangers are not uni-dimensional nor do they generally occur in isolation. The purpose of following each list of drug dangers with a list of mediating and moderating effects is to avoid over-simplifying the dangers associated with substances and also, to suggest some of the areas that may be appropriate for intervention in order to reduce dangers among those who may be unwilling to stop their use of a particular drug.

However, there are fundamental limitations to this approach. Drugs are not, of themselves, dangerous, with the risk residing in the interaction between the substance, the individual, the method of consumption and the context of use. Among the main variables that will shape risk relating to substance use are amount and purity, mediated by physiological and psychological factors in the user (such as tolerance, expectation and body mass), the route of administration and whether it is used in a safe and familiar environment. While it is not possible to list all of these possible combinations for each of the drugs (and more crucially for all of the possible drug interactions), the public health anxieties around blood-borne diseases would suggest that paying some attention to the issue of route of drug administration may prove illustrative.

Route specific dangers

One of the key variables mediating dangers is route of administration. Substances that are injected are associated with risks for blood-borne diseases, not only HIV, but also Hepatitis B and Hepatitis C. Use by injection is also associated with local site damage including skin abscesses, gangrene and lymphoedema. In addition, these problems can be exacerbated by both adulterants in the drug and by poor injecting technique,

possibly resulting in deep vein thrombosis. Furthermore, chronic injecting can lead to vein loss resulting in the use of particularly dangerous injecting sites such as the groin or neck. Thus, one possibility for intervention is to persuade entrenched users to switch to a different route of administration.

Although less dangerous than injecting, there are health problems associated with the other main routes of administration. Intranasal use (snorting) is associated with impaired breathing, nosebleeds and ulceration or inflammation of nasal mucosa, while swallowing of tablets may result in the longer term in liver damage. The key here may be education about the effects of use by different methods (see Tables 15-17 below)

Table 15: Adverse effects of the use of drugs by injection.

Route Specific Adverse Effects Use of Drugs by Injection

Local infections (skin and injection site)
skin abscess, cellulitis, necrotising fascitis, gangrene, septic thrombophlebitis, lymphodoema caused by adulterants/ contaminants in street drugs, clumsy or unhygienic injecting technique

Bacterial infections leading to distant problems
joint & bone infections, osteomyelitis, septic arthritis, septicaemia (possible consequence - endocarditis)

Viral infection from sharing contaminated injecting equipment
HIV, hepatitis B, hepatitis C

Blood vessel occlusion
Inert adulterants used to dilute drug eg non soluble particles such as talc, starch and chalk may not all be removed by filtration & may become microemboli in the bloodstream. These particles may form granulomas in the lung which may impair gaseous diffusion giving rise to dyspnoea, hypoxia, pulmonary hypertension or emphysema. Embolisation of insoluble particles can also cause retinopathy (accumulation of obstructive particles in retinal blood vessels and impairment of sight can occur) & thrombus formation (deep vein thrombosis).

Stigmata
Repeated intravenous injection over a prolonged period of time may cause needle marks, scarring due to abscesses, bruising, discolouration of skin along lines of veins due to insoluble particles accumulating within the skin.

Rare adverse effects

Injection of air embolus

Potential hazard leading to heart inefficiency & possible failure, but difficult to achieve via hand held syringe (unlikely at street level).

Intra arterial injection of irritant substances containing solid particles

Swelling distal to injection site, pain, discolouration, sensory and motor deficit. Subsequent pattern of events will depend on the site of injection & the tissues affected eg thrombosis of digits leading to gangrene, deep vein thrombosis, and haemorrhage.

Direct irritant effects of drug

Most drugs are not themselves irritant, the exception being temazepam which causes irritation of tissues or veins after injection leading to abscess, tissue necrosis, venous fibrosis, phlebitis. Irritant effects of injectable preparations are largely attributed to adulterants or additives eg citric acid to aid dissolution in heroin, ammonia in crack cocaine. Other potentially irritant adulterants in street drugs include quinine & sodium bicarbonate. Talcum powder may be used as cutting agent in heroin & damages organs where it collects.

Substance specific & route specific adverse effects

Temazepam gel capsules

Temazepam gel (no longer prescribed in the form of gel-filled capsules in the UK) may solidify in blood vessels after injection causing ischaemia &/or act as a focus for thrombus formation. Temazepam is insoluble and solid particles may cause vascular blockade via microembolism. Severe rhabdomyolysis has been described necessitating fasciotomy or limb amputation and causing renal failure. Other effects include deep vein thrombosis, pulmonary embolus and critical ischaemia of digits leading to amputation.

