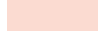


The scope of addiction medicine

- Epidemiology of substance use 3
- Spectrum of substance use and core clinical diagnoses 18
- Neurobiology of the dependence syndrome 20
- Underlying conditions and risk factors 24
- Natural history of substance use and related disorders 27
- What can we do about alcohol and other substance use problems? 32



The use of psychoactive substances has formed an integral part of human society for millennia, but there are considerable differences in the nature of substances used and the reasons for their use. Thousands of naturally occurring substances exist and these have been supplemented over the past 200 years by synthetic compounds produced in the search for medications or simply for hedonic purposes. Worldwide 48% of the total adult population (approx 2 billion people), consume alcohol at least occasionally, 33% (approx 1.3 billion people) smoke tobacco, principally in the form of cigarettes, and 5% of adults (approx 200 million people) use illicit drugs. Increasingly, the pattern of substance use involves the use of multiple substances, often with different pharmacological effects.

Cigarette smoking, which peaked in many western countries in 1940s and 50s, when 75% of men and 30% of women smoked, has declined greatly in response to concerted public health campaigns and legislation, for example, in Australia and some Scandinavian countries the prevalence is 16–20% of both men and women. Elsewhere in Europe the prevalence of cigarette smoking reaches approx 50%, and in Southeast Asia and East Asia the prevalence has risen hugely over the past 2–3 decades.

The pattern of illicit drug use varies widely across the world. In part, it reflects traditional use of certain drugs, and elsewhere the effects of trafficking and the creation of markets for these substances. The most commonly used illicit drug is cannabis, the use of which involves up to 10–15% of the adult population in many countries of Africa and the Middle East, Europe, Australasia, and North America. Illicit opioid use affects approx 1% of the adult population in several countries in Europe, Southeast Asia, and North America, but there has been a downturn in use in some Southeast Asian countries and Australia since 2000. The geographical pattern of psychostimulant use varies between cocaine and amphetamine-type stimulants. Traditional use of coca leaf in the northern countries of South America continues, and there has been high-level importation of cocaine into the USA, Canada, and several Western European countries. In contrast, in Southeast Asia and the Middle East, Japan, and Australia, amphetamine-type stimulants are more commonly used. Recently, there has been an upsurge in the use of amphetamines in the West Coast of the United States of America and this form of use is presently spreading eastwards across the country.

Substance use contributes substantially to the global burden of disease. Tobacco is the fourth commonest risk factor causing disease burden and measured by disability adjusted life years (DALYs). Alcohol consumption is the 5th commonest disease burden and illicit drugs are also in the top 20 causes of disease. Substance use disorders expend 4–5% of global gross domestic product (GDP), with alcohol causing 1–2%, tobacco 1%, and illicit drugs 0.5%.

Epidemiology of substance use

Alcohol

Alcohol consumption per head of population has been substantially higher in western countries, such as Europe, North America, and Australasia than elsewhere. In most of these countries alcohol consumption has plateaued or declined in recent years and ranges from 6 to 15 L of absolute alcohol per annum. Consumption has greatly increased in many countries where historically alcohol intake was low, notably in countries of East and Southeast Asia. By contrast, countries in the Middle East where Islam is the predominant religion and forbids the use of alcohol, have overall low levels of alcohol consumption, which are below 1 L per year and in some countries are essentially zero.

Globally, just over half the adult population does not drink alcohol, with abstinence rates being higher in poorer countries (Table 1.1). Much of the variation in *per capita* alcohol consumption between countries and regions of the world reflects variations in abstinence rates; amongst drinkers there is less variation in alcohol consumption. The majority of people who drink have a detrimental drinking pattern and a considerable proportion of alcohol is consumed in potentially harmful ways. Detrimental drinking patterns seem to be more common amongst poorer than amongst richer drinking populations.

Across regions of the world, the rank-ordering of the percentage of the population who drink alcohol generally follows the rank ordering in terms of *per capita* purchasing power parity (PPP), with there being more drinkers in richer regions than in poorer. This does not hold true for the two lowest income groups in Table 1.1, which were separated on the basis of their rates of abstinence. Generally, the gender differences in abstinence are much greater in the three developing country regional groups than in the two developed regional groups. In the absence of strong cultural or religious bars, it is likely that abstinence rates are likely to decline as affluence increases.

At the level of the individual country, the relationship between economic level and alcohol abstinence rate is relatively close up to a PPP level of (International Dollars) I\$7000. Beyond a PPP of I\$7000, there is little relation between the degree of affluence of a country and the adult rate of abstinence. Within countries, when categorizing the population by three daily income categories (<US\$1/day, US\$1–2/day, and >US\$2/day), people with higher incomes are more likely to use alcohol than people with lower incomes. Below a PPP of I\$10,000, adult *per capita* consumption increases by 1.2 L of pure alcohol per year for each increase in I\$1000 PPP, with the relationship flattening after I\$10,000.

Analysis of trends in alcohol consumption for the WHO regions finds that the European, African, and the Americas all reached their highest consumption about the same time, in the early 1980s, although the level of alcohol consumption is much higher in the European Region than in the other regions. The Eastern Mediterranean Region displays a steady low consumption. The two regions showing recent and continuing increases in alcohol consumption are the Southeast Asian Region (although still very low) and the Western Pacific Region. Based on recent trends in

alcohol consumption, it is reasonable to assume that in most regions of the world, alcohol consumption is likely to remain reasonably stable over the next 10–20 years. The exceptions to this are the countries of the Southeast Asian Region and the low to middle income countries of the Western Pacific Region (constituting nearly half of the world's population), where alcohol consumption is likely to increase.

Alcohol-related harm

The World Health Organization's global burden of disease study has estimated the impact of alcohol consumption on the burden of disease for the year 2002 (Table 1.2). The disability adjusted life year (DALY) estimates the number of healthy years of life lost due to alcohol. For example, while a year of perfect health will count as 1 and a year of death will be 0, a year of damaged health that significantly affects quality of life will be somewhere in between. DALYs measure a gap in health between the current position and what could be achieved.

Overall, alcohol is estimated to cause a net harm of 4.4% of the global burden of disease, indicating that the beneficial effects of alcohol are small compared with the detrimental effects. Alcohol causes a greater health burden for men than for women. Neuropsychiatric disorders, mainly made up of alcohol use disorders, constitute the category linked to most alcohol-attributable burden of disease, with unintentional injury being the second most important category. Contrary to the assumption by many that cirrhosis is the most important form of alcohol-induced morbidity and mortality, it only contributes to 10% of the burden of disease caused by alcohol. The health burden is considerable both for acute and chronic health consequences.

The highest burden of alcohol-related harm is found in the European Region, followed by the Americas and the Western Pacific Region. In all of these regions there are economically rich sub-regions (Western Europe, North America, Japan, Australia and New Zealand) with relatively higher alcohol consumption. The sub-region with the highest burden of alcohol-related harm is the Eastern part of the European Region, with the Russian Federation as the most populous country. The region with the least alcohol-attributable burden of disease is the Eastern Mediterranean Region, where in many countries alcohol is forbidden by law because of religious reasons. Intentional and unintentional injuries account for a higher proportion of alcohol-caused burden of disease in lower-income countries, whereas alcohol use disorders and cancers account for larger proportions of the burden in higher-income countries. The alcohol burden accounted by cardiovascular disease is highest in Eastern Europe and central Asia and in the lower-drinking poorest parts of the world. The global burden of disease study has limitations, since not all disease conditions where alcohol has a causal impact are included because of lack of data; this is especially relevant for communicable diseases, such as tuberculosis and human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS).

