Chapter 13

Illicit drug use

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Summary

Estimating mortality directly attributable to illicit drug use such as overdose death—the most tangible adverse heath effect of illicit drug use—is difficult because of variations in the quality and quantity of mortality data. As a result, it is necessary to make indirect estimates, involving estimates of the prevalence of illicit drug use. However, it is difficult to make even indirect estimates because the use of these drugs is illegal, stigmatized and hidden. Nonetheless, efforts must be made to estimate the contribution that illicit drug use makes to the global burden of disease, because it is a pattern of behaviour that has a substantial adverse effect on the health of those who engage in it. In cohort studies of treated drug users the problematic use of illicit drugs has been associated with an increased overall rate of mortality, and with an elevated rate of a number of individual causes of death, four of which were estimated here: AIDS, overdose, suicide and trauma.

Definitions of the variable of interest are difficult because of deficiencies in the data collected by countries on illicit drug use, and by disagreements over what constitutes "problematic" illicit drug use. The definition used here was long-term regular injecting use of opioids, amphetamines or cocaine. Data on the prevalence of problematic illicit drug use were derived from a range of sources that used variable methods of deriving estimates.

A literature search was conducted of all studies that estimated the prevalence of problematic drug use. Available data on prevalence in countries with data were used to estimate the prevalence of problematic illicit drug use for subregions.[1] A search was also completed for cohort studies of drug users that had estimated mortality due to the four individual causes of death, and to all causes of death. Data on the number of years of follow-up were extracted from each study and a weighted average annual mortality rate was calculated for each of the four causes

of death, and for their sum. A standardized mortality ratio (SMR) was also derived from previous estimates of the excess mortality from all causes attributable to illicit drugs. Estimates were made for some causes by applying an attributable fraction obtained from sources such as the Joint United Nations Programme on HIV/AIDS (UNAIDS) (for HIV-related deaths) to estimates of total deaths for some causes. The median estimate of a range of estimates was used as the estimate for each subregion. Estimates were limited to persons aged 15–54 years.

In 2000, the median number of global deaths attributed to illicit drugs estimated by summing the four causes of death was 194 058. There were an additional 10 000 deaths from overdose above and beyond those coded as drug use disorders (added to unintentional injuries) or when coded drug use disorder deaths were higher than estimated overdose deaths. The median 2000 estimate derived using the all-cause method was 197 383. Both estimates had wide uncertainty intervals around them (113 494 to 276 584 for sum of four causes; and 101 751 to 322 456 for all-cause estimates). When morbidity attributable to illicit drug use is added to the estimated mortality, this risk factor accounts for 0.8% of global disability-adjusted life years (DALYs). The distribution of numbers of deaths between subregions varied between the two methods. These variations in the estimates reflect the considerable uncertainty about prevalence of drug use in different subregions and uncertainty about the applicability of mortality data derived in developed countries to mortality among illicit drug users in developing countries.

The current estimates suggest that illicit drug use is a significant cause of premature mortality among young adults. This is an underestimate of total disease burden because: (i) there are deficits in data on mortality attributable to the use of some illicit drug (most notably cannabis and the newer synthetic drugs like MDMA[2]); (ii) there are differences across subregions in the quality of data available on the causes of mortality that *were* included in the current estimates; (iii) there is an absence of data that would permit estimates of some other causes of mortality and morbidity attributable to illicit drug use, such as hepatitis B and hepatitis C and violence. There is a need for better data on: the prevalence of illicit drug use in developed and developing countries, and on the mortality and morbidity attributable to problematic drug use.

1. Introduction

The use of legally proscribed psychotropic substances for non-medical purposes appears to be increasing in many parts of the world (Frischer et al. 1994; UNDCP 2000; UNODCCP 2000) but it is difficult to quantify the rate of increase. It is difficult to estimate the prevalence of this behaviour and its adverse health consequences in individual societies because this behaviour is illicit and therefore often hidden. Even estimating mortality related to illicit drug use, the most tangible adverse

heath effect, is difficult for reasons that are discussed below (Thorley et al. 1977). Nonetheless, efforts must be made to estimate the contribution that illicit drug use makes to the global burden of disease because it is a pattern of behaviour that has a substantial adverse effect on the health and well-being of those who engage in it, producing substantial loss of life and disability (Hulse et al. 1999).

The global burden of death and disability attributable to illicit drugs was first estimated by Donoghoe (1996), as part of the Global Burden of Disease (GBD) project (Murray and Lopez 1996). Donoghoe estimated that illicit drug use was responsible for 100 000 deaths globally in 1990, the majority of which (62%) occurred in developing countries. Murray and Lopez (1996) pointed out that this estimate may be too low because of difficulties in reliably estimating the prevalence of illicit drug use and its adverse health effects. Donoghoe's estimate was based on the attributable fractions of various causes of mortality and morbidity attributed to illicit drug use by English et al. (1995), who reviewed all studies published up to 1993. The great majority of these studies, which were principally cohort studies, were conducted in the United States of America and Europe.

Since these estimates were made, there has been an apparent increase in illicit drug consumption in developed societies (Australian Bureau of Criminal Intelligence 2000; EMCDDA 2000; Frischer et al. 1994; UNODCCP 2000), and increased incidence of HIV contracted as a result of sharing of injecting equipment by illicit drug users in developing societies (Stimson 1993). This suggests that Donoghoe's 1990 estimates are likely to substantially underestimate the contribution that illicit drug use makes to the global burden of disease in 2000.

In this chapter, we have attempted to estimate the burden of disease due to illicit drug use by combining a range of sources of data on the prevalence of use and indicators of outcome. We also outline the definitions of the "exposure" variable used in making estimates, and outline the causes of burden considered in this chapter. As will become clear, estimates made of this cause of burden are difficult to make given: (i) paucity of data on the prevalence of illicit drug use around the world; (ii) the fact that data on causes of death related to illicit drug use are not well-recorded, so it is necessary to rely on indirect estimates derived from inaccurate prevalence estimates; and (iii) an absence of evidence on the risk of mortality and morbidity due to some causes among illicit drug users.

1.1 Exposure variable

Substances included

Illicit drug use includes the non-medical use of a variety of drugs that are prohibited by international law. These drugs include: amphetamine-type stimulants,[3] cannabis,[4] cocaine,[5] heroin[6] and other opioids,[7] and MDMA (ecstasy). In order to estimate mortality and morbidity attrib-

utable to illicit drug use, we need to clearly define what is and is not included in this risk factor.

This chapter will focus on the burden attributable to amphetamines, cocaine and opioids. Other substances that are illegal in most countries, such as ecstasy, solvents and cannabis, have not been included in the present analysis as there is currently insufficient research information to quantify the health risks associated with these drugs. Thus, their exclusion should not be interpreted as meaning that the use of these drugs is safe. Rather, it reflects a paucity of research on the harm caused by their use.

Relationship to dose, frequency and route of administration

The risk of premature mortality and morbidity from illicit drug use is dependent on dose, frequency and route of administration. Consequently it is necessary to define what is meant by "use" when defining the exposure variable "illicit drug use". The mortality risks of illicit drug consumption increase with increasing frequency and quantity of consumption (Fischer et al. 1997). 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 since a single occasion of use and infrequent use, the most common patterns of use reported in population surveys, are associated with a small increase in mortality. More accurate estimates of the burden of disease attributable to illicit drugs require estimates of the prevalence of the most hazardous patterns of illicit drug use. These are found in highest prevalence among dependent drug users who typically inject drugs daily or near daily over periods of years. This pattern of use exposes users to the highest chance of fatal overdose (Warner-Smith et al. 2001) and of contracting bloodborne viral diseases (Ross et al. 1992).

The World Health Organization (WHO), following the International Classification of Diseases, defines problem drug use as "harmful drug use" and "drug dependence". Harmful drug use is defined by clear evidence that the substance use is responsible for physical (e.g. organ damage) and psychological harm (e.g. drug-induced psychosis). Drug dependence, as defined in the International Statistical Classification of Diseases and Related Health Problems, tenth revision (ICD-10), requires the presence of three or more indicators of drug dependence (WHO 1993). These include: a strong desire to take the substance; impaired control over the use; 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 is spent obtaining, using and recovering from drug use; and the user continuing to take other drugs despite associated problems. The problems should have been experienced for at least one month at some time during the previous year. 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" (UNDCP 2000).

Most prevalence estimates vary with the assumptions made and the methodology employed. Data provided by the UNDCP 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. Even if such surveys were feasible in all countries, it is generally accepted that surveys underestimate harmful illicit drug use (Hall et al. 2000b).

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) has invested considerable resources in developing methods for the collection of data on the prevalence of harmful illicit drug use that are both valid and comparable (EMCDDA 1997). While these standards have been developed for use within the European Union the global adoption of such standards may greatly improve estimates of drug-related harm. The EMCDDA defines "problem drug use" as injecting drug use (IDU) or long duration or regular use of opioids, cocaine or amphetamines (EMCDDA 1999). The EMCDDA definition is the one that we have adopted in estimating mortality attributable to illicit drugs.

Illicit drugs not included in current estimates of mortality

Cannabis

Cannabis has a high prevalence of use in many developed societies (Hall et al. 1999b) but there is a lack of well-controlled studies showing that its use increases mortality (Hall and Solowij 1998; WHO 1997). For example, we identified two cohort studies that have examined the effects of regular, prolonged cannabis use on risks of cancer. One of these reported no increase in overall cancer rates among cannabis users (although there were slightly increased rates of prostate and cervical cancer) (Sidney et al. 1997b). A case–control study found a doubling of the odds of aerodigestive cancers among heavy users of cannabis (Zhang et al. 1999) but it was difficult to disentangle the effects of cannabis smoking from those of tobacco smoking because many cannabis users also smoked tobacco (Andreasson and Allebeck 1990).

There are two prospective epidemiological studies of mortality among cannabis users. A Swedish study over 15 years of mortality among male military conscripts found an increased risk of premature death among men who had smoked cannabis 50 or more times by age 18 years (Andreasson and Allebeck 1990). Violent and accidental deaths were the major contributor to this excess. However, the association between mortality and cannabis use disappeared after multivariate statistical adjustment for alcohol and other drug use. Sidney et al. (1997a) re-

ported a 10-year study of mortality in cannabis users among 65 171 members of the Kaiser Permanente Medical Care Program aged between 15 and 49 years. The sample comprised 38% who had never used cannabis, 20% who had used less than six times, 20% who were former users, and 22% who were current cannabis users. Regular cannabis use had a small association with premature mortality (relative risk of 1.3) that was wholly explained by increased AIDS deaths in men, probably because cannabis use was a marker for male homosexual behaviour in this cohort. It is too early to conclude that cannabis use does not increase mortality because the average age at follow-up was only 43 years, and cigarette smoking and alcohol use were only modestly associated with premature mortality. For these reasons, we have not included any estimate of cannabis' effects on overall premature mortality.

Cannabis produces dose-related impairments in cognitive and behavioural functions that may potentially impair driving an automobile or operating machinery (Chait 1992). These impairments are larger and more persistent in difficult tasks involving sustained attention (Chait 1992). The most serious possible consequence of acute cannabis use is a motor vehicle accident if a user drives while intoxicated (Hall et al. 1994).

The effects of recreational doses of cannabis on driving performance in laboratory simulators and standardized driving courses have been reported as similar to blood alcohol concentrations between 0.07% and 0.10% (Hall et al. 1994). However, studies of the effects of cannabis on driving under more realistic conditions on roads have found much more modest impairments (Bates and Blakely 1999; Robbe 1994; Smiley 1999). This is probably because cannabis users are more aware of their impairment and less inclined to take risks than alcohol users (Smiley 1999).

Epidemiological studies of motor vehicle accidents have produced equivocal results because most drivers who have cannabinoids in their blood also have high blood alcohol levels (Hall et al. 1994, 2001). Studies with reasonable numbers of persons who have *only* used cannabis have not found clear evidence of increased culpability in these drivers (Bates and Blakely 1999; Chesher 1995). For these reasons we have not included any estimate of the contribution that cannabis makes to motor vehicle fatalities.

Other illicit drugs

Estimating the contribution that MDMA (ecstasy), hallucinogenic substances and inhalants make to premature mortality presents similar problems to cannabis (Boot et al. 2000). While there are case reports of deaths associated with MDMA intoxication (Dowling et al. 1987; Henry et al. 1992; Parr et al. 1997) these appear to be rare by comparison with overdose deaths due to opioids and cocaine in developed societies with good mortality data, such as Australia (Ridolfo and Stevenson

2001). The illicit use of pharmaceuticals and anabolic steroids have also been excluded from further analysis because difficulties in measuring (i) the prevalence of their harmful use and (ii) mortality attributable to their use mean that it is not possible to calculate relative risks. Similarly, the failure to include solvents stems largely from a lack of good evidence on the prevalence and extent or harm attributable to their use.

The exposure variable for illicit drug use in this analysis is, therefore, injection or long duration of use of amphetamines, cocaine or opioids. The failure to include cannabis, MDMA, hallucinogens and inhalants in our estimates of burden of disease attributable to illicit drugs reflects our ignorance of their health risks; it does not imply that the use of these drugs is without risk to users.

Counterfactual exposure distribution

The *theoretical* minimum counterfactual exposure distribution is zero illicit drug use. There may be countries in the world that can truly claim to have zero illicit drug use but there must be few of these now. Even countries that have the policy goal of achieving a drug-free society, such as Sweden, do not have zero illicit drug use. Arguably, once illicit drug use and dependence have appeared in a society, it is unrealistic to expect to be able to return to a zero level of illicit drug use. It may be reasonable to aim to reduce the prevalence of the most harmful types of illicit drug use and to minimize the harm that their use causes.

