Estimating non-AIDS mortality among injecting drug users: A review of cohort studies

Louisa Degenhardt
National Drug and Alcohol Research Centre
University of New South Wales
Sydney NSW 2052

Acknowledgement: *The work involved in the collection of much of the mortality data from cohort studies was completed in collaboration with Professor Wayne Hall, Dr Michael Lynskey and Mr Matthew Warner Smith as part of the Comparative Risk Assessment for Illicit Drugs in the 2000 Global Burden of Disease study (Degenhardt, Hall, Lynskey, & Warner-Smith, 2004).*

Table of Contents

1. Introduction

The injection of illicit drugs appears to be increasing in many parts of the world (ABCI, 2000; EMCDDA, 2000; Frischer, Green, & Goldberg, 1994; UNODCCP, 2000). Estimating mortality related to illicit drug use is difficult, for reasons that are discussed below (Thorley, Oppenheimer, & Stimson, 1977). Nonetheless, efforts must be made to estimate the mortality rate among injecting drug users (IDU) because it clearly has a substantial adverse effect on the health and well-being of those who engage in it, producing substantial loss of life (Hulse, English, Milne, & Holman, 1999).

One of the most widely discussed causes of death among IDU is that of deaths related to HIV/AIDS. In 2003, it was estimated that almost 38 million persons were living with HIV, and that HIV cause almost 3 million deaths (UNAIDS, 2004). Injecting drug use is thought to be the primary factor underlying the spread of HIV in Eastern Europe, Central Asia, Latin America, and for at least 10% of cases in high income countries (UNAIDS, 2004).

Given the importance of IDU in the transmission of HIV in many areas of the world and the consequent burden that this implies for many communities around the globe, it is important to make valid estimates of AIDS mortality among this group (Garnett, Grassly, Boerma, & Ghys, 2004; Ghys et al., 2004; Stover, 2004; Walker et al., 2004). In order to make such estimates, it is important to have good estimates of the prevalence of injecting drug use and of HIV among this group. It is also important, however, to take account of the fact that IDU have all-cause mortality rates that far exceed that of the general population: previous work has suggested that this group is approximately 13 times more likely to die than their peers (English et al., 1995; Hulse et al., 1999).

HIV is not the only cause of premature death among this group (see below). It is important, then to take account of this increased non-AIDS mortality to ensure valid estimates of AIDS mortality are produced. The current review was completed in order to provide estimates of the additional background mortality among IDU compared to the general population.

1.1. Defining injecting drug use

Injecting drug use may involve the use of a variety of drugs that are prohibited by international law. These drugs most commonly include: amphetamine-type stimulants,[1] cocaine,[2] heroin[3] and other opioids[4]. It is necessary to define clearly what is and is not included in this risk factor. This paper will focus on the mortality related to the use of amphetamines, cocaine and opioids. Other substances that may be injected (such as benzodiazepines and MDMA[5]

---

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

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

[3] Heroin: an opioid drug derived from the opium poppy.

[4] 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.

[5] *MDMA: 3,4 methylenedioxymethamphetamine, a synthetic drug that is used as a stimulant.*

(or "ecstasy") have not been included in the present analysis as there is currently insufficient research information to quantify the health risks associated with these drugs, and in the case of emerging drugs such as MDMA, are rarely injected even by those who regularly inject the drug (White et al., in press). 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.

The mortality risks of illicit drug use increase with increasing frequency and quantity of consumption (Fischer, Kendall, Rehm, & Room, 1997). 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, Darke, Lynskey, & Hall, 2001) and of contracting blood borne viral diseases (Ross, Wodak, Loxley, Stowe, & Drury, 1992). As will become clear, most of the evidence on mortality among IDU comes from cohort studies conducted with persons in treatment for their drug use, most of whom will have had such patterns of use.

1.2. Mechanisms of death among

Injecting drug use is an important risk factor for the transmission of blood-borne viral infections (BBVI), the most commonly cited of which are the human immunodeficiency virus (HIV) and hepatitis C virus. Good evidence suggests increased incidence HIV contracted as a result of sharing of injecting equipment by injecting drug users (IDU) in developing societies (Beyrer et al., 2003; Garten et al., 2004; Reid & Costigan, 2002; Stimson, 1993).

The major illicit drugs are known to have adverse effects in overdose that can be fatal. Opioids, for example, cause respiratory depression that can cause death, and this is especially likely to occur if opioids are used in combination with other CNS depressant drugs such as alcohol and benzodiazepines (Darke & Zador, 1996; Warner-Smith et al., 2001). Stimulant drugs, such as cocaine and amphetamines, can cause fatal cardiac arrhythmias and strokes (Goldfrank & 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, hepatitis B and hepatitis C infections are efficiently spread by contaminated blood in shared injection equipment (Donoghoe & Wodak, 1998; MacDonald, Crofts, & Kaldor, 1996).

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, Joyce, & Mulder, 1998, 1999). Opioid-dependent persons in treatment report very high rates of attempted suicide (Darke & Ross, 2000).

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 & Hall, 1995; Darke & Ross, 1997; Gossop, Marsden, & Stewart, 1998). Opioids are also intoxicating substances that adversely affect driving, although they are much less commonly found in persons killed in fatal car crashes. Nonetheless, there is evidence to suggest that drug driving occurs frequently among IDU (Darke, Kelly, & Ross, 2004)

2. Method

2.1. 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.

2.1.1. 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) (literature published prior to 1993).

2.1.2. 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. *Cohort, or case-control*
3. *Mortality*
4. *Morbidity*
5. *Suicide, or accidents, or HIV , or assault*

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

2.1.3. Inclusion criteria

The following inclusion criteria were used:

- *cohort studies on the use of opioids, cocaine or amphetamines and mortality;*
- *studies in which standardized mortality ratios (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.*

2.1.4. Exclusion criteria

The following exclusion criteria were used:

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

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

2.2. Mortality documented among IDU

Several studies have calculated standardized mortality ratios 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). 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 have who 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.

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

2.2.1. 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. This means that it is necessary to supplement such data with indirectly derived estimates from cohort studies that have examined the rate of deaths due to AIDS among injecting drug users.

2.2.2. Other causes

Overdose

"Overdose" refers to two ICD-10 classifications of cause of death: (a) accidental or intentional fatal poisoning caused by specific drugs, and (b) 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. Studies examining this issue are listed in the Appendix.

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 & Lenaars, 1989; Domino & Takahashi, 1991). Studies examining this issue are listed in the Appendix.

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. Studies examining this issue are listed in the Appendix.

3. Results

3.1. All cause mortality

In determining the mortality rate among IDU, it is necessary to rely on the results of cohort studies that have conducted long-term follow-up of individuals identified as such. English et al. (English et al., 1995) identified a total of 13 such studies investigating mortality associated with illicit opioid use up to 1993 (Barr, Antes, Ottenberg, & Rosen, 1984; Bewley, Ben-Arie, & James, 1968; Cherubin, McCusker, Baden, Kavaler, & Amsel, 1972; Engstrom, Adamson, Allebeck, & Rydberg, 1991; Frischer et al., 1993; Ghodse, Sheehan, Taylor, & Edwards, 1985; Haastrup & Jepson, 1984; Hser, Anglin, & Powers, 1993; Joe, Lehman, & Simpson, 1982; Perucci, Davoli, Rapiti, Abeni, & Forastiere, 1991; Thorsen & Haarstrup, 1975; Vaillant, 1973).

A further 16 studies were identified that have been published since 1993, excluding studies which used previously published data (Capelhorn, Dalton, Halder, Petrenas, & Nisbet, 1996; Eskild, Magnus, Samuelson, Sohlberg, & Kittelsen, 1993; Friedman, Williams, Singh, & Frieden, 1996; Fugelstad, Annell, Rajs, & Agren, 1997; Fugelstad, Rajs, Bottiger, & de Verdier, 1995; Galli & Musicco, 1994; Goedert et al., 1995; Goldstein & Herrera, 1995; Keenan, Dorman, & O'Connor, 1993; McAnulty, Tesselaar, & Fleming, 1995; Oppenheimer, Tobutt, Taylor, & Andrew, 1994; Orti et al., 1996; Robertson, Ronald, Raab, Ross, & Parpia, 1994; van Haastrecht et al., 1996; Wahren, Brandt, & Allebeck, 1997; Zaccarelli et al., 1994).