Cocaine

Cocaine injectors may be at particular risk as the drug has local anaesthetic properties which can mask the pain of damage.

Anabolic-androgenic steroids

Steroid users may have additional risks regarding injection as intra-muscular injection is administered in the buttocks out of sight of the user therefore their technique may be more clumsy and increase chances of infection. In addition, the chance of sharing injecting equipment may be increased as larger bore needles are needed for intra-muscular injection of these viscous solutions & these may not be as easily available as the narrower gauge intravenous varieties.

Table 16: Adverse effects associated with intranasal use of drugs

Route Specific Adverse Effects Intranasal Use (Snorting)

Damage to nasal passages leading to:

- impaired breathing
- minor nosebleeds
- irritation & possible perforation of nasal septum
- ulceration of nasal mucosa
- vasoconstriction of mucous membranes & subsequent vasodilation sometimes causing rhinitis (inflammation of mucous membrane)
- dental erosion if substance snorted through nose then into mouth
- local anaesthetic effect of cocaine resulting in difficulty swallowing

Table 17: Adverse effects associated with oral use of drugs.

Route Specific Adverse Effects Use of Drugs by Oral Route (Swallowing, Smoking, Inhalation)

Cannabis
irritant effects of smoke on respiratory system (cough, sore throat, bronchospasm in asthmatic people)

Cocaine
general respiratory problems due to vasoconstrictive effects, coughing, wheezing, chest pain, black sputum, lung damage

risk of acute death higher for crack cocaine than cocaine hydrochloride due to rapidity of onset – route specific smoking

Volatile Substances
intense cooling in mouth, throat may cause laryngeal spasm blocking airways & subsequent death by asphyxiation

inhalation of volatile material from a plastic bag may result in hypoxia and neurological impairment

irritant properties of solvents can produce erythema around mouth & nose, inflammation of abrasions or spots around the mouth, coughing, tearing and salivation

Opiates (Heroin, Methadone)
respiratory problems may result from chasing heroin eg asthma

spongiform encephalopathy – extremely rare major neurological problems in heroin smokers / chasers which does not seem to occur in injectors

Reading the substance specific tables

The tables are designed to provide both overviews about the types of difficulty that are associated with experimental or regular use of a range of drugs, classified according to a number of key domains of risk. They represent a reference guide for establishing the main types of health, psychological and social problems that are likely to follow from different patterns of use. Here it is possible to examine main effects according to drug type, frequency of use and the primary domain influenced by the use.

The following table (c, for each of the substances) attempts to indicate why other factors – associated with either the users or the context of use – are likely to shift the risks outlined in the two tables above. The authors sought to compromise in the complexity of the information provided so that the general overview by substance could be interpreted by the reader in terms of the riskiness associated with individual users and the factors that surround the using occasion.

As is evident from the tables, there are different profiles of danger across the classes of substances, which partly reflects 'real' differences between the drug classes but which is also indicative of the different priorities for research and the amounts of information available about certain drugs. For some drugs, like the new synthetic drugs, this is because of their relative youth, but for others, like the hallucinogens and volatile substances, it is a result of the low priority accorded them by research scientists and policy-makers alike. For other substances, like anabolic steroids and benzodiazepines, the situation is complicated by the variation in use patterns, with differing profiles of 'danger' for those who chronically use at therapeutic dose levels and those who use for shorter periods of time but use massively increased doses. For example, it is not unknown for bodybuilders to use 200 times the recommended dose of an anabolic steroid.

In order to gain an accurate picture of the potential dangers associated with use of certain substances, we also require a probability risk estimation to assess the likelihood of an adverse effect occurring in any one individual. This is the area in which prevalence of use impacts upon the salience of certain types of danger. Hall (1999) highlighted the fact that the danger of a drug is related to both the prevalence of its use and the likelihood of any harms.