One approach to defining a *plausible* counterfactual exposure would be to use developed countries with the lowest prevalence of illicit drug use as the basis for the estimate. Countries like Finland and Sweden may be suggested as examples. The weakness with this strategy is that illicit drug use trends are dynamic and countries that currently have low rates may show increases in rates of use (as has recently happened in Sweden) as availability of illicit drugs increases and more favourable social attitudes develop towards illicit drug use among young adults.

It is also not clear what are feasible minimum counterfactuals. It is not clear whether prevention programmes, such as school-based and other intervention programmes, can prevent problem drug use (National Research Council 2001). These programmes have been most widely implemented and evaluated in the United States. After reviewing this evidence, the United States National Research Council recently concluded that the

> effectiveness of most of these approaches for reducing substance use is unknown . . . Some prevention approaches are effective at delaying the initiation or reducing the frequency of tobacco, alcohol and marijuana use [but] . . . the magnitude of these effects are generally small . . . [and it] is not clear that preventing or reducing the use of gateway substances translates into a reduced use of cocaine or other illegal drugs (pp. 233–234).

These conclusions have been supported by a recent study of the likely impact of the most effective school-based prevention programmes, which concluded that they would have, at best, very modest effects in preventing cocaine use (Caulkins et al. 1999).

There is better evidence that some treatment programmes (e.g. opioid agonist maintenance treatment) can substantially reduce illicit opioid use and premature mortality from drug overdose[8] among opioid-dependent persons (Warner-Smith et al. 2001). In the case of opioid-dependent persons, one could examine the effects that enrolling 10%, 20%, 30%, etc. of persons who were dependent on illicit opioids in opioid maintenance treatment would have on illicit opioid use, overdose deaths and disability produced by illicit opioid dependence. Similar estimates could be made of the expected reduction in HIV/AIDS among injecting drug users from the introduction of needle and syringe exchange and distribution programmes.

1.2 Data sources

To provide data on the prevalence and risks of illicit drug use, a series of extensive computer searches using databases listed below was conducted. The specific parameters of these searches are also listed.

Databases searched

We carried out a citation search of Medline, Psychinfo and Web of Science, a search of reference lists of identified papers, including a literature search provided by English et al. (1995), which covered the literature published prior to 1993.

Search terms

1. *Illicit drug*, or *substance use*, or *substance abuse*, or *drug use*, or *drug abuse*, or *heroin*, or *opiates*, or *cocaine*, or *amphetamine*—limited to human studies published in the English language.
2. *Prevalence*
3. *Cohort*, or *case–control*
4. *Mortality*
5. *Morbidity*
6. *Suicide*, or *accidents*, or *HIV*, or *assault*

Strategy: combine 1 and 2; 1 and 3 and 4; 1 and 3 and 5; 1 and 3 and 6.

2. Risk factor exposure

2.1 Prevalence studies

Given the lack of reliable direct estimates of the health consequences of illicit drug use, it was necessary to make indirect estimates of burden. Hence, the first challenge in quantifying the burden of disease attributable to illicit drugs was to determine the prevalence of exposure to this risk factor. Illicit drug use differs from other risk factors in the GBD project in that one of its defining features, its illegality, makes it difficult to quantify. This presents two problems. First, illicit drug-using individuals are "hidden" and are thus difficult to identify. Second, even if all drug users can be located and interviewed, they may attempt to conceal their use of these drugs.

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 such drug users (Hartnoll 1997). The preferred strategy is to look for convergence in estimates produced by a variety of different methods of estimation (EMCDDA 1997, 1999). 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, and those who are in treatment or the criminal justice system) to estimate the size of the hidden population of illicit drug users.

A large number of studies purporting to be prevalence studies do not present credible prevalence data. Prevalence data reported in peer-reviewed literature are scarce and often unrepresentative. In addition, the range of methodologies used makes comparisons between studies difficult. For this reason, other sources of data were sought to complement prevalence estimates reported in the peer-reviewed literature.

2.2 Prevalence of problematic illicit drug use

For the purposes of estimating global mortality, data collated by the UNDCP (2000) provides a convenient and comprehensive tabulation of the most recent international prevalence data. The aggregated prevalence data for subregions are displayed in Table 13.1. The principal advantage of using UNDCP data is that it provides a readily accessible set of estimates for the majority of countries in the world. The quality of the data collected and reported by the UNDCP varies across countries and regions from high quality national survey data to key informant and indicator data of uncertain validity.

In some cases, prevalence data provided by the UNDCP were supplemented by data from other agencies, such as the EMCDDA, and the Asian Harm Reduction Network (AHRN). In regions where these addi-

tional data were available, they were used in indirect estimation methods as an additional source of prevalence estimates, thus meaning that these regions had additional estimates of causes of mortality.

UNDCP 2000 DATA ON THE PREVALENCE OF 12-MONTH USE AMONG PERSONS AGED >15 YEARS

Table 13.1 shows the population estimates of each of the 14 subregions, as well as the UNDCP-derived prevalence estimates of problematic use of the three substances considered in current estimates. It can be seen that problematic cocaine use is largely restricted to the Americas, the European Union and the developed countries of Oceania. Conversely, opioid abuse appears to be restricted to Asia and eastern and central Europe, as well as the developed countries of Oceania, the European Union and North America. Patterns of use in developing countries appear to reflect proximity to production areas and trafficking routes that supply the drug markets of developed "consumer" countries.

A challenge when estimating the prevalence of illicit drug consumption is to avoid double counting individuals who use more than one substance. There is strong evidence (principally from developed countries) that few drug users use one drug exclusively (Darke and Hall

Table 13.1 Prevalence (%) of problematic illicit drug use in the past 12 months among persons aged >15 years, by subregion (UNDCP-derived estimates of prevalence)[a]

Subregion	*Population >15 years (000s)*	*Opioids*	*Cocaine*	*Amphetamine*
AFR-D	159577	0.09	0.26	0.31
AFR-E	190152	0.01	0.05	0.12
AMR-A	255420	0.13	0.78	0.20
AMR-B	297625	0.03	0.24	0.20
AMR-D	44658	0.07	0.43	0.11
EMR B	86853	0.55	—	0.02
EMR-D	204039	0.41	—	0.14
EUR-A	339446	0.11	0.18	0.24
EUR-B	161213	0.09	0.01	0.10
EUR-C	152432	0.19	0.01	0.04
SEAR-B	206870	0.04	—	0.10
SEAR-D	818521	0.15	—	—
WPR-A	129888	0.04	0.28	0.22
WPR-B	1131503	0.02	—	0.34

— No data available, assumed to be negligible.

[a] Some estimates for subregions are based on data from a small number of countries in the subregion.

1995; Topp et al. 1999). Rather, most users nominate a drug of choice but regularly use a wide range of substances (Darke and Hall 1995; Klee et al. 1990). Thus combining estimates of the size of each population will overestimate the size of the drug-using population. Given that many opioid and stimulant users are polydrug users, and that these drugs are the most harmful illicit drugs, the simplest approach to this problem may be to use the prevalence of regular users of opioids and/or stimulants in each country as the prevalence estimate for problem illicit drug use.

In order to address this issue, a range of three prevalence estimates was derived from the above UNDCP data:

- a low estimate, which assumed that 50% of each of the prevalence estimates was unique and therefore additive;
- a medium estimate which assumed that 75% of each of the prevalence estimates was unique and therefore additive; and
- a high estimate, which assumed that the prevalence estimates were completely additive (i.e. that those who used opioids were a separate group from those who used cocaine and amphetamines).

In order to estimate the proportion of persons who had used these drugs *problematically* in the past year, data from the 1997 Australian National Survey of Mental Health and Well-Being were used. This survey was a structured diagnostic interview of a representative sample of Australian adults aged ≥18 years (Hall et al. 1999d; Henderson et al. 2000). It assessed persons who had used opioids and stimulant drugs for symptoms of DSM-IV[9] defined abuse and dependence. Of those who had reported using these drugs within the past year, 28% met criteria for DSM-IV abuse or dependence.

In the current calculations, therefore, it was assumed that 28% of those who had used these drugs within the past year were problematic users of these drugs.

It must be noted that prevalence estimates were not available for all countries in all subregions. In making estimates from UNDCP data, where countries had no reported prevalence estimates, subregional estimates of prevalence were used by deriving a weighted average prevalence rate from the data that were available from countries in the subregion. This weighted average rate was used in making subregional estimates. Some subregions therefore had estimates based upon only some countries within the subregion, which may make these estimates less representative:

- AFR-D: prevalence estimates based upon estimates provided for Cameroon, Chad, Ghana, Mauritius, Nigeria, Senegal and Sierra Leone;

- AFR-E: prevalence estimates based upon estimates provided for Ethiopia, Kenya, Namibia, Rwanda, South Africa, Uganda, the United Republic of Tanzania and Zimbabwe;
- AMR-D: prevalence estimates based upon estimates for Bolivia, Ecuador and Peru;
- EMR-D: prevalence estimates based upon estimates provided for Egypt, Morocco and Pakistan; and
- WPR-B: prevalence estimates based upon estimates provided for China, the Lao People's Democratic Republic, Malaysia, the Philippines, the Republic of Korea and Viet Nam.

EMCDDA estimates of "problem drug users"

These estimates were used to derive alternative estimates of prevalence in countries from EUR-A: Austria, Belgium, Croatia, Finland, France, Germany, Ireland, Italy, Luxembourg, the Netherlands, Norway, Spain, Sweden and the United Kingdom.

A weighted prevalence rate was derived from these estimates for the whole of EUR-A. The EMCDDA produced low and high estimates of "problem drug users" for countries in the European Union using a variety of estimation methods including capture-recapture and back-projection methods. Both these estimates were used to make lower and upper estimates of prevalence using these data. A median estimate was also calculated when making median estimates for each of the four major causes of mortality, and for all-cause mortality.

AHRN estimates of IDU in the Asian region

Numbers from the AHRN were used to make estimates of the prevalence of IDU in these countries (IDU in this case was taken to represent the prevalence of "problem drug use" used in the other two estimates). Weighted prevalence estimates of IDU prevalence were only made in the subregion they were classified under if two or more countries reported (see www.ahrn.net). The countries were as follows:

- SEAR-B: Indonesia (no estimate made);
- SEAR-D: Myanmar (no estimate made);
- WPR-A: Japan, Singapore;
- WPR-B: Cambodia, China, Malaysia, Mongolia, the Philippines, the Republic of Korea and Viet Nam.

Table 13.2 shows the prevalence estimates produced from the EMCDDA and AHRN sources. Comparison with estimates in Table 13.1 reveals that the estimates are fairly similar.

In the current chapter, we have used *all* available estimates of prevalence to make a range of estimates of each cause of mortality. Hence, for

Table 13.2 Alternative estimates of prevalence of problematic drug use in three subregions

Subregion	*EMCDDA low estimate (%)*	*EMCDDA high estimate (%)*	*AHRN (%)*
EUR-A	0.2	0.4	NA
WPR-A	NA	NA	0.3
WPR-B	NA	NA	0.01

NA Not applicable.

example, EUR-A has two sources of prevalence estimates: EMCDDA estimates (low and high) and UNDCP estimates (low, median and high). This approach was taken so as to make estimates based on as much of the available data as possible.

3. Health outcomes

3.1 Premature mortality

The major causes of premature death among illicit drug users are relatively directly related to their patterns of drug use. Evidence for these causes comes from studies of premature mortality among cohorts of illicit drug users who have been treated in Europe and North America. (It must be remembered that there is a range of issues surrounding the use of such cohort studies in deriving global estimates of mortality rates, which are discussed in section 6.2.)

Notwithstanding these issues, illicit drug users have elevated rates of four main causes of premature death by comparison with age peers who do not use illicit drugs, namely, drug overdose, HIV/AIDS, suicide and trauma.

Overdose

"Overdose" refers to two ICD-10 classifications of cause of death: (i) accidental or intentional fatal poisoning caused by specific drugs, and (ii) poisoning deaths occurring among dependent drug users that are attributed to drug dependence. Despite the conceptual simplicity of drug overdose deaths it has been difficult to quantify the number of such deaths with any precision, even in developed countries, for reasons that are discussed below.

HIV/AIDS

The connection between illicit drug use and HIV/AIDS largely arises from injection as the route of drug administration via drug users sharing

contaminated injecting equipment. This means that it is necessary to establish the prevalence of injecting drug use, rather than harmful drug use *per se*, in order to calculate the proportion of incident HIV cases that can be attributed to harmful drug use. This can be accomplished by extrapolating from data on the prevalence of injecting drug use among persons who are illicit drug users as indicated in studies in the peer-reviewed literature. It can also be estimated by the proportion of HIV/AIDS cases that are attributed to IDU in each country. One issue that exists concerns a lack of data from some countries on the prevalence of AIDS cases that are attributable to IDU. In the current study, we have only used UNAIDS estimates of mortality attributable to injecting drug use.

Suicide

Suicide is a cause of death in the ICD-10 but, as with overdose deaths, the reliability with which this cause of death is diagnosed may vary between countries depending on a number of variables. Cultural variations in attitudes towards suicide may influence coroners' and mortality registrars' willingness to classify a death as intentional (Domino and Lenaars 1989; Domino and Takahashi 1991).

Trauma

Trauma includes homicide, motor vehicle accidents and other forms of accidental death. It is likely that this will be underestimated since few cohort studies report mortality rates from all forms of trauma and it is difficult to calculate attributable fractions for these causes because many trauma deaths in drug users may not be recognized as being drug-related.

