

**TRENDS IN OPIATE OVERDOSE
DEATHS IN AUSTRALIA 1979-1995**

Wayne Hall & Shane Darke

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Executive Summary

This report analysed data on trends in opioid overdose mortality between 1979 and 1995 inclusive. Its major aim was determine whether there had been a statistically significant increase in the rate of such overdose deaths. A secondary aim was to examine trends in the demographic characteristics of persons who died of opioid overdose, defined as deaths due to opioid dependence and accidental opiate poisoning.

The number of opioid overdose deaths rose from 70 in 1979 to 550 in 1995. 78% of the deaths were male. The rate (per million of the adult population aged 15 to 44) significantly increased from 10.7 to 67.0. The increase was more marked among males than females, increasing 6.8 times for males (from 15.3 in 1979 to 104.6 in 1995) and 4.7 times for females (from 5.9 in 1979 to 27.9 in 1995).

Overdose mortality rates varied between different jurisdictions. Among males, New South Wales consistently accounted for around a half of all overdose fatalities, and its rate was almost twice that in Victoria, and three times that in the remaining states. There was a similar pattern among females.

The average age at death increased from 24.2 years in 1979 to 30.1 years in 1995. The highest mortality rate was observed among those aged between 25 and 24 years. The rate of increase in overdose mortality was greater among men and women aged 35 to 44 years and 25 and 34 years than among those aged between 15 and 24 years. An analysis by birth cohort showed that 46% of male overdose deaths and 50% of female overdose deaths in the period occurred among those born between 1960 and 1969. Deaths among persons born between 1950 and 1959 accounted for 38% of male and 33% of female deaths.

Most of the increase in opioid overdose mortality between 1979 and 1995 occurred among persons who initiated heroin use in the 1970s and 1980s. Recent initiations of heroin use among those born between 1970 and 1979 have begun to be reflected in an increased rate of opioid overdose deaths. If the mortality experience of initiates born since 1970 replicates that of the two earlier cohorts (1950-59 & 1960-69) there will be another epidemic of overdose mortality in 10 to 15 years.

Increased heroin purity and the use of alcohol and benzodiazepines in conjunction with heroin have probably played some role in the increased overdose mortality but the magnitude of the contributions awaits further research. Research is required on changes in: the numbers of opioid dependent persons; heroin purity; risk factors among fatal and nonfatal opiate overdoses; and patterns of heroin and polydrug use among heroin users, especially during the 1991-1995 period.

These data suggest that more effort needs to be made to recruit older dependent heroin users into methadone treatment which substantially reduces the risks of overdose. Those who decline treatment need to be persuaded of the overdose risks of using opioids in combination with alcohol and benzodiazepines. Consideration also needs to be given to trialing naloxone distribution to heroin users to reduce overdose fatalities, and to trialing "injecting rooms" in some high risk locations.

1.0 Background

There are good reasons to be concerned about an apparent increase in the rate of opioid overdose deaths. First, there has been a substantial increase in the absolute number of such deaths from 70 in 1979 to 550 in 1995. Second, opioid overdoses now represent a substantial proportion of premature deaths among young Australians. In 1995, overdose deaths comprised 8% of male and 5% of female deaths in young adults between the ages of 15 and 44. Third, the media have recently reported geographic and temporal clusters of fatal and nonfatal overdoses. Reports of overdose deaths among young adults, and the media attention they have received, have created an impression that the frequency of opioid overdose has dramatically increased in recent years, especially among young adults.

In April 1997, the Commonwealth Department of Health and Family Services (on behalf of the Illicit Drugs Expert Working Group) asked the National Drug and Alcohol Research Centre to assess the statistical and policy significance of apparent trends in opiate related overdose deaths in Australia between 1979 and 1995.

This report critically examines the data on opioid overdose deaths over the period 1979 to 1995 with a view to answering the following questions:

1. Has there been a statistically significant increase in the rate of opioid overdose deaths over the period?
2. If there has been an increase, has it been similar for men and women, for persons in different age groups, and for persons in different jurisdictions?
3. What are the most plausible explanations of any such increase?
4. Can these explanations be distinguished on the available data?
5. If the explanations cannot be distinguished, what additional information needs to be collected that would identify the most probable reasons for an increase?
6. What are the most potentially effective ways of reducing opioid overdose fatalities in Australia?

1.1 Opiate-related Mortality

Longitudinal studies report annual mortality rates between 1% and 3% among dependent opioid users (e.g. Engstrom et al, 1991; Frischer et al, 1997; Haarstrup & Jepsen, 1988; Oppenheimer et al, 1994; Segest et al, 1990; Tunving, 1988). These rates are between six and 22 times those expected among their peers (Haarstrup & Jepsen, 1988; Frischer et al, 1997; Oppenheimer et al, 1994). English et al (1995) pooled the data from 12 major longitudinal studies of mortality among heroin users before the advent of HIV/AIDS and found that premature mortality rate was 13.2 times higher among dependent heroin users than peers of the same age and gender who had not used heroin.

In the past decade there has been a pandemic of HIV among injecting drug users in many parts of the world, although not in Australia which has maintained low rates of infection among injecting drug users for over a decade (Feachem, 1995). Despite the AIDS pandemic, overdose deaths remain the major cause of mortality among opioid users (Cottrell et al, 1985; Eskild et al, 1993; Frischer et al, 1993; Frischer et al, 1997; O'Doherty & Farrington, 1997; Oppenheimer et al, 1994; Perucci et al, 1991).

