MORTALITY AMONGST ILLICIT DRUG USERS

Over the past 40 years the rate of illicit drug use worldwide has risen dramatically, and with it the number of deaths reported among drug-using populations. What are the clinical, ethical, and psychopathological implications of these deaths? In this book, Shane Darke and his team provide the first full, synthetic review of the epidemiology, causes, prevalence, demography, and associated risk factors of illicit-drug-related mortality. In addition, they examine and evaluate interventions to reduce these deaths. The major causes of death among illicit drug users are overdose, disease, suicide, and trauma. Each is independently examined. This is an important book for all clinicians and policy-markers involved in issues relating to illicit drug use.

SHANE DARKE is Associate Professor at the National Drug and Alcohol Research Centre at the University of New South Wales. He is also Australasian Regional Editor of *Addiction* and an associate editor of *Drug and Alcohol Dependence.*

LOUISA DEGENHARDT is Senior Lecturer at the National Drug and Alcohol Research Centre at the University of New South Wales. She is also Senior Investigator of the Illicit Drug Reporting System and the National Illicit Drug Indicators Project.

RICHARD MATTICK is Professor and Director of the National Drug and Alcohol Research Centre at the University of New South Wales. He is a Member of the Editorial Boards of *Drug and Alcohol Review*, and the *Cochrane Review Group of Drugs and Alcohol*.

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MORTALITY AMONGST ILLICIT DRUG USERS: EPIDEMIOLOGY, CAUSES, AND INTERVENTION

SHANE DARKE, LOUISA DEGENHARDT & RICHARD MATTICK

National Drug and Alcohol Research Centre
University of New South Wales
Australia

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Why illicit drug-related deaths matter

1.1 Introduction

Over the course of the past 40 years, the use of illicit drugs has increased dramatically in developed nations. Over this period there have been substantial increases in the use of cannabis, opioids, cocaine, amphetamine, and, more recently, amphetamine-like substances such as MDMA ("ecstasy") (cf. Chapter 2). While the initial increase in illicit drug use occurred within developed nations, recent years have seen large increases in illicit drug use in the developing world. In particular, since the 1990s there have been substantial increases in rates of drug use and drug-related problems in countries such as China, India, and the Republics of the former Soviet Union (Degenhardt et al., 2004a; United Nations Office for Drug Control, 2005).

Clearly, the use of illicit drugs has become an issue worldwide, although the nature of the problem may well vary from nation to nation. In some nations cocaine may be the primary focus, whilst in others opiates may dominate clinical concern. A natural corollary of any increase in the use of illicit substances of any sort, however, is an increase in rates of illicit drug-related death. The use of illicit drugs carries risks for morbidity and mortality, either directly related to the drug itself (e.g. overdose) or as a consequence of such use (e.g. intoxicated driving). As will be seen repeatedly throughout this book, rates of death amongst illicit drug users are substantially higher than those seen amongst the non-drug using population (cf. Chapter 3).

It is undeniable that both drug use and drug-related mortality have increased. The question posed in this chapter, however, is does this matter? Are there ethical reasons why this should be a concern to society or, indeed, for devoting a book to examining these deaths? It could be argued, for example, that such deaths are by nature self-inflicted, and that the deaths of illicit drug users may well be beneficial to society. After all, it could be said that nobody forces illicit

drug users to expose themselves to risk by taking drugs, and the reduction in crime and disease represented by their deaths may constitute a net gain to society. Whilst the authors of this book may not concur with this view, the issue of why such deaths are a matter for public concern is one that does require addressing, before embarking upon a detailed exploration of these deaths and the means to reduce them. There are a number of ethical and utilitarian arguments that emphasise the importance of drug-related death to society. Broadly speaking, these fall into the following areas: (i) ethical responsibility to prevent avoidable death, (ii) the costs of such deaths to society, (iii) the natural history of drug use, and (iv) the impact of such deaths on the families of drug users.

1.2 Why illicit drug-related deaths matter

1.2.1 Ethical responsibility to prevent avoidable death

The first thing to note in any discussion of whether illicit drug-related mortality matters is the extent of the problem. As will be more fully discussed in Chapter 3, it was estimated that in 2000 alone there were approximately 200,000 deaths worldwide attributable to illicit drug use (Degenhardt et al., 2004a). This figure is undoubtedly a conservative underestimate of the true level of mortality (cf. Chapter 3). As would be expected, given the epidemiology of illicit drug use (cf. Chapter 2), the majority of deaths occur amongst younger people, with the average age at death being approximately 30 years.

As a general rule, the prevention of premature death is uncontroversial. Few would argue that premature death due to leukaemia, for example, does not matter, or that the victims in some way deserved to die. Drug use, however, raises passions that are rarely seen when discussing death due to other causes. Unlike a disease brought on by some external factors, death due to drug use is essentially self-inflicted. The ethical responsibility thus falls upon the user, who has taken the decision to use and, typically, to continue to use illicit drugs. The distinction between drug use mortality and other forms of mortality is thus between what could be termed a "lifestyle choice" compared to death due to extraneous causes beyond the control of the individual.

As with so many appealing dichotomies, however, a simple contrast between a self-chosen pathway to death and other forms of mortality does not withstand close scrutiny. There is a clear implicit assumption of unrestricted free will in the assertion that drug-use behaviours are self-determined. Leaving the issue of free will versus determinism aside, the literature demonstrates clear precursors

for increased risk of illicit drug use and substance dependence (cf. Chapter 2). In particular, the development of problematic illicit drug use has been strongly associated with what has been referred to as a "shattered childhood" (Rossow & Lauritzen, 2001). This term includes a general clinical picture of parental psychopathology, parental drug and alcohol problems, early loss of parents, and, most importantly, childhood sexual and physical abuse (Rossow & Lauritzen, 2001). The development of drug-dependence problems is thus not a random occurrence, but is strongly associated with a set of factors likely to increase psychological distress and, not surprisingly, problematic drug use. Consistent with this picture of a "shattered childhood", levels of serious psychopathology such as major depression are extremely high amongst dependent illicit drug users (Darke & Ross, 1997a; Dinwiddie et al., 1992; Lynskey et al., 2004; Teesson et al., 2005). The majority of problematic drug users thus come from backgrounds that increase their risk of serious psychopathology and of dependent drug use. Much of this drug use may, in fact, be seen as attempts to self-medicate distressing effect.

The second point to raise concerning the "choice" of a drug using lifestyle is that, as will be seen in later chapters, the majority of drug-related fatalities occur amongst dependent drug users. Substance dependence is, of course, a well-recognised psychiatric diagnosis, defined in both the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (American Psychiatric Association, 2000) and the International Classification of Diseases (ICD-10) (World Health Organization, 1993). The syndrome includes both physical (e.g. withdrawal) and psychological (e.g. salience of the substance in the person's life) symptoms. Like many other psychiatric disorders (e.g. major depression, anxiety disorders, schizophrenia) drug dependence is strongly associated with substantially increased risk of premature death (Harris & Barraclough, 1998). Broadly speaking, the core feature of substance dependence is a loss of control over use of the substance in question. The person may be physically dependent on the drug, experiencing drug tolerance and withdrawal symptoms, and continue to use despite repeated efforts at abstinence. The point here is that, by definition, to invoke drug use as a choice when the person had been diagnosed as having lost control over their drug use is absurd. There are clear psychosocial factors that heighten the risk of illicit drug use and, once dependence has developed, to speak of choice makes little sense.

Moreover, the typical onset of illicit drug use, and of drug dependence, occurs in the teenage years (Chen & Kandel, 1995; Degenhardt et al., 2000; Kandel et al., 1992), *prior* to the person becoming an adult deemed ethically or legally responsible for their own behaviours. Legally, societies do not hold

children to be sufficiently developed cognitively or ethically to make informed, free choices of great magnitude. The use of illicit drugs, clearly, is a behaviour that carries enormous implications for health and welfare. To hold children or adolescents ethically responsible for a self-chosen pathway to death, particularly when adverse events in childhood so strongly predict such behaviours, is inconsistent and absurd. While the person may die an adult, the dependence that leads to this death, typically, was acquired as a minor.

Even if we assume that drug-related deaths are self-inflicted, however, it is unclear how they could be distinguished from other fatalities that *are* universally deemed worthy of clinical interest and intervention. The self-inflicted death *par excellence*, clearly, is death by suicide. Even if it is assumed that drug use, and dependent drug use, is a freely chosen pathway to mortality, drawing a distinction between death due to drug use and death due to suicide is difficult. If killing oneself, or attempting to kill oneself, is a matter for clinical and societal concern, then death from drug use is surely a similar matter for concern. No logical distinction can be drawn. Of course, problematic drug use might well be seen as a form of prolonged self-destruction, further blurring distinctions between drug-related mortality and suicide. Certainly as noted previously, there are high rates of depression and suicidal ideation amongst dependent drug users. In fact, suicide itself is a major cause of death amongst illicit drug users, as will be discussed at length in Chapter 7.

The problem of distinguishing self-inflicted deaths from other deaths that are worthy of intervention, however, extends far beyond the prime example of suicide. Let us take the cases of licit drug-related death, due to tobacco- or alcohol-related disease. To be consistent, these too would have to be deemed unworthy of intervention, as the use of these drugs was also a freely chosen lifestyle choice. So too would deaths resulting from motor vehicle accidents attributable to excessive speed (a freely chosen behaviour) or obesity-related illness due to excessive eating. The argument is never consistently applied, yet no logical or ethical distinction can be drawn between mortality due to illicit drug use and other deaths that *are* deemed worthy of concern.

1.2.2 Costs to society

The second broad issue to consider is the cost to society of drug-related mortality. As noted above, it could be argued that drug users constitute a substantial cost to society primarily through crime and disease. Given these costs, the attrition through death of illicit drug users may well be seen as a reduction of the burden that drugs impose upon society.

There is no doubt that drug use, and dependent drug use in particular, does place a substantial cost burden upon societies. In particular, there is a strong association between dependent drug use and crime (Flynn et al., 2003; Gossop et al., 1998; Kaye et al., 1998). It is important to note that this association, specifically, is between drug use crimes committed by dependent drug users to acquire money to purchase drugs, such as robbery or drug dealing. Importantly, however, the frequency of acquisitive crime has been demonstrated to co-vary with the frequency of illicit drug use. As the frequency of drug use declines, so also does the rate of acquisitive crime (Flynn et al., 2003; Gossop et al., 1999; Hser et al., 1998; Simpson et al., 1997). In fact, one of the major societal benefits of drug-treatment programmes is that criminal behaviours decline markedly as a result of such treatment.