3.1.1. All-cause mortality rate derived from all cohort studies

English et al. (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 & Jepson, 1984; Hser et al., 1993; Joe et al., 1982; Perucci et al., 1991; Thorsen & Haarstrup, 1975; Vaillant, 1973). Through extensive literature searches a further 17 studies were identified, excluding studies which used previously published data (Bargagli, Sperati, Davoli, Forastiere, & Perucci, 2001; Capelhorn et al., 1996; Eskild et al., 1993; Friedman et al., 1996; Fugelstad et al., 1997; Fugelstad et al., 1995; Galli & Musicco, 1994; Goedert, Fung, Felton, Battjes, & Engels, 2001; Goedert et al., 1995; Goldstein & 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 summarised in Table 2 were all identified studies that followed up cohorts of problem or injecting drug users.

A total of 170 434 participants were included, which involved a total of 1 160 380 person-years of observation, during which time 14 718 deaths were recorded. The weighted average all-cause mortality rate was 1.2684% per annum, with a 95%CI of the average rate estimated as between 0.9298% per annum and 1.6069% per annum.

3.1.2. All-cause mortality rate derived only from cohort studies reporting on AIDS deaths

The studies in Table 1 were studies that reported on the number of AIDS deaths in their cohorts, and also reported all cause mortality. In these studies, a total of 61 704 participants were included, which involved a total of 329 246 person-years of observation, during which time 7 267 deaths were recorded. The weighted average all-cause mortality rate was 2.2207% per annum, with a 95%CI of the average rate estimated as between 1.9059% per annum and 2.5084% per annum.

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, firstly, 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 2 studies). Secondly, with one exception (McAnulty et al., 1995) these studies drew their samples from people receiving treatment for drug-related problems. Thirdly, the majority 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.

3.1.3. AIDS mortality rate

Weighted average rates of mortality due to AIDS were estimated from the cohort studies included in this chapter. The weighted crude mortality rate from these studies was 0.6782% per annum. In order to make a range of estimates around this average rate, the standard error of the rate was calculated and 95% confidence intervals (95%CI) constructed around the rate and used as the lower (0.4888% per annum) and upper (0.8677% per annum) ranges of the mortality rates due to AIDS.

There was wide variation in the annual mortality rate attributed to HIV/AIDS. The wide variation in the importance of HIV/AIDS as a cause of mortality among injecting drug users is likely to reflect regional variations in the prevalence of HIV among injecting drug users and in access to preventive measures, such as sterile injecting equipment and opioid substitution treatment for heroin users. These issues are discussed below.

Table 1: Included outcome studies that examined rates of mortality due to AIDS among problematic drug users

Authors	Year	Site	*n*	Population studied	Follow-up *(years)*	Lost	Person-years	Drug used	Deaths	Crude mortality rate per 100
(Musto & Ramos, 1981)	*1981*	*New Haven, USA*	*91*	*Treatment*	*52*	*-*	*4 732*	*Morphine*	*0*	*0*
(Benson & Holmberg, 1984)	*1984*	*Gothenburg, Sweden*	*618*	*Drug using conscripts, rehab. & psych. patients, drug using welfare recipients*	*10*	*-*	*5 789*	*Cannabis, solvents, LSD, stimulants (opioids rare)*	*0*	*0*
(Bucknall & Robertson, 1986)	*1986*	*Edinburgh, Scotland*	*184*	*Heroin users attending a general practise*	*4*	*4*	*720*	*Heroin*	*0*	*0*
(Tunving, 1988)	*1988*	*Lund, Sweden*	*524*	*Persons in treatment for opioid, amphetamine, and both opioid and amphetamine*	*10*	*0*	*5 240*	*Opioids, amphetamines*	*0*	*0*
(Gronbladh, Ohund, & Gunne, 1990)	*1990*	*Sweden*	*368*	*Methadone and untreated*	*5–11*	*-*	*3 283*	*Heroin*	*0*	*0*
(Mientjes, van Ameijden, van den Hoek, & Coutinho, 1992)	*1992*	*Amsterdam, Netherlands*	*390*	*Methadone treatment*	*2.2*	*-*	*810*	*Opioids*	*3*	*0.37*
(Dukes, Robinson, & Robinson, 1992)	*1992*	*Wellington, New Zealand*	*997*	*Treatment*	*9.1*	*-*	*9 073*	*Injecting opioid users*	*0*	*0*
(Hser et al., 1993)	*1993*	*California, USA*	*581*	*Males in compulsory treatment*	*24*	*35*	*13 064*	*"Narcotics"*	*0*	*0*
(Eskild et al., 1993)	*1993*	*Oslo, Norway*	*1 009*	*HIV test centre clients*	*3.67*	*-*	*3 706*	*IDU*	*4*	*0.11*
(Oppenheimer et al., 1994)	*1994*	*London, England*	*128*	*Treatment*	*22*	*7*	*2 816*	*Heroin*	*0*	*0*
(Robertson et al., 1994)	*1994*	*Edinburgh, Scotland*	*203*	*GP*	*10*	*17*	*2 030*	*IDU*	*16*	*0.79*
(Zaccarelli et al.,	*1994*	*Rome, Italy*	*2 431*	*Treatment*	*3.2*	*-*	*7 872*	*IDU*	*89*	*1.13*

Authors	Year	Site	*n*	Population studied	Follow-up *(years)*	Lost	Person-years	Drug used	Deaths	Crude mortality rate per 100
1994)										
(Galli & Musicco, 1994)	*1994*	*Milan, Italy*	*2 432*	*Treatment*	*6.7*	*-*	*16 415*	*Methadone (94%)*	*144*	*0.88*
(Goedert et al., 1995)	*1995*	*Italy*	*4 962*	*Treatment*	*3.88*	*-*	*21 130*		*150*	*0.71*
(McAnulty et al., 1995)	*1995*	*Portland, USA*	*1 769*	*Not in treatment*	*1.78*	*-*	*3 149*	*IDU*	*0*	*0*
(Fugelstad et al., 1995)	*1995*	*Stockholm, Sweden*	*472*	*HIV+*	*3.8*	*-*	*1 793*		*7*	*0.39*
(Friedman et al., 1996)	*1996*	*New York, USA*	*858*	*Drug and alcohol dependants on welfare*	*8*	*-*	*6 864*	*Drugs and alcohol*	*84*	*1.23*
(van Haastrecht et al., 1996)	*1996*	*Amsterdam, Netherlands*	*632*	*HIV: methadone and STD clinic patients*	*4.4*	*18*	*2 781*		*12*	*0.43*
(Orti et al., 1996)	*1996*	*Catalonia, Spain*	*15 711*	*Hospital emergency departments and treatment*	*2.8*	*-*	*43 717*	*Opioids*	*472*	*1.08*
(Capelhorn et al., 1996)	*1996*	*Sydney, Australia*	*296*	*Methadone*	*13*	*39*	*3 484*	*Heroin*	*0*	*0*
(Fugelstad et al., 1997)	*1997*	*Stockholm, Sweden*	*1 640*	*Drug-related hospitalization*	*8*	*0*	*13 120*	*14% heroin; 35% amphetamine; 23% polydrug*	*18*	*0.14*
(Davoli et al., 1997)	*1997*	*Rome, Italy*	*3 955*	*Treatment*	*4*	*198*	*15 820*	*IDU*	*168*	*1.06*
(Zanis & Woody, 1998)	*1998*	*Philadelphia, USA*	*507*	*Methadone*	*1*	*5*	*507*	*Heroin*	*0*	*0*
(van Ameijden et al., 1999)	*1999*	*Amsterdam, Netherlands; Baltimore, USA*	*2 809*	*Treatment shelters and community agencies*	*6–9*	*-*	*15 107*	*IDU*	*0*	*0*
(Sanchez-Carbonell & Seus, 2000)	*2000*	*Catalonia, Spain*	*135*	*Treatment*	*10.5*	*-*	*1 418*	*Heroin*	*21*	*1.48*
(Goedert et al., 2001)	*2001*	*USA*	*6570*	*Methadone*	*6.7*	*-*	*44019*	*Heroin*	*330*	*0.75*
(Bargagli et al.,	*2001*	*Rome, Italy*	*11 432*	*Methadone, other treatment*	*18*	*39*	*80 787*	*Heroin*	*715*	*0.89*

Authors	**Year**	**Site**	***n***	**Population studied**	**Follow-up** *(years)*	**Lost**	**Person-years**	**Drug used**	**Deaths**	**Crude mortality rate per 100**
2001)										

– *no data*

n.a. not applicable

null statistically non-significant

Table 2: Included outcome studies that examined rates of all-cause mortality among problematic drug users