Prevalence issues

When interpreting prevalence statistics, we must remember that consumption of illicit drugs is not spread uniformly across age groups. The years between the ages of 16 and 35 are consistently found to be the peak periods for illegal drug consumption. In fact, above the age of 35, experience of illicit drugs is reasonably rare. If we look at prevalence statistics for the general population in the younger age groups we find elevated levels of use of all of the target illicit substances. However, this age effect is not apparent when looking at prevalence rates of alcohol and tobacco use. Use of these substances remains at a fairly constant level across age groups, although quantity of alcohol consumed decreases with age.

The British Crime Survey 2000 calculated population estimates of the number of 16-29 and 16-24 year olds using selected drugs in the last year and last month. This kind of information provides us with a baseline against which to assess a number of the critical parameters of danger – by measuring problem rates against the overall using population.

Table 18: 2000 estimates of number 16-29 year olds using drugs England & Wales. (British Crime Survey, 2000)

Substance	Best Estimates	
	Last Year	Last Month
Cannabis	2,115,000	1,345,000
Cocaine	457,000	178,000
Heroin	65,000	31,000
Any Class A Drug	763,000	373,000

Notes:
Total number of 16-29 year olds in England and Wales 2000 = 10,400,000
The category class A drug includes LSD, cocaine, crack, ecstasy, heroin, magic mushrooms and methadone

It would be extremely important to the completion of an assessment of dangerousness to have accurate prevalence and patterns data, against which to judge the prevalence of adverse outcomes and to establish both age and quantity-related parameters for harm. However, our attempts at assessing prevalence rates are beset by both logical and methodological problems (what the appropriate time period is for assessment, the reliability of self-report, the adequacy of information sources and so on) that this information can be regarded as indicative at best. For this reason, our understanding of the rate of occurrence of each adverse outcome is limited by a failure of

contextualisation – we cannot know the frequency of non-harmful preceding behaviours against which to measure, compare and assess. This has led to the use of triangulated methodologies in an effort to overcome these problems and a reliance on 'objective' measures such as fatality rates as a method of grounding these ephemeral and imprecise prevalence estimates.

Data on drug-related deaths

One of the questions that concerns policy makers, parents and users alike relates to the most extreme outcome of use – namely, what are the chances of death resulting from use. Drug related mortality measures the more extreme consequence of drug use, but one that seems relatively free from measurement problems. There are however, two problems in considering death data - one that relates to cause and one that relates to attribution. The causal question results from the distance of time between cause and the effect – if an individual's heart is weakened by chronic heavy drinking and they die from a heart attack, it is not obvious whether or not this is a 'alcohol-related' death. This has been the subject of much politicised debate, particularly in the discussions on smoking mortality. A second, related issue, concerns the proximal attribution of the death – thus, in the case of overdose, the death may be recorded as a heroin death in spite of the presence of excessive quantities of alcohol or benzodiazepines, while the coroner's inquest may record cause as vaguely as 'non-dependent drug abuse'. Thus, even death data must be considered in terms of the recording practices employed, the models of explanation favoured by those involved in the recording process and the limitations of the toxicological procedures used for assessing drug use post mortem.

All deaths in England and Wales which are sudden, unexpected or not natural and those for which the cause is unknown must be referred to a coroner for further investigation. The coroner's function is to establish the circumstances and cause of death. The coroner orders a post mortem to be conducted, collects information on the deceased from a variety of sources (police, medical records, relatives, friends, witnesses) and gives a verdict on the cause of death. The coroner's certificate is sent to the Registrar of Births and Deaths who register the death using the information provided on the coroner's certificate. The Office for National Statistics (ONS) receives a copy of the information on this registration form and uses this to compile their database on drug related deaths.

Box 3: Problems interpreting drug related mortality data

- the deceased may be a long term addict or occasional recreational user
- death may be accidental, suicide or even homicide
- death may be due to direct, indirect or long term effects of drug use
- dependent drug use is not always recorded as cause of death in a range of situations, such as where drug addict dies in fire, road traffic accident, of viral infection (HIV, hepatitis)
- drugs involved may be controlled drugs, prescribed substances, legally available substances such as alcohol or a mixture of these
- the drug may not be detected at post mortem or recorded on the death certificate
- whether a drug is detected may depend on which part of the body the sample is taken from
- whether a drug is detected may depend on how soon after death the post mortem is carried out
- there is much variation between coroners in facilities, resources and workloads and in the belief models they adhere to in relation to drug use and drug-related death
- what is recorded as verdict / cause of death is at the discretion of coroner (drug use may be omitted for reasons of stigma or because of family sensitivities)