In addition to crime, illicit drug use, and injecting drug use in particular, is strongly associated with disease and disease transmission. The sharing of used injecting equipment is a major transmission factor for human immunodeficiency virus (HIV), hepatitis C virus (HCV), and hepatitis B virus (HBV) (Karch, 2002). There are a range of other pathologies associated with drug use, including cardiovascular disease, pulmonary disease, renal complications, and neuropathology (Cherubin & Sapira, 1993; Karch, 2002). It is beyond question that regular illicit drug users are in poorer health than the non-drug using population, due to the complications of drug use. As with crime, however, the health of illicit drug users improves substantially after entering drug-treatment programmes (Gossop et al., 2002a).

While there are clearly substantial costs associated with illicit drug use, the deaths of large numbers of drug users also impose a substantial cost upon society. As noted above, the average age of illicit drug user deaths is around 30 years (Chapter 3). Given the relatively young age of such deaths, there is considerable lost productivity due to the truncated lifespan. It was recently calculated that in the year 2000 alone, nearly 7 million Disability Adjusted Life Years (DALYs), a measure of lost life and lost productive life, were attributable to death from illicit drug use (Degenhardt et al., 2004a). As will be discussed in Chapter 3, this is in all probability a substantial underestimate of the lost life and productivity incurred by illicit drug use.

The view that illicit drug users place a continuous burden upon society is predicated upon an assumption that problematic drug users always commit crime, and place burdens upon the health system. As noted above, however, sharp declines in criminality and improvement in both physical and psychological health are associated with drug-treatment programmes. Naturally, then, the burden imposed by criminal behaviours and poor health will decline, while

levels of social functioning improve. Problematic drug users may be a burden whilst using drugs, but this burden is ameliorated by treatment and declines with their drug use.

The above discussion primarily relates to dependent drug users. Typically, the picture of high levels of crime and extremely poor health presented above primarily pertains to a long-term heroin or cocaine user (Cherubin & Sapira, 1993; Karch, 2002). Whilst many deaths occur among unemployed, long-term opioid or cocaine users, as will be seen in subsequent chapters, a proportion of illicit drug use deaths occur amongst recreational users of cannabis or designer amphetamine-like drugs (e.g. MDMA "ecstasy") (Chapter 4). Cannabis, for example, is strongly associated with motor vehicle accidents (cf. Chapter 7), whilst deaths occurring from the use of drugs such as MDMA may result from hyperthermia or cardiac arrest (cf. Chapter 4). The psychosocial profile of such users is completely different from that of the regular, dependent opioid or cocaine user. These are typically employed, recreational users who are at low risk of serious diseases such as HIV or HCV. These are, in effect, typical young members of society. To characterise such productive young persons as a societal burden clearly would be absurd.

1.2.3 Natural history of drug use

The next point to consider, the natural history of drug use, follows on from the previous discussion on costs to society. As discussed above, illicit drug use typically commences in the mid-teenage years. Importantly, it peaks in the 20–30-year age group, and declines sharply in older age groups (Chen & Kandel, 1995; Degenhardt et al., 2000; Kandel et al., 1992). The natural history of illicit drug use is thus skewed towards the younger years. The point here is that the label "illicit drug user" is not an immutable lifetime description, but may refer to a relatively brief period. A person may well use illicit drugs during their 20s, but most will cease to do so in later years. The highest risk of illicit drug use, and of thus of mortality, is focussed over a relatively brief period in the person's life. If this high-risk period can be navigated safely, then the person may well cease to be an illicit drug user and cease to impose any illicit drug-related costs upon society. Even if we accept a view that illicit drug users are in some sense unworthy of concern, these same people may well cease to be illicit drug users after a relatively short period.

Dependent drug use, and opioid dependence in particular, may of course persist for substantially longer than the patterns described above (Hser et al., 2001). Even dependent opioid use, however, is cyclical in nature. Opioid users go through periods of use, followed by periods of treatment and abstinence (Darke

et al., 2005c; Flynn et al., 2003; Hser et al., 2001). Many dependent users may be seen to mature out of drug use, although this may take considerable time. As noted above, it is incontrovertible that drug-treatment programmes produce substantial improvements in the psychosocial profile of dependent drug users. As is the case with recreational drug users, there is a natural history associated with dependent drug use. A dependent drug user may be a high-risk person who imposes a societal burden. They may not, however, remain a dependent drug user, or continue to impose such a burden.

1.2.4 Families of drug users

Finally, we must consider the impact of illicit drug use deaths upon the families of these users. It is beyond question that the loss of loved ones through drug use matters greatly to the families of drug users. In considering whether drug use mortality is a legitimate matter for concern, the drug user must not be seen in isolation. The death of a drug user does not only affect the user themselves, but also those surrounding them. While it could be argued that the death was self-inflicted, this in no way applies to the anguish of relatives, partners, and friends of the deceased drug user. The effects upon the loved ones of deceased drug users are something that clearly must be considered when examining the impact of drug-related death. Apart from the lost societal productivity of the decedents themselves, drug deaths impose large burdens upon the families, and partners of deceased drug users.

Even if we were to restrict the argument to a strict utilitarian approach, and confine our analyses to the impacts upon broader society, there are good reasons to be concerned about familial loss through drug use. The most salient issue here clearly concerns the children of drug users. Early parental loss is associated with increased risk of the development of subsequent psychopathology, as well as increased risk of drug dependence and of suicide (Fergusson & Lynskey, 1995; Rossow & Lauritzen, 2001). One major advantage in keeping illicit drug users alive is that such actions may well reduce the costs to society of illicit drug use and drug-related death among the next generation. As noted above, most illicit drug use occurs over a relatively brief period in a person's life. If this period can be lived through, this may have substantial benefits for the families of drug users, both currently and in the future.

1.3 What do we need to know about illicit drug-related mortality?

Ultimately, whether illicit drug user deaths matter or not is a question that must be decided by the reader. If they do not matter, then there is nothing further to

say. If we do accept that high rates mortality amongst illicit drug users is a matter of concern, however, then what do we need to know about such deaths? First, we clearly need to understand the epidemiology of illicit drug use (Chapter 2). What are the drugs being used, and by whom? Second, what are the mortality rates associated with illicit drug use, and amongst whom are such deaths occurring (Chapter 3)? Third, what is causing such deaths, and how do these causes differ by substance (Chapters 4–7)? Finally, how can the rates of illicit drug user mortality be reduced (Chapter 8)? The ensuing chapters of this book will examine the epidemiology of illicit drug use, the epidemiology of drug-related death, the causes and factors associated with such deaths, and the efficacy of attempts to reduce drug-related mortality.

1.4 Summary

In summary, there are good reasons, apart from compassion for the victims, to regard illicit drug user mortality as a serious matter of public concern. Rates of illicit drug-related death have dramatically increased worldwide since the 1960s, and represent a major cause of death amongst younger people. Arguments that death due to illicit drug use is essentially self-inflicted and therefore not a matter for societal concern do not stand up to close scrutiny. There are well-delineated psychosocial factors that engender regular illicit drug use, and most drug-related fatalities occur amongst drug dependent individuals who have lost control of their drug use.

Whilst the use of illicit drugs imposes substantial costs upon societies, there are also substantial costs incurred through lost years of productivity from what are primarily deaths among young people. It is also the case that drug users do not necessarily remain drug users, and may move beyond drug use to make substantial contributions to society. Finally, drug users do not live in isolation. Drug-related mortality impacts upon the families of decedents, and increases the risks of serious psychopathology, drug dependence, and suicide amongst the children of deceased users.

Key points: Summary of why illicit drug use deaths matter

- Rates of illicit drug use and drug-related deaths have dramatically increased in the developed world since the 1960s, and in developing nations since the 1990s.
- Deaths due to illicit drug use are not due to a self-inflicted, freely chosen lifestyle. There are well-delineated psychosocial factors that engender regular illicit drug use.
- Most drug-related fatalities occur amongst drug dependent individuals who have lost control of their drug use. Moreover, drug use and dependence typically commences prior to the person having become an adult.
- The use of illicit drugs imposes substantial costs upon societies. There are also substantial costs to society, however, incurred through lost years of productivity from deaths among young people.
- Drug users do not necessarily remain drug users, and may move beyond drug use to make substantial contributions to society.
- Drug users do not live in isolation. Drug-related mortality impacts upon the families of decedents.

2

The global epidemiology of illicit drug use

2.1 Introduction

In this chapter, we outline the global epidemiology of illicit drug use. Illicit drug use includes the non-medical use of a variety of drugs that are prohibited by international law. These drugs include methamphetamine, amphetamine, MDMA (ecstasy), cannabis, cocaine, heroin, and other opioids. Table 2.1 briefly outlines the major drug classes. In order to estimate mortality attributable to illicit drug use, we need to define which drugs we are speaking about, and consider the relative prevalence of their use.

2.2 Drug use or drug use problems?

Most people who use psychoactive substances do so without experiencing any problems related to their use, but some do develop problems (Anthony et al.,

Table 2.1. Selected drugs and their actions

Drug type	Actions
Amphetamine type stimulants (ATS)	A class of sympathomimetic amines with powerful stimulant action on the central nervous system (CNS).
Cannabis	Generic term for psychoactive preparations derived from the *Cannabis sativa* plant (e.g. marijuana, hashish, hash oil).
Cocaine	An alkaloid CNS-stimulant drug derived from the coca plant.
MDMA	3,4-Methylenedioxymethamphetamine. Synthetic drug used as a (ecstasy) stimulant.
Opioids	Generic term applied to derivatives from the opium poppy, their synthetic analogues, and compounds synthesised in the body, which act upon the opioid receptors in the brain (e.g. heroin, opium, methadone). They have the capacity to relieve pain and produce a sense of euphoria, as well as to cause stupor, coma, and respiratory depression.

1994). The conceptualisation and measurement of these problems has undergone considerable change over the past three decades, with the emergence of the concept of a substance "dependence syndrome", influenced by Edwards and colleagues' work on alcohol dependence (Edwards & Gross, 1976). In 1977, Edwards and colleagues suggested that alcohol *dependence* could be thought of as a cluster of symptoms that were distinguishable from alcohol-related problems occurring in heavy drinkers (Edwards et al., 1977). The concept of a dependence syndrome has since been extended to substances such as cannabis, tobacco, amphetamines, opioids, and sedatives. Another category of problematic substance use has also been developed: the concept of substance *abuse.* This was developed in an attempt to classify persons who experienced clinically significant problems associated with their substance use, but who were not using the substance in a dependent manner.

The most recent operationalisation of the substance abuse and dependence syndromes is DSM-IV (American Psychiatric Association, 2000). DSM-IV Substance Abuse criteria require a pattern of substance use that causes clinically significant distress or impairment. DSM-IV Substance Dependence criteria require a cluster of three or more indicators (of a possible seven) that a person continues to use the substance despite significant substance-related problems (American Psychiatric Association, 2000). These include tolerance, withdrawal, indicators of impaired control over use, use despite problems, and the reduction of activities not related to substance use.