There is a very close relationship between total alcohol consumption and the prevalence of alcohol dependence, implying that when alcohol consumption increases, so does the proportion of people with alcohol

Table 1.1 Economic development status and alcohol consumption in 2002 (based on population weighted averages of 182 countries)

Level of mortality/ category of countries	Average GDP PPP in US\$	WHO- regions [†]	Adult total consumption in L/year [‡]	% Drinkers		Consumption per drinker in g/day pure alcohol	Average pattern of drinking [§]
				M	F		
High mortality; lowest consumption	2441	EMR-D, SEAR-D; Islamic Middle East and Indian subcontinent	1.7	19%	2%	33	2.9
Very high or high mortality; low consumption	2249	AFR-D, AFR-E, AMR-D; poorest countries in Africa and America	7.1	47%	32%	41	3.0
Low mortality emerging economies	5257	AMR-B, EMR-B, SEAR-B, WPR-B; better-off developing countries in America, Asia, Western Pacific Region	5.7	67%	36%	25	2.5

Table 1.1 (Contd.)

Level of mortality/ category of countries	Average GDP PPP in US\$*	WHO- regions†	Adult total consumption in L/year‡	% Drinkers		Consumption per drinker in g/day pure alcohol	Average pattern of drinking§
				M	F		
Developed countries	28,405	AMR A, EUR A, WPR A; North America, Western Europe, Japan, Australasia	10.7	81%	65%	32	1.8
Low child, and low or high adult mortality	6862	EUR B, EUR C; former Socialist countries in Central/Eastern Europe and Central Asia	11.7	77%	59%	37	3.5
World (population weighted from regions)			6.2	55%	34%	30	2.6

Source: World Health Organization 2007.

* GDP: Gross Domestic Product, a measure of the size of a country's economy; PPP: Purchasing Power Parity per capita, the country's per capita purchasing power for an equivalent basket of goods, expressed in International Dollars (US\$).

† The regional sub groupings are defined by WHO on the basis of high, medium, or low levels of adult and of infant mortality. A stands for very low child and very low adult mortality, B for low child and low adult mortality, C for low child and high adult mortality, D for high child and high adult mortality, and E for very high child and very high adult mortality.

‡ In litres of pure alcohol per resident aged 15 years and older per year (average of available data for 2001 to 2003); includes recorded and unrecorded consumption

§ Indicator of the hazard per litre of alcohol consumed, composed of several indicators of heavy drinking occasions plus the frequency of drinking with meals (reverse scored) and in public places (1 = least detrimental; 4 = most detrimental).

dependence, and vice versa. Although alcohol policy measures may have a significant impact on alcohol consumption and alcohol-related harms, there are a number of other factors that also affect the level and trends in alcohol consumption, and alcohol-related harms in a population. For example, in recent years there has been an increase in alcohol consumption in a number of low-income countries such as China, India, and South Korea, where abstention rates have been traditionally high, and where an increase in alcohol consumption has implied an increase in the proportion of the population that are drinkers. The consumption increase in these countries probably reflects economic development and increases in consumers' purchasing power, as well as increases in the marketing of branded alcoholic beverages.

Tobacco

Cigarette smoking and other forms of tobacco use are estimated to kill around 5 million people per year around the world. This number is likely to rise.

Smoking is the single greatest reversible risk factor for disease and death in the developed world, and was estimated as the third greatest risk factor (after alcohol and high blood pressure) in low mortality developing countries in 2002. Currently, it kills just less than one in 10 (8.8%) adults worldwide. Among males in developed regions, smoking is believed to cause more than a quarter (26.3%) of deaths.

The prevalence of smoking peaked in many western countries in the 1940s and 50s, when 75% of men and 30% of women smoked cigarettes. It has since declined greatly in response to concerted public health campaigns and legislation. In Australia and some Scandinavian countries the prevalence is now 16–20% of both men and women. Elsewhere in Europe the prevalence of cigarette smoking among males reaches up to 50%.

In contrast to the decline in smoking in the high-income countries, in Southeast and East Asia the prevalence has risen greatly over the past 2–3 decades, more in males, but increasingly also in females. Asia is an unashamed marketing target of the tobacco industry. More than 50% of males in Asia smoke today and one in every three cigarettes smoked in the world today is smoked in China, where there are said to be 1000 cigarette brands. Currently, 82% of the world's smokers live in low and middle income countries, with 38% of the world's smokers based in East Asia and the Pacific.

Lower socio-economic status is also the major risk factor for continuing smoking within developed countries and, similarly, low educational attainment is associated with higher smoking rates. In Australia, where there is a low overall prevalence of smoking, some isolated and disadvantaged Aboriginal communities have smoking rates of up to 80%.

Around the world more men than women smoke. Males in low income countries are more likely to be daily smokers than males in wealthier nations. In contrast, females are more likely to be daily smokers in wealthier nations than in low income nations.

Smoking typically starts before the age of 25, then the prevalence peaks at ages 30–49.

Table 1.2 The impact of alcohol consumption on the worldwide burden of disease, as expressed in the number of healthy life years lost (Disability adjusted life years, DALYs) due to alcohol in 2002

Disease category	Number of DALYs (thousands)	Percentage of the harms due to alcohol (in DALYs) attributed to each disease category
DALYs		
Maternal and perinatal conditions (low birth weight)	94	0.1
Cancer	6054	9.0
Diabetes mellitus	20	0.0
Neuropsychiatric disorders	23,115	34.3
Cardiovascular diseases	6598	9.8
Cirrhosis of the liver	6883	10.2
Unintentional injuries	17,146	25.5
Intentional injuries	7417	11.0
Total 'detrimental effects' attributable to alcohol	67,326	100.0
DALYs prevented		
Diabetes mellitus	-213	13.3
Cardiovascular diseases	-2039	86.7
Total 'beneficial effects' attributable to alcohol	-2351	100.0
Net DALYs		
Net DALYs attributable to alcohol	64,975	100.0
All DALYs	1,490,126	
Net DALYs attributable to alcohol as a percentage of all DALYs	4.4%	

Source: World Health Organization (2007).

Mental health disorders are also a risk factor for smoking. One third of individuals with major depression and a quarter of those with an anxiety disorder are dependent smokers. Persons with alcohol use disorders are more likely to smoke.

Impact of smoking

The World Health Organization estimates that smoking is the cause of 4% of the global burden of disease. One in two long-term regular smokers are likely to die as a result of their smoking. Half these deaths occur in middle

age (35–69 years). In developed countries smoking is responsible for much of the mortality gap between rich and poor.

Smoking is a well recognized risk factor for lung cancer, aerodigestive and other cancers, chronic obstructive pulmonary disease, other respiratory diseases and vascular diseases. It is also a risk factor for type 2 diabetes and for renal disease. As well as its chronic health effects, smoking is associated with acute harms from fire injuries.

Tobacco smoking in pregnancy is associated with lower birth weight babies.

Illicit drugs

Worldwide, an estimated 185 million adults use illicit drugs. The burden of disease associated with use of legal drugs outweighs that associated with illegal drugs.

The use of psychoactive drugs has received increasing attention worldwide in recent decades. There is much discussion about the extent of the problem, and drug use is thought to account for a significant share of the global burden of disease given the relatively low prevalence of illicit drug use in many regions of the world.

In this chapter, there is discussion of the major illicit drug types used, the epidemiology of use across the globe, and some discussion of the natural history and burden of disease related to these different drug types. There are differences across drug types in the magnitude and nature of harms.

'Illicit drug use' refers to the non-medical use of a variety of drugs including cannabis, amphetamine type stimulants (including methamphetamine, amphetamine, MDMA (3,4-methylenedioxymethamphetamine, ecstasy), cocaine, and opioids (including heroin) (Table 1.3). There are many other drugs used such as gamma-hydroxybutyrate (GHB), ketamine, and *d*-lysergic acid (LSD), but these are used by comparatively fewer persons in a more limited number of countries, and both the nature and extent of harm is less well documented, so the present chapter will focus upon the four major drug classes.