Authors	Year	Site	*n*	Population studied	Follow-up years	Lost	Person-years	Drug	No. of deaths	Crude mortality rate (per 100)
(Bewley et al., 1968)	*1968*	*United Kingdom*	*1 272*	*Heroin addicts known to Home Office*	*1.8*	*-*	*2 291*	*Heroin*	*85*	*2.7*
(Bewley & Ben-Arie, 1968)	*1968*	*London, England*	*100*	*Hospitalized male heroin addicts*	*2.25*	*-*	*225*	*Heroin*	*13*	*5.7*
(Vaillant, 1973)	*1973*	*New York, USA*	*100*	*Treatment, male*	*20*	*17*	*1 660*	*Narcotics*	*23*	*1.15*
(Concool, Smith, & Stimmel, 1979)	*1979*	*New York, USA*	*1 156*	*Treatment (84% methadone)*	*7*	*102*	*8 092*	*Heroin*	*45*	*0.56*
(Musto & Ramos, 1981)	*1981*	*New Haven, USA*	*91*	*Treatment*	*52*	*-*	*4 732*	*Morphine*	*40*	*0.84*
(Wille, 1981)	*1981*	*London, England*	*128*	*Treatment (Rx heroin)*	*10*	*-*	*1 280*	*Heroin*	*19*	*1.48*
(Joe et al., 1982)	*1982*	*34 treatment agencies in USA*	*3 324*	*Treatment*	*4*	*-*	*11 710*	*Opioids*	*179*	*1.52*
(Benson & Holmberg, 1984)	*1984*	*Gothenburg, Sweden*	*618*	*Drug using conscripts, rehab. & psych. patients, drug using welfare recipients*	*10*	*-*	*5 789*	*Cannabis, solvents, LSD, stimulants (opioids rare)*	*26*	*0.45*
(Haastrup & Jepson, 1984)	*1984*	*Copenhagen, Denmark*	*300*	*Treatment*	*7*	*19*	*1 967*	*Morphine*	*47*	*2.40*
(Bucknall & Robertson, 1986)	*1986*	*Edinburgh, Scotland*	*184*	*Heroin users attending a general practise*	*4*	*4*	*720*	*Heroin*	*7*	*0.972*
(Joe & Simpson, 1987)	*1987*	*18 treatment agencies in USA*	*697*	*Treatment*	*6*	*142*	*3 330*	*Opioids*	*52*	*1.56*
(Haastrup & Jepson, 1988)	*1988*	*Copenhagen, Denmark*	*300*	*First time entrants to treatment*	*11*	*30*	*2 970*	*Opioids*	*78*	*2.63*
(Tunving, 1988)	*1988*	*Lund, Sweden*	*524*	*Treatment: opioid, amphetamine, and both opioid and amphetamine*	*10*	*0*	*5 240*	*Opioids, amphetamines*	*62*	*1.18*

Authors	Year	Site	*n*	Population studied	Follow-up years	Lost	Person-years	Drug	No. of deaths	Crude mortality rate (per 100)
(Segest, Mygind, & Bay, 1990)	*1990*	*Copenhagen, Denmark*	*169*	*Methadone*	*8*	*-*	*1 352*	*Opioids*	*39*	*2.88*
(Gronbladh et al., 1990)	*1990*	*Sweden*	*368*	*Methadone and untreated*	*5–11*	*-*	*3 283*	*Heroin*	*96*	*2.92*
(Engstrom et al., 1991)	*1991*	*Stockholm, Sweden*	*1 630*	*Drug-related hospitalization*	*12*		*19 560*	*41% cocaine/amphetamine; 12% heroin; 16% polydrug; 31% other*	*446*	*2.3*
(Mientjes et al., 1992)	*1992*	*Amsterdam, Netherlands*	*390*	*Methadone*	*2.2*	*-*	*810*	*Opioids*	*29*	*3.58*
(Dukes et al., 1992)	*1992*	*Wellington, New Zealand*	*997*	*Treatment*	*9.1*	*-*	*9 073*	*Injecting opioid users*	*67*	*0.74*
(Keenan et al., 1993)	*1993*	*Ireland*	*45*	*Pregnant on methadone*	*6*	*-*	*270*	*Opioids*	*7*	*2.59*
(Hser et al., 1993)	*1993*	*California, USA*	*581*	*Males in compulsary treatment*	*24*	*35*	*13 064*	*"Narcotics"*	*161*	*1.23*
(Eskild et al., 1993)	*1993*	*Oslo, Norway*	*1 009*	*HIV test centre clients*	*3.67*	*-*	*3 706*	*IDU*	*87*	*2.35*
(Oppenheimer et al., 1994)	*1994*	*London, England*	*128*	*Treatment*	*22*	*7*	*2 816*	*Heroin*	*41*	*1.53*
(Robertson et al., 1994)	*1994*	*Edinburgh, Scotland*	*203*	*GP*	*10*	*17*	*2 030*	*IDU*	*40*	*1.97*
(Zaccarelli et al., 1994)	*1994*	*Rome, Italy*	*2 431*	*Treatment*	*3.2*	*-*	*7 872*	*IDU*	*181*	*2.30*
(Galli & Musicco, 1994)	*1994*	*Milan, Italy*	*2 432*	*Treatment*	*6.7*	*-*	*16 415*	*Methadone (94%)*	*413*	*2.52*
(Goedert et al., 1995)	*1995*	*Italy*	*4 962*	*Treatment*	*3.88*	*-*	*21 130*		*332*	*1.57*
(McAnulty et al., 1995)	*1995*	*Portland, USA*	*1 769*	*Not in treatment*	*1.78*	*-*	*3 149*	*IDU*		*1.05*
(Goldstein & Herrera, 1995)	*1995*	*Alburquerque, USA*	*1 013*	*Methadone*	*22*	*243*	*22 286 (16 940 excl. lost)*		*348*	*1.56 (2.05)*
(Fugelstad et al.,	*1995*	*Stockholm, Sweden*	*472*	*HIV+*	*3.8*	*-*	*1 793*		*69*	*3.85*

Authors	Year	Site	*n*	Population studied	Follow-up years	Lost	Person-years	Drug	No. of deaths	Crude mortality rate (per 100)
1995)										
(Friedman et al., 1996)	*1996*	*New York, USA*	*858*	*Drug and alcohol dependents on welfare*	*8*	*-*	*6 864*	*Drugs and alcohol*	*183*	*2.67*
(van Haastrecht et al., 1996)	*1996*	*Amsterdam, Netherlands*	*632*	*HIV: methadone and STD clinic patients*	*4.4*	*18*	*2 781*		*72*	*2.59*
(Orti et al., 1996)	*1996*	*Catalonia, Spain*	*15 711*	*Hospital ER and treatment*	*2.8*	*-*	*43 717*	*Opioids*	*1315*	*3.01*
(Capelhorn et al., 1996)	*1996*	*Sydney, Australia*	*296*	*Methadone*	*13*	*39*	*3 484*	*Heroin*	*42*	*1.21*
(Wahren et al., 1997)	*1997*	*Stockholm, Sweden*	*1 494*	*Hospitalized for drug dependence*	*22*	*-*	*32 868*	*57% stimulants; 39% opioids*	*521*	*1.59*
(Fugelstad et al., 1997)	*1997*	*Stockholm, Sweden*	*1 640*	*Drug related hospitalization*	*8*	*0*	*13 120*	*14% heroin; 35% amphetamine; 23% polydrug*	*214*	*1.63*
(Davoli et al., 1997)	*1997*	*Rome, Italy*	*3 955*	*Treatment*	*4*	*198*	*15 820*	*IDU*	*387*	*2.45*
(Ghodse, Oyefeso, & Kilpatrick, 1998)	*1998*	*United Kingdom*	*92 802*	*"Drug addicts" notified to Home Office*	*27*	*-*	*687 673*	*65% opioids*	*5310*	*0.77*
(Zanis & Woody, 1998)	*1998*	*Philadelphia, USA*	*507*	*Methadone*	*1*	*5*	*507*	*Heroin*	*13*	*2.56*
(van Ameijden et al., 1999)	*1999*	*Amsterdam, Netherlands; Baltimore, USA*	*2 809*	*Treatment shelters and community agencies*	*6–9*	*-*	*15 107*	*IDU*	*264*	*1.75*
(Sanchez-Carbonell & Seus, 2000)	*2000*	*Catalonia, Spain*	*135*	*Treatment*	*10.5*	*-*	*1 418*	*Heroin*	*41*	*3.4*
(Goedert et al., 2001)	*2001*	*USA*	*6570*	*Methadone*	*6.7*	*-*	*44019*	*Heroin*	*1351*	*3.07*
(Bargagli et al., 2001)	*2001*	*Rome, Italy*	*11 432*	*Methadone, other treatment*	*18*	*39*	*80 787*	*Heroin*	*1734*	*2.15*

– *no data*

n.a. *not applicable*

null *statistically non-significant*

3.1.4. Non-AIDS mortality rate among IDU

It is important to remember that the majority of the cohort studies were conducted in the pre-AIDS era. This is important in the present circumstances because injecting drug users with HIV/AIDS are more likely to die from other causes of mortality than those who are not HIV+ (Zaccarelli et al., 1994). This introduces an additional source of uncertainty in the estimates. Three estimates have therefore been produced in this study for the rate of mortality other than AIDS:

1. *A rate that is derived from all cohort studies reporting all-cause mortality, and reduced by the rate of AIDS mortality derived from studies reporting AIDS deaths;*
2. *A rate that is derived only from cohort studies that reported all-cause mortality and AIDS deaths;*
3. *And a median estimate, which is the midpoint of these two estimates.*

It is important to consider that studies not reporting AIDS mortality were conducted either before the AIDS era, or presumably were drawn form population where the HIV prevalence among IDU was low. This means that the estimate (1) will produce a lower estimate of mortality than (2) (van Haastrecht, Mientjes, van den Hoek, & Coutinho, 1994; Zaccarelli et al., 1994), which probably contained samples that typically had a higher prevalence of HIV among its participants. The median estimate (3) allows for some "averaging" of this difference.