Among opioid-related deaths in Australia during 1992, 51% were classified as due to dependence, 17% as due to accidental poisoning, and a further 15% were estimated to be due to suicide (English et al, 1995). Zador et al (1996) reported that 80% of heroin-related deaths in NSW during 1992 were classified as due to "dependence" (ICD-9 code 304.0). In an analysis of all heroin-related deaths in south western Sydney during 1995, pathologists and coroners attributed the cause of death to "narcotism" in 80% of cases (Darke et al, 1997).

There are problems with the classification of opioid "overdose" deaths. There is, for example, considerable difficulty in distinguishing between the categories of "accidental poisoning" and "dependence" (or "narcotism"). The category of "dependence" probably signifies that morphine was detected post-mortem in the blood of a person with a known history of opioid dependence who died some time after self-administering heroin (Brecher, 1972).

The uncertainty about the classification of opioid overdose deaths means that distinctions between the ICD-9 codes for deaths due to opioid dependence and accidental opiate poisoning are of limited use. Nonetheless, these two causes of death jointly capture those deaths among young adults in which opioids may have played a contributory role and so trends in the rate of such deaths are worth examining as indicators of changes in the contributions made by opioid use to premature death. In the analyses reported in this paper, no distinction has been made between deaths in young adults that have been attributed to opioid dependence and to accidental opiate poisoning.

The problems of classification reflect uncertainty about the causes of most opioid "overdoses" (Darke & Zador, 1996). The immediate cause of death is usually respiratory failure (Proudfoot, 1988) which has typically been attributed to the use of a quantity of heroin in excess of the person's tolerance to the drug (Darke & Zador, 1996). However, the blood levels of morphine (the metabolite of heroin) in persons who have died of a heroin overdose have been skewed towards the lower end of the range (e.g. Fugelstad, 1994; Kintz et al, 1989; Monforte, 1977; Zador et al, 1996) and in many fatal "overdoses" the blood morphine levels are no higher than in survivors

of "overdose" (Aderjan et al, 1995; Brecher, 1972; Fugelstad, 1994; Gutierrez-Cebollada et al, 1994).

A focus on the presence of opioids in the classification of opioid-related deaths has distracted attention from the role of other concurrent drug use in many of these fatalities. Cases in which only morphine has been detected at autopsy represent a minority of heroin overdose fatalities (e.g. Darke et al, 1997; Manning & Ingraham, 1983; Monforte, 1977; O'Doherty & Farrington, 1997; Oppenheimer et al, 1994; Risser & Schneider, 1994; Steentoft et al, 1988; Wahbah et al, 1993; Zador et al, 1996). The same pattern has recently been reported in methadone-related deaths (Sunjic & Zador, 1997; Zador & Sunjic, 1996).

The two additional drug classes that are most often detected in opioid overdose fatalities are alcohol and the benzodiazepines (Risser & Schneider, 1994; Darke et al, 1997; Fugelstad 1994; Goldberger et al, 1994; Manning & Ingraham, 1983; Monforte, 1977; Ruttenber & Luke, 1984; Sunjic & Zador, 1997; Zador et al, 1996; Zador & Sunjic, 1996). Both are CNS depressants that may contribute to the respiratory depression that is the proximal cause of death in such overdoses (Proudfoot, 1988). Forty five percent of NSW cases reported by Zador et al (1996) had alcohol detected, and 27% were positive for benzodiazepines. In both Australian and overseas studies, blood morphine levels are much lower among persons who die with high blood alcohol levels (Darke et al, 1997; Ruttenber et al, 1990; Zador et al, 1996).

Suicides in which opioids have been a contributory factor have not been included in the analyses. The analysis of drug-caused mortality by English et al (1995) estimated on the basis of a Western Australian study that opiates are a causal factor in 9% of suicides among persons aged between 15 and 40 years. Unfortunately, the ABS codes for cause of death do not distinguish between suicides in which opioid drugs have been a factor from those in which they have not. It has therefore not been possible to analyse trends in the contribution of opiate use to suicide. Given the scarcity of data on suicide among opiate users in Australia, and the overseas evidence that suggests heroin users have an increased suicide risk (Farrell et al, 1996), opiate-related suicide is deserving of further research.

1.2 Study Aims

The aims of the study were:

1. To determine whether the apparent increase in the number of opioid overdose deaths in Australia between 1979-1995 was statistically significant;
2. To examine the sex, age, and jurisdiction of residence of persons who died from an opioid overdose in Australia between 1979-1995;
3. To examine and, where possible, evaluate potential explanations of any increase in the rate of opioid overdose deaths in Australia;
4. To identify priorities for future research to improve our understanding of opioid overdose and increase our capacity to prevent its occurrence; and

5. To identify any policies and strategies that may reduce the rate of opioid overdose deaths.

2.0 Methods

Data were obtained from the Australian Bureau of Statistics (ABS) on the number of deaths attributed to opioid dependence (ICD-9 code 304.0/304.7) and accidental opioid poisoning (ICD-9 code E850.0) for the years 1979 to 1995 inclusive. The age at death was obtained for males and females in each jurisdiction and the whole of Australia. Data were also obtained from the ABS on the estimated numbers of men and women at each age between birth and 85 who were resident in each state, and in the whole of Australia, at June 30 of each year between 1979 and 1995 inclusive. These data were used to calculate age and sex-specific mortality rates.