Coroners' certificates do not include information on:

- how or where the drugs were obtained, quantities of drugs involved, where the drugs were taken, route of administration
- whether a toxicological exam was carried out within the post mortem

Problem of attribution given polydrug using repertoires. When more than one substance has been used:

- only those drugs which are tested for will be detected
- no indication of relative quantities is provided
- no indication is given of which substance is likely to be responsible for the death
- if both substances are mentioned on the death certificate, the death is recorded more than once under each substance
- the effects of longer term impact such as the chronic abuse of alcohol and tobacco are likely to be understated or ignored

Table 19: Number of deaths where target substance mentioned on death certificate. Source: Office for National Statistics database on drug related deaths.

SUBSTANCE	ANNUAL NUMBER DEATHS 1997	ANNUAL NUMBER DEATHS 2000
ALCOHOL	28, 000 (1996, Alcohol Concern) 4,917 cases alcohol specified on death certificate	5,635 cases alcohol specified on death certificate
TOBACCO	120,000 Source: Action on Smoking & Health ASH,1995	Updated statistics not available
ALL AMPHETAMINES	50	59
BENZODIAZEPINES	temazepam 104 diazepam 121 nitrazepam 15	temazepam 73 diazepam 83 nitrazepam 6
CANNABIS	13	11
COCAINE	39	80
MDMA/Ecstasy	12	36
HALLUCINOGENS (LSD magic mushrooms)	1	NOT REPORTED
VOLATILE SUBSTANCES	80	64
METHADONE	421	238
HEROIN AND/OR MORPHINE	445	926
TOTAL DEATHS WITH MENTION OF DRUGS ON DEATH CERTIFICATE (NOT INCL. ALCOHOL OR TOBACCO)	2,858	2,968

Note: Figures quoted for heroin and morphine deaths are combined because heroin rapidly decays into morphine in body.
Death data for drugs refers to drugs present in bloodstream at post-mortem examination and therefore cannot be assumed to be causes of death, at least in a direct sense.

Alternative approaches to risk

1. Ranking the dangers

In their chapter in "The Health Effects of Cannabis" (Kalant et al, 1999), Hall, Room and Bondy undertake a comparison of the health and psychological risks of alcohol, cannabis, nicotine and opiates. They do however point out a number of limitations with this approach:

1. difficulties in making causal inferences about the use of a drug and adverse effects

2. lack of information about the extent or seriousness of drug risks
3. the difficulties of making comparative appraisals of the public health significance of identified risks
4. the recognition that different drugs are used in different ways
5. the difficulty of predicting the consequences of changes in either the prevalence of use of specific drugs or in their routes of administration

Their first summary was of the "main adverse affects of regular heavy use of the most harmful form of each type of drug, as commonly used for non-medical purposes" (p487). They did this firstly on the basis of a literature review, differentiating between important effects (in terms of number of heavy users affected, marked as **) or those effects that are less well established or less important numerically (marked as *), see Table 20:

Table 20: Hall et al (1999) assessment of comparative adverse effects for heavy users of the most harmful form of alcohol, nicotine, opiates and cannabis

	Cannabis	Alcohol	Tobacco	Heroin
Traffic and other accidents	*	**		*
Violence and suicide		**		
Overdose death		*		**
HIV and liver infections		*		**
Liver cirrhosis		**		
Heart disease		*	**	
Respiratory disease	*		**	
Cancer	*	*	**	
Mental illness	*	**		
Dependence/addiction	**	**	**	**
Lasting effects on the foetus	*	**	*	*

The chapter then goes on to report a second expert assessment by two North Americans, Neal Benowitz and Jack Henningfield, who rated the four substance types on five dimensions related to the capacity of each drug to produce addiction and casualties (Hilts, 1995). In Table 21 below, the lower the score, the greater the likelihood comparatively (ie 1 is the most likely to lead to this problem and 4 the least).

Table 21: Comparative ratings of the dependence potential of cannabis, alcohol, tobacco and heroin (Hall et al, 1999)

	Cannabis	Alcohol	Tobacco	Heroin
Presence and severity of withdrawal symptoms	4	1	3	2
Reinforcement: Capacity to get users to use again and again	4	2	3	1
Tolerance: How much more needed by a regular user for the same effect	4	3	2	1
Dependence: Difficulty quitting and avoiding relapse: perceived need to use	4	3	1	2
Intoxication: Impairment of motor abilities, distortion of thinking and mood	3	1	4	2

In the table above cannabis is rated as having the lowest 'addictive' potential on four of the five criteria identified, with heroin most strongly linked to reinforcement and tolerance, tobacco to dependence and alcohol to intoxication and withdrawal severity.