All-cause mortality

Several studies have calculated standardized mortality ratios (SMRs) for problem drug users. These studies indicated that problem drug users have substantially increased mortality rates, with typical estimates suggesting that they are approximately 13 times more likely to die than their peers (English et al. 1995; Hulse et al. 1999).

3.2 Likely sources of morbidity attributable to illicit drug use

Premature *death* is the most serious adverse health outcome experienced by problem drug users; it is also the best-studied health outcome in this population. Nevertheless, the contribution that illicit drug use makes to the burden of disease is not exhausted by premature death.

First, each of the major causes of premature mortality probably causes substantial morbidity. Second, drug dependence, which is highly prevalent among problem drug users, is also a cause of disability. Third, evidence suggests that the prevalence of hepatitis B and hepatitis C viruses (HBV and HCV) is high among injecting drug users (Alter et al. 1990;

Anderson et al. 1994; Levine et al. 1994; MacDonald et al. 1996, 2000). Both of these viruses are associated with substantial morbidity and premature death due to the sequelae of chronic infection (Alter et al. 1990; MacDonald et al. 1996, 2000).

However, there is little good evidence that allows quantification of the morbidity related to the use of illicit drugs, and it is not possible to make estimates of the burden of disease caused by morbidity resulting from illicit drug use. This means that current estimates of the burden of disease attributable to illicit drug use significantly underestimate the total burden of illicit drug use. An American analysis of the economic costs of drug use (National Institute on Drug Abuse 1992) revealed that problematic illicit drug use cost the United States an estimated US$ 98 billion in 1992; of this, the figure for the impact of premature deaths was US$ 14.6 billion. Health care expenditure cost an estimated US$ 9.9 billion, and impaired productivity resulting from drug-related morbidity cost an additional US$ 14.2 billion—clearly, costs from mortality attributable to drug use in the United States were a fraction of those attributable to morbidity. This means that our estimates are likely to underestimate the global burden of disease attributable to illicit drugs. Future estimates of the global burden of disease would be substantially improved by research into the total morbidity that is attributable to illicit drug use.

Outlined below are some of the major outcomes of illicit drug use that may be significant sources of morbidity. Future research is required to better document the nature and extent of morbidity attributable to the use of illicit drugs. In the absence of such data, we assumed that for each of the four causes included, the population attributable fractions for mortality could also be used to estimate the proportion of morbidity explained by that cause. Equivalently, we assumed that if illicit drug use causes a certain proportion of AIDS mortality, it does so by increasing its incidence, also increasing AIDS-related morbidity by a similar proportion. While uncertain, this assumption is closer to underlying mechanisms than assuming that illicit drug use contributed to none of AIDS-related morbidity. This approach cannot be used to estimate morbidity due to conditions that do not cause deaths, such as, neuropsychological impairment.

Non-fatal overdose

The prevalence of non-fatal overdose is not well studied in problem drug users apart from among opioid users in some developed societies, where non-fatal overdose is a common event (Darke et al. 1996; Gossop et al. 1996; Warner-Smith et al. 2001). An unknown proportion of these cases requires acute medical treatment and hospitalization and some of these may develop persistent medical sequelae as a result of non-fatal overdoses, such as cognitive impairment (Darke et al. 2000) and other medical problems (Warner-Smith et al. 2001). There are no good esti-

mates of the prevalence of these outcomes that would permit an estimate to be made of their contribution to the burden of disease. It should be a research priority to obtain better estimates of the prevalence of these forms of morbidity in future studies of illicit drug users so that the contribution that illicit drug use makes to the burden of disease can be better understood.

AIDS

In developed societies, the widespread availability of anti-retroviral drugs has extended the life expectancy of persons living with HIV/AIDS (Donoghoe and Wodak 1998), with the result that HIV/AIDS may become a chronic condition. However, in these countries we rarely have data on the proportion of treated cases who acquired their infections as a result of IDU. We have assumed that the proportion of *treated* HIV/AIDS cases that are attributable to IDU is the same as the proportion of AIDS-related deaths that are attributed to IDU.

Hepatitis B and C

Many injecting drug users in developed countries are infected with HCV. In Australian needle and syringe attendees, for example, the prevalence of HCV infection is estimated at between 50% and 60% (National Centre in HIV Epidemiology and Clinical Research 1998). Chronic infection has been estimated to occur in 75% of infections, and 3–11% of chronic HCV carriers will develop liver cirrhosis within 20 years. Given the large number of injecting drug users infected with HCV, and the more protracted complications arising from this infection, the net health and economic cost of HCV transmitted by injecting drug use may be as high as, or considerably higher than, those of HIV. Data on the prevalence of this infection among injecting drug users in developed countries is limited; it is non-existent in many developing countries.

Similarly, the prevalence of HBV has been documented as quite high among injecting drug users in developed countries. There is, however, a lack of good evidence on (i) the prevalence of HBV among illicit drug users; (ii) the risk of premature mortality caused by this disease; and (iii) the extent of morbidity that it causes. HBV has therefore not been included in current estimates for these reasons. It would be desirable in future to include estimates of morbidity and disability that HBV and HCV cause among illicit drug users.

Attempted suicide

Recent studies in Norway (Rossow and Lauritzen 1999) and Australia (Darke and Ross 2000) have found high rates of self-reported suicide attempts among problematic opioid users (Darke and Ross 2000; Rossow and Lauritzen 1999). Survivors of such suicide attempts may require psychiatric and medical treatment and some suffer from medical sequelae. As with non-fatal overdose, there are no data that permit the

morbidity attributable to this cause among problem drug users, but estimates could be obtained by applying the same attributable fraction for suicide deaths to morbidity caused by attempted suicides.

Trauma

In developed societies there are approximately 20 cases of severe injury for every death caused by a motor vehicle accident (MVA) (English et al. 1995). We could assume the same is true for problem drug users if we had a credible estimate of the proportion of motor vehicle fatalities that were attributable to problem drug use. In the absence of this data we estimated the proportion of MVA morbidity attributable to illicit drugs by applying the same attributable fraction for MVA deaths to morbidity caused by motor vehicle accidents.

Psychiatric disorder

Studies of treated populations of opioid-dependent persons have found a high prevalence of major depression and anxiety disorders (Darke and Ross 1997). It is difficult to sort out cause and effect from these cross-sectional data so it is unclear in what proportion of these cases psychiatric disorders preceded and contributed to the development of problem drug use or vice versa. Nor is it clear to what extent pre-existing psychiatric disorders have been exacerbated by problem illicit drug use or vice versa. It is accordingly difficult to estimate what proportion of these disorders are attributable to problem illicit drug use. For these reasons such estimates have not been included in this chapter. Better understanding of the causal relationships between the two is a priority for future research.

3.3 Causality

The main evidence for believing that illicit drug use is a cause of premature death, morbidity and disability comes from cohort studies and cross-sectional studies of illicit drug users.

Mortality

The cohort studies have identified a number of causes of mortality that are more prevalent among problem illicit drug users than their peers, indicating an association between harmful illicit drug use and these causes of mortality. They have rarely been well controlled for potential confounders, such as social disadvantage, which is common among illicit drug users. English et al. (1995) have argued that the mortality excess among illicit drug users is too large to be wholly accounted for by social disadvantage. Moreover, there are good reasons for believing that the relationship is causal in the case of deaths caused by overdose and blood-borne virus infection. The major illicit drugs are known to have adverse effects in overdose that can be fatal. Opioids, for example, produce respiratory depression that can cause death, and this is especially likely to

occur if opioids are used in combination with other central nervous system depressant drugs such as alcohol and benzodiazepines (Darke and Zador 1996; Warner-Smith et al. 2001). Stimulant drugs, such as cocaine and amphetamines, can cause fatal cardiac arrhythmias and strokes (Goldfrank and Hoffman 1993; Platt 1997), which are very rare causes of death in young adults who do not use these drugs. Similarly, the viruses that cause HIV/AIDS, HBV and HCV infections are efficiently spread by contaminated blood in shared injection equipment (Donoghoe and Wodak 1998; MacDonald et al. 1996).

The case for illicit drug use being a contributory cause of suicide is less direct. Depression is a risk factor for suicide and it occurs at higher rates among illicit drug users. Intoxicating drugs like alcohol and opioids, and dependence on these drugs, have been shown in case–control and prospective studies to be risk factors for suicide (Beautrais et al. 1998, 1999). Opioid-dependent persons in treatment report very high rates of attempted suicide (Darke and Ross 2000).

The case for a causal connection between illicit drug use and trauma deaths is less direct still. Driving while intoxicated by alcohol is a well-known risk factor for fatal motor vehicle crashes (English et al. 1995) and the heavy use of alcohol is common among illicit drug users (Darke and Hall 1995; Darke and Ross 1997; Gossop et al. 1998). Opioids are also intoxicating substances that adversely affect driving, although they are much less commonly found in persons killed in fatal car crashes.

Morbidity

The case for a causal connection between illicit drug use and morbidity caused by drug overdose, HIV/AIDS and HCV, suicide and trauma are the same as for mortality. To these must be added psychiatric disorders and drug dependence. By definition, drug dependence is caused by regular illicit drug use and most regular illicit drug users are dependent on one or more of the drugs that they regularly use.

The causal relationship between psychiatric disorder and illicit drug use is less clear. The two are associated in the general population and this is not attributable to confounding by social and demographic variables (Degenhardt et al. 2001). The direction of the causal relationship is less certain. Conduct disorders, depression and anxiety disorders that develop in early adolescence may predispose young adults to become dependent on illicit drugs. These disorders may also arise as a result of the adverse effects that illicit drug dependence has on the lives of those affected by it, or the rigours of regular illicit drug use may prolong pre-existing depressive and anxiety disorders that may have resolved in its absence.

4. Risk factor–disease relationship

4.1 Outcome studies

Inclusion criteria

The following inclusion criteria were used:

- cohort studies on the use of opioids, cocaine or amphetamines and mortality;
- studies in which SMRs were reported. SMRs are the ratio of observed numbers of deaths in the cohort to the expected number of deaths in people of the same age and sex distribution in the general population; and
- studies in which crude mortality rates (CMRs) could be derived from the available data in the article.

Exclusion criteria

The following exclusion criteria were used:

- multiple reports of same data set;
- subsets of a cohort; and
- reviews, commentaries, letters and abstracts.

Table 13.3 shows those studies that were not included in the present analyses. CMRs were derived from data on the number of deaths, period of follow-up and number of participants. Where person-years were not calculated by the authors, persons lost to follow-up were assumed to be alive at the end of study period and included in our calculation of person-years observation (to maintain consistency with studies that did not report numbers lost to follow-up). Following previous research (Hulse et al. 1999) it was assumed that persons dying during the period of

Table 13.3 Outcome studies that were not included

Reference	*Reason for exclusion*
Vaillant (1966)	Data are a subset of Vaillant (1973)
Watterson et al. (1975)	Series of cross-sections, not longitudinal
Thorley et al. (1977)	Data are a subset of Wille (1981)
Wiepert et al. (1978)	Poorly defined cohort
Ghodse et al. (1985)	Study of death register, not a predefined cohort
Selwyn et al. (1989)	No cohort defined
Frischer et al. (1993)	Retrospective
Fischer et al. (1999)	No mortality reported

follow-up died in the middle of the period (when estimating the person-years at risk). CMRs are unadjusted, expressed as per cent mortality per annum.

4.2 Quantification of risk

In determining the risks associated with harmful illicit drug use, it is necessary to rely on the results of cohort studies that have conducted long-term follow-up of individuals identified as using illicit drugs. English et al. (1995) identified a total of 13 such studies investigating mortality associated with illicit opioid use up to 1993 (Barr et al. 1984; Bewley et al. 1968; Cherubin et al. 1972; Engstrom et al. 1991; Frischer et al. 1993; Ghodse et al. 1985; Haastrup and Jepson 1984; Hser et al. 1993; Joe et al. 1982; Perucci et al. 1991; Thorsen and Haarstrup 1975; Vaillant 1973). Through extensive literature searches we identified a further 16 studies that have been published since 1993, excluding studies which used previously published data (Capelhorn et al. 1996; Eskild et al. 1993; Friedman et al. 1996; Fugelstad et al. 1995, 1997; Galli and Musicco 1994; Goedert et al. 1995; Goldstein and Herrera 1995; Keenan et al. 1993; McAnulty et al. 1995; Oppenheimer et al. 1994; Orti et al. 1996; Robertson et al. 1994; van Haastrecht et al. 1996; Wahren et al. 1997; Zaccarelli et al. 1994). The studies summarized in Tables 13.4–13.8 were all studies identified that followed up cohorts of problem or injecting drug users.

The general limitations of cohort studies have been discussed elsewhere (Dart 1995; Feldman 1993; Freeman 1996). The particular limitations of the cohort studies that are most relevant to this project are, first, that these studies were conducted exclusively in developed countries (principally the United States with 11 studies, western Europe with 22 studies and the Western Pacific with two studies). Second, with one exception (McAnulty et al. 1995) these studies drew their samples from people receiving treatment for drug-related problems. Third, the majority of the studies have been done on opioid users, usually injectors. There is much less data on mortality among problem stimulant users. Finally, the majority of cohort studies were conducted in the pre-AIDS era. These limitations will be discussed in more detail later in this chapter.

In studies of all-cause mortality (Table 13.8), a total of 152 432 subjects were included, which involved a total of 1 035 574 person-years of observation, during which time 11 633 deaths were recorded. The weighted average all-cause mortality rate was 1.12% per annum. Pooled crude death rates from the specific causes of death identified by English et al. (1995) were calculated from data reported in these studies (see Tables 13.4–13.7).