Data on deaths from opioid dependence and accidental poisoning were combined to give the total number of opioid "overdose" deaths occurring in each year for males and females. Most analyses were performed on deaths among persons aged between 15 and 44, the age group within which the overwhelming majority of heroin use occurs in Australian adults (English et al, 1995). Analyses of mortality in different birth cohorts used an extended age range of 15 to 54 years.

The following statistical analyses were performed. First, the sex and age specific mortality rates were calculated for each year for males and females in three age groupings: 15 to 24 years; 25 to 34 years and 35 to 44 years. Second, these rates were used to calculate a standardised mortality rate for each year for persons, male and females. These rates were standardised to the 1979 Australian adult population aged 15 to 44 years. Third, overdose mortality over the study period was compared between New South Wales, Victoria and the remaining states and territories.

Fourth, the statistical significance of changes in rates were assessed by multiple logistic regression analysis of the odds of an opioid overdose death occurring with sex, year of death and age group as predictors. If there has been an increase in the rate of overdose deaths this will be reflected in a statistically significant increased odds of overdose death for each year during the period (after adjustment for sex, age group and any significant interactions between sex, age and year). Fifth, multiple linear regression analyses were performed to discover whether the average age at death had changed between 1979 and 1995.

Sixth, rates of death were calculated for men and women in birth cohorts defined by having a date of birth between 1940-1949, 1950-1959, 1960-1969, 1970-1979. This was done to determine whether overdose mortality risk depended upon the age at which persons had initiated heroin use. These birth cohorts defined persons who differed in when they were at risk of initiating heroin use (see Appendix A). Persons born between 1940 and 1949 probably had the lowest risk of initiation since most had passed the age of 25 before the first recorded post-war epidemic of heroin use in Australia in the late 1960s and early 1970s (Manderson, 1993). Persons born between 1950 and 1959 were at the maximum risk of initiating heroin use (ages 15 to 25) around the time of the epidemic of heroin use in the mid 1970s. Persons born between 1960 and 1969 were passing through adolescence and early adult life in the middle 1980s when there was another increase in the initiation of heroin use. Those born between 1970 and 1979 are now approximately mid way through the period of maximum risk of initiating heroin use.

3.0 Results

3.1 Overall Mortality

The numbers of deaths attributed to opioid dependence or accidental poisoning between 1979 and 1995 increased in absolute numbers (see Table 1 in Appendix B). The number of such fatalities in Australia among young adults between 15 and 44 years rose from 70 in 1979 to 550 in 1995. The standardised mortality rate (per 1,000,000 of population) for the period 1979 to 1995 increased from 10.7 in 1979 to 67.0 in 1995 (see Figure 1). This represents an approximate six-fold increase in the rate of overdose mortality over the study period (see Table 2 in Appendix B). It represented a total of 3313 (78%) male and 957 female (22%) deaths between 1979 and 1985 among persons aged between 15 and 44.