The World Health Organization (WHO), following the International Classification of Disease (ICD-10), defines problem drug use as "harmful drug use" and "drug dependence". Harmful drug use is defined by clear evidence that substance use is responsible for physical (e.g. organ damage) and psychological harm (e.g. drug-induced psychosis). Drug dependence, as defined in ICD-10, requires the presence of three or more indicators of drug dependence (World Health Organization, 1993). These include a strong desire to take the substance, impaired control over use of the substance, a withdrawal syndrome on ceasing or reducing use, tolerance to the effects of the drug, requiring larger doses to achieve the desired psychological effect, a disproportionate amount of the user's time being spent obtaining, using and recovering from drug use, and the user continuing to take drugs despite associated problems. These problems must have been experienced at some time during the previous year for at least 1 month.

The United Nations Drug Control Programme (UNDCP) identifies "problem drugs" based on "the extent to which use of a certain drug leads to treatment demand, emergency room visits (often due to overdose), drug-related morbidity (including HIV/AIDS, hepatitis, etc.), mortality and other drug-related social ills"

(United Nations Drug Control Programme, 2000). It is important to note that in the majority of cases, it is problematic or dependent patterns of drug use, rather than occasional or experimental use, that best predict mortality from drug use.

2.3 How common is illicit drug use?

The use of drugs for non-medical purposes appears to be increasing in many parts of the world (United Nations Office for Drug Control, 2005). One of its defining features, its illegality, makes it difficult to quantify how many drug users there are (European Monitoring Centre for Drugs and Drug Addiction, 1997, 1999b). This is for a number of reasons. First, illicit drug-using individuals are "hidden" and may be difficult to identify. Second, even if drug users can be located and interviewed, they may attempt to conceal their drug use. Third, prevalence estimates vary with the method used and assumptions made. Data provided by the United Nations Drug Control Programme do not have the same reliability as large-scale household surveys of the type generally conducted in developed countries. Unfortunately, the expense of conducting such surveys makes their use in developing countries unfeasible.

There are no well-tested and widely accepted "gold standard" methods for producing credible estimates of the number of people who make up the "hidden population" of illicit drug users (Hartnoll, 1997). The preferred strategy is to look for convergence in estimates produced by a variety of different methods (European Monitoring Centre for Drugs and Drug Addiction, 1997, 1999b). 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) to estimate the size of the hidden population.

Prevalence data reported in peer-reviewed literature are scarce and often unrepresentative. There has been even less research on the epidemiology of *substance use disorders* in the general population than there has on *substance use*. Some exceptions are the US Epidemiological Catchment Area (ECA) study and the US National Comorbidity Study (NCS), which found that the most commonly used substances were also the most commonly *misused* substances (Anthony & Helzer, 1991; Anthony et al., 1994). The same was also found in the more recent Australian National Survey of Mental Health and Well-Being (Hall et al., 1999c).

It is important to remember that there is strong evidence (principally from developed countries) that few drug users use one drug exclusively (Darke & Hall,

1995; Darke & Ross, 1997; Dinwiddie et al., 1996; Gossop et al., 2002; Hubbard et al., 1997; Klee et al., 1990; Ross & Darke, 2000). Rather, most users nominate a drug of choice but regularly use a wide range of substances.

2.3.1 Cannabis

Cannabis is the most widely used illicit drug in most developed and many developing countries (Hall et al., 1999b). There are notable differences in the prevalence of cannabis use across developed countries. Rates appear higher in the UK, some western European countries, the USA, Canada, and Australia (with adult lifetime rates of use that can reach around 35–40%) than in countries such as Romania and Belgium (where rates are around 1–7%) (Hall et al., 2001). The more limited data available from developing countries in Africa, the Caribbean, Asia, and South America suggest that rates of cannabis use are much lower in these countries than in Europe and English-speaking countries (Hall et al., 2001, 1999b). In all countries, rates of past year use are highest among young adults.

2.3.2 Amphetamine-type stimulants

Increases have been noted in recent years in the market for amphetamine-type stimulants (ATS) in many countries (United Nations Office of Drug Control). Production and consumption of ATS appear to have increased considerably in recent years, notably around the Pacific Rim – North America, South-East Asia, and Oceania (United Nations Office for Drug Control, 2005). Many countries in these regions have noted the increased use of crystal methamphetamine, first in the Philippines, Korea, Taiwan, and Japan (Laidler & Morgan, 1997; Matsumoto et al., 2000; Shaw, 1999; Suwaki, 1991), and later in the US (Laidler & Morgan, 1997; Morgan & Beck, 1997; National Drug Intelligence Centre, 2003). In recent years, crystal methamphetamine use has been increasing in availability in areas of Oceania (Farrell et al., 2002; McKetin et al., 2005a, b; Topp et al., 2002; Wilkins, 2002).

The United Nations estimated that there were 26 million methamphetamine or amphetamine users globally in 2003 (United Nations Office for Drug Control, 2004). In European countries, lifetime prevalence of amphetamine use typically ranges from 0.1% to 6%, although rates are higher in the UK (up to 12%) (European Monitoring Centre for Drugs and Drug Addiction, 2005). In the USA, the prevalence of amphetamine use was estimated at 8.3% (Substance Abuse and Mental Health Services Administration, 2005).

Similar increases also appear to have occurred for "ecstasy", the name for tablets sold purporting to contain MDMA (United Nations Office for Drug Control, 2005). Ecstasy use has traditionally been concentrated in developed countries in North America, Europe, and Australia (United Nations Office for Drug Control, 2005). In Australia, ecstasy use among the general population has increased from 1% in 1988, to 7.4% in 2004 (Australian Institute of Health and Welfare, 2005). Indeed, ecstasy is now the second most widely used illicit drug in Australia among young adults aged 20–29 years. This is consistent with the trends seen in Europe, with ecstasy becoming more commonly used than amphetamines (European Monitoring Centre for Drugs and Drug Addiction, 2005).

2.3.3 Cocaine

Cocaine use is largely restricted to the Americas, which is not surprising given that production of cocaine occurs almost exclusively in that region (United Nations Office for Drug Control, 2005). It has been estimated that there are 14 million cocaine users globally, of which two-thirds are found in these regions. Worldwide, the prevalence of cocaine use has been estimated at 0.3% (United Nations Office for Drug Control, 2005), but cocaine use has historically been significantly higher than this in the USA (Johnston et al., 2003), which experienced a so-called "epidemic" of cocaine use (particularly in "crack" cocaine form) during the 1980s (Agar, 2003; Miech et al., 2005). Although crack cocaine use has declined in the USA since that time (Bowling, 1999), the prevalence of cocaine use remains more prevalent in that country than in comparable countries such as Australia (Johnston et al., 2003). In the USA in 2004, 14% of those aged 12 years or older reported lifetime use of cocaine use, and 2.4% reported having used it during the previous 12 months (Substance Abuse and Mental Health Services Administration, 2005).

Recent years may have seen an increase in the availability and use of cocaine in Europe, and increases in the use of "crack" cocaine (Home Office, 2004). Recent population surveys estimate that between 0.5% and 6% of the European population have tried cocaine, with rates in Italy (4.6%), Spain (4.9%), and the UK (6.8%) being higher than elsewhere in Europe (European Monitoring Centre for Drugs and Drug Addiction, 2005).

2.3.4 Heroin and other opioids

The prevalence of opioid use is relatively low in comparison with other illicit drugs. Estimates produced by the United Nations suggest that globally, just

over 15 million people had used opioids in the previous year (United Nations Office for Drug Control, 2004). This corresponded to approximately 0.4% of the global population aged between 15 and 64 years. Of these people, just over 9 million were estimated to use heroin, or approximately 0.2% of the global population aged 15 to 64 years (United Nations Office for Drug Control, 2004).

According to the UNODC, over half of the world's opioid users are to be found in the Asian countries surrounding Afghanistan and Myanmar, the two biggest opium cultivating countries (United Nations Office for Drug Control, 2004). Four million opioid users are estimated to be found in Europe (mostly in Eastern Europe). North and South America combined account for about 2.5 million opioid users, and Oceania (which includes Australia) has been estimated to have 0.1 million users. Both Europe and Oceania have a prevalence of opioid use higher than the global average: 0.75% and 0.5% of the population aged 15 to 64, respectively (United Nations Office for Drug Control, 2004).

There have been recent changes in opioid use globally. Use appears to be stable or declining in Western Europe, East and South-East Asia, Pakistan, and some Central Asian countries. China has experienced considerable increases in the extent of heroin use over the past decade, with the number of registered "addicts" reaching 1 million in 2003, a 15-fold increase since 1990 (United Nations Office for Drug Control, 2005).

There have been particularly marked decreases in problems related to heroin use in Australia since 2001 (Degenhardt et al., 2005b, c, e), and possibly in the number of regular heroin users (Degenhardt et al., 2004b, 2005c), as a result of a marked reduction in heroin supply and apparently sustained changes in the structure and extent of heroin trafficking into the country.

2.4 Risk factors for illicit drug use

Simple prevalence estimates of the proportion of the population that have *ever* used an illicit drug are likely to be associated with a low average risk of mortality. This is so because a single occasion of use and infrequent use are the most common patterns of reported use in population surveys, and these patterns are associated with only a small increase in mortality.

There are some global demographic factors that strongly predict illicit drug use. In general, males are more likely than females to use most psychoactive substances (Greenfield & O'Leary, 1999; Johnston et al., 2000a, b; Kandel, 1991). There are indications, however, that this gender difference in rates of use may be diminishing in more recent birth cohorts. While marked gender differences exist in the prevalence of substance use among older birth cohorts, these differences

became smaller in more recent birth cohorts (Degenhardt et al., 2000). Illicit drug users are also likely to be married/de facto than those who have not used illicit drugs (Kandel, 1991; Kandel et al., 1997; Warner et al., 1995).

Substance use (particularly illicit substance use, but also alcohol and tobacco use) is strongly associated with a person's age. Young people are by far the most likely age group to report using psychoactive substances within the past year (Bachman et al., 1997; Makkai & McAllister, 1998). Recent use (e.g. past year) typically declines in adulthood, reflecting the adoption of roles such as child-rearing, marriage, and employment (Bachman et al., 1997).