Table 13.4 Included outcome studies that examined rates of mortality due to AIDS among problematic drug users

Site	Reference	n	Population studied	Follow-up (years)	Lost	Person-years	Drug used	Crude mortality rate per 1000
Australia, Sydney	Capelhorn et al. (1996)	296	Methadone	13	39	3 484	Heroin	0
Italy	Goedert et al. (1995)	4962	Treatment	3.88	—	21 130	…	0.71
Italy, Milan	Galli and Musicco (1994)	2432	Treatment	6.7	—	16 415	Methadone (94%)	0.88
Italy, Rome	Davoli et al. (1997)	3955	Treatment	4	198	15 820	IDU	1.06
Italy, Rome	Perucci et al. (1991)	4200	Methadone treatment	8	Nil	33 600	Opioids	0.05
Italy, Rome	Zaccarelli et al. (1994)	2431	Treatment	3.2	—	7872	IDU	1.13
Netherlands, Amsterdam	Mientjes et al. (1992)	390	Methadone treatment	2.2	—	810	Opioids	0.37
Netherlands, Amsterdam	van Haastrecht et al. (1996)	632	HIV– methadone and STD clinic patients	4.4	18	2781	…	0.43
New Zealand, Wellington	Dukes et al. (1992)	997	Treatment	9.1	—	9073	Injecting opioid users	Nil
Norway, Oslo	Eskild et al. (1993)	1009	HIV test centre clients	3.67	—	3706	IDU	0.11
Spain, Catalonia	Orti et al. (1996)	15711	Hospital emergency departments and treatment	2.8	—	43 717	Opioids	1.08
Spain, Catalonia	Sanchez-Carbonell and Seus (2000)	135	Treatment	10.5	—	1418	Heroin	1.48
Sweden	Gronbladh et al. (1990)	368	Methadone and untreated	5–11	—	3283	Heroin	0
Sweden, Gothenburg	Benson and Holmberg (1984)	618	Drug using conscripts, rehab. & psych. patients, drug using welfare recipients	10	—	5789	Cannabis, solvents, LSD, stimulants (opioids rare)	0
Sweden, Lund	Tunving (1988)	524	Persons in treatment for opioid, amphetamine, and both opioid and amphetamine use	10	0	5240	Opioids, amphetamines	0

continued

Table 13.4 Included outcome studies that examined rates of mortality due to AIDS among problematic drug users (*continued*)

Site	*Reference*	*n*	*Population studied*	*Follow-up (years)*	*Lost*	*Person-years*	*Drug used*	*Crude mortality rate per 1000*
Sweden, Stockholm	Fugelstad et al. (1995)	472	HIV+	3.8	—	1 793	…	0.39
Sweden, Stockholm	Fugelstad et al. (1997)	1 640	Drug-related hospitalization	8	Nil	13 120	14% heroin; 35% amphetamine; 23% polydrug	0.14
United Kingdom, England, London	Oppenheimer et al. (1994)	128	Treatment	22	7	2 816	Heroin	Nil
United Kingdom, Scotland, Edinburgh	Bucknall and Robertson (1986)	184	Heroin users attending a general practice	4	4	720	Heroin	0
United Kingdom, Scotland, Edinburgh	Robertson et al. (1994)	203	GP	10	17	2 030	IDU	0.79
USA, CA	Hser et al. (1993)	581	Males in compulsory treatment	24	35	13 064	"Narcotics"	0
USA, CT, New Haven	Musto and Ramos (1981)	91	Under treatment for drug abuse when recruited	52	—	4 732	Morphine	0
USA, New York	Friedman et al. (1996)	858	Drug and alcohol dependants on welfare	8	—	6 864	Drugs and alcohol	1.23
USA, OR, Portland	McAnulty et al. (1995)	1 769	Not in treatment	1.78	—	3 149	IDU	0
USA, PA, Philadelphia	Zanis and Woody (1998)	507	Methadone	1	5	507	Heroin	0
Netherlands, Amsterdam; USA, MD, Baltimore	van Ameijden et al. (1999)	2 809	Treatment shelters and community agencies	6–9	—	15 107	IDU	0

— No data.

4.3 Overview of methods of estimating the mortality burden of illicit drugs

Methods for estimating mortality attributable to harmful illicit drug use can be "direct" or "indirect". Direct methods count the number of deaths attributed to illicit drug use by applying attributable fractions to ICD-classified causes of death in national mortality registers. Indirect methods involve estimating mortality by multiplying measures of mortality risk (e.g. relative risk) by the prevalence of the risk factor in the population.

Direct methods

The first method, which requires the greatest amount of data, uses the attributable fraction of mortality attributed to harmful illicit drug use calculated for a population for which direct measures of specific cause mortality data are available. This attributable fraction is then used to extrapolate the mortality attributable to harmful illicit drug use in another population.

This method has the advantage of excluding deaths in those exposed that are *not* due to the risk factor. The source of mortality data to use with this method is the All-Cause Mortality Database compiled by WHO. Attributable fractions for illicit drug use (which have been calculated in countries where direct estimates have been made) can be applied to these data.

In some countries direct measures of mortality are available from mortality registers. This is straightforward, in principle, for deaths caused by overdose, which has an attributable fraction of 1. Aside from individual country mortality registers, other sources of directly measured mortality data include HIV/AIDS surveillance data available from agencies such as UNAIDS and the United States Census Bureau.

The difficulties involved in applying this method are exemplified by the case of "overdose" deaths. This is the only cause of death that is wholly attributable to harmful illicit drug use so all mortality due to this cause must be the result of the risk factor. It is the cause of death that should be the most easily quantified. However, the great many difficulties inherent in assigning any particular case to this cause of death have been well documented (Advisory Council on the Misuse of Drugs 2000; Danish National Board of Health 1997; WHO 1998).

In most United Nations Member States, cause of death is classified according to ICD-10 codes, which specify whether the cause of death was intentional poisoning (suicide), unintentional poisoning or dependence. Despite the existence of ICD-10 criteria for classification of cause of death, countries differ in the way that deaths are registered and causes of death are classified (Danish National Board of Health 1997; WHO 1998). For example there is one European country in which: "... it is well known that about 90% of drug-related deaths are coded

with the code for unknown cause of death" (p. 51) (Sanchez-Carbonell and Seus 2000).

A recent report by the Home Office has been critical of the system for recording drug-related deaths in the United Kingdom (Advisory Council on the Misuse of Drugs 2000). It noted that deaths may not be classified as drug-related if they are not referred to the coroner (as may happen when a certifying doctor is unaware that the deceased was a drug user) or the death is due to an indirect effect of harmful drug use, such as a viral infection. There also appears to be a great deal of variation between individual coroners in their preparedness to record deaths as drug related. The report notes that: "there are coroners working in areas of known high drug prevalence who never certify a death as related to drug misuse" (p. 80).

Other sources of variation identified in the British report were that neither post-mortem nor toxicological analysis are formally required for suspected drug-related deaths; that the verdicts available to the coroner are not mutually exclusive; that coroners do not have the necessary skills to distinguish between the verdicts available to them, most notably "dependence on drugs" and "non-dependent abuse of drugs"; and that there is no requirement of the coroner to identify the drugs involved (Advisory Council on the Misuse of Drugs 2000).

There are also variations between countries in how much information is gathered about the circumstances or cause of death (Danish National Board of Health 1997; WHO 1998). In Australia, for example, autopsy is routinely conducted on all suspected overdose deaths, making forensic and toxicological data the basis for the classification of cause of death. This, however, is a far from universal practice. In the United States, only 20% of drug-related deaths are subject to autopsy (WHO 1998). Similarly, the immediate cause of death is recorded in death registers but contributing factors may or may not (Danish National Board of Health 1997; WHO 1998). This can cause large differences in rates of drug-related deaths based on death register data.

For causes other than overdose, where the attributable fraction is less than 1, the difficulties involved in attributing a death to illicit drug use are compounded. In addition to the caveats discussed above, the simple fact that there is a complete absence of such data in the majority of countries in the world necessitates the use of indirect methods to estimate mortality attributable to harmful drug use.

Indirect methods

Indirect methods of estimating mortality can be used when directly recorded data are unavailable or unreliable. The estimates provided by these methods can be validated against direct methods in countries where reliable mortality data are available. For the vast majority of countries in the world, indirect methods provide the only indicator of the extent

of the health consequences of harmful illicit drug use, because of the absence of epidemiological data on drug-related mortality. Three indirect methods can be used to estimate the burden of mortality attributable to illicit drugs.

The simplest method is to multiply mortality rates in cohort studies by the estimated prevalence of problem illicit drug use in the country. This provides an estimate of deaths caused by illicit drugs for each of the causes of death that we have considered.

Key informant data

A final source of data is that which researchers in the drug and alcohol field can provide. The WHO Management of Dependence Project surveyed drug researchers in Member States and asked them to provide estimates of the prevalence of harmful drug use and resultant mortality in their country, using the best available data. The sources range in quality from large-scale population surveys to educated guesses based on clinical experience, but such consultations provide an independent source of estimates against which to check the sources outlined above.

Only 15 responses were returned and in most cases responses either reported on published data or data whose validity was difficult to evaluate. This source has not been included formally in current estimates. Future attempts to estimate the contribution that illicit drug use makes to global burden of disease may include such data.

Key informants may also be of use to judge the accuracy and validity of estimates of mortality attributable to the different causes of death. Such key informants are extremely invaluable and note has been made in the text of instances in which key informants reported that our estimates were likely to be underestimates.

4.4 Methods used for each cause of mortality

AIDS

UNAIDS estimates of death related to IDU were used. No upper and lower estimates were obtained.

Drug overdose

It should be noted that rates derived from research on opioid overdoses were included in these calculations and separate estimates of the number of persons dying from stimulant-related overdoses have not been made. There is a lack of good data on rates and/or risk of dying from stimulant-related overdoses. However, it is likely that in countries which have a higher prevalence of cocaine use, cocaine-related overdoses may account for a considerable proportion of all fatal drug overdoses. In the United States, for example, the Drug Abuse Warning Network indicated that in 1999, 28% of single-drug overdoses were due to co-

caine (National Institute on Drug Abuse, personal communication, 2002).

Our approach has been to assume that overdose rates derived from research on opioid overdose may be applicable to stimulant drugs. In estimates made of overdose deaths, rates of drug use (which include opioids, amphetamines and cocaine) were multiplied by the rate of opioid overdoses derived from cohort studies. Hence, it has been assumed that the same rate of overdose deaths applies to these other drugs as it does to opioid drug use. In the estimates derived from "all-cause" rates in cohort studies, overdoses due to amphetamines and cocaine use will be included in this rate. Direct estimates made from the WHO Mortality Database included only deaths due to opioids so may be an underestimate.

In this chapter, data used to derive a number of estimates of the number of persons dying from overdoses were derived from the following sources.

Direct estimates: attributable fractions combined with data from WHO all-cause mortality database

An attributable fraction was derived from EUR-A countries. This involved obtaining estimates of the total number of deaths coded in ICD as attributed to mental disorders and accidental poisoning due to opioids. The median attributable fraction of these countries was 0.1164. This attributable fraction was applied to all other subregions to enable a direct estimate to be made.

Data were taken from the WHO all-cause mortality database on deaths attributed to mental disorders and accidental poisoning. Not all countries reported such data. In making estimates for subregions when some data were missing from countries in the subregion, an average overdose rate was calculated using the available data, and this rate was used to estimate the total number of trauma deaths in the subregion. It must be noted that many countries in some subregions did not report data in the WHO database, and some subregions had no countries that reported such data; the following subregions had estimates made from only few countries in the subregion, or had no estimates made:

- AFR-D: Mauritius;
- AFR-E: no estimate;
- AMR-B: Argentina, Belize, Brazil, Costa Rica and El Salvador;
- AMR-D: no estimate;
- EMR-B: Kuwait;
- EMR-D: no estimate;
- EUR-C: Armenia, Azerbaijan, Bulgaria, Kyrgyzstan, Poland, Romania and Slovakia;

- SEAR-B: Thailand;
- SEAR-D: the Democratic People's Republic of Korea;
- WPR-B: no estimate.

Indirect estimates: cohort-derived mortality rate

A weighted average mortality rate was calculated from cohort studies (see Table 13.5 for included studies). The average was 0.43% per annum (to 2 decimal places). The upper and lower 95% confidence intervals of this rate were 0.25% per annum and 0.64% per annum.

Suicide

Suicide was considered as a cause of mortality among illicit opioid users only. Hence, when making indirect estimates of deaths, only rates of opioid use were considered in analyses. Median estimates are reported. Where only one source of data was available in estimating a cause of mortality, then the median of this was used, and the lowest and highest estimate used for the range. If more than one source of estimates was available for a subregion, then the lowest and highest *median* estimates were used as the range.

Direct estimates: attributable fractions combined with data from WHO all-cause mortality database

An attributable fraction of 0.09 was used to calculate the proportion of all suicides that were among opioid users. This attributable fraction was derived from an Australian study reported by English et al. (1995). Data were taken from the WHO all-cause mortality database on the number of deaths due to suicide by country, for persons aged >15 years. The year for which data were available varied. For those countries that had more than one year of data, the most recent year's data were used.