Table 1.3 Major illicit drug groups

Cannabis	A generic term for psychoactive preparations (e.g. marijuana, hashish, and hash oil) derived from the cannabis sativa plant
Amphetamines	A class of sympathomimetic amines with powerful stimulant action on the central nervous system
Cocaine	An alkaloid central nervous system stimulant that is derived from the coca plant
Opioids	Derivatives of the opium poppy (such as heroin and morphine), their synthetic analogues, and compounds synthesized in the body, which act upon the opioid receptors in the brain. They have the capacity to relieve pain and produce a sense of euphoria, as well as cause stupor, coma, and respiratory depression

How common is illicit drug use?

The illegality of illicit drug use makes it difficult to quantify the levels of drug use because the drug-users are 'hidden' and thus difficult to identify, and even when they can be located and interviewed, they may attempt to conceal their drug use. The United Nations Office on Drugs and Crime (UNODC) publish estimates of the prevalence of past year illicit drug use, but the quality of the data used varies dramatically from country to country, from high quality national survey data, to key informant and indicator data of uncertain validity. Nonetheless, until there is a concerted attempt to collect high quality data they remain the only source of estimates for some countries.

Cannabis is the most widely used illicit drug and is used in every region of the world. In 2004, around 162 million adults (an estimated 4% of the global adult population) were thought to have used cannabis in the previous year, a 10% increase on estimated rates of global use in the mid-1990s. Patterns of cannabis use have been most extensively studied in developed countries such as the USA, Canada, Australia, and Europe. Europe generally has lower rates of use than Australia, Canada, and the USA. The limited data from low and middle income countries suggest that with exceptions (e.g. South Africa) rates of cannabis use are much lower in Africa, Asia, and South America than in Europe and English-speaking countries. There may be pockets of high level use within a country. For example, in some remote Aboriginal communities in Australia more than 60% of adults are reported to use cannabis regularly.

The term 'amphetamine type stimulants' (ATS) refers to a range of drugs related to amphetamine. Methamphetamine and amphetamine are the major ATS available worldwide, followed by MDMA. The diversion of prescription stimulant drugs such as dexamphetamine has been reported, but this is less of a problem than illicitly produced ATS. Use appears to be increasing in many parts of the world, but many countries have scant or no data on the prevalence, routes and forms of use. Problematic use of amphetamines appears more prevalent in East and Southeast Asia, North America, South Africa, New Zealand, Australia, and a number of European countries.

Cocaine is reportedly the least widely used of the illicit drugs: around 13 million adults were thought to have used cocaine in 2006, with use heavily concentrated in North America, Latin America, and some European countries. The reported prevalence of cocaine use in other high income countries is typically much lower than that in the US.

Illicit opioids are the third most common form of illicit drug use. Globally, illicit opioids were estimated to have been used by around 16 million people in the early 2000s. In high income countries, estimates of dependence are typically below 1% of adults aged 15 or more. Most research on the epidemiology and natural history of opioid use focuses upon dependent users. The distinction between 'use' and 'dependence' is an important one that is briefly discussed below.

Use versus problematic use: an important distinction

Not all drug use causes evident harm to users. Efforts have been made on an international level to classify the behaviours or symptoms

associated with use that does cause problems to the user. It is this problematic use towards which most health care interventions are targeted.

The International Classification of Diseases (ICD) distinguishes between 'harmful drug use' and 'drug dependence'. Harmful drug use is defined by clear evidence that the substance use is responsible for physical (e.g. organ damage) and psychological harm (e.g. drug-induced psychosis). In ICD10 drug dependence involves a cluster of behavioural, cognitive, and physiological phenomena that develop after repeated substance use and that typically include a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal state.

It is difficult to produce credible estimates of the number of people who make up the 'hidden population' of such dependent or problematic drug users, yet it is this group who probably suffer the bulk of problems related to their drug use and who are in most need of treatment—drug treatment and treatment for general medical health problems. The preferred strategy is to look for convergence in estimates produced by a variety of different methods of estimation. These methods are of two broad types, *direct* and *indirect*. Direct estimation methods attempt to estimate the number of illicit drug users in representative samples of the population. Indirect estimation methods attempt to use information from known populations of illicit drug users (such as those who have died of opioid overdoses or been treated) to estimate the size of the hidden population of illicit drug users.

Examining the harms related to drug use: morbidity and mortality

In the first Global Burden of Disease estimates (1990 and 2001 estimates), there was good evidence suggesting that there had been an increase globally in the extent of mortality related to injecting drug use and dependent use of opioids, cocaine or amphetamines. In the next iteration of these estimates, (see <http://www.gbd.unsw.edu.au>) attempts will be made to extend estimates to include cannabis given its prevalence of use and the expansion of the evidence on potential harms related to its use.

The best evidence that illicit drug use is a cause of premature death comes from cohort studies of illicit drug users, which have limitations. It is likely that the estimates of disease burden to date have been underestimated because we simply have too little data on the nature and magnitude of harms related to different drugs, and because even where we know drugs cause harm, too few studies have estimated the course of drug use and associated harm over time and across different country contexts. Existing estimates could not estimate morbidity and mortality related to cannabis use; more recently, evidence increasingly suggests that cannabis may increase risks of some cancers (related to smoking of the drug) and motor vehicle accidents.

1 Degenhardt L, Hall W, Lynskey M, Warner-Smith M. Illicit drug use. In: Ezzati M, Lopez AD, Rodgers A, Murray R, eds. *Comparative Quantification of Health Risks: Global and Regional Burden of Disease Attributable to Selected Major Risk Factors*, 2nd edn. Geneva: World Health Organization, 2004; 1109–1176.

Illicit drug use

Cannabis

The best data on the prevalence of cannabis use and its correlates comes from the United States, Canada, and Australia, where the levels of use appear to have been the highest. Rates in Europe have increased over the past decade. Generally, rates of use have been higher among young people in high income countries, but rates of recreational use may be increasing among young people in low and middle income countries.

Studies conducted in the United States suggest that cannabis typically begins in the mid to late teens, and is most prevalent in early adulthood. Most cannabis use is irregular, with very few users engaging in long-term daily use. In the USA and Australia, it is thought that about 10% of those who ever use cannabis become daily users, and another 20–30% use weekly. Transitions in life roles such as entry into full-time employment, getting married, or having children, are associated with reductions in or cessation of use for many people. The largest decreases are seen in cannabis use among males and females after marriage, and especially during pregnancy and after childbirth in women.

Heavy (daily) cannabis use over a period of years increases the risks of experiencing problems. Daily cannabis users are more likely to be male, less well educated, and more likely to regularly use other drugs. Weekly or more frequent use in adolescence appears to carry significant risk for dependence in early adulthood. Population surveys suggest that cannabis use disorders are the most common forms of drug problems after alcohol and tobacco. In Australia, the prevalence of past-year cannabis use disorders has been estimated at around 2%. An estimated lifetime risk of 9% for dependence has been estimated among persons who ever used cannabis.

Risk is not confined to older users. Among a cohort of young people in Australia, the prevalence of cannabis dependence in the past year was 7%, with almost 75% of daily users meeting dependence criteria. In countries such as Australia, New Zealand, and the United States, around one in six young people who ever use cannabis develop symptoms of dependence. Those at highest risk may have a history of poor academic achievement, deviant behaviour in childhood and adolescence, non-conformity and rebelliousness, poor parental relationships, and a parental history of drug and alcohol problems. There is increasing evidence of a substantial genetic contribution to the likelihood of using and developing dependence upon cannabis.

Psychostimulants

The term 'amphetamine type stimulants' refers to a range of drugs related to amphetamine, which share stimulant properties that increase the activity of the central nervous system and produce effects similar to adrenaline. Methamphetamine and amphetamine are now the major ATS available worldwide. ATS have recently become the focus of increasing attention worldwide because of a substantial increase in the production of these drugs over the past decade, and increasing consumption and harm related to their use. After cannabis, ATS are the most widely used illicit drugs, in both high and low income countries.

Because it is derived from a plant, cocaine use has typically been more concentrated in regions where the coca plant is grown or those nearby. The US has had by far the greatest problem with cocaine (and 'crack' cocaine) dependence worldwide, particularly in the 1990s. More recently, there have been increases in the availability and use of cocaine in Western Europe. The use of cocaine is much more uncommon in Asia, Oceania, and African countries.