The median non-AIDS mortality rate was estimated to be 1.07% per 100 person years (see Table 3). The lower limit of this estimate (using the methods described above) was 0.59% per annum, and the upper limit was 1.54% per annum.

Table 3: Estimates of mortality per 100 person years amongIDU

	All-cause mortality	*AIDS mortality*[4]	**Non-AIDS mortality**
Lower range[1]	*1.2684*	*0.6782*	**0.5902**
Upper range[2]	*2.2207*	*0.6782*	**1.5425**
Median estimate[3]	*1.7446*	*0.6782*	**1.0664**

1. Lower estimate: weighted crude mortality rate obtained when all cohort studies were included

2. Upper estimate: weighted crude mortality rate obtained when only cohorts reporting numbers of AIDS deaths included

3.Median estimate: median of these two estimates

4. Estimate produced from cohort studies in Table 1.

4. Discussion

The current paper derived weighted mortality rates for IDU based upon cohort studies that comprised a total of 170 434 participants involving 1 160 380 person-years of observation, during which time 14 718 deaths were recorded.

The weighted crude AIDS mortality rate from studies that reported on the number of AIDS deaths was approximately 0.68% per annum. The median non-AIDS mortality rate was estimated to be 1.07% per 100 person years. The lower limit of this estimate was 0.59% per annum, and the upper limit was 1.54% per annum. Hence, it is estimated that among IDU, non-AIDS deaths outnumber AIDS deaths by around 1.6 : 1.

The above estimate of non-AIDS mortality among IDU will be incorporated in the UNAIDS/WHO recommended methods (Garnett et al., 2004) and will be applied in future HIV and AIDS estimates in countries. Especially in countries where IDU make up a substantial proportion of people living with HIV, the addition of this adjustment in the estimation of mortality is expected to result in a more accurate estimate of mortality due to AIDS. This kind of improvement is important as the estimates of HIV prevalence and AIDS mortality form the basis for important planning processes in countries, including the estimation of the number of people in need of antiretroviral treatment (WHO & UNAIDS, 2004).

4.1. Methodological caveats

4.1.1. Sources of inaccuracy or variation

A number of potential sources of inaccuracy need be acknowledged in these estimates.

First, environmental, cultural or behavioural factors, which are also likely to interact, may affect mortality rates. 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 (NSP) 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, Jolley, & Kaldor, 1997). An illustration of this was provided by Lurie and Drucker (1997) who assessed the impact of NSP 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 affect mortality rates. 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.

4.1.2. Limitations of cohort studies

Cohort studies of drug users have a number of limitations that are listed below.

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 & Seus, 2000; Zanis & Woody, 1998). These studies have found that the relative risk of death while in treatment varied from less than 0.2 to 0.8 compared to those out of treatment, 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 blood-borne 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, Lamb, & Iguchi, 1995; Chaisson, Osmond, Brodie, Sande, & Moss, 1989). They may also be more likely to engage in sex for drugs (Chiasson et al., 1991; Darke, Ross, Cohen, Hando, & Hall, 1995; Edlin, Irwin, Faraque, McCoy, & Word, 1994). Due to limited data, however, mortality has been calculated using data pooled from users of all drugs.

Extrapolation across regions

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 differential in mortality rates between the general population and problem drug users in developing countries. Applying the RR from developed countries to developing ones may therefore overestimate the mortality attributable to illicit drug use in the latter. For this reason, the crude mortality rate has been presented here.

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.

Conclusions – cohort studies

Despite the limitations of cohort studies, they are the most robust form of epidemiological evidence on the relationship between problem illicit drug use and mortality. Cohort studies therefore provide the best basis on which to estimate risk and identify mortality outcomes.

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 standardized mortality ratios 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). In the present case, mortality rates have been used, so it is likely that there may be a slight underestimate of IDU-related mortality in developing countries as a result.

4.2. Research priorities

1. *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.*
2. *There is also a need for cohort studies of IDU who are not in treatment, since there is evidence to suggest that rates of mortality are higher among this group.*
3. *There is a global need for better surveillance systems to collect data on mortality.*
4. *Other specific data collection needs include the following:*
    a. *improve the consistency of procedures used to identify and register drug-related deaths;*
    b. *systematic monitoring of mortality by drug type, especially in developing countries and countries with high HIV prevalence; and*
    c. *measurement of the coverage and nature of services in place to reduce mortality.*

4.3. Conclusions

There is a considerable amount of data from cohort studies of illicit drug users that can be used to estimate the rate or mortality 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 IDU. 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. Deaths due to AIDS form only part of that increased risk.

References

ABCI. (2000). Australian Illicit Drug Report 1998-1999. Canberra: Australian Bureau of Criminal Intelligence.

Bargagli, A. M., Sperati, A., Davoli, M., Forastiere, F., & Perucci, C. A. (2001). Mortality among problem drug users in Rome: An 18-year follow-up study, 1980-97. Addiction, 96(10), 1455-1463.

Barr, H. L., Antes, D., Ottenberg, D. J., & Rosen, A. (1984). Mortality of treated alcoholics and drug addicts: the benefits of abstinence. Journal of Studies on Alcohol, 45, 440-452.

Beautrais, A. L., Joyce, P. R., & Mulder, R. T. (1998). Psychiatric illness in a New Zealand sample of young people making serious suicide attempts. New Zealand Medical Journal, 111(1060), 44-48.

Beautrais, A. L., Joyce, P. R., & Mulder, R. T. (1999). Cannabis abuse and serious suicide attempts. Addiction, 94(8), 1155-1164.

Benson, G., & Holmberg, M. B. (1984). Drug-related mortality in young people. Acta Psychiatrica Scandanavia, 70, 525-534.

Bewley, T. B., Ben-Arie, O., & James, I. P. (1968). Morbidity and mortality from heroin dependence. 1. Survey of heroin addicts known to home office. British Medical Journal, 1, 725-726.

Bewley, T. H., & Ben-Arie, O. (1968). Morbidity and mortality from heroin dependence. 2. Study of 100 consecutive patients. British Medical Journal, 1, 727-730.

Beyrer, C., Jittiwutikarn, J., Teokul, W., Razak, M. H., Suriyanon, V., Srirak, N., Vongchuk, T., Tovanabutra, S., Sripaipan, T., & Celentano, D. D. (2003). Drug use, increasing incarceration rates, and prison-associated HIV risks in Thailand. AIDS & Behavior, 7(2), 153-161.

Bucknall, A. B. V., & Robertson, J. R. (1986). Deaths of heroin users in a general practise population. Journal of the Royal College of General Practitioners, 36, 120-122.

Bux, D., Lamb, R., & Iguchi, M. (1995). Cocaine use and HIV risk behaviour in methadone maintenance patients. Drug and Alcohol Dependence, 37, 29-35.

Capelhorn, J. R. M., Dalton, M. S. Y. N., Halder, F., Petrenas, A.-M., & Nisbet, J. G. (1996). Methadone maintenance and addicts' risk of fatal heroin overdose. Substance Use and Misuse, 31, 177-196.

CDC. (2001). Centre for Disease Control, National Centre for HIV, STD and TB Prevention. Surveillance reports. Retrieved, 2001, from the World Wide Web: http://www.cdc.gov/hiv/stats/hasr1201.htm

Chaisson, R. E., Osmond, D., Brodie, B., Sande, M. A., & Moss, A. R. (1989). Cocaine use and HIV infection in intravenous drug users in San Francisco. JAMA, 261(4), 561-565.

Cherubin, C., McCusker, J., Baden, M., Kavaler, F., & Amsel, Z. (1972). The epidemiology of death in narcotic addicts. American Journal of Epidemiology, 96, 11-22.