Not all countries reported such data. In making estimates for subregions in which some data were missing from countries in the subregion, an average suicide rate was calculated using the available data. This rate was used to estimate the total number of suicide deaths in the subregion. It must be noted that many countries in some subregions did not report data in the WHO database, and in some subregions there were no countries that reported such data. The subregions in which estimates were made from only few countries, or which provided no estimates are as follows:

- AFR-D: Mauritius;
- AFR-E: no estimate;
- AMR-B: Argentina, Belize, Brazil and Costa Rica;
- AMR-D: no estimate;

Table 13.5 Included outcome studies that examined rates of mortality due to overdose among problematic drug users

Site	*Reference*	*n*	*Population studied*	*Follow-up (years)*	*Lost*	*Person-years*	*Drug*	*Crude mortality rate per 1000*
Australia, Sydney	Capelhorn et al. (1996)	296	Methadone	13	39	3 484	Heroin	0.66
Denmark, Copenhagen	Haastrup and Jepson (1984)	300	Treatment	7	19	1 967	Morphine	1.37
Italy	Goedert et al. (1995)	4962	Treatment	3.88	—	21 130	…	0.30
Italy, Milan	Galli and Musicco (1994)	2432	Treatment	6.7	—	16 415	Methadone (94%)	0.92
Italy, Rome	Davoli et al. (1997)	3955	Treatment	4	198	15 820	IDU	0.58
Italy, Rome	Perucci et al. (1991)	4200	Methadone	8	Nil	33 600	Opioids	0.24
Italy, Rome	Zaccarelli et al. (1994)	2431	Treatment	3.2	—	7 872	IDU	0.55
Netherlands, Amsterdam	van Haastrecht et al. (1996)	632	HIV– methadone and STD clinic patients	4.4	18	2 781	…	0.56
New Zealand, Wellington	Dukes et al. (1992)	997	Treatment	9.1	—	9 073	Injecting opioid users	0.25
Norway, Oslo	Eskild et al. (1993)	1009	HIV test centre clients	3.67	—	3 706	IDU	1.56
Spain, Catalonia	Orti et al. (1996)	15711	Hospital ER and treatment	2.8	—	43 717	Opioids	1.09
Sweden	Gronbladh et al. (1990)	368	Methadone and untreated	5–11	—	3 283	Heroin	1.74
Sweden, Gothenburg	Benson and Holmberg (1984)	618	Drug-using conscripts, rehab. & psych. patients, drug-using welfare recipients	10	—	5 789	Cannabis, solvents, LSD, stimulants (opioids rare)	0.05 (poisoning)
Sweden, Lund	Tunving (1988)	524	Treatment: opioid, amphetamine, and both opioid and amphetamine	10	0	5 240	Opioids, amphetamines	0.67

Sweden, Stockholm	Engstrom et al. (1991)	1630	Drug-related hospitalization	12	—	19560	41% cocaine/ amphetamine; 12% heroin; 16% polydrug; 31% other	0.16
Sweden, Stockholm	Fugelstad et al. (1995)	472	HIV+	3.8	—	1793	…	2.29
Sweden, Stockholm	Fugelstad et al. (1997)	1640	Drug-related hospitalization	8	Nil	13120	14% heroin; 35% amphetamine; 23% polydrug	0.82
Sweden, Stockholm	Wahren et al. (1997)	1494	Hospitalized for drug dependence	22	—	32868	57% stimulants; 39% opioids	0.09
United Kingdom	Ghodse et al. (1998)	92802	"Drug addicts" notified to Home Office	27	—	687673	65% opioids	0.38
United Kingdom, England, London	Oppenheimer et al. (1994)	128	Treatment	22	7	2816	Heroin	0.64
United Kingdom, England, London	Wille (1981)	128	Treatment (Rx heroin)	10	—	1280	Heroin	0.86
United Kingdom, Scotland, Edinburgh	Bucknall and Robertson (1986)	184	Heroin users attending a general practice	4	4	720	Heroin	0.55
United Kingdom, Scotland, Edinburgh	Robertson et al. (1994)	203	GP	10	17	2030	IDU	0.74
USA, CA	Hser et al. (1993)	581	Males in compulsory treatment	24	35	13064	"Narcotics"	0.40
USA, CT, New Haven	Musto and Ramos (1981)	91	Treatment	52	—	4732	Morphine	0

continued

Table 13.5 Included outcome studies that examined rates of mortality due to overdose among problematic drug users (*continued*)

Site	*Reference*	*n*	*Population studied*	*Follow-up (years)*	*Lost*	*Person-years*	*Drug*	*Crude mortality rate per 1000*
USA, NM, Albuquerque	Goldstein and Herrera (1995)	1013	Methadone	22	243	22 286 (16 940 excl. lost)	…	0.53 (0.70)
USA, New York	Concool et al. (1979)	1156	Treatment (84% methadone)	7	102	8092	Heroin	0.07
USA, New York	Friedman et al. (1996)	858	Drug and alcohol dependents on welfare	8	—	6864	Drugs and alcohol	0.12
USA, New York	Vaillant (1973)	100	Treatment, male	20	17	1660	Narcotics	0.35
USA, OR, Portland	McAnulty et al. (1995)	1769	Not in treatment	1.78	—	3149	IDU	0.41
USA, PA, Philadelphia	Zanis and Woody (1998)	507	Methadone	1	5	507	Heroin	1.18
USA, 18 treatment agencies	Joe and Simpson (1987)	697	Treatment	6	142	3330	Opioids	0.75
USA, 34 treatment agencies	Joe et al. (1982)	3324	Treatment	4	—	11 710	Opioids	0.59
Netherlands, Amsterdam; USA, MD, Baltimore	van Ameijden et al. (1999)	2809	Treatment shelters and community agencies	6–9	—	15 107	IDU	0.50

— No data.

- EMR-B: Kuwait;
- EMR-D: no estimate;
- SEAR-B: Thailand;
- SEAR-D: the Democratic People's Republic of Korea;
- WPR-B: no estimate.

Indirect estimates: cohort-derived crude mortality rates

The crude mortality rate due to suicide from cohort studies was also estimated (see Table 13.6 for included studies). The weighted average rate of death per annum due to suicide was 0.24% (shown here to 2 decimal places). In order to make a range of estimates around this average rate, the standard error of the rate was calculated and 95% confidence intervals constructed around the rate. These were used as the lower and upper ranges of the mortality rates due to suicide: these were 0.15% per annum and 0.33% per annum, respectively.

Trauma

It must be noted that there are significant problems with estimates of rates/attributable fractions due to trauma, since cohort studies reported different sorts of trauma, and different numbers of causes. In the attributable fraction method of calculation, only road traffic accidents were used to calculate the number attributable to illicit drug use as it is unclear the extent to which homicides or other trauma deaths are due to illicit drug use.

Median estimates are reported. Where only one source of data was available in estimating a cause of mortality, then the median of this estimate was used, and the lowest and highest estimates were used for the range. If more than one source of estimates was available for a subregion, then the lowest and highest *median* estimates were used as the range.

Direct estimates: attributable fraction combined with data from WHO all-cause mortality database

Data were taken from the WHO all-cause mortality database on the number of deaths due to motor vehicle or other road traffic accidents (ICD-9 codes E470–E474 and E479) by country. Not all countries reported such data. In making estimates for subregions when data were missing from some countries, an average trauma rate was calculated using the available data. This rate was used for estimating the total number of trauma deaths in the subregion. It must be noted that many countries in some subregions did not report data in the WHO database, and some subregions had no countries that reported such data. In the following subregions estimates were made from only few countries, or no estimates were made:

Table 13.6 Included outcome studies that examined rates of mortality due to suicide among problematic drug users

Site	*Reference*	*n*	*Population studied*	*Follow-up (years)*	*Lost*	*Person-years*	*Drug*	*Crude mortality rate (per 1000)*
Australia, Sydney	Capelhorn et al. (1996)	296	Methadone	13	39	3484	Heroin	0.14
Denmark, Copenhagen	Haastrup and Jepson (1984)	300	Treatment	7	19	1967	Morphine	0.61
Italy, Milan	Galli and Musicco (1994)	2432	Treatment	6.7	—	16415	Methadone (94%)	0.06
Italy, Rome	Perucci et al. (1991)	4200	Methadone	8	Nil	33600	Opioids	0.03
Italy, Rome	Zaccarelli et al. (1994)	2431	Treatment	3.2	—	7872	IDU	0.04
Netherlands, Amsterdam	van Haastrecht et al. (1996)	632	HIV– methadone and STD clinic patients	4.4	18	2781	…	0.36
New Zealand, Wellington	Dukes et al. (1992)	997	Treatment	9.1	—	9073	Injecting opioid	0.09
Norway, Oslo	Eskild et al. (1993)	1009	HIV test centre clients	3.67	—	3706	IDU	0.24
Sweden	Gronbladh et al. (1990)	368	Methadone and untreated	5–11	—	3283	Heroin	0.09
Sweden, Gothenburg	Benson and Holmberg (1984)	618	Drug-using conscripts, rehab. & psych. patients, drug-using welfare recipients	10	—	5789	Cannabis, solvents, LSD, stimulants (opioids rare)	0.29
Sweden, Lund	Tunving (1988)	524	Treatment: opioid, amphetamine, and both opioid and amphetamine	10	0	5240	Opioids, amphetamines	0.33
Sweden, Stockholm	Engstrom et al. (1991)	1630	Drug-related hospitalization	12	—	19560	41% cocaine/ amphetamine; 12% heroin; 16% polydrug; 31% other	0.79

Sweden, Stockholm	Fugelstad et al. (1995)	472	HIV+	3.8	—	1793	…	0.50
Sweden, Stockholm	Fugelstad et al. (1997)	1640	Drug-related hospitalization	8	Nil	13120	14% heroin; 35% amphetamine; 23% polydrug	0.22
Sweden, Stockholm	Wahren et al. (1997)	1494	Hospitalized for drug dependence	22	—	32868	57% stimulants; 39% opioids	0.30
United Kingdom, England, London	Oppenheimer et al. (1994)	128	Treatment	22	7	2816	Heroin	0.07
United Kingdom, England, London	Wille (1981)	128	Treatment (Rx heroin)	10	—	1280	Heroin	0.08
United Kingdom, Scotland, Edinburgh	Bucknall and Robertson (1986)	184	Heroin users attending a general practice	4	4	720	Heroin	0.14
USA, CT, New Haven	Musto and Ramos (1981)	91	Treatment	52	—	4732	Morphine	0.02
USA, NM, Albuquerque	Goldstein and Herrera (1995)	1013	Methadone	22	243	22286 (16940 excl. lost)	…	0.05 (0.07)
USA, New York	Vaillant (1973)	100	Treatment, male	20	17	1660	Narcotics	0.20
USA, PA, Philadelphia	Zanis and Woody (1998)	507	Methadone	1	5	507	Heroin	0
Netherlands, Amsterdam; USA, MD, Baltimore	van Ameijden et al. (1999)	2809	Treatment shelters and community agencies	6–9	—	15107	IDU	0.59

— No data.

- AFR-D: no estimate;
- AFR-E: no estimate;
- AMR-B: Argentina, Belize, Brazil, Costa Rica, El Salvador and Paraguay;
- AMR-D: no estimate;
- EMR-B: Kuwait;
- EMR-D: no estimate;
- SEAR-B: Thailand;
- SEAR-D: no estimate;
- WPR-B: the Philippines and the Republic of Korea.

The attributable fraction derived by Ridolfo and Stevenson (2001) of 0.015 was used to calculate direct estimates of trauma due to illicit drugs.

Indirect estimates: cohort-derived crude mortality rates

Indirect estimates of the number of road traffic accident deaths due to illicit drug use were also made using pooled estimates of the rates of death due to trauma from cohort studies (Table 13.7). Rates of traumatic injury were also high in this group: the weighted average rate of death per annum due to trauma was 0.35%. In order to make a range of estimates around this average rate, the standard error of the rate was calculated and 95% confidence intervals constructed around the rate. These were used as the lower and upper ranges of the mortality rates due to trauma: these were 0.23% per annum and 0.46% per annum, respectively (shown here only to 2 decimal places).

All-cause mortality

Median estimates are reported. Where only one source of data was available in estimating a cause of mortality, then the median of this was used, and the lowest and highest estimate used for the range. If more than one source of estimates was available for a subregion, then the lowest and highest *median* estimates were used as the range.

Direct estimates: attributable fractions combined with data from WHO all-cause mortality database

Data were taken from the WHO all-cause mortality database on the total number of deaths by country, for persons aged between 15 and 54 years. The year for which data were available varied so the data from the most recent year were used in those countries that had more than one year of data.