Psychostimulants are most commonly taken orally, intranasally, the vapours inhaled (smoking), or injected. A dependence syndrome upon amphetamine and cocaine is well described. Dependence has been associated with mental health, physical, occupational, relationship, financial, and legal problems. It is likely that most of the harm related to psychostimulant use occurs among those who have developed dependent use of the drug. Users with a history of other drug and mental health problems may be at greater risk of developing dependence. There has been concern about associations between psychostimulant use and HIV risk, much of which has focused on risky sexual behaviour.

Available data strongly suggest that both route of administration and forms used are important factors affecting the nature and extent of associated harms. The increase in use of the crystalline form of methamphetamine, for example, has been associated with increased problems related to dependent and binge patterns of use. Smoking and injecting have also been associated with a higher risk of dependent or problematic use than swallowing or snorting of the drug. There is evidence that 'smoking' crystal methamphetamine and 'crack' cocaine also carries harms related to the inhalation of possibly toxic chemicals and possibly blood borne virus transmission through the sharing of smoking implements.

Few studies have documented the natural history of psychostimulant use, in sharp contrast to the literature on cannabis and even opioids. Our current understanding derives largely from cross-sectional studies, typically involving convenience samples, or treatment or prison settings. US prospective studies have suggested that relapse following treatment for psychostimulant dependence is common. The concentration of work in treatment or prison populations makes it difficult to draw inferences about amphetamine use in the general population, since most users will never come into contact with either treatment or law enforcement agencies. As a result, little is known about the aetiology and consequences of psychostimulant use that does not come to the attention of police or treatment services. This is an area where much more needs to be known given the increases thought to be occurring in the use of these drugs.

Opioids

Cohort studies of dependent opioid users have suggested that users may continue to use opioids for decades, with periods of use interrupted by time spent in treatment, prison, and for some, extended periods of abstinence. Such cohort studies have largely been conducted in high income countries—in Asia, for example, the context of opium (and, more recently, heroin and pharmaceutical opioids) use is quite different from the USA and we know much less about the natural history of opioid use in these countries. Nonetheless, the evidence available to date suggests that

opioid dependent persons may struggle to control their use for significant portions of their lives. Data from the US have suggested that one in four persons who use opioids illicitly may develop dependence upon them.

Although opioids are used by far fewer people than cannabis, opioid dependence is associated with substantial mortality and morbidity that appears to far exceed that of cannabis use or dependence. Reviews have suggested that opioid dependent persons may be 13 times more likely to die than peers of the same age and sex. Multiple reasons exist for this: drug overdose, accidents and trauma, suicide, the consequences of blood borne viral infections, such as HIV and hepatitis C virus (HCV), and generally poorer physical health contribute to shorter life expectancy and poorer quality of life for this group. Although heroin has typically been thought to be the primary opioid accounting for problems related to opioid dependence, in many countries (particularly in the United States, South Asia and Eastern Europe) dependence upon pharmaceutical opioids is an increasing problem.

Summary and implications: illicit drugs

The discussion above has attempted to provide a broad overview of the epidemiology of four major drug types. Although we have some data on the scope of the problem, because of the illegal nature of such drug use there is much that we do not understand about the extent, context, and natural history of illicit drugs, particularly in low and middle income countries where drug use seems to be increasing. We still have much to learn about the extent of drug use, and the nature and magnitude of harms that may result.

Although much remains to be understood about illicit drug use, based upon what we do know, several things are certain:

- There is considerable and possibly increasing demand for drugs in the general population
- Demand for and consumption of drugs is dynamic, with current trends suggesting increasing demand for stimulant drugs
- Drug supply may both respond to and drive demand for drugs
- Responses to drug use must reflect these drivers.

From Table 1.4 we see that Australia, New Zealand, USA and Canada rank highest among the prevalence of adult illicit drug users in the world with Singapore, Japan and Sweden the lowest. Cannabis is the most widely used illicit substance in the world.

Although opioid use has plateaued in recent years, the use of amphetamine type substances has increased.

While Tables 1.5 and 1.6 show estimates of prevalence for countries or regions, within any population there are subgroups with far higher prevalence of substance used disorders. Higher rates are particularly common in disadvantaged or marginalized groups. For example, major population surveys in Australia indicate that 2% of the population have, at some time, self injected drugs, compared with 62% of street kids. Among street kids, injecting is epidemic. The most widely injected drugs across Australia were opiates (26%), amphetamines (8-10%), cocaine (2%), and benzodiazepines (2%).

Table 1.4 Percentage of the population aged 15–64 who have used any illicit drug in the past year

	Opiates	Cannabis	Cocaine	Amphetamines	Ecstasy
Australia	0.5	13.3	1.2	3.8	4.0
New Zealand	0.5	13.4	0.5	3.4	2.2
UK	0.9				
England & Wales		10.8	2.4	1.5	2.0
Scotland		7.9	1.4	1.4	1.7
Ireland	0.6	5.1	1.1	0.4	1.1
Italy	0.8	7.1	1.2	0.2	0.4
France	0.4	9.8	0.3	0.2	0.3
Germany	0.3	6.9	1.0	0.9	0.8
Sweden	0.1	2.2	0.2	0.2	0.4
USA	0.6	12.6	2.8	1.5	1.0
Canada	0.4	16.8	2.3	0.8	1.1
Singapore	0.004	0.004	0.0002	0.005	0.004
Japan	0.1	0.1	0.03	0.4	0.1
Russian Federation	2.0	3.9	0.1	0.2	0.1

NB: Data come from different years between 1999 and 2004; the year of the survey may vary between countries and, for different substances, within countries. Data from: United Nations Office on Drugs and Crime. World Drug Report. Vienna, Austria: United Nations 2006. Available at http://www.unodc.org/unodc/en/world_drug_report.html

While illicit drugs attract great public concern, in terms of morbidity, mortality, and social costs, they are far outweighed by the costs from tobacco. For example, in Australia in the late 1990s the annual social cost of tobacco smoking was estimated at AUD 21.3 billion, compared with alcohol AUD 7.6 billion and illicit drugs AUD 6.1 billion.

Table 1.5 Estimated worldwide use of licit and illicit drugs and global burden of disease

	Worldwide use by adults Estimated in 2002	Global burden of disease (DALYs in 2000)	Burden of disease in developed regions (2000)	Deaths world-wide (2000)	Deaths in developed regions (2000)
Licit drugs:					
Tobacco	1.1 billion	4.1%	12.2%	8.8%	18.0%
Alcohol	2 billion	4.0%	9.2%	3.2%	3.9%
Illicit Drugs:	185–200 million	0.8%	1.8%	0.4%	0.5%

Adapted from: Anderson P. Global use of alcohol, drugs and tobacco. *Drug and Alcohol Review* 2006; 25: 489–502; and Rehm J, Taylor B, Room R. Global burden of disease from alcohol, illicit drugs and tobacco. *Drug and Alcohol Review* 2006; 25: 503–513.

Table 1.6 Estimated worldwide use of illicit drugs in the early 2000s

Illicit drugs	Any illicit drug: 200 million
Cannabis	146.2–162.4 million
Amphetamines	25–29.6 million
Illicit opioids	15.3–15.9 million
Cocaine	13.3–13.4 million
Ecstasy	8.3–9.7 million

Adapted from: Anderson P. Global use of alcohol, drugs and tobacco. *Drug and Alcohol Review* 2006; 25: 489–502.

Summary: epidemiology of alcohol, tobacco and illicit drug use

The misuse of licit and illicit drugs increases the burden of disease to the individual, the country, and the world. In addition to criminal activity, injecting use of illegal drugs is a major risk factor for spread of infections, particularly hepatitis C and HIV, secondary to sharing of needles and injecting equipment. However, the health and economic cost of the use of tobacco and alcohol outweighs the cost of illicit substances. It is, in fact, the legal drugs (tobacco and alcohol) that have the greatest cost.