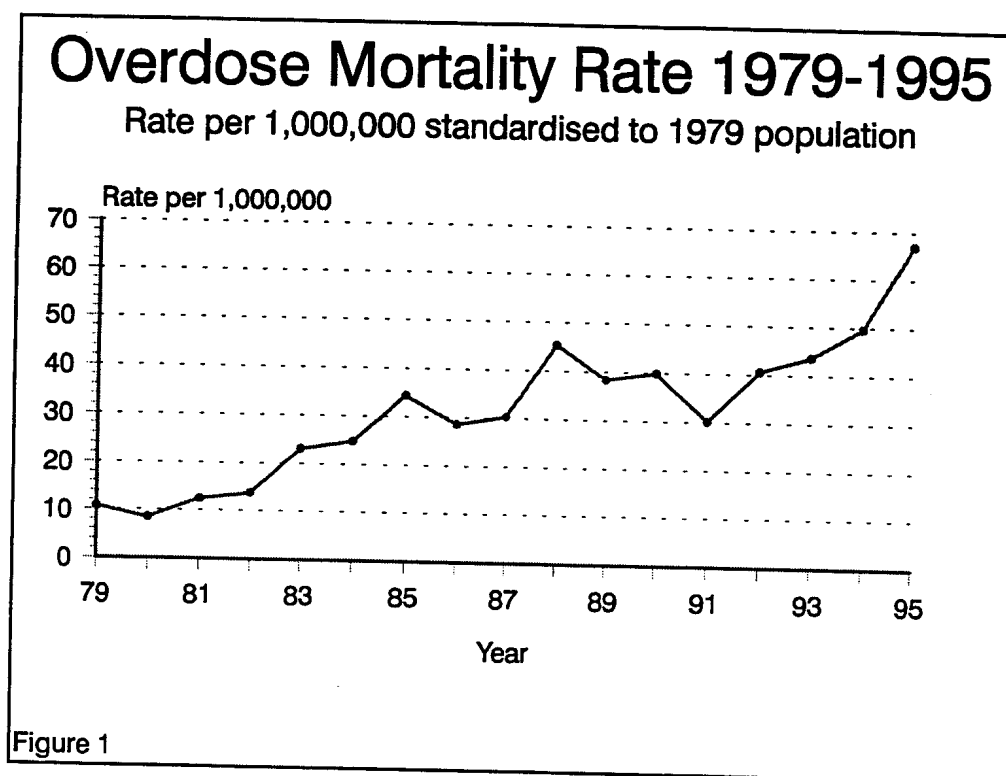
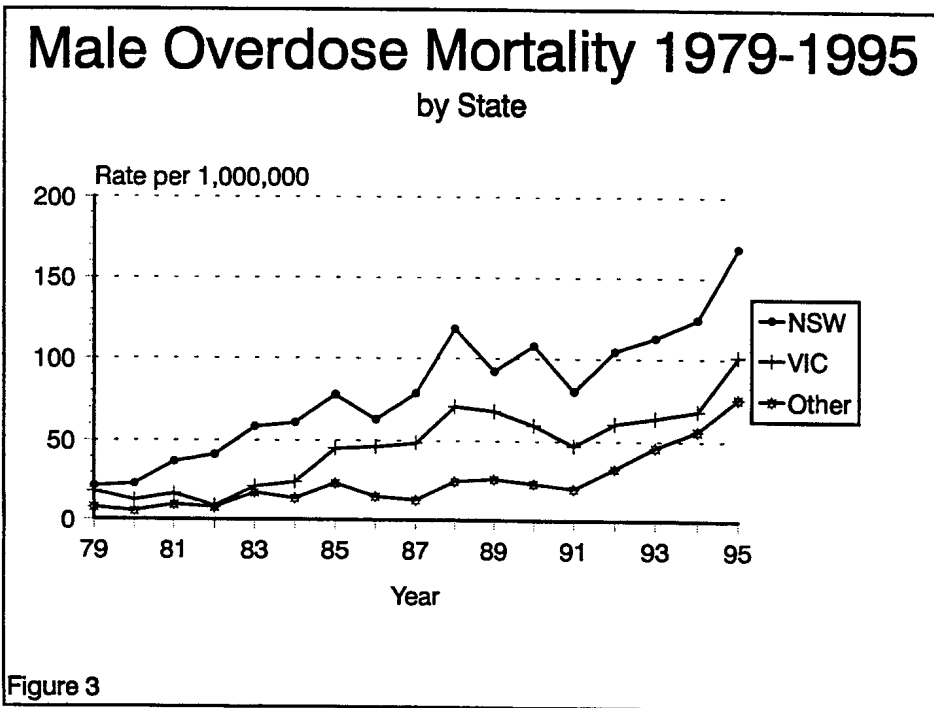
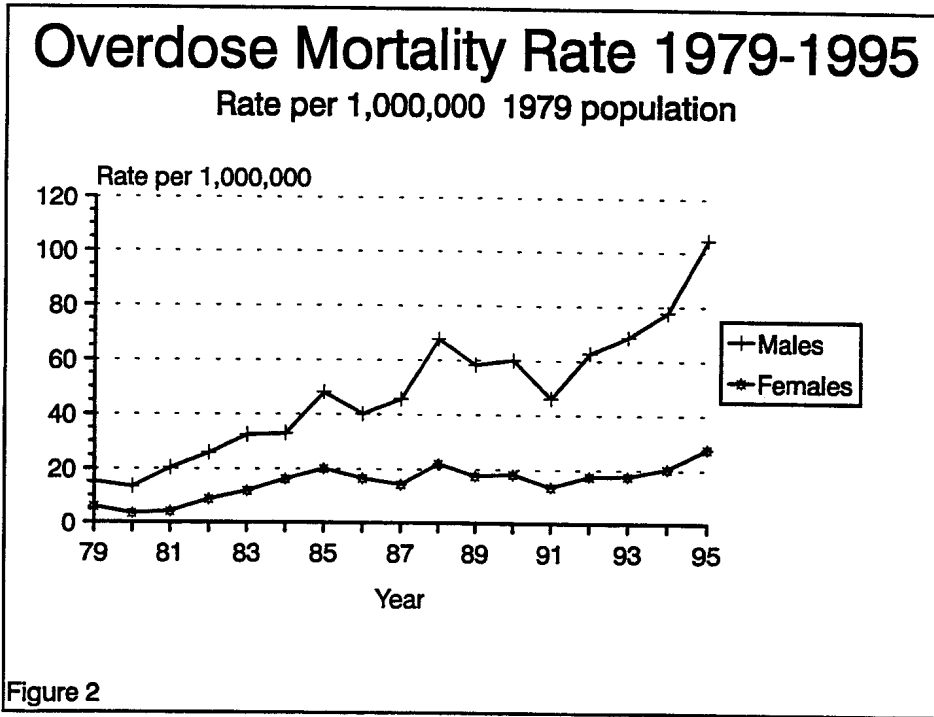


Figure 2, which shows the standardised mortality rates for males and females, indicates that there was a more marked increase among males than females. For males, the rate increased 6.8 times, from 15.3 in 1979 to 104.6 in 1995. For females, the rate increased 4.7 times, from 5.9 in 1979 to 27.9 in 1995 (see Table 2, Appendix B). This probably reflects a combination of the greater likelihood of opioid dependence among males than females (Anthony & Helzer, 1991; Anthony et al, 1994) and greater risk taking among males than females (Plant & Plant, 1992).