Chiasson, M., Stoneburner, R., Hildebrandt, D., Ewing, W., Telzak, E., & Jaffe, H. (1991). Heterosexual transmission of HIV-1 associated with the use of smokable freebase cocaine (crack). AIDS, 5, 1121-1126.

Concool, B., Smith, H., & Stimmel, B. (1979). Mortality rates of persons entering metadone maintenance: a seven-year study. American Journal of Drug and Alcohol Abuse, 6(3), 345-353.

Darke, S., & Hall, W. (1995). Levels and correlates of polydrug use among heroin users and regular amphetamine users. Drug and Alcohol Dependence, 39, 231-235.

Darke, S., Kelly, E., & Ross, J. (2004). Drug driving among injecting drug users in Sydney, Australia: prevalence, risk factors and risk perceptions. Addiction, 99, 177-185.

Darke, S., & Ross, J. (1997). Polydrug dependence and psychiatric comorbidity among heroin injectors. Drug & Alcohol Dependence, 48(2), 135-141.

Darke, S., & Ross, J. (2000). The relationship between suicide and overdose among methadone maintenance patients. NDARC Technical Report No. 100. Sydneyt: National Drug and Alcohol Research Centre, University of NSW.

Darke, S., Ross, J., Cohen, J., Hando, J., & Hall, W. (1995). Injecting and sexual risk-taking behaviour among regular amphetamine users. AIDS Care, 7(1), 19-26.

Darke, S., & Zador, D. (1996). Fatal heroin "overdose": A review. Addiction, 91(12), 1765-1772.

Dart, J. K. (1995). The use of epidemiological techniques to assess risk: the epidemiology of mocrobial keratitis. Eye, 9, 679-683.

Davoli, M., Perucci, C., Rapiti, E., Bargagli, A. M., D'Ippoliti, D., Forastiere, F., & Abeni, D. (1997). A persistent rise in mortality among injecting drug users in Rome, 1980 through 1992. American Journal of Public Health, 87, 851-854.

Degenhardt, L., Hall, W., Lynskey, M., & Warner-Smith, M. (2004). Chapter 13. Illicit drug use. In M. Ezzati & A. D. Lopez & A. Rodgers & R. Murray (Eds.), Comparative Quantification of Health Risks: Global and Regional Burden of Disease Attributable to Selected Major Risk Factors (2nd edition ed., Vol. 2, pp. 1109-1176). Geneva: World Health Organization.

Domino, G., & Lenaars, A. A. (1989). Attitudes toward suicide: A comparison of Canadian and U.S. college students. Suicide and Life-Threatening Behaviour, 19, 345-359.

Domino, G., & Takahashi, Y. (1991). Attitudes towards suicide in Japanese and American medical students. Suicide and Life-Threatening Behaviour, 21, 345-359.

Donoghoe, M., & Wodak, A. (1998). Health and social consequences of injecting drug use. In G. Stimson & D. Des Jarlais & A. Ball (Eds.), Drug injecting and HIV infection: Global dimensions and local responses (pp. 42-57). London: UCL Press.

Dukes, P. D., Robinson, G. M., & Robinson, B. J. (1992). Mortality of intravenous drug users: attenders of the Wellington Drug Clinic, 1972-89. Drug and Alcohol Review, 11, 197-201.

Edlin, B., Irwin, K., Faraque, S., McCoy, C., & Word, C. (1994). Intersecting epidmics - crack cocaine use and HIV infection among inner city young adults. Multcenter Crack Cocaine and HIV Infection Study Team. New England Journal of Medicine, 331, 1422-1427.

EMCDDA. (2000). Annual report on the state of the drugs problem in the European Union. Lisbon: European Monitoring Centre for Drugs and Drug Addiction.

English, D., Holman, C., Milne, E., Winter, M., Hulse, G., Codde, S., Corti, B., Dawes, V., De Klerk, N., Knuiman, M., Kurinczuk, J., Lewin, G., & Ryan, G. (1995). The quantification of drug caused morbidity and mortality in Australia, 1995. Canberra: Commonwealth Department of Human Services and Health.

Engstrom, A., Adamson, C., Allebeck, P., & Rydberg, U. (1991). Mortality in patients with substance abuse: a follow-up in Stockholm County, 1973-1984. The International Journal of the Addictions, 26, 91-106.

Eskild, A., Magnus, P., Samuelson, S. O., Sohlberg, C., & Kittelsen, P. (1993). Differences in mortality rates and causes of death between HIV positive and HIV negative intravenous drug users. International Journal of Epidemiology, 22, 315-319.

Feldman, U. (1993). Epidemiologic assessment of risks of adverse reactions associated with intermittent exposure. Biometrics, 49, 419-428.

Fischer, B., Kendall, P., Rehm, J., & Room, R. (1997). Charting WHO-goals for licit and illicit drugs for the year 2000: are we "on track"? Public Health, 111, 271-275.

Freeman, J. (1996). Quantitative epidemiology. Infection control and hospital epidemiolgy, 17, 249-255.

Friedman, L. N., Williams, M. T., Singh, T. P., & Frieden, T. R. (1996). Tuberculosis, AIDS, and death among substance abusers on welfare in New York city. The New England Journal of Medicine, 334, 828-833.

Frischer, M., Bloor, M., Goldberg, D., Clark, J., Green, S., & McKeganey, N. (1993). Mortality among injecting drug users: a critical reappraisal. Journal of Epidemiology and Community Medicine, 47, 59-63.

Frischer, M., Green, S. T., & Goldberg, D. (1994). Substance abuse related mortality: a worldwide review. Austria: United Nations International Drug Control Programme.

Fugelstad, A., Annell, A., Rajs, J., & Agren, G. (1997). Mortality and causes and manner of death among drug addicts in Stockholm during the period 1981-1992. Acta Psychiatrica Scandanavia, 96, 169-175.

Fugelstad, A., Rajs, J., Bottiger, M., & de Verdier, M. G. (1995). Mortality among HIV-infected inravenous drug addicts in relation to methadone treatment. Addiction, 90, 711-716.

Galli, M., & Musicco, M. (1994). Mortality of intravenous drug users living in Milan, Italy: role of HIV-1 infection. AIDS, 8, 1457-1463.

Garnett, G., Grassly, N. C., Boerma, J. T., & Ghys, P. D. (2004). Maximizing the global use of HIV surveillance data through the development and sharing of analytical tools. Sexually Transmitted Infections, 80 (supplement 1), i1-i4.

Garten, R. J., Lai, S., Zhang, J., Liu, W., Chen, J., Vlahov, D., & Yu, X. F. (2004). Rapid transmission of hepatitis C virus among young injecting heroin users in Southern China. International Journal of Epidemiology, 33(1), 182-188.

Ghodse, A. H., Oyefeso, A., & Kilpatrick, B. (1998). Mortality of drug addicts in the United Kingdom 1967-1993. International Journal of Epidemiology, 27, 473-478.

Ghodse, A. H., Sheehan, M., Taylor, C., & Edwards, G. (1985). Deaths of drug addicts in the United Kingdom 1967-81. British Medical Journal, 290, 425-428.

Ghys, P. D., Brown, T., Grassly, N. C., Garnett, G., Stanecki, K. A., Stover, J., & Walker, N. (2004). The UNAIDS Estimation and Projection Package: a software package to estimate and project national HIV epidemics. Sexually Transmitted Infections, 80 (supplement 1), i5-i9.

Goedert, J., Fung, M., Felton, S., Battjes, R., & Engels, E. (2001). Cause-specific mortality associated with HIV and HTLV-II infections among injecting drug users in the USA. AIDS, 15, 1295-1302.

Goedert, J. J., Pizza, G., Gritti, F. M., Costigliola, P., Boschini, A., Bini, A., Lazzari, C., & Palareti, A. (1995). Mortality among drug users in the AIDS era. International Journal of Epidemiology, 24, 1204-1210.

Goldfrank, L., & Hoffman, R. (1993). The cardiovascular effects of cocaine - update. In H. Sorer (Ed.), Acute cocaine intoxication: Current methods of treatment. Research Monograph No. 123 (pp. 70-109). Rockville, MD: National Institute on Drug Abuse.

Goldstein, A., & Herrera, J. (1995). Heroin addicts and methadone treatment in Alburquerque: A 22 year follow-up. Drug and Alcohol Dependence, 40, 139-150.

Gossop, M., Marsden, J., & Stewart, D. (1998). NTORS at one year. London: Department of Health.

Gronbladh, L., Ohund, L. S., & Gunne, L. M. (1990). Mortality in heroin addiction: impact of methadone treatment. Acta Psychiatrica Scandanavia, 82, 223-227.