Use of one psychoactive substance often does not occur in isolation. Those with alcohol use disorders are more likely to smoke tobacco; most illicit drug users are polysubstance users and often use non-injectable drugs as well, particularly nicotine, alcohol, benzodiazepines, cannabis, and prescribed and proprietary drugs.

It is difficult to get accurate figures on the prevalence of misuse of many psychoactive substances. For example, it is difficult to differentiate between illicit benzodiazepine use and its prescribed use, and so the true epidemiology of benzodiazepine misuse is unknown. A range of other substances are misused. For example, the misuse of volatile solvents is a problem in many countries particularly among disadvantaged youth, for example petrol sniffing among adolescent Aboriginal and Torres Strait Islander population in remote Australia. A range of proprietary (over the counter) medications are misused, but there are little data on the extent of this.

In the health care setting, substance misuse is commonly encountered, either as overt or covert cause for the consultation, or as an incidental finding. For example, in a primary care setting up to one-third of patients have a disorder related to alcohol and tobacco use, or use of other drugs. In general hospitals, the figure is often greater than this. In mental health services, co-morbid substance use disorders affect half or more of patients.

Further reading

- Anderson P. Global use of alcohol, drugs and tobacco. *Drug and Alcohol Review* 2006; **25**: 489–502.
- Collins DJ, Lapsley HM. *Counting the cost: estimates of social costs of drug abuse in Australia 1998–1999*. National Drug strategy Monograph series No 49. Canberra: Commonwealth Department of Health and Aging, 2002.
- Degenhardt L, Mathers B, Guarinieri M, Panda S, Phillips B, Strathdee S, et al. *The global epidemiology of methamphetamine injection: A review of the evidence on use and associations with HIV and other harm*. Sydney: National Drug and Alcohol Research Centre, University of NSW, 2007.
- Ezzati M, Lopez A, Rodgers A, Vander Hoorn S, Murray C. The Comparative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. *Lancet* 2002; **360**: 1347–1360.
- Rehm J, Taylor B, Room R. Global burden of disease from alcohol, illicit drugs and tobacco. *Drug and Alcohol Review* 2006; **25**: 503–513.
- World Health Organization (2007). *WHO Expert Committee on Problems Related to Alcohol Consumption*. Available at: http://www.who.int/substance_abuse/expert_committee_alcohol/en/index.html

Spectrum of substance use and core clinical diagnoses

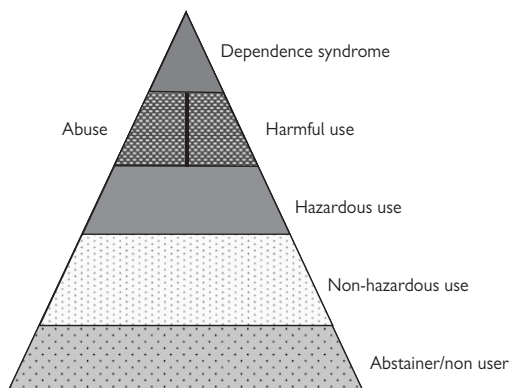


Fig. 1.1 The spectrum of substance use and problems.

Definitions

For any psychoactive substance there is a range of use from that which causes little or no problems through to dependent use. Alcohol and other substance use can be classified conveniently into five categories. These represent the diagnosis made when using international diagnostic systems.

Hazardous drinking or substance use: is repetitive use at levels that places a person at risk of harm of medical or psychological complications.

Harmful drinking or substance use: is a repetitive pattern of use that causes actual physical damage (e.g. liver disease, hypertension, cancers), or psychological harm (depression, anxiety; ICD10).

Substance abuse: repetitive pattern of drinking or use of a substance which results in social complications, e.g. financial, occupational and legal problems (*Diagnostic and Statistical Manual*, 4th edn: DSM-IV).

Dependence: represents an established syndrome of repetitive substance use, which is driven by internal forces. Dependence can be defined as a cluster of psychological, behavioural, and cognitive syndromes that comprise an inner drive to repetitive pattern of drinking or using drugs, pre-occupation with substance use, and sometimes withdrawal symptoms (ICD10 or DSM-IV).

A diagnosis of dependence is made if three or more of the following symptoms have occurred repeatedly within the past year:

- Impaired control over substance use—subjective awareness of an impaired capacity to control use
- A strong desire or sense of compulsion to use—subjective awareness of this compulsion; craving
- Preoccupation with substance use to the neglect of other responsibilities or interests
- Tolerance—increased amounts of the substance are required in order to achieve the desired effects
- Withdrawal symptoms on cessation or reduction of substance use
- Relief or prevention of withdrawal symptoms by further substance use
- Persistence of substance use despite clear evidence of overtly harmful consequences.

(Adapted from ICD10 criteria for dependence)

Dependence exists in various degrees of severity, but craving is a common feature of most forms of dependence and a common reason for relapse. This forms the rationale for use of anti-craving agents in the prevention of relapse. The colloquial term 'addiction' is often used to describe drug dependence just as the term 'alcoholism' is used for alcohol dependence.

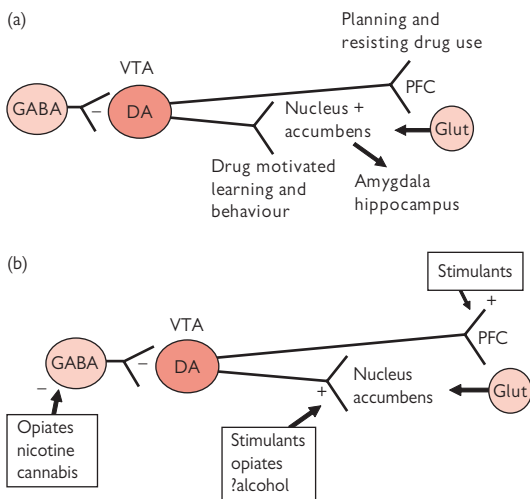
Withdrawal syndrome occurs when neurones have adapted to the chronic presence of a psychoactive substance. Cessation of substance use then results in abnormal neuronal function. It only occurs when dependence on that substance is present. However, the extent to which a withdrawal syndrome occurs is dependent on the substance, its level and pattern of use, and on inter-individual differences. Not all dependent users experience withdrawals.

Repetitive use of alcohol or other psychoactive substances may also lead to complications, which may be physical, neuropsychiatric, or social. Furthermore, substance use disorders may co-exist with other underlying illnesses, such as chronic pain, or psychiatric illnesses, such as anxiety disorders, depression, or schizoaffective illnesses ('Dual diagnosis').

Neurobiology of the dependence syndrome

There have been remarkable advances in the neuroscience of drug and alcohol dependence in the past decade. The target sites of action of most misused substances have been identified at the molecular and cellular level, and the brain circuits that underpin drug reward (pleasure) have been identified. Furthermore, the higher level control systems that regulate behaviours, such as planning, wanting, and resisting drug use are becoming understood in humans through the use of techniques such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) scanning.

Animal studies—mostly in rodents, although with some key confirmatory ones in primates—have revealed a brain circuit that appears to be common to the rewarding effects of most if not all drugs, as well as other reinforcing behaviours, such as eating, thirst, and sexual drives. This brain circuit comprises a dopamine pathway that runs from the ventral tegmental area into the ventral part of the striatum (the nucleus accumbens) and into the prefrontal cortex. Activation in this pathway is believed to lead to the learning of associations between behaviours and the relevance that they have for the individual. The landmark discovery here was that the self-administration of cocaine to rats is associated with a great release of dopamine in the nucleus accumbens (Fig.1.2a). Subsequently, this group and many others revealed that most other drugs that are misused will also do this (the main exception being the benzodiazepines). From this developed the dopamine theory of addiction—addictive substances release dopamine—this is pleasurable so the behaviour is repeated (reinforced). However, as drugs stimulate greater dopamine release than natural reinforcing activities, such as food, water, and sex, they ‘hijack’ the system, thus directing motivation and behaviour to drug use, rather than other activities. For instance, rats allowed to electrically stimulate this brain circuit do so relentlessly, not stopping to eat or drink, to the point where they may die unless the electricity is turned off; a phenomenon that has striking parallels with some human binge drug use. In Fig. 1.2b the pathway is shown along with the sites at which drugs act. Some, e.g. cocaine, work at the level of the dopamine terminals to cause dopamine release; others, e.g. the opioids and cannabis, act to switch off an inhibitory gamma amino-butyric acid (GABA) neuron that normally gates the firing of the dopamine neurons, so indirectly lead to dopamine release.