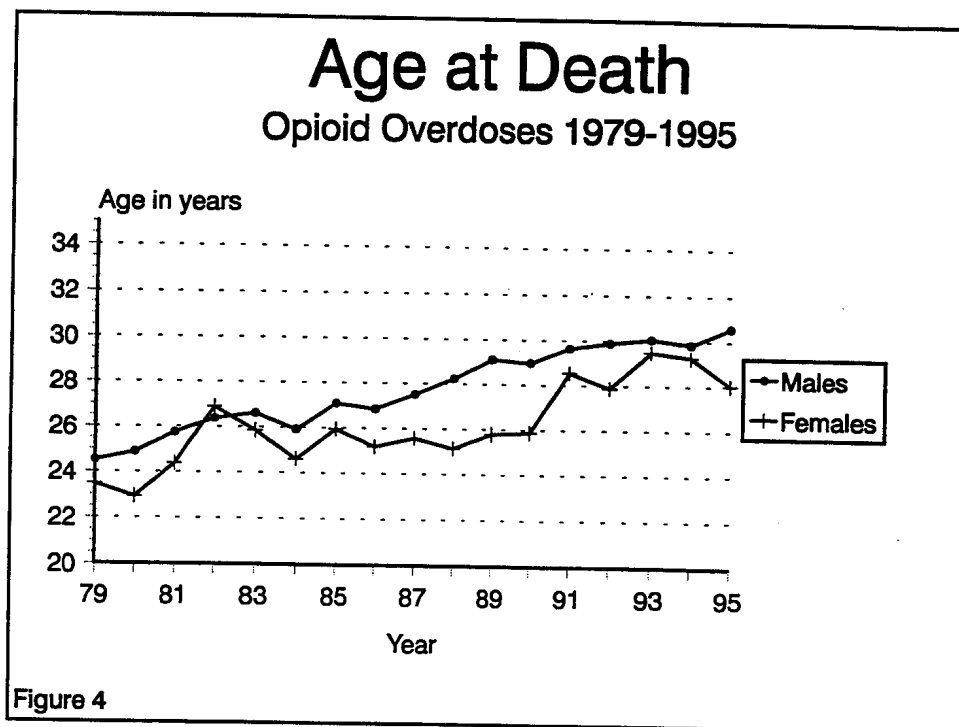
Overdose mortality rates also varied between the different jurisdictions, especially among males (see Figure 3). For the purposes of description, the jurisdictions were divided into New South Wales, Victoria and the other states and territories. Among males, New South Wales accounted for around a half of all overdose fatalities, and its rate was almost twice that in Victoria, and three

times the rate in the remaining states (see Tables 3 and 4 in Appendix B). There were less marked differences between states in female mortality rates. A logistic regression analysis confirmed that these differences were statistically significant (see Appendix C.1 for details). These differences in overall overdose mortality closely parallel differences between the jurisdictions in rates of enrolment in methadone maintenance treatment (Hall, 1996a), and probably reflect real differences in the prevalence of opioid dependence between different jurisdictions.



3.2 Mortality and age

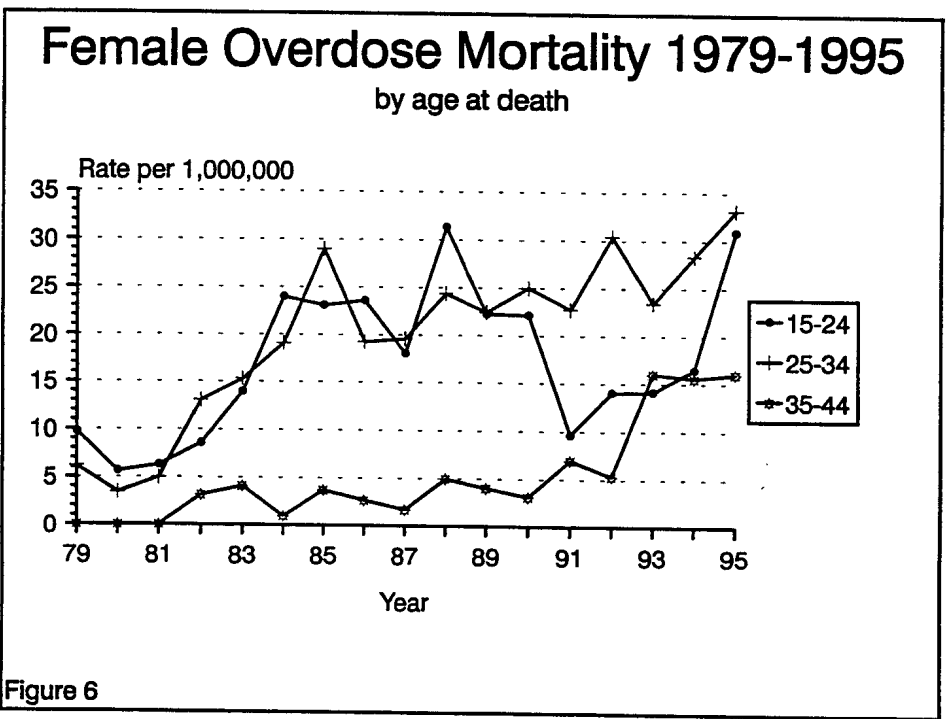
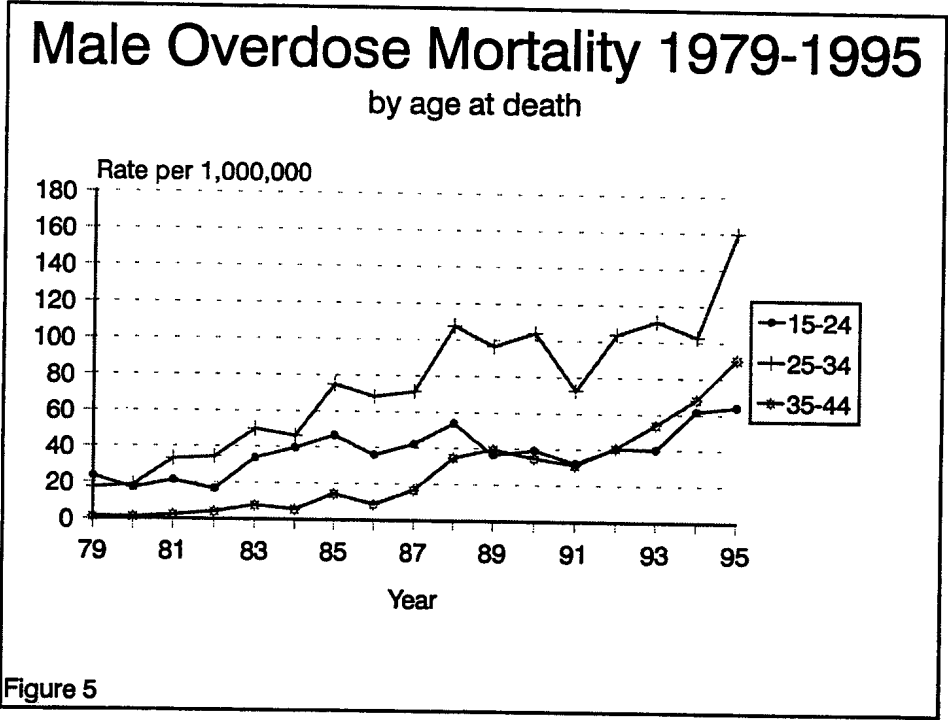
The average age at death for males increased from 24.5 in 1979 to 30.6 years in 1995 while the average age for females increased from 23.5 years to 28.0 years over the same period (see Figure 4 and Table 5, Appendix B). A multiple regression analysis confirmed that there was a significant linear relationship between age at death and year of death (see Appendix C.2). Age at death increased by 4.2 months per year and men were on average 21 months older at death than women, reflecting the fact that women are often introduced to heroin use by older male sexual partners (Hall et al, 1993; Hser et al, 1987).