Haastrup, S., & Jepson, P. W. (1984). Seven year follow-up of 300 young drug abusers. Acta Psychiatrica Scandanavia, 70, 503-509.

Haastrup, S., & Jepson, P. W. (1988). Eleven year follow-up of 300 young opioid addicts. Acta Psychiatrica Scandinavica, 77, 22-26.

Hser, Y., Anglin, D., & Powers, K. (1993). A 24-year follow-up of Californian narcotics addicts. Archives of General Psychiatry, 50, 577-584.

Hulse, G., English, D., Milne, E., & Holman, C. (1999). The quantification of mortality resulting form the regular use of illicit opiates. Addiction, 94(2), 221-230.

Hurley, S., Jolley, D., & Kaldor, J. (1997). Effectiveness of needle-exchange programmes for prevention of HIV infection. Lancet, 349(9068), 1797-1800.

Joe, G. W., Lehman, W., & Simpson, D. D. (1982). Addicts death rates during a four-year posttreatment follow-up. American Journal of Public Health, 72(7), 703-709.

Joe, G. W., & Simpson, D. D. (1987). Mortality rates among opioid addicts in a longitudinal study. American Journal of Public Health, 77(3), 347-348.

Keenan, E., Dorman, A., & O'Connor, J. (1993). Six year follow-up of forty five pregnant opiate addicts. Irish Journal of Medical Science, 162, 444-445.

Lurie, P., & Drucker, E. (1997). An opportunity lost: HIV infections associated with a lack of needle-exchange programmes in the USA. The Lancet, 349, 604-608.

MacDonald, M., Crofts, N., & Kaldor, J. (1996). Transmission of hepatitis C virus: rates, routes, and cofactors. Epidemiologic Reviews, 18(2), 137-148.

McAnulty, J. M., Tesselaar, H., & Fleming, D. W. (1995). Mortality among injection drug users identified as "out of treatment". American Journal of Public Health, 85, 119-120.

Mientjes, G. H., van Ameijden, E. K., van den Hoek, A. J. A. R., & Coutinho, R. A. (1992). Increasing morbidity without rise in non-AIDS mortality among HIV-infected intravenous drug users in Amsterdam. AIDS, 6, 207-212.

Muller, M. (1982). The Health of Nations: A North-South investigation. London: Faber and Faber.

Musto, D. F., & Ramos, M. R. (1981). A follow-up study of the New Haven morphine maintenance clinic of 1920. The New England Journal of Medicine, 304(18), 1071-1077.

Oppenheimer, E., Tobutt, C., Taylor, C., & Andrew, T. (1994). Death and survival in a cohort of heroin addicts from London clinics: a 22-year follow-up study. Addiction, 89, 1299-1308.

Orti, R. M., Domingo-Salvany, A., Munoz, A., MacFarlane, D., Suelves, J. M., & Anto, J. M. (1996). Mortality trends in a cohort of opiate addicts, Catalonia, Spain. International Journal of Epidemiology, 25, 545-553.

Perucci, C. A., Davoli, M., Rapiti, E., Abeni, D. D., & Forastiere, F. (1991). Mortality of intravenous drug users in Rome: a cohort study. American Journal of Public Health, 81, 1307-1310.

Platt, J. J. (1997). Cocaine Addiction: Theory, Research, and Treatment. Cambridge, Massachusetts: Harvard University Press.

Reid, G., & Costigan, G. (2002). Revisiting "The Hidden Epidemic": A situation assessment of drug use in Asia in the context of HIV/AIDS. Melbourne: The MacFarlane Burnet Institute for Medical Research and Public Health.

Robertson, J. R., Ronald, P. M., Raab, G. M., Ross, A. J., & Parpia, T. (1994). Deaths, HIV infection, abstinence and other outcomes in a cohort of injecting drug users followed up for 10 years. British Medical Journal, 309, 369-372.

Ross, M., Wodak, A., Loxley, W., Stowe, A., & Drury, M. (1992). Staying negative. Summary of the results of the Australian National AIDS and Injecting Drug Use Study. Sydney: ANAIDUS.

Sanchez-Carbonell, X., & Seus, L. (2000). Ten-year survival analysis of a cohort of heroin addicts in Catalonia: the EMETYST project. Addiction, 95, 941-948.

Segest, E., Mygind, O., & Bay, H. (1990). The influence of prolonged stable methadone maintenance treatment on mortality and employment: an 8-year follow-up. The International Journal of the Addictions, 25, 53-63.

Stimson. (1993). The global diffusion of injecting drug use: Implications for human immunodeficiency virus infection. Bulletin on Narcotics, 45(1), 3-17.

Stover, J. (2004). Projecting the demographic consequences of adult HIV prevalence trends: the Spectrum Projection Package. Sexually Transmitted Infections, 80 (supplement 1), i14-i18.

Thorley, A., Oppenheimer, E., & Stimson, G. V. (1977). Clinic attendance and opiate prescription status of heroin addicts over a six-year period. British Journal of Psychiatry, 130, 565-569.

Thorsen, K., & Haarstrup, S. (1975). Follow-up of 97 young non-psychotic male opiate abusers: relationship between achieving abstinence, age and duration of abuse. Acta Psychiatrica Scandanavia, 51, 289-296.

Tunving, K. (1988). Fatal outcome in drug addiction. Acta Psychiatrica Scandanavia, 77, 551-566.

UNAIDS. (2001). Joint United Nations Programme on HIV/AIDS. Retrieved, 2001, from the World Wide Web: http://www.unaids.org/

UNAIDS. (2004). 2004 Report on the global AIDS epidemic. 4th global report. Geneva: UNAIDS/04.16E.

UNODCCP. (2000). World Drug Report 2000. Oxford: Oxford University Press.

Vaillant, G. E. (1973). A 20-year follow-up of New York narcotic addicts. Archives of General Psychiatry, 29, 237-241.

van Ameijden, E. J. C., Krol, A., Vlahov, D., Flynn, C., van Haastrecht, H. J. A., & Coutinho, R. A. (1999). Pre-AIDS mortality and morbidity among injection drug users in Amsterdam and Baltimore: an ecological comparison. Substance Use and Misuse, 34, 845-865.

van Haastrecht, H. J., Mientjes, G. H., van den Hoek, A. J., & Coutinho, R. A. (1994). Death from suicide and overdose among drug injectors after disclosure of first HIV test result. Aids, 8(12), 1721-1725.

van Haastrecht, H. J. A., van Ameijden, E. J. C., van den Hoek, J. A. R., Mientjes, G. H. C., Bax, J. S., & Coutinho, R. A. (1996). Predictors of mortality in the Amsterdam cohort of human immunodeficiency virus (HIV)-positive and HIV-negative drug users. American Journal of Epidemiology, 143(4), 380-391.

Wahren, C. A., Brandt, L., & Allebeck, P. (1997). Has mortality in drug addicts increased? A comparison between two hospitalized cohorts in Stockholm. International Journal of Epidemiology, 26, 1219-1226.

Walker, N., Stover, J., Stanecki, K., Zaniewski, A. E., Grassly, N. C., Garcia-Calleja, J. M., & Ghys, P. D. (2004). The workbook approach to making estimates and projecting future scenarios of HIV/AIDS in countries with low-level and concentrated epidemics. Sexually Transmitted Infections, 80 (supplement 1), i10-i13.

Warner-Smith, M., Darke, S., Lynskey, M., & Hall, W. (2001). Heroin overdose: causes and consequences. Addiction, 96(8), 1113-1125.

White, B., Day, C., Degenhardt, L., Kinner, S., Fry, C., Bruno, R., & Johnston, J. (in press). Prevalence of injecting drug use and associated risk behaviour among regular ecstasy users. Journal of Urban Health.

WHO. (2001). World Health Organization All-Cause Mortality Database. Retrieved, 2001, from the World Wide Web: http://www-nt.who.int/whosis/statistics/menu.cfm

WHO, & UNAIDS. (2004). "3 by 5" progress report December 2004. Geneva: World Health Organization.

Wille, R. (1981). Ten-year follow-up of a representative sample of London heroin addicts: clinic attendance, abstinence and mortality. British Journal of Addiction, 76, 259-266.

Zaccarelli, M., Gattari, P., Rezza, G., Conti, S., Spizzichino, L., Vlahov, D., Ippolito, G., Lelli, V., & Valenzi, C. (1994). Impact of HIV infection on non-AIDS mortality among Italian injecting drug users. AIDS, 8, 345-350.

Zanis, D. A., & Woody, G. E. (1998). One-year mortality rates following methadone treatment discharge. Drug and Alcohol Dependence, 52, 257-260.