One hypothesis to explain why some people seem more likely to develop problematic substance use is that they inherit an increased susceptibility (*vulnerability*) to the development of such problems. Substance use disorders are likely to cluster within families. Researchers have attempted to develop models of vulnerability to substance use disorders, in which vulnerability is the product of genetic and/or environmental factors. Research with twins suggests that there is a significant genetic component (*heritability*) that increases the likelihood of dependence on a range of substances. Twin studies have produced estimates of the heritability of cannabis abuse and dependence (ranging from 62% to 79%) (Kendler & Prescott, 1998a; Tsuang et al., 1998), and also for dependence upon heroin, sedatives, and stimulants (Kendler & Prescott, 1998b; Tsuang et al., 1996, 1998). The exact nature of these genetic vulnerabilities is not known. Thus far, there have been no single candidate genes discovered which are directly related to substance abuse (Altman et al., 1996). It is likely that genetic influences involve multiple genes or the incomplete expression or function of several genes that influence how drugs are metabolised and how rewarding their effects are (Kendler, 1999; Schuckit, 1999).

There are several social and environmental factors that have been strongly related to substance use and substance use disorders. These are in keeping with the findings of twin studies showing that while there is a strong genetic component accounting for vulnerability to substance dependence, there is also a substantial *environmental* component (e.g. Kendler & Prescott, 1998a, b; Kendler et al., 1999). A number of these factors will be outlined below.

There is abundant evidence that people who engage in antisocial behaviour are more likely to have, or develop, substance use problems. Adolescents with conduct disorders are significantly more likely to develop substance use disorders than those without such conduct problems (Cicchetti & Rogosch, 1999; Gittelman et al., 1985). In general, it appears that the earlier, more varied and more serious a child's antisocial behaviour, the more likely it will be continued into adulthood,

with substance misuse considered one of these antisocial behaviours (Costello et al., 1999; Robins, 1978). Furthermore, children or young people with anxiety or depressive symptoms are more likely to begin substance use at an earlier age, and more likely to develop substance use problems (Cicchetti & Rogosch, 1999; Costello et al., 1999; Henry et al., 1993; Loeber et al., 1999).

The peer environment also has a large influence on substance use behaviours. Substance use usually begins with peers, and peer attitudes to substance use have been shown to be highly predictive of adolescent substance use (Fergusson & Horwood, 1997; Hoefler et al., 1999; Newcomb et al., 1986). This may be because those who use substances are more likely to choose to spend time with other people who use such substances. There is, however, no direct evidence on the influence of peers on the development, or maintenance, of substance *dependence* (Institute of Medicine, 1996).

Families also have a strong effect upon the likelihood that people will develop substance use problems (Hawkins et al., 1992; Lynskey et al., 1998). This occurs in a number of ways. First, modelling of substance use by parents and other family members has been shown to affect adolescent substance use behaviour. For example, parental substance use has been associated with the initiation of alcohol and cannabis use (Hawkins et al., 1992), while older brothers' substance use and attitudes towards substance use have been associated with younger brothers' substance use (Brook et al., 1988). Second, there is evidence that if parents hold permissive attitudes towards the use of specific substances by their children, their children will be more likely to use such substances (Hawkins et al., 1992). Third, the nature of family relationships has an effect upon the likelihood that adolescents will develop problematic substance use. The risk of substance misuse is higher if there is family discord, poor or inconsistent behavioural management by parents, or low levels of bonding within the family (Hawkins et al., 1992).

The socio-cultural background of a person will also affect the likelihood that they develop substance use problems. There are clear links between social disadvantage and poorer global health outcomes (Graham & Power, 2004; Wilkinson & Marmot, 2003). More particularly, there are strong links of disadvantage with substance use, which suggest increased vulnerability of the disadvantaged to the initiation of substance use, and thus be exposed to its associated problems (Anthony et al., 1994; Hawkins et al., 1992; Kandel et al., 1997). Disadvantage may be conceptualised at three levels: individual disadvantage, family disadvantage, and community disadvantage. At the level of individual disadvantage, lower socioeconomic individuals are more likely to have problematic use across a range of substances, including tobacco, alcohol,

and illicit drugs (Anthony et al., 1994; Hawkins et al., 1992, Hemmingsson et al., 1997; Muntaner et al., 1998). More specifically, markers for individual disadvantage such as unemployment and lower educational levels have been associated with the use of illicit drugs such as cannabis, amphetamines, and heroin (Institute of Medicine, 1996; Kandel, 1991; Kandel et al., 1997; Lynskey & Hall, 2000; Warner et al., 1995).

When considering the disadvantage of an individual and potential for illicit drug use, childhood family disadvantage must also be taken into consideration (Bradley & Corwyn, 2002; Graham & Power, 2004). Lower parental socioeconomic status has been associated with a number of risk factors for the development of substance use and dependence such as childhood abuse, childhood neglect, depression, and hopelessness (Bradley & Corwyn, 2002; Galea et al., 2004; Graham & Power, 2004; Poulton et al., 2002). The more specific subsequent effects of such childhood factors upon mortality due to suicide amongst drug users are discussed in a later section (Chapter 6).

Finally, community disadvantage is associated with a range of health and social problems (Bobashev & Anthony, 1998; Galea et al., 2004; Petronis & Anthony, 2003; Weatherburn & Lind, 2001). In particular, disadvantaged communities have higher rates of initiation into alcohol and illicit drug use, and of substance use problems (Bobashev & Anthony, 1998; Fergusson & Horwood, 1997; Galea et al., 2004; Hawkins et al., 1992; Institute of Medicine, 1996; Petronis & Anthony, 2003; Weatherburn & Lind, 2001). For instance, the incidence of fatal opioid and cocaine overdose, a clear marker of use of these drugs, has been associated with the poverty of a district (Marzuk et al., 1997). Impoverished social environments tend to have high rates of crime, delinquency, and substance availability. In the case of the disadvantaged community, we see a clustering of the disadvantages discussed above with limited educational opportunities, lower levels of employment, and higher levels of stress upon individuals and families.

2.5 Summary

Cannabis is the most commonly used illicit drug in many societies. Stimulant drugs such as amphetamines, ecstasy, and cocaine are typically the next most commonly used drugs. Opioid drugs are the least commonly used drugs worldwide.

Substance use has been consistently linked to a number of social and demographic characteristics, with males, younger persons, unemployed persons, those with less education, those who are not married, and those from lower

socioeconomic backgrounds all more likely to report licit and illicit substance use. Disadvantage at the individual, family, and community level all increase the likelihood of substance use. In general, these same factors have also been related to an increased risk of problematic substance use.

A multitude of theories have been proposed to explain why some people develop problematic substance use. Genetic factors appear to play a part: twin studies indicate these components have a significant role in developing dependence upon the most commonly used substances. There is also consistent evidence that a range of environmental factors will increase the likelihood of problematic substance use. These include economic disadvantage, family conflict, modelling of substance use or parents' permissive attitudes towards substance use, as well as childhood conduct disorder and emotional problems.

There are a number of approaches to explain why some people become problematic substance users. Each level of explanation (biological, psychological, socio-cultural) has been supported by empirical research. These different levels, however, remain to be integrated into a more comprehensive model of addiction.

Key points: Summary of illicit drug use epidemiology

- There is a clinical distinction between substance use, substance abuse, and substance dependence.
- Cannabis is the most commonly used illicit drug in many societies.
- Stimulant drugs such as amphetamines, ecstasy, and cocaine are typically the next most commonly used drugs.
- Opioid drugs are the least commonly used illicit drugs worldwide.
- Substance use has been linked to social and demographic characteristics: being male, younger age, unemployment, less education, unmarried, lower socioeconomic background.
- Genetic factors appear to play a significant role in developing dependence upon the most commonly used substances.
- Environmental factors will increase the likelihood of problematic substance use: family conflict, modelling of substance use, permissive parental attitudes towards substance use, childhood conduct disorder, emotional problems.
- Individual, family, and community disadvantage all increase the likelihood of illicit drug use and dependence.

3

Mortality amongst illicit drug users

3.1 Introduction

In this chapter we examine the epidemiology of illicit drug-related death. Specifically, this chapter presents rates of mortality amongst illicit drug users from all causes, the demography of cases, and the associated risk factors. As any discussion of illicit drug-related mortality must necessarily discuss the issues surrounding the estimation of drug-related mortality, they are examined first. Rates of death due to specific causes will be examined in subsequent chapters, as will the specific factors associated with these causes.

3.2 Problems in estimating mortality

A number of problems arise when attempting to estimate global mortality attributable to illicit drug use (cf. Degenhardt et al., 2004a). Part of the problem arises from the very fact that the drugs in question are illicit, and that these deaths thus occur amongst "hidden" populations. Whilst a death may be attributable to illicit drug use, the use of these drugs may well have been concealed by the individual. As such, the link to illicit drug use may not be formally recognised as the cause of death, or as a factor associated with the death. A good example is the completed suicide of an illicit drug user, an issue addressed in detail in a later chapter. If the suicide method is by means of an illicit drug overdose, then the death will be clearly attributable to illicit drug use. If, however, the suicide is performed by means that do not involve drugs (e.g. hanging), association of the death with illicit drug use may not be made. The decedent may be an illicit drug user, the death may be due to depression associated with drug use, but unless the illicit drug using status of the individual is known, such an attribution will not occur. Reported death rates amongst hidden populations are thus, in all likelihood, underestimates.

It is also obvious that the quality of official statistics on the prevalence of illicit drug use, and of illicit drug-related mortality, will vary enormously from country to country. A wealthy, first world country is far more likely to have the resources and infrastructure to devote to collecting official statistics on mortality and its specific causes than would a poorer nation. Estimates of mortality and the total burden of disease attributable to illicit drug use in some regions will, by necessity, be speculative.

Whilst this is true, there are also environmental, cultural, and behavioural factors that vary between countries, and will affect estimates made for those countries (Degenhardt et al., 2004a). One major factor that will affect mortality rates among illicit drug using populations is the provision of drug-dependence treatment. Enrolment in drug treatment has been associated with substantially reduced drug use, as well as reduced risk of overdose and acquiring human immunodeficiency virus (HIV) (Darke et al., 2005f; Flynn et al., 2003; Gossop et al., 1999, 2000; Gronbladh et al., 1990; Stewart et al., 2002; Teesson et al., in press; Ward et al., 1998). The extent to which drug treatment is provided in a country, and is able to be accessed by dependent drug users, will thus impact substantially upon the rates of drug-related mortality amongst these populations. Provision and access to treatment will vary greatly, even between countries that are broadly similar, and mortality rates may thus vary widely.

Similarly, countries differ substantially in relation to blood-borne disease prevention programmes, such as the provision of sterile injecting equipment to injecting drug users (IDU). To the extent that such programmes reduce rates of blood-borne viral infections amongst illicit drug users, and subsequent death, there will be an impact upon mortality rates. As with treatment, differences in approaches to the containment of blood-borne infections may be substantial between otherwise similar countries, facing similar viral threats.