2. Capture rates

The issue of the relative impact of prevalence of use on danger is the basis for the capture rate approach. Although it is important to know prevalence, it is just as important to be able to work out how many of those who try a drug will go on to use it regularly or to become dependent on it – the 'capture rate' for a drug. Much of this information comes from the American National Comorbidity Survey (Anthony, Warner and Kessler, 1994). In a national household survey, they asked about lifetime use and lifetime dependence for a range of psychoactive substances. An estimated 24% of the total sample had developed tobacco dependence at some point in their lives, 14% alcohol dependence and 7% dependence on an illicit drug. However, significantly more people had used alcohol or tobacco than had ever used illicit drugs. Therefore, the authors also calculated the proportion of those who had ever used a drug who had gone on to develop dependence (see table 22 below):

Table 22: Prevalence, dependence & 'capture' rates by target substance (Anthony, Warner & Kessler, 1994)			
Drug	Proportion who have used (%)	Proportion who have developed dependence (%)	Proportion of dependence among users (%)
Tobacco	75.6	24.1	31.9
Heroin	1.5	0.4	23.1
Cocaine	16.2	2.7	16.7
Alcohol	91.5	14.1	15.4
Cannabis	46.3	4.2	9.1

Although alcohol is most commonly used, the transition from use to self-reported dependence for alcohol is relatively low. In addition, while almost half of those surveyed have tried cannabis, less than 10% of these have gone on to become dependent. In contrast, almost one third of those who have ever smoked a cigarette and almost ¼ of those who have ever tried heroin have gone on to become dependent. Similar to the findings of Hall and colleagues(1999) in their ranking approach, what this would suggest is that tobacco has the greatest potential for dependence followed by heroin, then cocaine and alcohol. Cannabis has the lowest 'addictability' of all the drugs listed above.

However, the capture rate approach may be misleading as it assumes that the people who have ever tried heroin are the same as the people who have ever tried alcohol so that the capture score is a property of the drug and not of the user. Yet we know that being offered drugs in adolescence has been associated with poor neighbourhoods (Crum et al, 1996), with divorced parents (Grady et al, 1986) and with prior use of alcohol or tobacco (Steinbecka et al, 1993). For this reason, the frequency of the shift from experimentation to dependence reflects not only the addictiveness of the drug, but also the characteristics of those who are willing to experiment with it.

General developmental issues & danger

The second implication of the capture rate approach is that it suggests that drug dangers can be characterised as aspects of drug-using careers. This implies that many young people will start using drugs and committing crimes in the early teenage years, their use will peak in late adolescence and generally decline through their early twenties.

The developmental approach has generally involved a consideration of 'risk' factors as the key determinants of harm or danger, particularly for younger users but with certain risks permeating across the life course. These include background characteristics such as parental drug use and family income, anti-social personality, low intelligence and other factors that may increase the risk of all kinds of lifetime problems. In addition, contemporary - contextual factors that influence drug-using decisions may include availability, opportunity, peer influence and expectancies about what the drug will do. This distinction allows us to incorporate both general factors that will shape risk-taking behaviour across the life course with factors that will determine the outcome of a particular risk situation.

Individual Vulnerability

In reviewing the substance specific tables, it becomes clear that biological, psychological and social factors all significantly impact on the dangers of drug use. In trying to explicate these relationships, researchers must consider variables which indicate potential differences between groups. Two such areas of investigation that have provided evidence on such mediating factors are gender and co-morbidity.

Gender

Traditionally, research on drug use has included only male subjects and results have been generalised to women. This, in part, reflects a social bias and a reluctance to include women of child-bearing age in studies for fear of biological injury; but also reflects the fact that substance use occurs more frequently in men. It now appears that this difference, at least from a macro perspective, is related to opportunities for use as opposed to differences in vulnerability (Van Etten et al, 1999). However, research has also shown that with regard to specific substances, there are marked differences in the biological and behavioral impacts of drug use according to gender.