Appendix – cohort studies reporting on other causes of mortality among IDU

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 some countries, particularly the United States, which have a higher prevalence of problematic cocaine use, cocaine-related overdoses may account for a considerable proportion of all drug-related overdoses. In the United States, for example, the Drug Abuse Warning Network indicated that in 1999, 28% of single-drug overdoses were due to cocaine (NIDA, 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.

A weighted average mortality rate was calculated from cohort studies (see Table 3 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

The crude mortality rate due to suicide from cohort studies was also estimated (see Table 4 for included studies). The weighted average rate of death per annum due to suicide was 0.24% per annum (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 due to trauma, since cohort studies report different sorts of trauma, and different numbers of causes. Indirect estimates of the number of road traffic accident deaths due to illicit drug use were made using pooled estimates of the rates of death due to trauma from cohort studies (Table 5). Rates of traumatic injury were also high in this group: the weighted average rate of death per annum due to trauma was 0.35% per annum. 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).

Table 3: Outcome studies that examined rates of mortality due to overdose among problematic drug users

Authors	Year	Site	n	Population studied	Follow-up years	Lost	Person-years	Drug	Crude mortality rate per 1000
(Vaillant, 1973)	1973	New York, USA	100	Treatment, male	20 years	17	1 660	Narcotics	0.35
(Concool et al., 1979)	1979	New York, USA	1 156	Treatment (84% methadone)	7 years	102	8 092	Heroin	0.07
(Musto & Ramos, 1981)	1981	New Haven, USA	91	Treatment	52 years	-	4 732	Morphine	0
(Wille, 1981)	1981	London, England	128	Treatment (heroin)	10 years	-	1 280	Heroin	0.86
(Joe et al., 1982)	1982	34 treatment agencies in USA	3 324	Treatment	4 years	-	11 710	Opioids	0.59
(Benson & Holmberg, 1984)	1984	Gothenburg, Sweden	618	Drug using conscripts, rehab. & psych. patients, drug using welfare recipients	10 years	-	5 789	Cannabis, solvents, LSD, stimulants (opioids rare)	0.05 (poisoning)
(Haastrup & Jepson, 1984)	1984	Copenhagen, Denmark	300	Treatment	7 years	19	1 967	Morphine	1.37
(Bucknall & Robertson, 1986)	1986	Edinburgh, Scotland	184	Heroin users attending a general practice	4 years	4	720	Heroin	0.55
(Joe & Simpson, 1987)	1987	18 treatment agencies in USA	697	Treatment	6 years	142	3 330	Opioids	0.75
(Tunving, 1988)	1988	Lund, Sweden	524	Treatment: opioid, amphetamine, and both opioid and amphetamine	10 years	0	5 240	Opioids, amphetamines	0.67
(Gronbladh et al., 1990)	1990	Sweden	368	Methadone and untreated	5–11 years	-	3 283	Heroin	1.74
(Perucci et al., 1991)	1991	Rome, Italy	4 200	Methadone	8 years	Nil	33 600	Opioids	0.24
(Engstrom et al., 1991)	1991	Stockholm, Sweden	1 630	Drug-related hospitalization	12 years	-	19 560	41% cocaine/amphetamine;12% heroin;	0.16

Authors	Year	Site	n	Population studied	Follow-up *years*	Lost	Person-years	Drug	Crude mortality rate per 1000
								16% polydrug; 31% other	
(Dukes et al., 1992)	*1992*	*Wellington, New Zealand*	*997*	*Treatment*	*9.1 years*	*-*	*9 073*	*Injecting opioid users*	*0.25*
(Hser et al., 1993)	*1993*	*California, USA*	*581*	*Males in compulsory treatment*	*24 years*	*35*	*13 064*	*"Narcotics"*	*0.40*
(Eskild et al., 1993)	*1993*	*Oslo, Norway*	*1 009*	*HIV test centre clients*	*3.67*	*-*	*3 706*	*IDU*	*1.56*
(Oppenheimer et al., 1994)	*1994*	*London, England*	*128*	*Treatment*	*22 years*	*7*	*2 816*	*Heroin*	*0.64*
(Robertson et al., 1994)	*1994*	*Edinburgh, Scotland*	*203*	*GP*	*10*	*17*	*2 030*	*IDU*	*0.74*
(Zaccarelli et al., 1994)	*1994*	*Rome, Italy*	*2 431*	*Treatment*	*3.2*	*-*	*7 872*	*IDU*	*0.55*
(Galli & Musicco, 1994)	*1994*	*Milan, Italy*	*2 432*	*Treatment*	*6.7*	*-*	*16 415*	*Methadone (94%)*	*0.92*
(Goedert et al., 1995)	*1995*	*Italy*	*4 962*	*Treatment*	*3.88*	*-*	*21 130*		*0.30*
(McAnulty et al., 1995)	*1995*	*Portland, USA*	*1 769*	*Not in treatment*	*1.78*	*-*	*3 149*	*IDU*	*0.41*
(Goldstein & Herrera, 1995)	*1995*	*Alburquerque, USA*	*1 013*	*Methadone*	*22*	*243*	*22 286 (16 940 excl. lost)*		*0.53 (0.70)*
(Fugelstad et al., 1995)	*1995*	*Stockholm, Sweden*	*472*	*HIV+*	*3.8*	*-*	*1 793*		*2.29*
(Friedman et al., 1996)	*1996*	*New York, USA*	*858*	*Drug and alcohol dependents on welfare*	*8*	*-*	*6 864*	*Drugs and alcohol*	*0.12*
(van Haastrecht et al., 1996)	*1996*	*Amsterdam, Netherlands*	*632*	*HIV: methadone and STD clinic patients*	*4.4*	*18*	*2 781*		*0.56*
(Orti et al., 1996)	*1996*	*Catalonia, Spain*	*15 711*	*Hospital ER and treatment*	*2.8*	*-*	*43 717*	*Opioids*	*1.09*
(Capelhorn et al.,	*1996*	*Sydney, Australia*	*296*	*Methadone*	*13*	*39*	*3 484*	*Heroin*	*0.66*

Authors	Year	Site	n	Population studied	Follow-up *years*	Lost	Person-years	Drug	Crude mortality rate per 1000
1996)									
(Wahren et al., 1997)	*1997*	*Stockholm, Sweden*	*1 494*	*Hospitalized for drug dependence*	*22*	*-*	*32 868*	*57% stimulants; 39% opioids*	*0.09*
(Fugelstad et al., 1997)	*1997*	*Stockholm, Sweden*	*1 640*	*Drug related hospitalization*	*8*	*Nil*	*13 120*	*14% heroin 35% amphetamine 23% polydrug*	*0.82*
(Davoli et al., 1997)	*1997*	*Rome, Italy*	*3 955*	*Treatment*	*4*	*198*	*15 820*	*IDU*	*0.58*
(Ghodse et al., 1998)	*1998*	*United Kingdom*	*92 802*	*"Drug addicts" notified to Home Office*	*27*	*-*	*687 673*	*65% opioids*	*0.38*
(Zanis & Woody, 1998)	*1998*	*Philadelphia, USA*	*507*	*Methadone*	*1*	*5*	*507*	*Heroin*	*1.18*
(van Ameijden et al., 1999)	*1999*	*Amsterdam, Netherlands; Baltimore, USA*	*2 809*	*Treatment shelters and community agencies*	*6–9*	*-*	*15 107*	*IDU*	*0.50*

– *no data*

n.a. *not applicable*

null *statistically non-significant*

Table 4: Outcome studies that examined rates of mortality due to suicide among problematic drug users

Authors	Year	Site	n	Population studied	Follow-up *(years)*	Lost	Person-years	Drug	Crude mortality rate **(per 1000)**
(Vaillant, 1973)	*1973*	*New York, USA*	*100*	*Treatment, male*	*20 years*	*17*	*1 660*	*Narcotics*	*0.20*
(Musto & Ramos, 1981)	*1981*	*New Haven, USA*	*91*	*Treatment*	*52 years*	*-*	*4 732*	*Morphine*	*0.02*
(Wille, 1981)	*1981*	*London, England*	*128*	*Treatment (Rx heroin)*	*10 years*	*-*	*1 280*	*Heroin*	*0.08*
(Benson & Holmberg, 1984)	*1984*	*Gothenburg, Sweden*	*618*	*Drug using conscripts, rehab. & psych. patients, drug using welfare recipients*	*10 years*	*-*	*5 789*	*Cannabis, solvents, LSD, stimulants (opioids rare)*	*0.29*
(Haastrup & Jepson, 1984)	*1984*	*Copenhagen, Denmark*	*300*	*Treatment*	*7 years*	*19*	*1 967*	*Morphine*	*0.61*
(Bucknall & Robertson, 1986)	*1986*	*Edinburgh, Scotland*	*184*	*Heroin users attending a general practise*	*4 years*	*4*	*720*	*Heroin*	*0.14*
(Tunving, 1988)	*1988*	*Lund, Sweden*	*524*	*Treatment: opioid, amphetamine, and both opioid and amphetamine*	*10 years*	*0*	*5 240*	*Opioids, amphetamines*	*0.33*
(Gronbladh et al., 1990)	*1990*	*Sweden*	*368*	*Methadone and untreated*	*5–11 years*	*-*	*3 283*	*Heroin*	*0.09*
(Perucci et al., 1991)	*1991*	*Rome, Italy*	*4200*	*Methadone*	*8 years*	*Nil*	*33 600*	*Opioids*	*0.03*
(Engstrom et al., 1991)	*1991*	*Stockholm, Sweden*	*1630*	*Drug-related hospitalization*	*12 years*	*-*	*19 560*	*41% cocaine/amphetamine; 12% heroin; 16% polydrug; 31% other*	*0.79*
(Dukes et al., 1992)	*1992*	*Wellington, New Zealand*	*997*	*Treatment*	*9.1 years*	*-*	*9 073*	*Injecting opioid*	*0.09*
(Eskild et al., 1993)	*1993*	*Oslo, Norway*	*1009*	*HIV test centre clients*	*3.67*	*-*	*3 706*	*IDU*	*0.24*