While estimating illicit drug-related death rates raises problems, estimating the extent to which these rates exceed population rates is also problematic. Standardised mortality ratios (SMRs), the ratio of observed to expected deaths, are typically derived from studies conducted amongst European and North American drug using cohorts. Caution must be exercised when extrapolating these mortality ratios to other settings, particularly third world countries, as there will be substantial differences in population death rates in a country such as the US compared to poor countries with limited medical resources. Whilst, for example, heroin users may die at a rate 20 times greater than that seen amongst the general US population, the excess mortality due to heroin use may be substantially *lower* in a third world nation, as overall population mortality is substantially *higher*.

Cohort studies provide a valuable means of estimating illicit drug user mortality rates, and are used in meta-analyses to determine these rates (e.g. Hulse et al., 1999). Two points must be borne in mind here. First, for logistical reasons, most cohorts have been initially recruited through treatment populations. Those entering drug treatment may thus not reflect death rates seen amongst the broader illicit drug using population. Second, the majority of studies have focussed on opioid users, and relatively few studies have examined rates across different drug classes.

Finally, there are specific problems that relate to causal attribution. As discussed above, unless a case of suicide is by means of a drug overdose, the causal role of illicit drug use in such a death may be overlooked. Disease also presents problems, as it is a dynamic factor in such deaths. The acquired immune deficiency syndrome (AIDS) pandemic amongst IDU from the 1980s onwards changed the nature and rates of death amongst IDU, as have the new anti-retroviral regimes that have prolonged life amongst those infected with HIV. Finally, trauma, which is discussed in detail in a later chapter, is difficult to quantify in official statistics. Illicit drug use, and injecting drug use in particular, is likely to involve increased risk of death through injury or violence. It is unlikely that such deaths would be classified as drug-related in any official statistics. Rates of death through trauma are thus likely to be underestimated.

The above all indicate that a number of caveats must be borne in mind when estimating death rates amongst illicit drug users. In all likelihood, these estimates will be conservative. Despite these caveats, however, a large amount of data exists that can be considered. As will be seen, despite the above caveats, these studies show a large degree of consistency. All sources indicate high mortality rates amongst illicit drug using populations and, further, that these rates are greatly in excess of those of the general population. Given that, as will be seen in the ensuing chapters, there is wide and continuing exposure among illicit drug users to a range of mortality risk factors at rates far beyond those seen in the general population, these findings make causal sense. Whilst the specifics of drug-related deaths may be debated, and appropriate caveats borne in mind, the overall patterns and trends of such deaths are consistent and indicate a major clinical and social problem.

3.3 Mortality amongst illicit drug users

The most comprehensive attempt to quantify the global burden of disease, and more specifically of mortality, attributable to substance use and dependence was recently published by the World Health Organization (Ezzati et al., 2004).

Table 3.1. Deaths and Disability Adjusted Life Years (DALYs) attributed to illicit drug use in 2000, with comparisons to alcohol and tobacco

Region	Males (% of cases)	Females (% of cases)	All (% of cases)
Africa	23,828 (87.2)	3,504 (12.8)	27,332 (100)
Asia/Pacific	50,487 (83.6)	9,882 (16.4)	60,369 (100)
Europe	21,875 (66.4)	11,081 (35.6)	32,956 (100)
Middle East	12,797 (83.0)	2,626 (17.0)	15,423 (100)
North America	22,599 (56.0)	17,757 (44.0)	40,356 (100)
South/ Central America	13,424 (64.1)	7,523 (35.9)	20,947 (100)
Total illicit drug deaths[*]	145,010 (73.5)	52,373 (26.5)	197,383 (100)
DALYs	5,402,000	1,477,000	6,879,000
Alcohol[+] total deaths	1,638,000 (91)	166,000 (9)	1,804,000 (100)
DALYs	761,562,000	693,911,000	1,455,473,000
Tobacco[#] total deaths	3,840,000 (80)	1,000,000 (20)	4,830,000 (100)
DALYs	48,177,000	10,904,000	59,081,000

[*]Degenhardt et al. (2004a); [+]Rehm et al. (2004); [#]Ezzati, M. & Lopez, A. (2004).

Estimates were made of the mortality attributable to substance dependence in the year 2000, based upon a mixture of direct (e.g. specific cause of death figures, such as overdose) and indirect estimates (e.g. extrapolation of mortality rates form large cohort studies). On the basis of these analyses, it was estimated that 197,383 deaths that were attributable to illicit drug use occurred in 2000 alone (Table 3.1) (Degenhardt et al., 2004a). As would be expected, given the difficulties involved in making such estimates, there was a wide confidence interval around this estimate, with an upper estimate of 322,456 cases. As can be seen, and consistent with the rise in illicit drug use seen around the world (United Nations Office for Drug Control, 2005), illicit drug use deaths were not restricted to any one world region.

The same study also estimated the Disability Adjusted Life Years (DALYs) due to illicit drug use mortality. DALYs are defined as the sum of years of potential life lost due to premature mortality, and the years of productive life lost due to disability. They are thus a combination measure of lost life and disability. In 2000, it was estimated that over 6.87 million DALYs were attributable to illicit drug use, which represents 0.8% of all global DALYs for that year (Degenhardt et al., 2004a).

By way of comparison, Table 3.1 also presents mortality estimates for both alcohol (Rehm et al. 2004) and tobacco (Ezzati & Lopez, 2004). As would be expected, given the far more extensive use of these substances, the estimated mortality is substantially higher than for illicit drugs. In 2000, it was estimated that there were 1.8 million deaths attributable to alcohol and 4.8 million for tobacco. These licit substances thus clearly cause more deaths per year than do illicit drugs. However, despite the illicit nature of the drugs in question, and substantially lower prevalence of use, the estimated number of illicit drug deaths in 2000 was 11% of those attributed to alcohol.

Mortality rates of large-scale cohorts of illicit drug users are presented in Table 3.2. As can be seen, in the majority of studies the mortality rate exceeds 15 per thousand person years. How this compares to the general population is demonstrated by the SMRs pertaining to these studies. In all of these studies, mortality rates were far in excess of those seen amongst the general population of the countries in which they were conducted. In fact, in the majority of these studies the excess mortality was more than 10 times that of non-drug users matched for age and gender.

3.4 Factors associated with illicit drug-related mortality

3.4.1 Drug class

The nature and extent of risks associated with illicit drug use will clearly vary according to the type of substance used. Perhaps the major risk associated with opioid use is overdose, discussed in detail in Chapter 5, which constitutes a substantial proportion of opioid-related deaths. Overdose is also a risk for stimulant use, although the mechanisms differ from those of opioids, and there does not appear to be the clear dose response seen in opioids (cf. Chapter 4). Injectors of any drug will be at risk of infection with blood-borne viruses, such as HIV or hepatitis C, if they engage in the sharing of injecting equipment (Karch, 2002).

Deaths due to other drug classes are less well-documented than those seen amongst opioid and stimulant users. Whilst not large in number, deaths due to methylenedioxymethamphetamine (MDMA) have been documented, and have been related to cardiac arrhythmia, hyperthermic collapse, dehydration, or excessive water consumption (Karch, 2002; Schifano, 2004). Cannabis, the most widely used illicit drug, has no risk of overdose or infection through the sharing of injecting equipment. Cannabis-related mortality is primarily due to the long-term effects of route of administration on the respiratory system or traumatic motor vehicle accidents (Kalant et al., 1999; Kelly et al., 2004).

Table 3.2. All cause mortality rates amongst illicit drug user cohorts

Study	Country/Period	Sample	Drug	Standardized mortality ratio	Crude mortality rate (per 1000 person years)
Bargagli et al. (2001)	Italy 1980–1997	Treatment	Heroin	17.3; Male 15.4, Female 37.8	21.5
Bartu et al. (2004)	Australia 1985–1998	Hospital/psychiatric admissions	Opioids, amphetamine	–	1.8
Benson & Holmberg (1984)	Sweden 1968–1978	Conscripts, rehabilitation and psychiatric patients, welfare recipients	Cannabis, solvents, last stage of delirium (LSD), stimulants	26.0	4.5
Bewley et al. (1968)	UK 1947–1966	Notified addicts	Heroin	28.0	27.0
Brugal et al. (2005)	Spain 1992–1999	Treatment	Heroin	–	0.4
Bucknall & Robertson (1986)	UK 1981–1985	General Practitioner attendees	Heroin	11.6	9.7
Caplehorn et al. (1996)	Australia 1979–1991	Treatment	Heroin	–	12.1
Cherubin et al. (1972)	US 1964–1968	Notified addicts	Heroin	–	6.4–12.8
Cooncool et al. (1979)	US 1969–1976	Treatment	Heroin	1.5	5.6
Cotrell et al. (1985)	UK 1971–1982	Notified addicts	Heroin	–	18.6
Davoli et al. (1997)	Italy 1980–1992	Treatment	IDU	Male 21.2, Female 38.5	24.5
Dukes et al. (1992)	New Zealand 1971–1989	Treatment	Opioids	2.4; Male 1.8, Female 4.7	7.4
Engstrom et al. (1991)	Sweden 1973–1984	Drug-related hospitalisation	Amphetamine, cocaine, heroin	5.3; Male 5.8, Female 4.6	23.0
Eskild et al. (1993)	Norway 1985–1991	HIV test centre	IDU	31.0; Male 25.0, Female 58.0	23.5
Friedman et al. (1996)	US 1984–1992	Welfare recipients	Drugs and alcohol	5.2	28.4

(*Contd.*)

Table 3.2. (*Contd.*)

Study	Country/Period	Sample	Drug	Standardized mortality ratio	Crude mortality rate (per 1000 person years)
Frischer et al. (1997)	UK 1982–1994	Treatment	IDU	22.0; Male 16.1, Female 37.7	20.8
Fugelstad et al. (1995)	Sweden1986–1990	HIV + drug addicts	Heroin	–	38.5
Fugelstad et al. (1997)	Sweden 1981–1992	Drug-related hospitalisation	Heroin, amphetamine	–	16.3
Galli & Musicco (1994)	Italy 1980–1991	Treatment	IDU	20.5; Male 19.5, Female 54.2	25.2
Ghodse et al. (1998)	UK 1967–1993	Notified "Drug addicts"	Opioids	7–13; Male 2.9–16.9, Female 5.0–21.0	7.7
Goedert et al. (1995)	Italy 1980–1990	Treatment	Heroin	18.0	15.7
Goldstein & Herrera (1995)	US 1979–1993	Treatment	Heroin	Male 4.0, Female 11.1	15.6
Gossop et al. (2002b)	UK 1995–1999	Treatment	Heroin, amphetamine	6.0	–
Gronbladh et al. (1990)	Sweden 1967–1988	Treatment, untreated	Heroin	63.1 (street), 8.4 (methadone)	29.2
Haarstrup & Jepson (1988)	Denmark 1973–1984	Treatment	Opioids	–	26.3
Hser et al. (1993)	US 1962–1986	Treatment	Narcotics	–	12.3
Joe et al. (1982)	US 1969–1979	Treatment	Opioids	1.7; Male 1.7, Female 1.8	15.2
Joe & Simpson (1987)	US 1978–1984	Treatment	Opioids	6.9	15.6
Langendam et al. (2001)	Holland, 1985–1996	Treatment/community	Heroin, cocaine	–	30.2
McAnulty et al. (1995)	US 1989–1991	Not in treatment	IDU	8.3	10.5
Musto & Ramos (1981)	US 1918–1973	Treatment	Morphine	–	8.4