VTA = ventral tegmental; PFC = prefrontal cortex DA = dopamine glutamate

Fig. 1.2 (a) The dopamine reinforcement pathway. (b) The dopamine reinforcement pathway: sites of drug action.

More recently, it has been discovered that the state of dopamine neurotransmission may itself influence vulnerability to repeated drug use. A landmark human imaging study by Volkow and colleagues revealed that human volunteers with a lower density of dopamine D2 receptors in the striatum gained more pleasure from IV stimulant administration than those with a higher level. Attempts were made to back-translate this to animal models with remarkable results. It has now been shown both in monkeys and rats that the baseline density of D2 receptors predicts the extent of cocaine use when access is allowed—low levels of receptors before exposure to drug leads to great regular use of cocaine. In mice, low levels of these receptors are associated with alcohol intake and if the level is changed, e.g. by transfecting a virus that adds receptors to the nucleus accumbens, then preference declines. Moreover, repeated use of some drugs, especially stimulants and perhaps alcohol, leads to a reduction in the number dopamine D2 receptors so a vicious cycle of use and repeated use can be predicted (see Fig. 1.3).

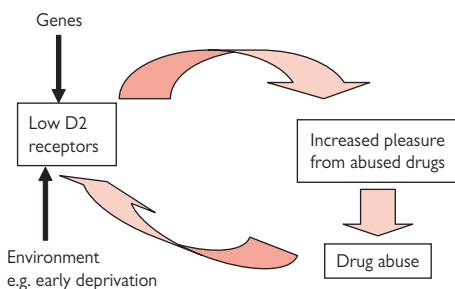


Fig. 1.3 Dopamine can help explain social aspects of addiction also.

One powerful aspect of this dopamine receptor theory is that it can help explain other factors that are known to relate to drug use, e.g. stress and social deprivation, as each of these in animals has been shown to lead to reduced D2 receptor number or function. It also leads to testable predictions about the role of dopamine receptor mutations that may alter neurotransmitter function as vulnerability markers (Fig. 1.3).

It is too simplistic to believe that, in the human, all drug reinforcement can be explained simply in terms of changes in the dopamine system. For instance, not all drugs have been shown to release dopamine in humans, the opioids being the most obvious exception. Also, dopamine blocking drugs, e.g. neuroleptics, have little impact on human drug-taking so it is likely that other neurotransmitter systems play a part in human addiction. There is a good body of evidence to support an involvement of the brain endogenous opioid system—the endorphins—in addiction also. These peptides provide natural reinforcement, as well as regulating pain behaviour and may be released in parallel with, or in place of, dopamine to provide reward, for instance from alcohol and cocaine. There is also good and growing imaging evidence that brain opioid receptors are abnormal in some addictions and that this may be associated with craving and relapse, as well as being a possible vulnerability factor to dependence. The involvement of endogenous opioids in addiction probably explains why opioid antagonists, such as naltrexone and nalmefene have utility in the treatment of alcohol, as well as heroin addiction.

Another critical aspect of drug misuse is the role of high level cortical processing in behaviour. It has been known for a long time that persons who misuse drugs, especially when addicted, have numerous deficits in mental functions, such as attention, memory planning, and impulse regulation. The use of new imaging techniques has revealed that these processes reside in sub-regions of the frontal cortex, particularly the orbitofrontal cortex and its limbic projection regions, especially the amygdala, and clear abnormalities of these brain regions have now been observed in many different addictions. The idea that addiction represents a fundamental remodelling of these pathways leading to long-term consequences for self regulation has been put forward by Volkow and has a lot of support (Fig. 1.4).

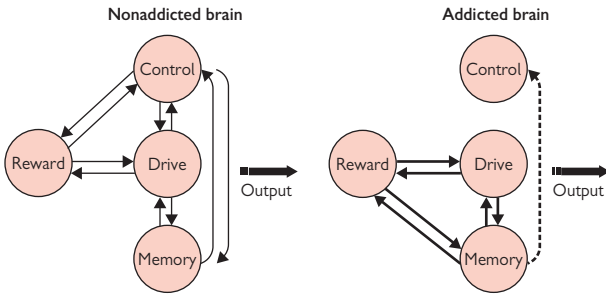


Fig. 1.4 Changed reciprocal brain control relationships in addiction (from Volkow).

The extent to which these reflect predisposing factors or are a consequence of drug induced damage is still under investigation, and both are likely to be relevant to differing extents in different people. Also there may well be particular aspects of dysfunction that explain a particular person's problems, e.g. in one person impulsivity may be the major problem, whereas in others compulsion to use may predominate. This offers a new approach to targeting treatments at the major risk factor in a person and also the prospect of new pharmacological approaches such as cognition enhancers.

Following repeated drug use, pathways of reward drive and memory become over-established and detached from higher-level control centres, so perpetuating drug use.

Underlying conditions and risk factors

When are individuals more likely to become dependent on drugs or alcohol?

Dependence develops on the basis of an interaction between:

- The pharmacological properties of the drug (Table 1.7)
- Individual vulnerability
- The influence of the environment.

Pharmacological properties of drugs that pose a risk for dependence

- Pleasurable effects (rewarding- see previous section)
- Effects are rapid in onset and are, therefore, more positively reinforcing
- Psychoactive substances, including alcohol, which with repeated exposure, induce tolerance as a neuro-adaptive response. More of the drug is required to produce the same effect. This may be due to changes in neurons including receptor properties, ionic flux, and intracellular chemical pathways
- As a consequence of this neuro-adaptation, in many cases withdrawal symptoms occur on cessation or reduction of substance use. This provides negative reinforcement of abstinence, is associated with strong craving, and so encourages return to substance use.

Individual vulnerability

Influenced by:

Genetic factors: these are estimated to account for 50–60% of the risk of developing alcohol dependence, particularly in males. In addition, up to half the variance in drinking patterns in non dependent people is genetically determined. Less data is available for illicit drugs, but genetic influences are believed to be involved.

Genetic influences are polygenic, but some influences may be mediated through:

- **Personality traits:** Impulsivity, risk taking and rebelliousness are associated with increased risk of substance use disorders
- **Different metabolism of or response to psychoactive substances:**
 - For example, adolescent boys with a strong family history of alcohol problems show a reduced sensitivity to the effects of alcohol even at the time of their first drinking, so from the very start drink they more than their peers
 - In some Asian populations, an unpleasant flushing reaction to alcohol, based on a deficiency of aldehyde dehydrogenase activity, protects against alcohol dependence.

Psychiatric disorders: e.g. anxiety, depression, schizophrenia, personality disorder, post-traumatic stress disorder (PTSD) are all associated with increased risk of substance use disorders.