Research on cocaine and tobacco has demonstrated significant differences between men and women. For example, women appear to be more sensitive to the cardiovascular effects of cocaine (Lucas et al, 1996), but may be more protected from the negative effects on the brain and on cognitive functioning (Stein et al, 1997). Women also appear to use greater amounts of the drug in shorter intervals. In the case of tobacco, while both sexes are equally vulnerable to dependence, men smoke a larger quantity of cigarettes, with higher nicotine counts and there are indications that they inhale more deeply. Despite this

women are less successful at quitting and tend to have higher rates of relapse (Perkens et al, 1999).

Considering vulnerability towards dependence, gender does not appear to impact on capture rates for the majority of substances; however, it has been documented that women are more likely to abuse prescription drugs while men are more likely to abuse alcohol and cannabis (NIDA, 1998).

The implications of recognising gender differences can be best illustrated with regard to the transmission of blood borne disease. Women infected with HIV progress to full-blown AIDS with half the viral load as men, in approximately the same time. According to the National Institute on Drug Abuse (USA), drug abuse causes a greater percentage HIV infection in women, related to both an increased likelihood of engaging in unsafe sexual practices with infected partners and sharing of injecting equipment. Considerably more work needs to be carried out on risk which assesses the impact of gender on both chronic and acute risk, but, for the moment, policy makers and practitioners need to be aware that gender may be a significant factor in determining relative levels of drug-related risk.

Co-morbidity / Dual Diagnosis

While the Department of Health has prioritized research into dual diagnosis as part of the Drug Misuse Research Initiative (see DH website), it is important to acknowledge that there are likely to be additional risks associated with individuals who have mental health problems and are using substances. The extent of this overlap was indicated by the Epidemiological Catchment Area (ECA) study (Robins & Regier, 1991) which found that, amongst those with any drug disorder, the mental health disorders were common – particularly anxiety (28%); affective disorders (26%); antisocial personality disorders (18%) and schizophrenia (7%) (Regier et al, 1990).

This group have greater treatment needs yet are frequently more chaotic as a consequence of their dual diagnosis and so may be harder to both engage and then retain in treatment. Dual diagnosed individuals have higher rates of incarceration and criminal involvement (Tessler & Dennis 1989), they are at greater risk for suicide (Moselhy & Conlon, 2001), violence (Boles & Johnson 2001) and physical health problems (Kendrick et al, 1994) all of which contribute to a low quality of life (Booth & Blow, 2001). For this reason, this group is at particular risk of increased drug involvement and subsequently for experiencing a greater range of problems as a consequence of use. Therefore, it is critical that, in assessing drug risks and dangers, that mental

health issues are accorded prominence and that, in planning treatment services, adequate resources are made available for dealing with the complex needs of this population.

The normalisation of drug use

The increase in availability of a wide range of drugs has been accompanied by changes in the perception of drug use across social groups in the direction of increased acceptance and acceptability, particularly for cannabis and the new synthetic drugs which are not associated with disease spread, acquisitive crime or violent behaviour. This has led to increased accessibility of illicit drugs, both socially and economically, to a wider range of potentially vulnerable populations such as younger adolescents, resulting in Government initiatives which emphasise primary prevention. However, under such circumstances, the physical developmental risks may be exacerbated by increased access in vulnerable populations (those socially excluded or absent from formal education, children of drug using parents, those with mental health problems and those living in care) which may compound the dangers outlined for the (adult) populations identified in the tables. Thus, a social context in which drugs are more readily available across a wider range of populations may result in unprecedented levels of drug-related harm in the more vulnerable social groups.

Harm Reduction

One method of diversifying approaches to meet the spread of substance use across populations, has involved the implementation of interventions based on a harm reduction philosophy. The harm reduction approach aims to remove or ameliorate some mediating variables that increase risk from drug use. As documented in the substance summaries, it is often these risk variables (and not the drug itself), particularly those associated with route of administration and lifestyle, which have the greatest negative impact on the user. The degree to which such approaches have been successfully introduced also has an impact on overall and specific harm.

The legal context

The legal status of drugs of misuse and the way in which the relevant legislation is applied (and also how it is perceived) has an impact on how such drugs are used and consequently the particular related harms. The illegality of a drug can affect how it is used and level of involvement in criminal activity is in part

affected by this. The legal context therefore has an impact on overall harm as described in the tables.