Oppenheimer et al. (1994)	UK 1969–1991	Treatment	Heroin	11.9; Male 11.2 Female 13.9	15.3
Orti et al. (1996)	Spain 1985–1991	Treatment, Hospital	Opioids	–	30.1
Oyefesso et al. (1999b)	UK 1974–1993	Notified teenage addicts	Opioids	12.3; Male 10.7, Female 21.2	4.7
Perucci et al. (1991)	Italy 1980–1988	Treatment	Opioids	10.1; Male 9.3, Female 18.1	7.1
Quaglio et al. (2001)	Italy 1985–1998	Treatment	IDU	12.9; Male 8.9, Female 21.7	–
Rehm et al. (2005)	Switzerland 1994–2000	Treatment	Heroin	9.7; Male 8.4, Female 17.2	10.6
Rossow (1994)	Norway 1968–1992	Treatment	"Addicts"	–	24.0
Sanchez-Carbonell & Seus (2000)	Spain 1985–1995	Treatment	Heroin	28.5	34.0
Tunving (1988)	Sweden 1970–1984	Treatment	Opioids, amphetamine	5.4 (opiates) 2.5 (amphetamine)	11.8
Vaillant (1973)	US 1952–1970	Treatment, males	Narcotics	–	11.5
Van Ameijden et al. (1999a)	Holland 1985–1995	Treatment and community agencies	IDU	–	17.5
Van Haarstrecht et al. (1996)	Holland 1985–1993	Treatment, STD patients	IDU	–	25.9
Vlahov et al. (2004)	US 1988–2000	New onset IDU	IDU	3.1–8.1	32.6
Wahren et al. (1997)	Sweden 1970–1974	Hospitalised for drug dependence	Stimulants, opioids	6.9; Male 7.6, Female 5.4	15.9
Watterson et al. (1975)	US 1970–1974	Treatment	Opioids	–	13.0
Wille (1981)	UK 1969–1979	Treatment	Heroin	–	14.8
Zaccarelli et al. (1994)	Italy 1985–1991	Treatment	IDU	Male HIV + 30.3, HIV − 11.1 Female HIV + 19.4, HIV − 4.9	23.0
Zanis & Woody (1998)	US 1993–1994	Methadone	Heroin	–	25.6

In addition to the innate risks associated with a drug, the pattern of drug use in a particular country will greatly affect the distribution of drug-related death. In Europe, opioids are by far the principal cause of drug-related death (European Monitoring Centre for Drugs and Drug Addiction, 2004). By contrast, in the US opiates and cocaine figure prominently in deaths, most particularly in combination (Coffin et al., 2003; Department of Health and Human Services, 2005). In all of these regions, relatively small proportions of cases are attributed to amphetamine, MDMA, or cannabis.

When examining the rates of death due to different drugs, it must be borne in mind that polydrug use, of both licit and illicit substances, is the norm amongst illicit drug users (e.g. Darke & Hall, 1995; Darke & Ross, 1997; Dinwiddie et al., 1996; Gossop et al., 2002a; Hubbard et al., 1997; Klee et al., 1990; Ross & Darke, 2000). This makes attribution to a particular drug difficult in many cases. This is illustrated by the strong association between heroin and cocaine seen in the US and elsewhere (Coffin et al., 2003; Darke et al., 2005a). Also, the caveats regarding hidden populations must be borne in mind. National statistics on illicit drug deaths will be biased towards clear overdoses, so may not reflect the overall mortality associated with a particular drug.

Few cohort studies have directly compared mortality rates across drug classes, a possible reflection of the predominance of opiate users in such cohorts. The few that have, however, consistently report significantly higher death rates amongst primary opiate users, but also report elevated death rates for stimulant users (Bartu et al., 2004; Engstrom et al., 1991; Fugelstad et al., 1997; Tunving, 1988; Wahren et al., 1997). Bartu et al. (2004) reported that opiate users were 1.4 times more likely to die than amphetamine users in their cohort, and were 2.4 times more likely to die from overdose. Fugelstad et al. (1997) also reported a substantially higher mortality rate (3.2 times) amongst opiate users when compared to amphetamine users. Many of the deaths amongst primary amphetamine users in this study were, in fact, due to heroin overdose, a good illustration of the problems polydrug use presents for causal attribution. Higher SMRs amongst opiate compared to stimulant users were reported by Engstrom et al. (1991) (18 versus 9), Tunving (1988) (5 versus 2.5), and Wahren et al. (1997) (22 versus 10). Overall, the data indicate that opiate use carries the highest risk of death, and overdose is the obvious candidate to explain this elevated risk (Bartu et al., 2004; Engstrom et al., 1991; Fugelstad et al., 1997; Tunving, 1988; Wahren et al., 1997).

More widespread polydrug use appears to increase the risk of death amongst illicit drug users (Gossop et al., 2002a; Van Ameijden et al., 1999a; van Haarstrecht et al., 1996). In particular, heavy alcohol use (Cooncool et al., 1979; Friedman et al., 1996; Gossop et al., 2002a; Hser et al., 1998, 2001; Joe et al.,

1982; Musto & Ramos, 1981; van Ameijdan et al., 1999a; van Haarstrecht et al., 1996) and benzodiazepine use (Caplehorn, 1996; Gossop et al., 2002a; van Ameijdan et al., 1999a; van Haarstrecht et al., 1996) appear to substantially increase mortality rates. A partial explanation for these findings is that both alcohol and benzodiazepines are central nervous system (CNS) depressants, and increase the risk of overdose when used in conjunction with opioids. Concomitant alcohol use also increases the toxicity of cocaine, and is strongly associated with cocaine toxicity deaths (Coffin et al., 2003; Darke et al., 2005a; Karch, 2002). Heavy alcohol use is also associated with liver disease, while both alcohol and benzodiazepine dependence increase the risk of suicide (Harris & Barraclough, 1997). There is also a strong relationship between these drugs and death due to trauma (Gill, 2001; Greenberg et al., 1999; Kelly et al., 2004). Given all this, when these licit substances are used in combination with illicit drugs, it is not surprising that the risk of death increases. The relationship between polydrug use and mortality is crucial, and is discussed further throughout this book.

3.4.2 Gender

Consistent with the epidemiology of illicit drug use (Chapter 2), the majority of deaths worldwide attributable to illicit drug use occur amongst males (Table 3.1). These estimates indicate that males constitute approximately three quarters of deaths, and of DALYs. Males have also dominated deaths in the major cohort studies (Table 3.3), ranging to 87% of cases (Gossop et al., 2002b).

Whilst males constitute the bulk of fatal cases, the SMRs associated with *female* mortality are generally greater than those of males (Table 3.2). The discrepancy between male and female SMRs has been consistently reported in studies from different countries, and is quite pronounced in many studies, for example, 15.4 versus 37.8 (Bargagli et al., 2001), 21.2 versus 38.5 (Davoli et al., 1997), 4.0 versus 11.1 (Goldstein & Herrera, 1995), 8.4 versus 17.2 (Rehm et al., 2005). What this means is that female illicit drug users are substantially more likely to die than non-drug using females, than are males when compared to non-drug using males. Thus, in the Bargagli et al. (2001) study, female drug users were 37 times more likely to die than non-drug using females, while males in the cohort were 15 times more likely to die than non-drug using males.

The fact that males represent the majority of fatalities is expected, as they constitute the majority of illicit drug users. How, then, do we interpret the reverse situation in the case of SMRs? There are two possibilities. First, the female illicit drug users are more risky than their male counterparts. The fact that females are substantially less likely to use illicit drugs than males may mean that those

Table 3.3. Demographic characteristics of illicit drug-related deaths in major cohort studies

Study	Country/Period	Drug	Mean age at death	Gender (% male)
Bargagli et al. (2001)	Italy 1980–1997	Heroin	32.9	81
Bartu et al. (2004)	Australia 1985–1998	Opioids, amphetamine	34.6	66
Benson & Holmberg (1984)	Sweden 1968–1978	Cannabis, solvents, LSD, stimulants	–	84
Brugal et al. (2005)	Spain 1992–1999	Heroin	39.0	77
Bucknall & Robertson (1986)	UK 1981–1985	Heroin	Male 28.3 Female 22.0	86
Cherubin et al. (1972)	US 1964–1968	Heroin	28.3	85
Cooncool et al. (1979)	US 1969–1976	Heroin	35.1	–
Cotrell et al. (1985)	UK 1971–1982	Heroin	29.9	–
Davoli et al. (1997)	Italy 1980–1992	IDU	–	83
Dukes et al. (1992)	New Zealand 1971–1989	Opioids	32.3	69
Engstrom et al. (1991)	Sweden 1973–1984	Amphetamine, cocaine, heroin	–	66
Eskild et al. (1993)	Norway 1985–1991	IDU	–	65
Friedman et al. (1996)	US 1984–1992	Drugs and alcohol	–	79
Frischer et al. (1997)	UK 1982–1994	IDU	26.3	66
Fugelstad et al. (1997)	Sweden 1981–1992	Heroin, amphetamine	–	75
Galli & Musicco (1994)	Italy 1980–1991	IDU	–	82
Ghodse et al. (1998)	UK 1967–1993	Opioids	30.6	78
Gossop et al. (2002b)	UK 1995–1999	Heroin, amphetamine	30.6	87
Gronbladh et al. (1990)	Sweden 1967–1988	Heroin	–	80
Hser et al. (1993)	US 1962–1986	Narcotics	40.2	–
McAnulty et al. (1995)	US 1989–1991	IDU	–	73
Musto & Ramos (1981)	US 1918–1973	Morphine	55.9	–
Oppenheimer et al. (1994)	UK 1969–1991	Heroin	–	70
Orti et al. (1996)	Spain 1985–1991	Opioids	–	75
Oyefesso et al. (1999a)	UK 1974–1993	Opioids	23.0	76
Perucci et al. (1991)	Italy 1980–1988	Opioids	–	84
Quaglio et al. (2001)	Italy 1985–1998	IDU	31.3	84
Rossow (1994)	Norway 1968–1992	"Addicts"	–	81
Sanchez-Carbonell & Seus (2000)	Spain 1985–1995	Heroin	31.0	76
Tunving (1988)	Sweden 1970–1984	Opioids, amphetamine	27.6	84
Van Haarstrecht et al. (1996)	Holland 1985–1993	IDU	–	68
Wahren et al. (1997)	Sweden	Stimulants, opioids	–	75
Wille (1981)	UK 1969–1979	Heroin	30.8	74
Zaccarelli et al. (1994)	Italy 1985–1991	IDU	–	79

who do so are a self-selected, and riskier population than the more commonly seen male drug user. Several factors, however, contradict this possibility. The prevalence of the psychiatric diagnoses that most directly measure impulsivity, risk, and deviance (Antisocial Personality Disorder (ASPD) and Borderline Personality Disorder (BPD)) in many studies are no higher amongst female drug users than amongst males (Darke et al., 1998, 2005d; Gill et al., 1992; Luthar et al., 1996). If females were comparatively more "deviant" than males, we would most certainly expect to see higher rates of these disorders.