This age group (15–54 years) was chosen as the age group within which excess mortality rates would occur among problem illicit drug

Table 13.7 Included outcome studies that examined rates of mortality due to trauma among problematic drug users

Site	*Reference*	*n*	*Population studied*	*Follow-up (years)*	*Lost*	*Person-years*	*Drug*	*Crude mortality rate (per 1000)*
Australia, Sydney	Capelhorn et al. (1996)	296	Methadone	13	39	3484	Heroin	0.23
Italy	Goedert et al. (1995)	4962	Treatment	3.88	—	21130	…	1.8
Italy, Milan	Galli and Musicco (1994)	2432	Treatment	6.7	—	16415	Methadone (94%)	0.15
Italy, Rome	Davoli et al. (1997)	3955	Treatment	4	198	15820	IDU	0.25
Italy, Rome	Perucci et al. (1991)	4200	Methadone	8	Nil	33600	Opioids	0.15
Italy, Rome	Zaccarelli et al. (1994)	2431	Treatment	3.2	—	7872	IDU	0.20
Netherlands, Amsterdam	van Haastrecht et al. (1996)	632	HIV– methadone and STD clinic patients	4.4	18	2781	…	0.18
New Zealand, Wellington	Dukes et al. (1992)	997	Treatment	9.1	—	9073	Injecting opioid users	0.12
Norway, Oslo	Eskild et al. (1993)	1009	HIV test centre clients	3.67	—	3706	IDU	0.22
Spain, Catalonia	Orti et al. (1996)	15711	Hospital ER and treatment	2.8	—	43717	Opioids	0.37
Sweden	Gronbladh et al. (1990)	368	Methadone and untreated	05–11	—	3283	Heroin	0.06
Sweden, Gothenburg	Benson and Holmberg (1984)	618	Drug-using conscripts, rehab. & psych. patients, drug-using welfare recipients	10	—	5789	Cannabis, solvents, LSD, stimulants (opioids rare)	0.07
Sweden, Lund	Tunving (1988)	524	Treatment: opioid, amphetamine, and both opioid and amphetamine	10	0	5240	Opioids, amphetamines	0.15

continued

Table 13.7 Included outcome studies that examined rates of mortality due to trauma among problematic drug users (*continued*)

Site	*Reference*	*n*	*Population studied*	*Follow-up (years)*	*Lost*	*Person-years*	*Drug*	*Crude mortality rate (per 1000)*
Sweden, Stockholm	Engstrom et al. (1991)	1630	Drug-related hospitalization	12	—	19560	41% cocaine/ amphetamine; 12% heroin; 16% polydrug; 31% other	0.35
Sweden, Stockholm	Fugelstad et al. (1995)	472	HIV+	3.8	—	1793	…	0.11
Sweden, Stockholm	Fugelstad et al. (1997)	1640	Drug-related hospitalization	8	Nil	13120	14% heroin; 35% amphetamine; 23% polydrug	0.21
Sweden, Stockholm	Wahren et al. (1997)	1494	Hospitalized for drug dependence	22	—	32868	57% stimulants; 39% opioids	0.22
United Kingdom, England, London	Oppenheimer et al. (1994)	128	Treatment	22	7	2816	Heroin	0.14
United Kingdom, England, London	Wille (1981)	128	Treatment (Rx heroin)	10	—	1280	Heroin	0.16

United Kingdom, Scotland, Edinburgh	Bucknall and Robertson (1986)	184	Heroin users attending a general practice	4	4	720	Heroin	0.14
USA, CA	Hser et al. (1993)	581	Males in compulsory treatment	24	35	13064	"Narcotics"	0.35 (incl. suicide)
USA, CT, New Haven	Musto and Ramos (1981)	91	Treatment	52	—	4732	Morphine	0.08
USA, NM, Albuquerque	Goldstein and Herrera (1995)	1013	Methadone	22	243	22286 (16940 excl. lost)	…	0.27 (0.35)
USA, New York	Vaillant (1973)	100	Treatment, male	20	17	1660	Narcotics	0.1
USA, New York	Concool et al. (1979)	1156	Treatment (84% methadone)	7	102	8092	Heroin	0.26
USA, OR, Portland	McAnulty et al. (1995)	1769	Not in treatment	1.78	—	3149	IDU	0.16
USA, PA, Philadelphia	Zanis and Woody (1998)	507	Methadone	1	5	507	Heroin	0
USA, 18 treatment agencies	Joe and Simpson (1987)	697	Treatment	6	142	3330	Opioids	0.45
USA, 34 treatment agencies	Joe et al. (1982)	3324	Treatment	4	—	11710	Opioids	0.38
Netherlands, Amsterdam; USA, MD, Baltimore	van Ameijden et al. (1999)	2809	Treatment shelters and community agencies	6–9	—	15107	IDU	0.25

— No data.

users compared to non-users. After calculating mortality rates among this age group, an SMR of 13 was used to calculate the rate of all-cause mortality death among problematic illicit drug users. This was taken from previous studies estimating the excess rates of mortality in this group (English et al. 1995; Hulse et al. 1999). It was assumed for these calculations that the resulting rate of death applied to all illicit drug users. This will underestimate the mortality rate among the minority of illicit drug users who are older than 54 years.

Some countries did not have any death data included in the WHO database. For these countries no individual estimates were made. However, in making calculations for subregions, a weighted average of the all-cause mortality rates was calculated using the data from countries that were included. It was assumed that the countries for which no data were available had the average rate of the other countries in the subregion from which they came. Some subregions, however, had no countries which had appropriate estimates. Those subregions in which there were few or no countries for which estimates could be made were as follows:

- AFR-D: Mauritius;
- AFR-E: South Africa;
- AMR-B: Argentina, Belize, Brazil, Costa Rica, El Salvador and Paraguay;
- AMR-D: no estimate;
- EMR-B: Kuwait;
- EMR-D: no estimate;
- SEAR-B: Thailand;
- SEAR-D: no estimate;
- WPR-B: the Philippines and the Republic of Korea.

Indirect estimates: cohort-derived crude mortality rate

Crude all-cause mortality rates were also derived from cohort studies included in this project (see Table 13.8). A weighted average all-cause mortality rate was calculated (1.12% per annum), with a 95% CI of the average rate estimated as between 0.78% per annum and 1.46% per annum.

Table 13.8 Included outcome studies that examined rates of all-cause mortality among problematic drug users

Site	*Reference*	*n*	*Population studied*	*Follow-up (years)*	*Lost*	*Person-years*	*Drug*	*Standardized mortality ratio*	*No. of deaths*	*Crude mortality rate (per 1000)*
Australia, Sydney	Capelhorn et al. (1996)	296	Methadone	13	39	3 484	Heroin	...	42	1.21
Denmark, Copenhagen	Haastrup and Jepson (1984)	300	Treatment	7	19	1 967	Morphine	20	47	2.40
Denmark, Copenhagen	Haastrup and Jepson (1988)	300	First time entrants to treatment	11	30	2 970	Opioids	...	78	2.63
Denmark, Copenhagen	Segest et al. (1990)	169	Methadone	8	—	1 352	Opioids	...	39	2.88
Ireland	Keenan et al. (1993)	45	Pregnant on methadone	6	—	270	Opioids	...	7	2.59
Italy	Goedert et al. (1995)	4962	Treatment	3.88	—	21 130	...	18	332	1.57
Italy, Milan	Galli and Musicco (1994)	2432	Treatment	6.7	—	16 415	Methadone (94%)	13.5	413	2.52
Italy, Rome	Davoli et al. (1997)	3955	Treatment	4	198	15 820	IDU	21.2 (Males) 38.5 (Females)	387	2.45
Italy, Rome	Perucci et al. (1991)	4200	Methadone	8	Nil	33 600	Opioids	10.1	239	0.71
Italy, Rome	Zaccarelli et al. (1994)	2431	Treatment	3.2	—	7 872	IDU	(Males) 30.3 HIV+ 11.1 HIV– (Females) 19.4 HIV+ 4.9 HIV–	181	2.30

continued

Table 13.8 Included outcome studies that examined rates of all-cause mortality among problematic drug users (*continued*)

Site	*Reference*	*n*	*Population studied*	*Follow-up (years)*	*Lost*	*Person-years*	*Drug*	*Standardized mortality ratio*	*No. of deaths*	*Crude mortality rate (per 1000)*
Netherlands, Amsterdam	Mientjes et al. (1992)	390	Methadone	2.2	—	810	Opioids	…	29	3.58
Netherlands, Amsterdam	van Haastrecht et al. (1996)	632	HIV– methadone and STD clinic patients	4.4	18	2781	…	…	72	2.59
New Zealand, Wellington	Dukes et al. (1992)	997	Treatment	9.1	—	9073	Injecting opioid users	2.44	67	0.74
Norway, Oslo	Eskild et al. (1993)	1009	HIV test centre clients	3.67	—	3706	IDU	…	87	2.35
Spain, Catalonia	Orti et al. (1996)	15711	Hospital ER and treatment	2.8	—	43717	Opioids	…	1315	3.01
Spain, Catalonia	Sanchez-Carbonell and Seus (2000)	135	Treatment	10.5	—	1418	Heroin	28.5	41	3.4
Sweden	Gronbladh et al. (1990)	368	Methadone and untreated	5–11	—	3283	Heroin	63 street 4 methadone	96 26	2.92 0.45
Sweden, Gothenburg	Benson and Holmberg (1984)	618	Drug-using conscripts, rehab. & psych. patients, drug-using welfare recipients	10	—	5789	Cannabis, solvents, LSD, stimulants (opioids rare)	…		
Sweden, Lund	Tunving (1988)	524	Treatment: opioid, amphetamine, and both opioid and amphetamine	10	0	5240	Opioids, amphetamines	5.4 (opioids) 2.5 (amphetamines)	62	1.18
Sweden, Stockholm	Engstrom et al. (1991)	1630	Drug-related hospitalization	12	—	19560	41% cocaine/ amphetamine; 12% heroin; 16% polydrug; 31% other	5.3 (18.3 for opioid users; 9.0 for cocaine/ amphetamine)	446	2.3

Sweden, Stockholm	Fugelstad et al. (1995)	472	HIV+	3.8	—	1 793	…	…	69	3.85
Sweden, Stockholm	Fugelstad et al. (1997)	1 640	Drug-related hospitalization	8	Nil	13 120	14% heroin; 35% amphetamine; 23% polydrug	…	214	1.63
Sweden, Stockholm	Wahren et al. (1997)	1 494	Hospitalized for drug dependence	22	—	32 868	57% stimulants; 39% opioids	6.9	521	1.59
United Kingdom	Bewley et al. (1968)	1 272	Heroin addicts known to Home Office	1.8	—	2 291	Heroin	28	85	2.7
United Kingdom	Ghodse et al. (1998)	92 802	"Drug addicts" notified to Home Office	27	—	687 673	65% opioids	7.0	5310	0.77
United Kingdom, England, London	Bewley and Ben-Arie (1968)	100	Hospitalized male heroin addicts	2.25	—	225	Heroin	…	13	5.7
United Kingdom, England, London	Oppenheimer et al. (1994)	128	Treatment	22	7	2 816	Heroin	11.9	41	1.53
United Kingdom, England, London	Wille (1981)	128	Treatment (Rx heroin)	10	—	1 280	Heroin	…	19	1.48
United Kingdom, Scotland, Edinburgh	Bucknall and Robertson (1986)	184	Heroin users attending a general practice	4	4	720	Heroin	11.6	7	0.972
United Kingdom, Scotland, Edinburgh	Robertson et al. (1994)	203	GP	10	17	2 030	IDU	…	40	1.97
USA, CA	Hser et al. (1993)	581	Males in compulsory treatment	24	35	13 064	"Narcotics"	…	161	1.23
USA, CT, New Haven	Musto and Ramos (1981)	91	Treatment	52	—	4 732	Morphine		40	0.84

continued

Table 13.8 Included outcome studies that examined rates of all-cause mortality among problematic drug users (*continued*)

Site	*Reference*	*n*	*Population studied*	*Follow-up (years)*	*Lost*	*Person-years*	*Drug*	*Standardized mortality ratio*	*No. of deaths*	*Crude mortality rate (per 1000)*
USA, NM. Albuquerque	Goldstein and Herrera (1995)	1013	Methadone	22	243	22286 (16940 excl. lost)	…	4.0 (Males) 6.8 (Females)	348	1.56 (2.05)
USA, New York	Concool et al. (1979)	1156	Treatment (84% methadone)	7	102	8092	Heroin	1.5	45	0.56
USA, New York	Friedman et al. (1996)	858	Drug and alcohol dependents on welfare	8	—	6864	Drugs and alcohol	…	183	2.67
USA, New York	Vaillant (1973)	100	Treatment, male	20	17	1660	Narcotics	…	23	1.15
USA, OR, Portland	McAnulty et al. (1995)	1769	Not in treatment	1.78	—	3149	IDU	8.3		1.05
USA, PA, Philadelphia	Zanis and Woody (1998)	507	Methadone	1	5	507	Heroin	…	13	2.56
USA, 18 treatment agencies	Joe and Simpson (1987)	697	Treatment	6	142	3330	Opioids	6.9	52	1.56
USA, 34 treatment agencies	Joe et al. (1982)	3324	Treatment	4	—	11710	Opioids	14 (<21 years) 10 (21–30 years) 4 (>30 years)	179	1.52
Netherlands, Amsterdam; USA, MD, Baltimore	van Ameijden et al. (1999)	2809	Treatment shelters and community agencies	6–9	—	15107	IDU	…	264	1.75

— No data.

5. Estimated mortality attributable to illicit drug use, 2000

5.1 Burden of mortality attributable to specific causes

Table 13.9 shows the median indirect estimates of the number of deaths attributed to illicit drug use in 2000 for each of the 14 subregions (Table 13.10 also shows low and high range estimates around these medians).

AIDS

The second largest individual cause of death was AIDS, with a global median estimate of 59 000 deaths. The largest proportion of these deaths was estimated to have occurred in WPR-B (17 000). The other two subregions in which the greatest number of deaths from AIDS related to illicit drug use were EMR-D (11 000) and SEAR-B (11 000).

There is some indication that the estimates for some subregions may be too low. The United States Centers for Disease Control and Prevention reported that in 1999, 5932 AIDS-related deaths occurred in the United States that were attributed to IDU (see http://www.cdc.gov/hiv/stats/hasr1202.htm). Similarly, reports from UNAIDS experts indicate that estimates for EUR-C may also be too low, with reports that in the Ukraine alone, approximately 3440 deaths occurred due to AIDS in 1999 (UNAIDS, personal communication, 2001). While some reviewers commented that South-East Asian estimates were higher than they expected, recent work has indicated that the number of AIDS deaths in Thailand (one of the countries in this region) was higher than previously estimated (A. Lopez, personal communication, 2001). Recent work in the South-East Asia Region is consistent with the possibility that AIDS-related deaths have been underestimated in this region (Reid and Costigan 2002).

Overdose

Opioid overdose was the next largest cause of death among illicit drug users, with a median estimate of 69 152 deaths globally. The two subregions that accounted for the largest number of opioid overdose deaths were SEAR-D (22 989) and EMR-D (12 852), followed by EUR-C and AMR-A.