Age-specific mortality rates for males (see Figure 5) and females (see Figure 6) between 1979 and 1995 varied between the three age groups. Among men the mortality rate was consistently higher among those aged 25 to 34 years while among women there were less marked differences in rates between those aged 15 to 24 and 25 to 34 years. In men and women the steepest rate of increase was among those aged between 35 and 44 years, followed by that persons aged between 25 and 34 years at death (see Tables 6 and 7 in Appendix B).

A multiple logistic regression analysis of mortality rates for opioid overdoses indicated that there was a substantial increase in the odds of an opioid overdose death between 1979 and 1995. The model included significant interaction terms (see Appendix C.3 for details) indicating that the rate of increase in the risk of opioid overdose death over the period 1979-1995 differed between men and women and the three age groups, and that the relationships between age group and year differed between men and women. The analysis suggests that the rate of increase in the odds of an overdose death was greatest among men and women who were 35 years or older at the time of their death.

1.

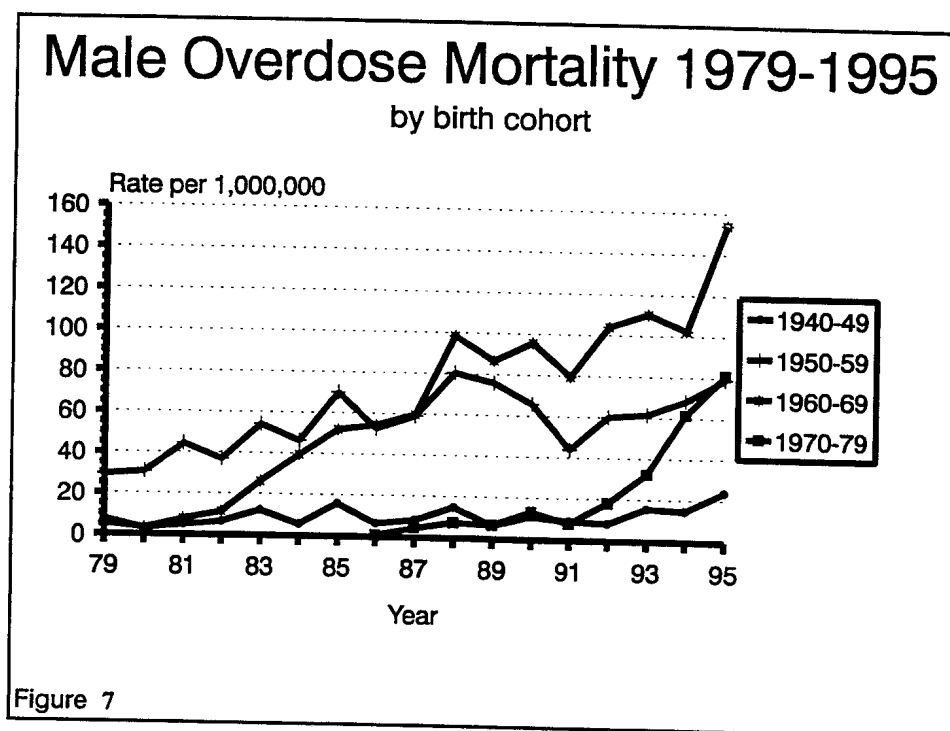


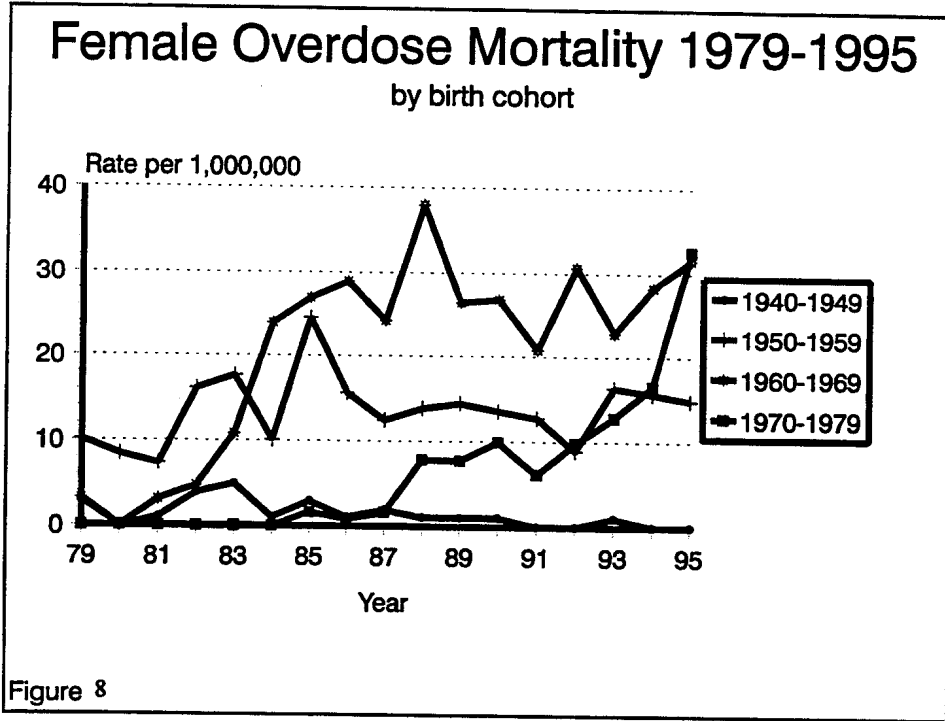
3.3 Age Cohort and Mortality

An analysis was also made of overdose mortality by birth cohort. Four cohorts were defined as having a date of birth between: 1940-49, 1950-1959, 1960-1969, and 1970-1979 (see Figures 7 and 8, and Tables 8 and 9). As explained above, these birth cohorts identified persons who differed substantially in their degree of exposure to heroin use during the period of maximum risk of initiation (namely ages 15 to 25).

The analysis showed that 46% of all male and 50% of all female overdose deaths between 1979 and 1995 occurred among those who were born between 1960 and 1969. Deaths among persons born between 1950 and 1959 accounted for 38% of male and 33% of female deaths over the same period. Of the deaths that occurred between 1991 and 1995, 50% occurred among men who were born between 1960 and 1969, and 27% occurred among those who were born between 1950 and 1959. Deaths among persons born since 1970 accounted for 18% of male and 27% of female deaths between 1991 and 1995.