More importantly, when gender-specific mortality rates have been reported, or the gender proportions of deaths compared to baseline, there is no observable difference between male and female death rates (Bargagli et al., 2001; Bartu et al., 2004; Caplehorn 1996; Frischer et al., 1997; Fugelstad et al., 1997; Galli & Mustico, 1994; Goldstein & Herrara, 1995; Gossop et al., 2002a; Gronbladh et al., 1990; McAnulty et al., 1995; Oppenheimer et al., 1994; Orti et al., 1996; Oyefesso et al., 1999a; Perucci et al., 1991; Rossow, 1994; Sanchez-Carbonell & Seus, 2000; Tunving 1988; Van Haarstrecht et al., 1996; Wahren et al., 1997; Watterson et al., 1975; Wille, 1981; Zaccarelli et al., 1994). If anything, these studies indicate slightly *higher* rates amongst males. Thus, females *within* drug using cohorts appear no more likely to die than male members of the cohort.

The more likely explanation for higher female SMRs is the lower base population mortality rates seen amongst females. If the mortality rates of male and female illicit drug users are similar, then the SMRs of females drug users will be far greater compared to other females, than for male drug users compared to other males. While the chances of death may be similar for both male and female drugs users, the excess risk faced by females compared to their non-drug using female peers is substantially greater than that seen among males.

3.4.3 Age

In overall population terms, most deaths due to illicit drug use occur among the young. As can be seen from Table 3.3, the mean age at death in cohort studies has been generally in the vicinity of 30 years. An average age of death around 30 is consistent with studies of illicit drug-related fatalities (e.g. Darke & Zador, 1996; Karch et al., 1999; Schifano, 2004), and with estimates indicating that the highest proportion of deaths occur in the 25–34 and 25–44 years age brackets (Degenhardt et al., 2004a). The fact that these deaths occur amongst a relatively young age group is reflected in the large number of DALYs attributable to illicit drugs (Table 3.1).

Whilst in overall population terms these deaths occur among the young, in the context of drug using careers these are older, experienced drug users. As discussed previously, illicit drug use typically commences in the early- to mid-teenage years (Chen & Kandel, 1995; Degenhardt et al., 2000; Kandel et al., 1992). These deaths thus typically occur amongst a group that has been using illicit drugs for a decade or more. It is not the new, inexperienced user who appears to be most at risk, despite the pervasiveness of this view in media coverage which emphasises cases of very young illicit drug-related deaths. The bulk of cases occur amongst older drug users. Consistent with these findings, cohort studies of illicit drug users have repeatedly reported older age as an independent predictor of death during follow-up (Bartu et al., 2004; Brugal et al., 2005; Cooncool et al., 1979; Davoli et al., 1997; Dukes et al., 1992; Eskild et al., 1993; Friedman et al., 1996; Frischer et al., 1997; Gossop et al., 2002a; Goedert et al., 1995; Hser et al., 2001; Joe & Simpson, 1987; Joe et al., 1982; McAnulty et al., 1995; Oppenheimer et al., 1994; Quaglio et al., 2001; Watterson et al., 1975; Wahren et al., 1997; Zacarelli et al., 1994).

Why are older illicit drug users most at risk? When considering this we must remember that, whilst older, these deaths are not due to advanced age, which would be unremarkable. It is the period between the teenage years and the early 30s that is of most interest here. To comprehensively answer why it is older users who are most at risk, we must examine the causes of death, as will be done in detail in later chapters. Several possible factors emerge. First, there is the possibility of disease progression, particularly due to HIV or hepatitis C (Chapter 5). Older users may be sicker, and die due to illness. Second, the finding may relate to the cumulative risk associated with illicit drug use. In particular, the cumulative risk of overdose may be such that the risk of death is substantially higher at 30 than at 18. This finding may also represent some aspect of the natural history of illicit drug use, such as increased risk of overdose in later career stages (cf. Chapter 4). Of course, these potential explanations are not mutually exclusive. A person with hepatitis C may well be at greater risk of an overdose due to liver damage as the disease progresses. Whatever the case, when considering means by which to reduce illicit drug-related mortality, it must be borne in mind that it is the longer-term drug user who presents the highest risk, and is a major target for intervention.

3.4.4 Length of drug use career

A risk factor that is related to, but not identical with, age is the length of drug use career. Effectively this is the period between current age and the age of initiation

of drug use. As discussed in Chapter 1, illicit drug use careers are complex, and may include many cyclical periods of drug use, treatment, and abstinence (Darke et al., 2005c; Flynn et al., 2003; Hser et al., 2001). Longer length of career has, however, repeatedly been related to a higher risk of mortality (Brugal et al., 2005; Caplehorn et al., 1996; Cooncool et al., 1979; Eskild et al., 1993; Hser et al., 2001; McAnulty et al., 1995; Orti et al., 1996; Quaglio et al., 2001; van Haarstrecht et al., 1996; Vlahov et al., 2004). As was seen with age, it is not new users who are at the greatest risk of mortality. More so than age, length of drug use career is probably a proxy for cumulative risk exposure from factors such as overdose, viral infection, and trauma. A longer length of career may also reflect increased drug dependence and more problematic use, with consequent increased risk of death.

The findings from cohort studies on mortality risk relating to both age and length of use career indicate that it is the older, experienced user who is at greatest risk. It is important to note, however, that in recent years the age of initiation to both licit and illicit drug use has declined in many countries (Degenhardt et al., 2000). Such a trend has two implications. First, the age of death of drug users may begin to decline, as exposure to risks such as overdose and disease commences earlier. Second, earlier age of onset of drug use has been associated with higher levels of dependence and with more serious drug-related problems (Fergusson & Horwood, 1997; Grant & Dawson, 1998; Mills et al., 2004). After a decade of heroin use, for example, a heroin user who commenced use at age 15 will generally have more serious drug-dependency problems than one who commenced at 20. The consequences of earlier onset of drug use would, in all probability, exacerbate any trend towards earlier death amongst these populations. Indeed, such a trend has already been noted. In Australia, between the early 1970s and late 1990s, the age of death declined for each succeeding birth cohort (Hall et al., 1999a).

3.4.5 Drug-dependence treatment

One factor that appears to reduce mortality is treatment for drug dependence. Cohort studies have consistently found that retention in drug-treatment programmes substantially reduces mortality risk (Bartu et al., 2004; Brugal et al., 2005; Caplehorn et al., 1996; Davoli et al., 1993; Esteban et al., 2003; Fugelstad et al., 1995, 1997; Gronbladh et al., 1990; Quaglio et al., 2001; Segest et al., 1990; Watterson et al., 1975; Zanis & Woody, 1998). The extent of this reduction in mortality risk was illustrated dramatically by Gronbladh et al. (1990) in relation to methadone maintenance. Not in treatment "street" users had an

elevated rate of death 63 times that of the general population, compared to an 8-fold risk amongst those enrolled in treatment. Similarly, Zanis & Woody (1998) reported that 8% of patients discharged from methadone maintenance died over 12 months, compared to only 1% of those enrolled in treatment. Whilst treatment clearly cannot reduce the excess risk of death seen amongst illicit drug users to zero, cohort studies indicate that it does substantially reduce this risk. It should not, however, be assumed that any or all drug treatment reduces mortality risk. Rather, in the studies cited above it is prolonged, stable treatment that is most effective in reducing mortality risk. Indeed, as will be discussed in Chapter 4, there are specific situations in which mortality risk may actually *increase* (e.g. the induction phase of methadone, cessation of naltrexone maintenance). Despite these specific situations, the overall effect of treatment upon mortality is positive.

Why does stable drug treatment have such an impact upon mortality? This issue will be more fully explored in Chapter 8. Briefly, however, treatment outcome studies have repeatedly demonstrated that enrolment in the major treatment modalities is associated with large reductions in drug use (e.g. Darke et al., 2005c; Flynn et al., 2003; Gossop et al., 1999; Hubbard et al., 1997; Teesson et al., 2006). As well as substantial reductions in drug use, these studies also document reductions in crime, sharing of injecting equipment, psychopathology, as well as improvements in physical health. Better treatment outcomes have been associated with longer retention times and stability of treatment (Darke et al., 2005c; Flynn et al., 2003; Gossop et al., 1999; Hubbard et al., 1997; Simpson et al., 1997).

The reduction in mortality risk factors associated with drug treatment (Table 3.4) is of particular relevance. One major factor that treatment appears to impact upon is overdose. As will be discussed in Chapter 4, overdose represents a major cause of death amongst drug users, particularly opioid and cocaine users. Treatment has been demonstrated to reduce the risk of non-fatal overdose (Darke et al., 2005f; Stewart et al., 2002) and fatal overdose cases are rarely in drug treatment (Darke & Zador, 1996; Darke et al., 2005a; Davidson et al., 2003). This reduction in overdose risk is probably due to reduced rates of drug use and, in the case of opioid agonist therapies, a correspondingly high tolerance to opioids. Treatment has also been demonstrated to be protective against HIV infection, a consequence of the substantially reduced rates of sharing of injecting equipment associated with treatment (Ward et al., 1998). Two positive consequences of treatment for drug use then, are reductions in risk of death by overdose and disease. A recent study of the impact of drug treatment on suicide risk, however, indicated that treatment did not significantly reduce this risk

Table 3.4. Factors associated with illicit drug-related mortality

Risk factor	Comment
Drug class	Highest risk for opiates
Gender	Males comprise the majority of fatalities. SMRs of females higher than males.
Age	Higher risk for older drug users, with average age of death around 30 years.
Length of use career	Longer drug use careers associated with greater risk.
Treatment	Enrolment in drug treatment associated with substantially lower risk of death.
HIV infection	Higher mortality rates amongst HIV positive drug users.
Psychosocial functioning	Poorer psychosocial functioning associated with increased risk of death.