General discussion

The first point to make here is that the dangerousness of an individual substance is difficult to abstract from the context of its use – a context that is likely to include the individual taking the drug, their expectations and beliefs about the drug, the society that defines these beliefs, the likelihood of sanctions and the state of the individual at the time of consuming the drug.

The classification that has been provided in the drug tables has adopted a model of 'everything else being equal' that is only viable when making generalisations of this sort. However, this does not mean that there is no benefit to taxonomies of this sort – they form the basis on which actuarial calculations of the likelihood of particular negative outcomes can be calculated. The dangerousness of a drug cannot be generalised across all situations – the criterion to be used and the method of calculating both the likelihood of and the extent of the negative outcome need to be specified before comparisons across substances can be made.

A further point is about the temporal aspect of measurement. If it is accepted that the dangerousness of a drug is not exclusively a function of the pharmacological properties of the substance, then there are likely to be ephemeral factors (such as availability and purity, as well as societal responses such as legality) that will influence the likelihood of particular negative outcomes. The ability to measure shifts in these outcomes is also crucial to understanding shifting risk patterns, the efficacy of public health interventions and changing patterns of drug use. To this end it is critical not only that measures of dangerousness are maximised, but also that they are obtained consistently across time. It is here that the call for better information collection, analysis and dissemination is most clear.

Implications

Considerable work is required to provide an adequate answer to some of the problems of assessment set out in this report – some of which are epidemiological and some of which are underpinned by limitations in our current knowledge of the ways in which drugs are used. However, there are some intrinsic logical issues that prevent clear delineation of risks by substance use:

a. Factors related to the substance – in particular, the quantity and purity of the drug.
b. Factors in the consumer – their physiological frame and state, their history of consumption and consequences for tolerance, and psychological factors including expectations and psycho-adaptation to the drug. Individual factors will also be mediated by 'career' variables including age and developmental state.
c. Combination use – the concurrent or consecutive use of several drugs both within and across drug classes provides an enormous confounding effect on the prediction of effects, and may significantly increase risk.
d. Route of administration – while it is generally acknowledged that use by injection carries the most immediate risk it should not be assumed that other routes – smoking and swallowing in particular – are without hazards.

What has been outlined above is an attempt to provide a basic matrix in which the more commonly occurring effects are presented for the main psychoactive drugs along two dimensions – acute versus chronic and physical versus psycho-social. This is no more than an illustrative guide based on the experiences and acquired knowledge of academics and clinicians and is therefore biased in the direction of medical and psychiatric effects. As with the Hall et al (1999) review, the current report does not attempt to enumerate the positive effects that may be associated with substance use, although it readily acknowledges that part of the risk relates to this reinforcing quality and the 'functionality' of much substance use.

The guide provided, particularly in the tables, reflects a summary of the published literature and the views of the key informants, but each of these sources of information is restricted by the limitations in our knowledge base. Perhaps the most important of these is epidemiological in that, without baseline levels of use reporting, we do not have adequate denominators against which to assess the risk probabilities of adverse event occurrence. There is considerable scope for building on this work by improving our understanding of the 'why' questions at a social, psychological and anthropological level, of developing our clinical and physiological awareness of impact and of using these factors as hazard predictors. However, this is a huge task that assumes societal stasis and, for this reason, is unrealistic. It is hoped that, within a relatively short period of time, our research technologies and their assimilation within the broad multi-disciplinary frame of addiction science will significantly

improve on the data presented here. This can never be a precise science and individual variation will inevitably confound our attempts at precision. This does not mean that the attempt is not worthwhile and it is the bases of our approximations that will decide the viability of such risk assessments.