These data show that most of the increase in opioid overdose mortality over the whole period 1979 to 1995, and more than two thirds of overdose deaths between 1991 and 1995, occurred among persons who initiated heroin use in the 1970s and 1980s (see analysis in Appendix C.4). Recent initiations to heroin use among the youngest age cohort have just begun to be reflected in an increased rate of overdose deaths. If the mortality experience among the youngest birth cohort (1970-1979) replicates that in the older ones (1950-1959 and 1960-1969), then we can expect another epidemic of opioid overdose deaths in this birth cohort within 10 to 15 years.





4.0 Discussion

These analyses indicate that there has been a statistically significant six-fold increase in the rate of opioid overdose mortality between 1979 and 1995. The overdose mortality rate in New South Wales was approximately twice that in Victoria, and three times higher than that in the other Australian states and territories.

The rate of increase was much higher among males than females, and highest for men and women in the age group of 35 to 44 years. There was also a substantial rate of increase among those aged between 25 and 34 and a lower but still statistically significant increase among men and women aged between 15 and 24 years. This age-related pattern of opioid overdose mortality was reflected in an increase in the average age at death from 24.2 years in 1979 to 30.1 years in 1995.

Analysis of mortality by birth cohort indicated that most deaths occurred among older heroin users who had initiated their heroin use in the late 1970s and the early 1980s. Deaths among younger recruits to heroin use have increased but they have not been a major contributor to the recent increase in opioid overdose mortality rate.

The statistical analyses indicate that the increase in the incidence of opioid-related deaths in Australia during the period 1979 to 1995 was not due to chance. The following sections outline and evaluate possible explanations of the increase in the rate of opioid overdose deaths.

4.1. Changes in the classification of causes of death

The first explanation that must be considered is that the increase in opioid overdose mortality may reflect a change over the study period in the diagnostic practices of pathologists and the type of conclusions reached by coroners as to cause of death. There may have been, for example, an increased use by coroners and forensic pathologists of the categories of "opioid dependence" and "accidental opiate poisoning" as causes of death among young people. Another possibility is that deaths that may formerly have been certified as suicide may now be classified as "overdose" deaths.