The estimates may be too low for some subregions. For example, WPR-A, which includes Australia, had a median estimate of 825 deaths, with a high and low estimate of 954 and 696, respectively. Data from the Australian Bureau of Statistics indicates that in 2000, a total of 737 deaths occurred among persons aged 15–44 years (National Drug and Alcohol Research Centre 2000).

Suicide

Suicide among opioid users was estimated to account for 32 216 deaths in 2000. SEAR-D accounted for the greatest proportion of these deaths

Table 13.9 Median indirect estimates of mortality attributed to illicit drug use, by subregion

Subregion	*AIDS*	*Opioid overdose*	*Suicide*	*Trauma*
AFR-D	0	1 891	1 191	2 768
AFR-E	0	407	64	922
AMR-A	4 000	6 397	2 034	4 057
AMR-B	5 000	1 845	922	2 342
AMR-D	0	498	78	716
EMR-B	0	3 881	673	813
EMR-D	11 000	12 852	2 015	2 954
EUR-A	0	5 527	2 355	3 387
EUR-B	1 000	1 281	1 465	651
EUR-C	3 000	6 895	4 156	830
SEAR-B	11 000	955	576	797
SEAR-D	7 000	22 989	14 982	3 128
WPR-A	0	825	1 251	1 028
WPR-B	17 000	2 909	456	9 295
Total (median)	59 000	69 152	32 216	33 689

Note: There were an additional 10 000 deaths from overdose above and beyond those coded as drug use disorders (added to unintentional injuries) or when coded drug use disorder deaths were higher than estimated overdose deaths.

(14 982), with EUR-C accounting for the next largest. A similar number of deaths were estimated to be due to trauma (34 184). WPR- B had the largest numbers of deaths due to this cause (9295), followed by AMR-A (4057).

5.2 All-cause mortality attributable to illicit drugs

Table 13.11 compares two methods of calculating the total mortality attributable to illicit drug use: (i) adding the above four causes; and (ii) using estimates of "all-cause" mortality derived from cohort studies and attributable fractions. There are some reassuring similarities between the two sources, and some noteworthy discrepancies.

Overall, the global estimates were remarkably similar ("all-cause" estimate 197 383 vs "sum" estimate 194 058). Of note was the fact that the subregions that had discrepant estimates were largely developing subregions, and not the subregions from which the majority of cohort studies and attributable fractions had been derived. One of the subregions that accounted for the slightly lower estimates using the all-cause mortality method was SEAR-D, whose all-cause estimate (around 11 000) was only 23% of its sum estimate. In general, however, for most other subregions, estimates were within close range of each other, or the all-cause estimates were higher. The overall rate of death per 1 000

Table 13.10 Mortality range attributable to illicit drug use, by subregion

Subregion	*AIDS*	*Opioid overdose*	*Suicide*	*Trauma*	*All-cause*
AFR-D	**0**[a]	**1 891**	**1 191**	**2 768**	**19 046**
Low	0	1 526	354	1 235	9 754
High	0	2 256	2 028	4 807	28 338
AFR-E	**0**	**407**	**64**	**922**	**8 286**
Low	0	246	40	412	3 251
High	0	609	87	1 602	13 321
AMR-A	**4 000**	**6 397**	**2 034**	**4 057**	**40 356**
Low	4 000	5 144	806	718	23 186
High	4 000	7 649	3 261	7 397	54 647
AMR-B	**5 000**	**1 845**	**922**	**2 342**	**18 425**
Low	5 000	1 530	240	985	13 034
High	5 000	2 159	1 604	3 699	23 817
AMR-D	**0**	**498**	**78**	**716**	**2 522**
Low	0	300	49	319	1 070
High	0	744	107	1 243	3 985
EUR-A	0	**5 527**	**2 355**	**3 387**	**16 453**
Low	0	2 791	866	712	11 026
High	0	9 108	4 481	4 690	19 533
EUR-B	**1 000**	**1 281**	**1 465**	**651**	**5 794**
Low	1 000	214	336	473	2 923
High	1 000	2 348	2 595	829	8 665
EUR-C	**3 000**	**6 895**	**4 156**	**830**	**10 709**
Low	3 000	4 507	707	674	3 474
High	3 000	9 284	7 605	986	17 944
EMR B	**0**	**3 881**	**673**	**813**	**5 012**
Low	0	431	196	317	4 612
High	0	7 332	1 149	1 309	5 412
EMR D	**11 000**	**12 852**	**2 015**	**2 954**	**10 411**
Low	11 000	7 757	1 271	1 319	4 416
High	11 000	19 212	2 759	5 131	16 454
SEAR-B	**11 000**	**955**	**576**	**797**	**5 688**
Low	11 000	581	208	745	2 625
High	11 000	1 330	943	849	8 751
SEAR-D	**7 000**	**22 989**	**14 982**	**3 128**	**11 024**
Low	7 000	1 824	2 059	1 396	4 676
High	7 000	44 154	27 105	5 434	17 423
WPR-A	**0**	**825**	**1 251**	**1 028**	**9 916**
Low	0	696	109	246	6 375
High	0	954	2 394	1 809	13 457
WPR-B	**17 000**	**2 909**	**456**	**9 295**	**33 741**
Low	17 000	1 756	288	8 111	11 329
High	17 000	3 439	624	10 479	90 709
Total median	**59 000**	**69 152**	**32 216**	**33 689**	**197 383**
Low	59 000	29 303	8 330	17 622	101 751
High	59 000	110 577	56 742	50 264	322 456

[a] Figures in bold: the median estimates from Table 13.9.

Table 13.11 Estimates of total mortality attributed to illicit drug use, by subregion

Subregion	*Population (000s) >15 years*	*Sum of four causes of mortality*[a]	*Population mortality rate (per 1000)*	*All-cause mortality*[b]	*Population mortality rate (per 1000)*
AFR-D	159577	5850	0.04	19046	0.12
AFR-E	190152	1393	0.01	8286	0.04
AMR-A	255420	16488	0.06	40356	0.16
AMR-B	297625	10109	0.03	18425	0.06
AMR-D	44658	1292	0.03	2522	0.06
EMR-B	86853	5367	0.06	5012	0.06
EMR-D	204039	28821	0.14	10411	0.05
EUR-A	339446	11269	0.03	16453	0.05
EUR-B	161213	4397	0.03	5794	0.04
EUR-C	152432	14881	0.10	10709	0.07
SEAR-B	206870	13328	0.06	5688	0.03
SEAR-D	818521	48099	0.06	11024	0.01
WPR-A	129888	3104	0.02	9916	0.08
WPR-B	1131503	29660	0.03	33741	0.03
World	4178197	194058	0.05	197383	0.05

[a] Sum of the median estimates of the following four causes: AIDS, opioid overdose, suicide via opioids and trauma.

[b] Median estimates of all-cause mortality derived from SMR analyses and pooled CMRs.

persons aged ≥15 years due to illicit drug use, on a global level, was estimated at 0.5 per annum. The highest all-cause *mortality rate* was estimated to have occurred in AMR-A (0.16 per 1000 persons aged ≥15 years), followed by AFR-D (0.12 per 1000 persons aged ≥15 years). The lowest rates using all-cause estimates occurred within SEAR-D (0.01 per 1000), WPR-B (0.03) and SEAR-B (0.03).

The discrepancies between the two sources of estimates for developed societies suggested that in general (with the exception of AMR-A), the consistency between the two was reasonable. If anything, the all-cause method produced a higher estimate, which is consistent with the fact that the "four cause" method does not include an exhaustive list of all possible causes of death.

In some developing subregions (such as SEAR-D) there was marked discrepancy between the two sources of estimates. This could be due to higher rates of AIDS-related deaths among injecting drug users in these subregions, which were not adequately assessed by using the all-cause method (in which some cohort studies were carried out before AIDS became an issue).

Table 13.12 Proportion of causes of death attributed to illicit drug use among males, by subregion

Subregion	*Proportion among males*
AFR-D	0.89
AFR-E	0.83
AMR-A	0.56
AMR-B	0.63
AMR-D	0.72
EMR-B	0.85
EMR-D	0.82
EUR-A	0.59
EUR-B	0.64
EUR-C	0.79
SEAR-B	0.96
SEAR-D	0.83
WPR-A	0.93
WPR-B	0.79

5.3 Age and sex breakdowns

Our ability to make reliable and valid estimates of the age and sex breakdowns of deaths attributable to illicit drug use is extremely limited. Not only are estimates of the prevalence of drug use according to these characteristics limited (or absent) in many countries, it is also the case that evidence on the characteristics of persons dying from the causes examined here are limited. The estimates made below have been made with reference to limited data on the age and sex breakdowns of persons dying from AIDS, overdose, trauma and suicide.

Sex

We made the following estimates of the sex breakdown. This was completed by using estimates of the proportion of tobacco users who were males in each of the 14 subregions. These had been calculated in each subregion from the smoking risk factor for the GBD project. Table 13.12 shows the estimates for proportion of deaths among males in each of the subregions. Table 13.13 shows the resulting numbers of deaths attributable to illicit drugs by subregion and sex. Table 13.14 provides estimates of the total DALYs attributable to illicit drugs by subregion and sex.

Age groups

Similarly to the sex breakdowns, the age breakdowns are based on limited data concerning the age distribution of persons dying from the

Table 13.13 Number of deaths attributed to illicit drug use, by subregion and sex

Subregion	*Sum of four causes of mortalty*[a]	*All-cause mortality*[b]
AFR-D		
Males	5207	16951
Females	643	2095
AFR-E		
Males	1156	6877
Females	237	1409
AMR-A		
Males	9233	22599
Females	7255	17757
AMR-B		
Males	6369	11608
Females	3740	6817
AMR-D		
Males	930	1816
Females	362	706
EMR-B		
Males	4562	4260
Females	805	752
EMR-D		
Males	23633	8537
Females	5188	1874
EUR-A		
Males	6649	9707
Females	4620	6746
EUR-B		
Males	2814	3708
Females	1583	2086
EUR-C		
Males	11756	8460
Females	31251	2249
SEAR-B		
Males	12795	5460
Females	533	228
SEAR-D		
Males	39922	9150
Females	8177	1874
WPR-A		
Males	2887	9222
Females	217	694
WPR-B		
Males	23431	26655
Females	6229	7086
World		
Males	149425	145012
Females	44633	52371

[a] Sum of the median estimates of the following four causes: AIDS, opioid overdose, suicide via opioids and trauma.

[b] Median estimates of all-cause mortality derived from SMR analyses and pooled CMRs.

Table 13.14 Burden of disease (000s of DALYs) attributed to illicit drug use in the subregions, by sex

Subregion	*Males*	*Females*
AFR-D	428	134
AFR-E	460	150
AMR-A	594	185
AMR-B	586	13
AMR-D	193	59
EMR-B	376	64
EMR-D	478	109
EUR-A	599	172
EUR-B	130	39
EUR-C	340	102
SEAR-B	95	22
SEAR-D	703	116
WPR-A	173	76
WPR-B	256	55
World	5402	1477

four main causes of death considered here. It was assumed that no persons aged <15 years and no persons aged >54 years were problematic users of illicit drugs; the 15–54-year age group has typically been found to contain the vast majority of problematic illicit drug users (Anthony and Helzer 1991).

It was assumed that two-thirds of overdose deaths occurred among the 25–44-year age group, with on-sixth each occurring in the 15–24- and 45–54-year age groups, in line with previous research suggesting the bulk of deaths occur in such a pattern (Hall et al. 1999c, 2000c). Deaths related to illicit drug use that were due to trauma were assumed to be disproportionately distributed among younger age groups, with smaller proportions among those aged 35–54 years (see Table 13.15). With the knowledge that AIDS-related deaths usually occur years after contracting HIV, we assigned the deaths the same age distribution as the total HIV/AIDS deaths in each subregion.

6. Discussion

6.1 Methodological caveats

A number of potential sources of inaccuracy need be acknowledged in our estimates. First, there are a number of factors that determine the proportion of cases of any particular cause of mortality that are attribut-

Table 13.15 Estimated distribution of causes of death attributed to illicit drug use, by age

	Age (years)					
Cause of death	*<15*	*15–24*	*25–34*	*35–44*	*45–54*	*>54*
Overdose	0	1/6	1/3	1/3	1/6	0
Suicide	0	1/3	1/3	1/6	1/6	0
Trauma	0	1/3	1/3	1/6	1/6	0
Total[a]	0	0.13	0.34	0.29	0.24	0

[a] Weighted average of the three causes.

able to harmful illicit drug use. These include environmental, cultural or behavioural factors, which are also likely to interact. The risk of contracting HIV/AIDS through injecting drug use, for example, is greatly reduced by providing sterile injecting equipment, and the use of such equipment will be affected by attitudes towards needle sharing. In countries with needle and syringe programmes the attributable fraction of HIV due to injecting drug use is likely to be relatively small compared to similar countries that do not have needle and syringe programmes, even assuming a similar prevalence of other risk factors for HIV transmission in both countries (Hurley et al. 1997). An illustration of this was provided by Lurie and Drucker (1997) who assessed the impact of needle and syringe programmes on the development of the HIV epidemic in Australia and the United States. They estimated that between 10 000 and 25 000 HIV infections in the United States could have been prevented if needle exchange programmes were implemented as they had been in Australia.

Second, the availability of drug treatment programmes, medical care and a host of other factors that differ between otherwise similar countries may produce differences in the attributable fractions in those countries. For example, van Ameijden et al. (1999) compared mortality in cohorts of heroin users in Amsterdam and Baltimore. They found Amsterdam drug users had an overdose/suicide mortality rate approximately twice that of their counterparts in Baltimore. This was despite the fact that a greater proportion of users in Amsterdam were in methadone maintenance treatment, which has been shown to reduce the risk of overdose. This finding contrasts with a previous finding of the same research group, which attributed lower mortality rates from infectious disease in Amsterdam to drug users having better access to primary health care in Amsterdam than in New York (Mientjes et al. 1992). The variation in mortality rates that result from differences in the complex interactions

of determinants of mortality makes comparisons of cohort studies conducted in different countries problematic.