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Appendix 1

Glossary of Medical and Technical Terminology

Alcoholic Hepatitis	Inflammation of the liver resulting from chronic alcohol consumption, often leading to cirrhosis of the liver.
Anaesthetic	A drug or agent that is used to create partial or total loss of sensation.
Anterograde amnesia	Impairment of memory for events and experiences which occur after the amnesia-causing trauma.
Asphyxia	Pathological changes caused by a lack of oxygen in respired air, results in hypoxia.
Ataxia	Partial or complete loss of coordination of voluntary muscle movements; irregularity of muscle action.
Cardiac arrhythmia	Any variation from the normal rhythm of the heartbeat.
Cardiomyopathy	Disease of the heart muscle.
Cardiovascular	Pertaining to the heart and blood vessels.
Cerebral haemorrhage	Leakage of blood from the vessels in the largest part of the brain.
Cerebrovascular	Pertaining to the blood vessels in the brain.
Cirrhosis (liver)	Normal cells in the liver are replaced by scar tissue, impacting on ability to function. Complications can include internal bleeding, kidney failure, mental confusion, coma, fluid retention and infection.
Diuresis	Increased formation / excretion of urine by the kidneys.
Dyskinesia	Distortion or impairment of voluntary movements; the presence of involuntary movements (tic, spasm).
Dysphoria	Abnormal affect, usually associated with anxiety, restlessness, depression. (ant. Euphoria).

Euphoria	Extreme elation generally accompanied by optimism and a sense of well-being and heightened activity. May be unrealistic, contain delusions of grandeur or invulnerability, and manic activity. (ant. Dysphoria).
Foetal Alcohol Syndrome	A cluster of abnormal developmental features of a foetus resulting from alcohol consumption by the mother during pregnancy. Anatomical and psychological deficits can occur, including facial dysmorphism, microcephaly, growth deficiencies, mental retardation, hyperactivity, heart murmur and skeletal malformation.
Gynaecomastia	Excessive development of male breasts.
Hypothermia	Abnormally low body temperature. The condition needs treatment at body temperatures of 35C (95 F) or below, becomes life threatening below body temperatures below 32.2 C (90 F).
Hyperthermia	Abnormally high body temperature. Unrelieved can lead to collapse and death, particularly in the elderly. Also known as heatstroke or heat prostration.
Hypoglycaemia	Abnormally diminished concentration of glucose in the blood. May result in loss of consciousness, coma, and brain damage.
Hypoxia	A reduction of oxygen supply to bodily tissues.
Korsakoff's psychosis	An amnesic syndrome (anterograde) accompanied by an impaired ability to plan and organise, often found in chronic alcoholics. With continued drinking or detoxification in the absence of vitamin supplementation can produce irreversible cognitive impairment. The development of Korsakoff's psychosis may result from untreated Wernike's encephalopathy.
Ischaemia	A deficiency of blood in a part of the body usually due to obstruction of the arterial blood supply or inadequate blood flow.

Larynx	The organ of voice and air passage between pharynx and trachea, made up of muscles and cartilages.
Lymphoedema	Swelling of tissues below the skin caused by fluid accumulation and an obstruction of lymphatic drainage.
Mallory-Weiss tear	Tear in the lining of the stomach where it joins the oesophagus. Due to sudden increase in intra-abdominal pressure caused by retching, commonly associated with binge alcohol use.
Medulla Oblongata	The lowest subdivision of the brainstem, adjacent to the spinal chord; houses respiration and cardiac regulatory centres.
Microcephaly	A congenital abnormality of the central nervous system where the head circumference is significantly below the average for age and sex. May occur as a result of genetic or non-genetic factors, including fetal alcohol syndrome.
Myocardial Infarction (MI)	Deprivation of circulating blood to the heart, usually caused by a narrowing of the arteries resulting in the development of a blood clot, commonly known as a heart attack.
Myopathy	Any disease of a muscle.
Pancreatitis	Acute or chronic inflammation of the pancreas; due to autodigestion of pancreatic tissue by its own enzymes.
Peripheral neuropathy	Functional disturbance or pathological changes in the nervous system of the arms and legs.
Pharmacodynamics	The study of the biochemical and physiological effects of drugs and their mechanism of action on the human body.
Pharmacokinetics	The study of how the body's systems effect drugs. This includes absorption, distribution, biotransformation and excretion.
Pharynx	"The throat" or the passage between the mouth and the larynx and oesophagus.

Phenotype	The entire physical, biochemical and physiological makeup of an individual; determined both genetically and environmentally.
Poly neuropathy	A disease process that involves a number of peripheral nerves.
Tachycardia	Excessively rapid heart action; generally over 100 beats per minute.
Thrombosis (deep vein)	The development of blood clots which may break off and cause respiratory distress.
Wernicke's Encephalopathy	An acute brain disorder characterised by abnormal eye movement, unsteady on feet and disordered gait (ataxia), orientation problems and general mental confusion. This is the result of a deficiency in B1 thiamine and may be prevented by large doses of this vitamin.