(Darke et al., 2005e) (cf. Chapter 6). The effects of treatment upon trauma risk have not been quantified to date.

3.4.6 Disease

Illicit drug use is associated with increased risk for a range of diseases (Cherubin & Sapira, 1993; Karch, 2002). Most prominent amongst these is infection with HIV, hepatitis B and hepatitis C, transmitted through injecting with used injecting equipment and/or unprotected sexual activity. There are also specific pathologies related to the use of individual drugs. Cocaine and, to a lesser extent, amphetamine are cardiotoxic, and strongly associated with accelerated atherosclerosis, cerebrovascular accident, cardiomegaly, and cardiac infarction (Karch, 2002). There are also significant health effects of cannabis that relate to smoking as a route of administration (Kalant et al., 1999).

The impact of disease upon illicit drug user mortality is substantial (cf. Chapter 5), as the proportion of deaths attributable to disease illustrates, for example, Bargagli et al. (2001) (30%), Maxwell et al., (2005) (62%), Hser et al. (2001) (40%), Goedert et al. (1995) (73%). Since the advent of the HIV pandemic a large proportion, and in many studies the majority of disease-related deaths (e.g. Bargagli et al., 2001; Brugal et al., 2005; Davoli et al., 1997; Friedman et al., 1996; Vlahov et al., 2004), have been attributable to the consequences of HIV infection (Chapter 5).

The range of cohort studies that have examined baseline health status and risk of mortality is not extensive, and has overwhelmingly focused on baseline

HIV serostatus. Not surprisingly, given the risk to life it represents, positive HIV status is associated with significantly higher mortality rates (Eskild et al., 1993; Esteban et al., 2003; Friedman et al., 1996; Frischer et al., 1993, 1997; Fugelstad et al., 1997; Galli & Musicco, 1994; Goedert et al., 1995; Langendam et al., 2001; Orti et al., 1996; Quaglio et al., 2001; van Ameijdan et al., 1999a; van Haarstrecht et al., 1996; Vlahov et al., 2004; Zacarelli et al., 1994). For example, Vlahov et al. (2004) reported that mortality rates among HIV-positive cohort members were 7.3 times those of HIV negative cohort members. Similarly high excess mortality ratios amongst the HIV positive have also been consistently reported in other studies (e.g. Eskild et al., 1993; Esteban et al., 2003; Fugelstad et al., 1997). While the mortality rates of HIV negative drug users exceed those of the general population, rates among the HIV positive are elevated further. It is important to note that this excess mortality is not solely related to AIDS. Whilst not always noted, higher death rates amongst the HIV positives from causes other than AIDS have been reported by Eskild et al. (1993), Goedert et al. (1995), Quaglio et al. (2001), and Zacarelli et al. (1994).

On a broader level, both Hser et al. (1994, 2001) reported that physical disability amongst opiate users that was sufficient to interfere with holding a job increased the risk of mortality by 3.6 and 2.7 times respectively. Poorer global physical health has also been associated with an increased risk of death (Gossop et al., 2002a; Langendam et al., 2001). Both Langedam et al. (2001) and Van Haarstrecht et al. (1996) reported that being clinically underweight, a probable marker for poor health, was an independent predictor of mortality, even after controlling for HIV status.

3.4.7 Psychosocial functioning

The demographic characteristics of drug-related deaths typically reflect lower psychosocial functioning (Bartu et al., 2004; Darke & Zador, 1996; Darke & Ross, 2002; Davoli et al., 1993). Opioid overdose deaths predominantly occur among long-term, dependent, socially isolated heroin users with prison histories, who are typically unemployed as is also the case with cocaine (cf. Chapter 4). Suicide is strongly associated with poorer psychosocial functioning, social isolation, and psychological distress, both amongst the general population and amongst drug users in particular (cf. Chapter 6). Overall, the profile of drug user deaths suggests low levels of psychosocial functioning.

Few cohort studies have specifically related psychosocial functioning to mortality, reflecting an absence of good data on these variables. Those studies

that have examined these factors, however, are consistent with the profile of deaths due to illicit drugs derived form retrospective studies (Bartu et al., 2004; Davoli et al., 1993; Gossop et al., 2002a; Harlow, 1990; Haarstrup & Jepson, 1988; Kjelsberg et al., 1995; Langendam et al., 2001; Musto & Ramos, 1981; Segest et al., 1990; van Haarstrecht et al., 1996; Zanis & Woody, 1998). Even within a population that has high levels of social disadvantage and psychopathology, psychosocial dysfunction still predicts mortality. Periods of homelessness are common amongst dependent illicit drug users, and have been associated with increased risk of premature mortality (Darke & Ross, 2001; Gossop et al., 2002a; Langendam et al., 2001). This may partially reflect the fact that homelessness is a risk factor for suicide, both amongst the general population, and amongst illicit drug users in particular (Darke et al., 2001). Street injecting, a concomitant of homelessness amongst IDU, has also been associated with higher overdose risk and poorer vascular health (Darke et al., 2001; Klee & Morris, 1995). Homelessness also exposes an individual to greater risk of trauma and disease.

Unemployment and lower income levels have been specifically related to risk of mortality (Harlow, 1990; Musto & Ramos, 1981). It will also be recalled that disability sufficient to interfere with holding employment increases mortality risk (Hser et al., 1998, 2001). A lower level of education, a probable marker for lower income and/or unemployment, has also been associated with increased mortality risk (Davoli et al., 1993).

Poorer global psychosocial functioning has been specifically related to increased mortality risk (Haarstrup & Jepson, 1988), having unstable social groupings (Segest et al., 1990) and being single (Davoli et al., 1993; van Haarstrecht et al., 1996). Whilst the latter reflects the risks associated with lower levels of social support, it may also reflect the risk of fatal overdose when others are not available to intervene. This is clearly less likely when the drug user has a partner.

As mentioned earlier, illicit drug use is associated with high levels of psychopathology, particularly mood and anxiety disorders (Darke & Ross, 2001; Degenhardt et al., 2001; Dinwiddie et al., 1992; Teesson et al., 2005). Major depression, a common diagnosis amongst the dependent drug users who comprise the bulk of mortality cases, is a strong risk factor for attempted and completed suicide (Harris & Barraclough, 1997) and overdose (Best et al., 2000). Few cohort studies have measured psychopathology as a risk factor for mortality. Those that have, however, have reported an increased risk associated with psychiatric hospital admission (Bartu et al., 2004), major depression (Kjelsberg et al., 1995, Zanis & Woody, 1998), and anxiety (Gossop et al., 2002a).

Overall, dependent illicit drug use is associated with a poor psychosocial profile. Even within this population, however, a poorer psychosocial profile appears to further increase the risk of premature death.

3.5 Major causes of death amongst illicit drug users

It is apparent from the preceding sections that mortality rates amongst illicit drug users far exceed those seen amongst the general population. What then are the main causes of these elevated rates? These fall into four main areas: drug overdose, disease, suicide, and trauma. A brief overview of how these areas relate to drug users is presented below. Cause-specific death rates, epidemiology, toxicology, and risk factors for each of these areas will be fully explored in Chapters 4–7.

3.5.1 Drug overdose

Drug overdose is an area that, by definition, is specifically relevant to drug users. Overdose is clearly not going to be a cause of death amongst those who do not use such substances. In particular, overdose is a major cause of premature death among opioid users and cocaine users. Whilst less common, death due to the toxicity of amphetamine, or MDMA and other "party" drugs, does occur. Cannabis, whilst the most widely used illicit drug, is not a drug that causes overdose death, and does not figure in subsequent discussions of overdose. Drug overdose as a cause of death is explored fully in Chapter 4.

3.5.2 Disease

Unlike overdose, disease as a cause of death is relevant to both drug users and non-drug users alike. There are, however, specific disease risks associated with illicit drug use that occur at much lower levels amongst the general population. In particular, injecting drug use is strongly associated with the transmission of blood-borne viruses, such as HIV, HCV, and HBV. Disease as a cause of death is fully explored in Chapter 5.

3.5.3 Suicide

Suicide is a leading cause of death amongst illicit drug users, and occurs at rates far in excess of those of the general population (Chapter 6). This is not surprising, as amongst this group rates of psychopathology (and major depression

in particular) far exceed those in the non-drug using population. In addition, illicit drug users (opioid and cocaine users in particular), typically exhibit high levels of other risk factors for suicide. Despite high rates of suicide, and high rates of predisposing risk factors, suicide as a cause of death amongst injecting illicit drug users is substantially under-explored. Suicide as a cause of death is discussed fully in Chapter 6.

3.5.4 Trauma

There are a number of lifestyle factors surrounding illicit drug use that suggest that trauma may play a significant part in illicit drug user deaths. These include violence surrounding the use and procurement of highly expensive illegal drugs, high levels of risk due to crime and sex work performed to support drug use, high rates of psychiatric diagnoses that predispose individuals to impulsivity and violence, and the specific psychotropic effects of psychostimulant drugs. In addition, there is also a strong association between illicit drug use, motor vehicle trauma, and other traumatic events. Trauma as a cause of death is explored in Chapter 7.

3.6 Summary of illicit drug mortality

Estimating mortality attributable to illicit drug use is problematic due to factors such as these being hidden populations, differences in the quality of national official statistics, national differences in the provision of drug intervention programmes, and the inherent limitations of cohort studies. Within these limitations, however, it was estimated that approximately 200,000 deaths occurred in 2000 alone that were attributable to illicit drug use, representing over 6 million DALYs. The mortality rate in the majority of cohort studies exceeds 15 per thousand person years, with rates typically more than 10 times those of non-drug users. The majority of illicit drug-related deaths occur in males, the average age of death is in the vicinity of 30 years, and the highest risk of death is associated with opioid use. Factors that predict premature mortality include: being older, longer illicit drug use career, not being enrolled in a drug treatment programme, poorer health, and poorer psychosocial functioning. The major causes of death amongst illicit drug users are drug overdose, disease, suicide, and trauma.

Key points: Summary of all cause illicit drug-related mortality

- It is estimated that there were 197,383 deaths worldwide attributable to illicit drug use in the year 2000 alone.
- These deaths were responsible for the total of 6,879,000 years of lost life and productive life in 2000.
- Approximately three quarters of cases are male, and the mean age at death is approximately 30 years old.
- Opioids are associated with the highest risk of death.
- Predictors of mortality include older age, longer illicit drug use careers, not being enrolled in drug treatment, poorer health, and poorer psychosocial functioning.
- The major causes of death amongst drug users are drug overdose, disease, suicide, and trauma.