Third, attributable fractions can only be reliably calculated in countries that collect accurate mortality data. These data are most likely to be found in developed countries vs developing countries (Muller 1982). Caution is required in applying fractions estimated in developed countries to developing ones.

6.2 Limitations of cohort studies

As mentioned earlier, the cohort studies of problem illicit drug users have a number of major limitations when used for the purpose of estimating the contribution of problem illicit drug use to the global burden of disease.

Treatment populations

The vast majority of cohort studies of mortality among illicit drug users have included people seeking treatment for problem drug use. A small number of studies have compared mortality of drug users while in and out of treatment (Capelhorn et al. 1996; Fugelstad et al. 1995; Gronbladh et al. 1990; Sanchez-Carbonell and Seus 2000; Zanis and Woody 1998). These studies have found that the relative risk of death while in treatment varied from less than 0.2 to 0.8, with a mean of approximately 0.4. These studies can be used to produce more accurate estimates of mortality by applying different mortality rates for proportions of users who are and are not in treatment.

Illicit drugs used

Injecting opioid users are over-represented in the cohort studies by comparison with cocaine and other stimulant users. The few studies that report separate data on problem illicit opioid and stimulant use suggest that mortality is higher among opioid users (Engstrom et al. 1991), probably because of the greater risk of fatal overdose from opioids. Stimulant users, by contrast, may be at higher risk of contracting diseases from bloodborne viruses such as hepatitis B and C from sharing injection equipment because they inject at a high frequency when bingeing on their drug of choice (Bux et al. 1995; Chaisson et al. 1989). They may also be more likely to engage in sex for drugs (Chiasson et al. 1991; Darke et al. 1995; Edlin et al. 1994).

Extrapolation across subregions

Applying direct measures of mortality from cohort studies in developed countries to populations in developing countries is problematic. Developing countries generally have all-cause mortality rates that are significantly higher than the developed countries in which most cohort studies are conducted (WHO 2001). Thus it may be that there is less of a dif-

ferential in mortality rates between the general population and problem drug users in developing countries. Applying the relative risks from developed countries to developing ones may therefore overestimate the mortality attributable to illicit drug use in the latter.

HIV/AIDS

The majority of cohort studies identified for this project were conducted before the HIV/AIDS epidemic began to affect mortality among injecting drug users. Changes in the epidemiology of HIV and other drug-related conditions since these studies were conducted may reduce the validity of using prevalence or incidence data to predict mortality. In some developed nations, for example, the incidence of HIV and AIDS may be declining but the large number of prevalent cases may still produce a high burden of mortality (CDC 2001; UNAIDS 2001). Conversely, countries that are still in the early stages of the epidemic may have a high incidence of HIV/AIDS cases that have not yet begun to contribute to mortality. In either case mortality estimates based on the number of incident cases may be inaccurate, for very different reasons. However, in the absence of better data on this issue, UNAIDS data on the number of AIDS deaths in the year 2000 have been used to estimate mortality, since there are significant problems with making estimates from incident cases.

Despite the limitations of cohort studies, they present the most robust epidemiological evidence on the relationship between problem illicit drug use and mortality. When quantifying the burden of mortality attributed to illicit drugs, therefore, cohort studies provide the best basis on which to estimate risk and identify mortality outcomes.

In terms of estimating risk, as we have described above, the use of annual mortality rates derived from studies of illicit drug users in developed countries may underestimate mortality in developing countries. By contrast, applying SMRs from the cohort studies to developed societies may overestimate the mortality rate of drug users in developing countries (which already have higher mortality rates in general), since it is probable that the higher the general mortality rate in any given country, the lower will be the SMR for illicit drug users in that country (Muller 1982). We have used UNAIDS estimates in the current study.

Other data sources can be used to validate estimates of risk derived from cohort studies in some developed societies. In populations where reliable mortality data are collected the attributable fraction of mortality due to a range of conditions that may be related to problem illicit drug use can be calculated. These fractions can then be applied to estimates of mortality in other countries using the WHO all-cause mortality database. The main weaknesses of this method are: that it does not take into account variations in the prevalence of the risk factor; it assumes homogeneity between the population from which the attributable fraction was derived and the population to which it is being applied;

and that cohort studies are representative of the population at risk. It is nonetheless an independent method of calculating mortality that can be used to check estimates of mortality derived by multiplying measures of risk by prevalence estimates.

6.3 Summary and conclusions

In summary, in this work we have attempted to estimate the extent of global mortality and morbidity attributable to illicit drug use in 2000. This required estimates of both the global prevalence of problem illicit drug use and the mortality attributable to it. Ideally, such data would include estimation of the numbers of problem, or dependent users, as these are the individuals at greatest risk for drug-related harm. Currently, there are poor data on the prevalence of problem illicit use in many developing countries and there is no consensus on the definition and operationalization of "problem drug use". UNDCP data, supplemented by other sources, provide the best available data, although these have major limitations.

Similarly, there is a considerable amount of data from cohort studies of individuals identified as problem illicit drug users that can be used to estimate the relative risks of death among this group. Unfortunately, most of these studies have been conducted in developed countries on problem opioid users and many were conducted prior to the AIDS pandemic among injecting drug users. A priority for future research must be to assess mortality among illicit drug users in developing countries and, in particular, to examine the extent to which the findings of studies conducted in developed countries are applicable to developing countries.

Furthermore, much of this research has been based on samples of people entering treatment for drug-related problems. Further work is needed to quantify mortality among problem drug users who are *not* in treatment. Nonetheless, it is clear from the existing cohort studies that problem illicit drug users have a greatly elevated risk of premature death from drug overdose, HIV/AIDS, suicide and trauma.

By comparison with the extensive literature on the health effects of tobacco and alcohol use, very little is known about the adverse health effects of illicit drug use. This situation reflects at least three factors: the recent history of illicit drug use in many countries; the low prevalence of its use in the population compared to alcohol and tobacco; and the fact that its illicit nature encourages users to conceal or deny their drug use, hence inhibiting research on its effects on mortality and morbidity.

In 2000, the median of the two methods of estimating the number of global deaths attributed to illicit drugs was 195 721. Estimates produced by both methods had wide uncertainty intervals around them (113 494 for sum of four causes; and 101 751 to 322 456 for all-cause estimates). When morbidity attributable to illicit drug use is added to the estimated mortality this risk factor accounts for 0.8% of global DALYs. The distribution of DALYs between subregions varied, reflecting variations in

drug use and death rates, with considerable uncertainty about the applicability of mortality data derived in developed countries to mortality among illicit drug users in developing countries.

Nonetheless, the current estimates suggest that illicit drug use is a significant cause of premature mortality among young adults in the developed and developing world. Our estimate is certainly an underestimate of total disease burden because: (i) there are deficits in data on mortality attributable to the use of some illicit drugs (most notably cannabis and the newer synthetic drugs like MDMA); (ii) there are differences across subregions in the quality of data available on the causes of mortality that *were* included in the current estimates; and (iii) there is an absence of data that would permit estimates of some other causes of mortality and morbidity attributable to illicit drug use, such as hepatitis B and C and violence.

Given public concerns about the effects of illicit drug use, and indications of a worldwide increase in the production and use of illicit drugs, better research must be done on the adverse health effects of their use. With that in mind we include a list of research priorities.

6.4 Research priorities

- There is a need for more rigorously designed prospective studies of mortality and morbidity among problem illicit drug users in developing countries, especially ones which have high rates of HIV/AIDS infection among injecting drug users, and which have experienced substantial increases in rates of such problem drug use in recent years.
- There is also a need for cohort studies of injecting drug users who are *not* in treatment, since there is evidence that rates of mortality are higher among this group.
- There is a need for better studies of morbidity attributable to non-fatal overdoses, bloodborne viral diseases such as hepatitis B and C, suicide attempts, and trauma among problem illicit drug users in both developed and developing countries.
- There is a global need for better surveillance systems to collect data on key drug-related consequences.
- There is a need for better prevalence estimates of problem illicit drug use in developed and developing countries, especially where there are indications of increased illicit drug use because of proximity to source countries.
- Other specific data collection needs include the following:
  - — improving the comparability and quality of data on the prevalence of drug use across regions;

— improving methods for accurately estimating the prevalence of, and burden associated with, illicit drug use among non-institutionalized populations;

— improving estimates of the number of "problem drug users" *per se*, to take into account polydrug use using consistent definitions of "problem drug use";

— obtaining mortality and morbidity data from developing regions from which more accurate methods to estimate the burden of illicit drug use can be derived for those regions;

— improving data on drug use among psychiatric patients, and data on psychiatric morbidity among drug users;

— developing more comparable and accurate mortality data by improving the consistency of procedures used to identify and register drug-related deaths across subregions, for both developed and developing subregions;

— systematic monitoring of mortality by drug type to provide data on mortality associated with non-opioid drugs, especially in the context of developing countries and countries with high HIV prevalence; and

— measurement of the coverage and nature of services in place to reduce burden, especially those aimed at reducing the transmission of bloodborne viruses.

7. Projections of illicit drug-related harm

There are a number of indications that rates of illicit drug use and illicit drug-related harm have risen in the past decade. First, developed countries with reasonable mortality data have shown steady increases in drug-related deaths, especially drug overdose deaths, over the past decade, for example, in Australia (Hall et al. 1999a); Spain (de la Fuente et al. 1995); and the United Kingdom (Hall et al. 2000c). Estimates derived from back projections of both overdose deaths and treatment entry in Australia have shown an increase in estimated number of dependent opioid users (Hall et al. 2000a, 2000b). Second, illicit drug use and drug-related harm such as overdoses and HIV/AIDS have been reported in an increasing number of countries where it was previously rare, such as in eastern Europe, the former Soviet Union, Asia and Africa (UNAIDS 2001; UNDCP 2000; UNODCCP 2000).

Despite indications that drug-related harm is increasing, it is difficult to predict future patterns of illicit drug use and drug-related harm for the following reasons.

First, there is a lack of good time series data on the prevalence of illicit drug use and data on drug-related harm may not be comparable over

time, even in countries with good mortality data systems, because of changes in classification systems (such as successive iterations of the ICD classification system), and because of improvements (and deterioration) in the quality of data that are collected.

Second, although the general trend has been for drug-related deaths to *increase* during the 1990s, there have also been a number of countries in which drug-related deaths have fallen sharply, often after various policy initiatives have been introduced. In France (Lepere et al. 2001) and Switzerland, for example, drug-related deaths have fallen markedly in the later half of the 1990s, probably in response to a marked expansion of opioid substitution treatment in both countries. In the past two years, Australia has also seen a substantial drop in opioid overdose deaths, after a steep rise from the early 1990s until 1999 (Degenhardt 2002). In this case, some of the early decrease may have been attributable to expanded treatment and educational initiatives to reduce overdose among opioid users. Since the beginning of 2001, the major driver of reduced overdose deaths in Australia has been a substantial drop in the availability of heroin (Weatherburn et al. 2001).

Third, there have been changes in the scale of illicit drug production and in the choice of drugs for illicit manufacture. For example, restrictions on opioid production in Afghanistan in the late 1990s may have reduced heroin supply to Europe, while the supply of cocaine and amphetamine type stimulants (ATS) increased (UNODCCP 2000). The net effect of these changes on drug-related harm is difficult to predict because the effects of ATS on mortality are less well studied and understood than that of opioids (Darke et al. 2000a).

7.1 Options for projection

A conservative option may be to assume that: (i) the current global problem will remain at about the current level, but that (ii) the distribution of burden will shift between developed and developing countries with declines in drug-related deaths in developed countries (resulting from expanded opioid substitution treatment) being offset by increases in drug-related deaths in developing societies.

A less conservative option would be to assume that in developed countries, rates of opioid use and opioid-related deaths will continue to rise, but at a slower rate (e.g. 50%) than that observed during the 1990s, because of expanded treatment availability. In developing countries, the rate of increase could be projected to follow the same pattern and magnitude as that observed in developed countries like Australia, which have reasonable time series data on trends in opioid-related deaths over the period when illicit opioid use was first introduced and spread (Hall et al. 2000b).

Substantial uncertainty intervals would need to be placed around these estimates to indicate our ignorance of underlying trends and to empha-

size the need to undertake better epidemiological research to improve our estimates of the global burden of disease attributable to illicit drug use.

Notes

1 See preface for an explanation of this term.

2 MDMA: 3,4 methylenedioxymethamphetamine, a synthetic drug that is used as a stimulant.

3 Amphetamine-type stimulant (ATS): one of a class of sympathomimetic amines with powerful stimulant action on the central nervous system.

4 Cannabis: a generic term for psychoactive preparations (e.g. marijuana, hashish and hash oil) derived from the *cannabis sativa* plant.

5 Cocaine: an alkaloid central nervous system stimulant drug that is derived from the coca plant.

6 Heroin: an opioid drug derived from the opium poppy.

7 Opioids: generic term applied to derivatives from the opium poppy, their synthetic analogues, and compounds synthesized in the body, which act upon the opioid receptors in the brain. They have the capacity to relieve pain and produce a sense of euphoria, as well as cause stupor, coma and respiratory depression.

8 Drug overdose: the use of any drug in such an amount that acute adverse physical or mental effects are produced. Overdose in this chapter refers to cases in which death is the outcome.

9 DSM-IV: American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, 4th edition.

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