Table 1.7 Commonly self administered psychoactive drugs (some common street names in brackets)

CNS depressants	CNS stimulants	Hallucinogens	Other
Alcohol	Amphetamines (<i>speed; uppers, goey, whiz, velocity</i>) Methamphetamines (<i>ice, shabu, crystal, yaba, crystal meth</i>)	Hallucinogens LSD (<i>acid</i>) Mescaline (<i>magic mushrooms</i>) Psilocybin (<i>magic mushrooms</i>)	Solvents— e.g. petrol, paint Inhalants e.g. amyl nitrite N ₂ O
Sedatives	Ecstasy—(<i>MDMA, e, Es, XTC, eckies</i>)	Ecstasy— (<i>empathogenic</i>)	Anabolic steroids
Benzodiazepines (<i>benzos, pills</i>)	Cocaine (<i>coke; crack; snow, charlie</i>)		
Z-drugs: zopiclone, zolpidem	Caffeine		
Barbiturates	Nicotine		
Opioids			
Heroin (<i>chasing the dragon</i> —inhaling heroin vapour)			
Opioid analgesics			
Codeine			
Morphine			
Pethidine			
Methadone			
Buprenorphine			
Oxycodone			
Pentazocine			
Dextromoramide			
Fentanyl			
Cannabis		Cannabis—in high doses (<i>dope; ganga; yandi; grass; weed; hashish</i>) May be smoked using a bong (water pipe) or as a joint—cigarette.	
GHB (<i>fantasy, liquid ecstasy, grievous bodily harm</i>)			
Ketamine (<i>special K</i>)			

Environmental influences

- **Adverse upbringing** including emotional deprivation, physical and sexual abuse, social disadvantage. Also the impact of these major stressors may result in anxiety, depression, or PTSD in later life and then an increased risk of substance use disorders in an attempt to self-medicate
- **Availability of substance:** low cost and ready availability
- **Cultural acceptance:** the degree to which a substance is legally and socially sanctioned, advertisement, traditional practices, and encouragement by peer group can markedly influence substance use
- **Employment:** certain occupational groups, e.g. bar tenders have an increased prevalence of alcohol and other drug misuse. This may be caused by the increased availability of alcohol and constant cues to drinking. Unemployment is an important risk factor for, as well as consequence of substance use
- **Role modelling:** modelling of substance use behaviour by family members, peers and other community members can encourage use.

Natural history of substance use and related disorders

The use of psychoactive substances ranges from single occasion, often experimental, use to the repeated high level use continuing over many years that is characteristic of substance dependence. Natural history of substance use and the core clinical syndromes, such as harmful use, substance abuse, and dependence derives from several sources. These include longitudinal or cohort studies, some being birth cohorts, or those established in childhood or teen years. Another group of natural history studies is based on persons identified as having a substance use disorder in population studies who are followed up over time. A third and relatively numerous type of natural history study comprises clinical populations attending treatment services. Some of these do not receive treatment or have minimal treatment, while others have a range of treatments for their disorder.

Alcohol

In countries with a high prevalence of alcohol consumption, consumption typically starts in the mid-late teens, although this varies according to the legal age for alcohol consumption, which ranges from 16 to 21 years. Young people's alcohol intake tends to be episodic, and consumption of large amounts in a single session has become increasingly common among both young men and young women in many Western countries. Intensity of drinking (number of drinks per session) declines from the mid-20s, but the frequency of consumption per week rises. Approximately 15–20% of the adult population consumes alcohol in a risky or hazardous way and of these, approximately one-third progress to alcohol dependence, with most of the others reducing their consumption to low risk levels by their 30s. Of the 5% of the population who have alcohol dependence, the course is quite variable. About one-third seek treatment within a few years of becoming dependent and this group provides much of our present knowledge of the natural history of this disorder. Untreated alcohol dependence shows a pronounced tendency to progress and following any periods of abstinence, to relapse. Reduction of alcohol consumption in alcohol dependent individuals to low risk levels is highly unusual especially in treatment populations where it is vanishingly small. Overall, untreated alcohol dependence results in the following outcomes over 10 years; 30% achieve recovery from their disorder, based on abstinence, 40% manifest continuing heavy consumption with progressive and continuing features of dependence, and 30% show a progressive downhill course characterized by frequent ever more severe relapse leading to death within this period. The natural history of treated alcohol dependence is influenced by the sociodemographic and cultural background of the person. Typically in people attending comprehensive public sector programmes, 45% have a good or relatively good prognosis, achieving abstinence in the long-term, with intermittent relapses in some cases; 35% show a less favourable course with periods of abstinence interspersed

with periods of heavy uncontrolled drinking, while 20% show a progressive downhill course which appears unresponsive to treatment. Among private sector facilities, rates of recovery over 10 years of 50–80% are claimed, although some studies have relied only on telephone interviews without objective measures of recovery status.

The natural history of an alcohol use disorder can be dramatically changed by the presence of physical or neuropsychiatric sequelae, for example, alcohol cirrhosis, one of the most common causes of death inpatients with alcohol use disorders, has an overall mortality rate of 50% at 5 years, comprising 70% of those who continue to drink heavily and 20% of those who abstain. Likewise, alcoholic cardiomyopathy has a bad prognosis with 60% of patients dying within 3 years. Alcohol dependence when complicated by depression, psychosis or suicidal behaviour also has a worse prognosis. The risk of suicide is 50 times greater in alcohol dependent people compared with the general population. Other common causes are motor vehicle accidents (the principal cause in many Western countries), accidental injury, drowning and homicide.

Sedative/hypnotic use

Numerous sedative hypnotic drugs are available on prescription, or in some countries can be purchased in pharmacies or (illegally) over the Internet.

The most commonly used drugs of this type are the benzodiazepines, of which approximately 30 are in common use, with different pharmacokinetic characteristics and clinical effects. Prior to the introduction of these drugs in the 1960s and 1970s, the most commonly available sedative hypnotics were the barbiturates and non-barbiturate drugs, such as methaqualone and chloral hydrate.

Most use of benzodiazepines is short term or confined to use to induce sleep. Approximately 30% of people who start taking benzodiazepines develop dependence on these drugs and this is well described as occurring at therapeutic doses of the equivalent of 15 mg diazepam daily for 3 months. Forty per cent will experience a withdrawal syndrome when the drug is discontinued under double blind conditions; this increases to 70% after 6 months' administration. The risk of dependence increases as the dose extends into supratherapeutic ranges. There is relatively little information on the natural history of benzodiazepine dependence, except that, without intervention, it tends to be long-term and there is a tendency to relapse after a period of non-use. Continuing use is characterized by increasingly levels of dependence, in common with the ever-present risk of the withdrawal syndrome when supply is interrupted. The natural history in treated populations varies widely, with abstinence rates of 70% at 1 year being reported in the people prescribed benzodiazepines legitimately, and also in elderly populations and ranging down to 20% in other studies and lower in street users of these drugs.

The last decade has seen the introduction of the so called 'z drugs', which include zolpidem and zopiclone. Little is known of the natural history of the z drugs other than that they also have dependence potential.

Cannabis

The extent of cannabis use is influenced by the form of cannabis used and several co-morbid factors. Cannabis is the most prevalent illicit drug worldwide. Of those who have ever smoked it, one-third have smoked it in the previous 12 months and approximately 10% have features of cannabis dependence. The natural history of cannabis use varies from the single occasion or experimental use in teenage years to periodic use in parties or other social occasions to regular daily use, which may extend up to 14–16 h of continual smoking per day. Information is scant on the natural history of various levels of cannabis use. Of those who have cannabis dependence, about 50% are still smoking regularly at 5 years and cannabis smoking of 30–40 years is well recognized. Studies conducted in the United States suggest that cannabis typically begins in the mid to late teens, and is most prevalent in early adulthood. Most cannabis use is irregular, with very few users engaging in long-term daily use. In the USA and Australia, it is thought that about 10% of those who ever use cannabis become daily users, and another 20–30% use weekly. Transitions in life roles, such as entry into full-time employment, getting married, or having children, are associated with reductions in or cessation of use for many people. The largest decreases are seen in cannabis use among males and females after marriage, and especially during pregnancy and after childbirth in women.

Opioid dependence

Dependence on opioids can develop from the use of heroin, opium and other illicit opioids, from prescribed or proprietary opioid medications, and from locally or home-produced opioids ('home bake'). Most of our knowledge of opioid dependence is of injecting heroin dependence. Surprisingly little is known of the course of prescribed opioid dependence over the long term.