Authors	Year	Site	n	Population studied	Follow-up (years)	Lost	Person-years	Drug	Crude mortality rate (per 1000)
(Oppenheimer et al., 1994)	1994	London, England	128	Treatment	22 years	7	2 816	Heroin	0.07
(Zaccarelli et al., 1994)	1994	Rome, Italy	2431	Treatment	3.2	-	7 872	IDU	0.04
(Galli & Musicco, 1994)	1994	Milan, Italy	2432	Treatment	6.7	-	16 415	Methadone (94%)	0.06
(Goldstein & Herrera, 1995)	1995	Alburquerque, USA	1013	Methadone	22	243	22 286 (16 940 excl. lost)		0.05 (0.07)
(Fugelstad et al., 1995)	1995	Stockholm, Sweden	472	HIV+	3.8	-	1 793		0.50
(van Haastrecht et al., 1996)	1996	Amsterdam, Netherlands	632	HIV: methadone and STD clinic patients	4.4	18	2 781		0.36
(Capelhorn et al., 1996)	1996	Sydney, Australia	296	Methadone	13	39	3 484	Heroin	0.14
(Wahren et al., 1997)	1997	Stockholm, Sweden	1494	Hospitalized for drug dependence	22	-	32 868	57% stimulants; 39% opioids	0.30
(Fugelstad et al., 1997)	1997	Stockholm, Sweden	1640	Drug related hospitalization	8	Nil	13 120	14% heroin; 35% amphetamine; 23% polydrug	0.22
(Zanis & Woody, 1998)	1998	Philadelphia, USA	507	Methadone	1	5	507	Heroin	0
(van Ameijden et al., 1999)	1999	Amsterdam, Netherlands; Baltimore, USA	2809	Treatment shelters and community agencies	6–9	-	15 107	IDU	0.59

– no data

n.a. not applicable

null statistically non-significant

Table 5: Outcome studies that examined rates of mortality due to trauma among problematic drug users

Authors	Year	Site	*n*	Population studied	Follow-up *(years)*	Lost	Person-years	Drug	Crude mortality rate (per 100)
(Vaillant, 1973)	*1973*	*New York, USA*	*100*	*Treatment, male*	*20 years*	*17*	*1 660*	*Narcotics*	*0.1*
(Concool et al., 1979)	*1979*	*New York, USA*	*1 156*	*Treatment (84% methadone)*	*7 years*	*102*	*8 092*	*Heroin*	*0.26*
(Musto & Ramos, 1981)	*1981*	*New Haven, USA*	*91*	*Treatment*	*52 years*	*-*	*4 732*	*Morphine*	*0.08*
(Wille, 1981)	*1981*	*London, England*	*128*	*Treatment (Rx heroin)*	*10 years*	*-*	*1 280*	*Heroin*	*0.16*
(Joe et al., 1982)	*1982*	*34 treatment agencies in USA*	*3 324*	*Treatment*	*4 years*	*-*	*11 710*	*Opioids*	*0.38*
(Benson & Holmberg, 1984)	*1984*	*Gothenburg, Sweden*	*618*	*Drug using conscripts, rehab. & psych. patients, drug using welfare recipients*	*10 years*	*-*	*5 789*	*Cannabis, solvents, LSD, stimulants (opioids rare)*	*0.07*
(Bucknall & Robertson, 1986)	*1986*	*Edinburgh, Scotland*	*184*	*Heroin users attending a general practise*	*4 years*	*4*	*720*	*Heroin*	*0.14*
(Joe & Simpson, 1987)	*1987*	*18 treatment agencies in USA*	*697*	*Treatment*	*6 years*	*142*	*3 330*	*Opioids*	*0.45*
(Tunving, 1988)	*1988*	*Lund, Sweden*	*524*	*Treatment: opioid, amphetamine, and both opioid and amphetamine*	*10 years*	*0*	*5 240*	*Opioids, amphetamines*	*0.15*
(Gronbladh et al., 1990)	*1990*	*Sweden*	*368*	*Methadone and untreated*	*5–11 years*	*-*	*3 283*	*Heroin*	*0.06*
(Perucci et al., 1991)	*1991*	*Rome, Italy*	*4 200*	*Methadone*	*8 years*	*Nil*	*33 600*	*Opioids*	*0.15*
(Engstrom et al., 1991)	*1991*	*Stockholm, Sweden*	*1 630*	*Drug-related hospitalization*	*12 years*	*-*	*19 560*	*41% cocaine/amphetamine;12% heroin; 16% polydrug; 31% other*	*0.35*
(Dukes et al., 1992)	*1992*	*Wellington, New Zealand*	*997*	*Treatment*	*9.1 years*	*-*	*9 073*	*Injecting opioid users*	*0.12*
(Hser et al., 1993)	*1993*	*California, USA*	*581*	*Males in compulsary treatment*	*24 years*	*35*	*13 064*	*"Narcotics"*	*0.35 (incl. suicide)*
(Eskild et al., 1993)	*1993*	*Oslo, Norway*	*1 009*	*HIV test centre clients*	*3.67*	*-*	*3 706*	*IDU*	*0.22*

Authors	Year	Site	*n*	Population studied	Follow-up (years)	Lost	Person-years	Drug	Crude mortality rate (per 100)
(Oppenheimer et al., 1994)	1994	London, England	128	Treatment	22 years	7	2 816	Heroin	0.14
(Zaccarelli et al., 1994)	1994	Rome, Italy	2 431	Treatment	3.2	-	7 872	IDU	0.20
(Galli & Musicco, 1994)	1994	Milan, Italy	2 432	Treatment	6.7	-	16 415	Methadone (94%)	0.15
(Goedert et al., 1995)	1995	Italy	4 962	Treatment	3.88	-	21 130		1.8
(McAnulty et al., 1995)	1995	Portland, USA	1 769	Not in treatment	1.78	-	3 149	IDU	0.16
(Goldstein & Herrera, 1995)	1995	Albuquerque, USA	1 013	Methadone	22	243	22 286 (16 940 excl. lost)		0.27 (0.35)
(Fugelstad et al., 1995)	1995	Stockholm, Sweden	472	HIV+	3.8	-	1 793		0.11
(van Haastrecht et al., 1996)	1996	Amsterdam, Netherlands	632	HIV - methadone and STD clinic patients	4.4	18	2781		0.18
(Orti et al., 1996)	1996	Catalonia, Spain	15 711	Hospital ER and treatment	2.8	-	43 717	Opioids	0.37
(Capelhorn et al., 1996)	1996	Sydney, Australia	296	Methadone	13	39	3 484	Heroin	0.23
(Wahren et al., 1997)	1997	Stockholm, Sweden	1 494	Hospitalized for drug dependence	22	-	32 868	57% stimulants; 39% opioids	0.22
(Fugelstad et al., 1997)	1997	Stockholm, Sweden	1 640	Drug related hospitalization	8	Nil	13 120	14% heroin; 35% amphetamine; 23% polydrug	0.21
(Davoli et al., 1997)	1997	Rome, Italy	3 955	Treatment	4	198	15 820	IDU	0.25
(Zanis & Woody, 1998)	1998	Philadelphia, USA	507	Methadone	1	5	507	Heroin	0
(van Ameijden et al., 1999)	1999	Amsterdam, Netherlands; Baltimore, USA	2 809	Treatment shelters and community agencies	6–9	-	15 107	IDU	0.25

– *no data*

n.a. *not applicable*

null *statistically non-significant*