With heroin use typically starting between the age of 16 and 19 years, heroin dependence typically is evident at the age of 18–19 years, i.e. after 2 years of use. There is, however, much variation in the rate of development of dependence, which may occur on some people in 6–8 weeks, whereas in others dependence may not develop until many years of intermittent use have occurred.

Among people with heroin dependence, the average duration of dependent heroin use, when untreated, is 10 years, but again there is a wide range and heroin dependence occurring over 20–30 years is well recognized. Heroin dependence thus conforms very clearly to the characteristic chronic and relapsing disorder that is characteristic of untreated established substance dependence syndromes. In the untreated state approximately 30% of heroin dependent individuals will have died at 10 years, most commonly of overdoses, but also of septicaemia and other bacterial complications, HIV/AIDS and hepatitis B- and C-induced liver disease, suicide, trauma, and accidents. Approximately 25% will have recovered, and be abstinent from opiates and other psychoactive substances. Some achieve recovery spontaneously and others through detoxification, other treatment, and involvement with self-help groups. Of the remaining 55%, about half will be using opiates on a regular basis, although in some cases it will have changed to a

sporadic pattern of use, based on supply or the finance to purchase it. The other half will be opioid free, but are using other substances in a harmful or dependent manner. Substances mostly used by this group are alcohol, benzodiazepines, and to some extent, psychostimulants.

The natural history of heroin dependence has been modified in recent years by the widespread availability of opioid substitutes, such as methadone and buprenorphine, and also by ready access in many (but not all) countries to sterile injecting equipment provided as part of a harm reduction approach. Opioid substitution reduces the death rate by 75%, so the mortality rate among IV heroin users is now under 10%. Sterile injecting equipment also reduces mortality and also morbidity from infections including blood borne viruses. By contrast, some forms of treatment are associated with no change or increased mortality and so the practitioner working with heroin-dependent people needs to select treatment very carefully. For example, naltrexone treatment with or without prior or rapid detoxification reduces opioid use, but mortality is the same as in an untreated population because of the risk of relapse into an opioid naïve state after treatment ceases. Periodic detoxification is associated with an increase in mortality rate of with the untreated state with 1-year death rate of up to 7% compared with 3% among untreated populations.

Psychostimulant use

Psychostimulant dependence in Western societies is a more recent phenomenon than opioid or cannabis dependence, and consequently less information is available on its natural history, especially in the long term.

Few studies have documented the natural history of psychostimulant use, in sharp contrast to the literature on cannabis and even opioids. Our current understanding derives largely from cross-sectional studies, typically involving convenience samples, or treatment or prison settings. US prospective studies have suggested that relapse following treatment for psychostimulant dependence is common. The concentration of work in treatment or prison populations makes it difficult to draw inferences about amphetamine use in the general population, since most users will never come into contact with either treatment or law enforcement agencies. As a result, little is known about the aetiology and consequences of psychostimulant use that does not come to the attention of police or treatment services. This is an area where much more needs to be known given the increases thought to be occurring in the use of these drugs.

Amphetamine dependence occurs in 30–40% of people who start using amphetamine repeatedly. Uptake of amphetamine use occurs typically from the ages of 17–25 years and dependence develops after an average period of use of 3–4 years, again with much variation. The natural history of amphetamine use differs according to the route of administration. The most common methods are smoking, per nasal use ('snorting') and intravenous use. In Australia, most amphetamine is injected, but the opposite applies in most European countries.

When people have developed amphetamine dependence, the course is again typically a chronic one with periods of non-use and episodes of relapse. Approximately 60% will still be amphetamine-dependent after 3 years, but the long-term natural history (over 10–20 years) has still to be determined. At 3 years, mortality is 5% with most of the deaths occurring from accidents, suicide, and homicide, and a smaller proportion as a result of blood borne infections.

Cocaine dependence develops in approximately 55% of people in Western societies who use cocaine repeatedly. As described earlier, cocaine is used in various forms, as in coca leaf in which the leaves are mixed with an alkali, chewed, and left to rest in the mouth. This is characteristic of its use in indigenous populations in South America. In Western societies, cocaine is used in two main forms, as purified cocaine hydrochloride that may be produced illicitly or obtained from medical supplies, and cocaine freebase, various forms of which are available including 'crack' cocaine. Purified cocaine tends to be used by more socio-economically advantaged people, while crack is used by lower socio-economic and often homeless people.

What can we do about alcohol and other substance use problems?

A range of prevention and intervention measures are available. As with any health problem, intervention may aim to prevent a problem, provide early intervention and treatment; or provide treatment or harm reduction in a well established disorder. The main body of the book is concerned with practical ways in which doctors and health care professionals can diagnose the various forms of alcohol and substance use disorders and provide practical assistance and treatment to people with a view to helping them recover or at least reduce the risk of harmful consequences. However, we should note that at a societal level, the most effective strategy to reduce alcohol and substance-related harm derives from population level approaches, such as legal controls on availability, random breath testing to reduce drink driving and public policies such as no smoking zones, supported by public and school-based education.

Other population-based strategies have specifically targeted blood borne viral infections, e.g. HIV/AIDS and, in more recent years, hepatitis C and B infections. Many countries have in recent years established campaigns and programmes to reduce the harm caused by alcohol and other substance use at a population level. These include the Australian National Campaign Against Drug Abuse and the UK 10-year drug strategy. An important role of doctors and health care practitioners is to support these broad community based measures within their own spheres of influence, while recognizing that the bulk of their work will be concerned with the practical issues of assessment, diagnosis, and treatment of their patients.

Where do we see the role of doctors and health care professionals in prevention? The main body of this text book will deal with the assessment, diagnosis and treatment of people with known or suspected substance dependence, and its related problems. In many cases, treatment is orientated to the goal of abstinence from substance use. In others the goal is maintenance on a substitute medication. Doctors and other health professionals also have an important role to play in early intervention for non-dependent substance use disorders. The following sections summarize the four main components of health care:

Prevention (primary intervention)

Aims to prevent hazardous alcohol and other substance use in the general population, e.g. by controls on availability (supply reduction), media, or school education campaigns (demand reduction), work place policies and addressing underlying risk factors, such as social disadvantage or psychiatric disorders, or by enhancing protective factors such as establishing links with family or community. In terms of practical health care, primary intervention can also be taken as intervention by a general practitioner or health care worker at the point of first contact with a patient who is drinking or using substances hazardously.

Early intervention (secondary intervention)

Actively identifies persons with hazardous alcohol or other substance use before dependence, or physical or psychosocial complications have arisen, and enables them to cease or reduce substance use. Advice or brief counselling at point of first contact is typically used. All health care professionals, including General Practitioners, hospital doctors, and nurses play a major role in early intervention. Early intervention has the potential of being the most effective approach to reduce substance-related harm in the population as a whole.

Treatment (tertiary intervention)

Aims to provide treatment for patients with established dependence or who have already experienced harm caused by substance use to help them cease substance use or be placed on maintenance medication in a therapeutic setting.

Harm reduction and palliation (quaternary intervention)

Involves providing health education and other measures (e.g. supply of clean injecting equipment, ignition interlocks to stop drink driving), to reduce the risk of physical, psychiatric, or medical complications among those who are still using alcohol or other substances in a risky manner. Harm reduction approaches may be used when an individual is trying to change their substance use, but still experiencing slips or relapses. It is also very important in the individual who is not yet able or willing to engage with treatment or to change their substance use. Harm reduction can not only reduce risk to the individual, but also to broader society (e.g. through reduced prevalence of blood borne viruses by means of needle and syringe exchange programmes, hepatitis B vaccination, and treatment of chronic hepatitis C infection).

In some individuals (e.g. those with well established alcohol-related brain damage who continue to drink) there may be little realistic prospect of cure. Palliation and harm reduction measures form an important part of treatment. With respect to alcohol dependence, thiamine is used to reduce the impact of alcohol on the central nervous system in an effort to reduce brain damage. Such an approach aims to relieve symptoms and maintain function and independence to the greatest extent possible. Provision of supervised accommodation is another example of harm reduction.