There are a number of reasons why changes in classification of cause of death are an unlikely explanation of the increased mortality rate. First, there has been a marked increase in fatalities attributed to opioids over the study period, so the change in diagnostic practice would have to be very marked to explain the six fold increase in mortality rate from these causes. Second, there is no evidence that such changes have occurred. Darke et al (1997) compared the conclusions as to cause of death by pathologists in heroin-related deaths in south western Sydney in 1992 and 1995. There was a doubling in the number of heroin-related fatalities in these years but the proportion of cases attributed to "narcotism" (opiate dependence) was 80% in both years, and in both years the majority of these deaths had other drugs detected at autopsy. Third, the change in diagnostic practice would have to have varied strongly with the age and sex of the deceased to explain the observed trends. For example, in order to explain the strong relationships between overdose death and birth cohort, the changes in certification of cause of death would need to be much more marked for males than females, and for older males born between 1950 and 1969. Fourth, a very similar pattern of results has recently been reported among opiate- and cocaine-related deaths in Spain between 1983 and 1991 (Sanchez et al, 1995). Fifth, a reclassification of suicides involving

opioids as overdose deaths is unlikely since one would expect to see higher blood morphine levels among persons who had intentionally overdosed on heroin.

For these reasons, it is unlikely that diagnostic categories have substantially altered over time. As a matter of prudence it would be wise to conduct more detailed analyses of the ways in which pathologists and coroners diagnose the causes of deaths in young adults in which opiates have been implicated as a contributory cause of death.

4.2. An increase in the number of heroin users

Assuming that the increase in opioid overdose deaths is not an artefact of changing diagnostic practices, an obvious explanation is that the number of persons who use heroin has increased between 1979 and 1995. This possibility is difficult to evaluate because of the lack of credible and precise estimates of the number of people who engage in an illegal and socially stigmatised act like using heroin (Hall, 1995).

Household surveys of drug use in Australia typically report that between 1% and 2% of the adult Australian population say that they have used heroin at some time in their lives (Commonwealth Department of Human Services and Health, 1994). These figures are likely to be underestimates for a number of reasons. First, household surveys probably under-sample heroin users. Their lifestyle makes them less likely to live in conventional living arrangements. They are also probably less likely to participate in household surveys, either because they are unavailable at the time the interviewer calls or they are reluctant to be interviewed. Second, if heroin users are sampled and agree to be interviewed, their heroin use is likely to be under-reported because it is illegal.

There are limited historical data on trends in opiate use in Australia. The first major epidemic of illicit heroin use after World War II occurred in Australia in the late 1960s and early 1970s (Manderson, 1993). This was when the first treatment centres were established and methadone maintenance treatment was introduced to Australia (Ward et al, 1992). There was another epidemic of heroin use in the early and middle 1980s which prompted the establishment of the National Campaign Against Drug Abuse in 1985. Secondary analysis of data on age of initiation among heroin users in a 1989 survey of injecting drug users in Sydney (ANAIIDUS, 1991) suggests that the peak initiations of heroin use were between 1970 and 1977 (for those born between 1940 and 1949), between 1978 and 1983 (for those born between 1950 and 1959), and between 1984 and 1986 (for those born between 1960 and 1969).

Heroin dependent persons appear to be those who are most at risk of fatal (Zador et al, 1996) and non-fatal heroin overdoses (Darke et al, 1996a, b). Heroin dependence can be defined as use of the drug over which the user has lost control, as indicated by the continued use of the drug in the face of problems that the user knows or believes are caused by their drug use, including legal difficulties, interpersonal problems and health problems. In Australia dependent heroin users are typically daily or near daily injectors of heroin who also use a range of other licit and illicit drugs (ANAIIDUS, 1991; Darke and Hall, 1995).

American community surveys of mental disorders, such as the Epidemiologic Catchment Area (Robins and Regier, 1991) and the National Comorbidity Surveys (Kessler et al, 1994), indicate

that between a quarter and a half of those who report ever having used heroin meet criteria for heroin dependence. This represents between 0.4% (Anthony et al, 1994) and 0.7% (Anthony and Helzer, 1991) of the American adult population.

There are no Australian survey data on the population prevalence of heroin dependence comparable to the ECA or the NCS. In their absence, a number of imperfect methods have been used to produce estimates of the number of dependent heroin users in Australia. The most recent "guesstimate" is that there were 59,000 dependent heroin users in Australia in 1991. The range of estimates was between 36,000 and 120,000, indicating considerable uncertainty about the total number (Hall, 1995). The midpoint of this range (59,000) is approximately equal to the larger of the US population prevalence estimates (namely, 0.7% of the adult population).

Given the obstacles to obtaining credible estimates, it is difficult to rule out the possibility that there has been a substantial increase in the number of heroin users over the study period. Indirect evidence, however, is against the hypothesis that any such increase explains the increased opioid overdose mortality between 1991 and 1995. The best guesses as to the change in number of dependent heroin users suggests that there has been an approximate doubling in their number during the time period (Hall, 1995). This is considerably less than the six fold increase required to explain the overdose mortality data. The increase in the age at death, and the marked differences in mortality for the different birth cohorts, also suggest that most of the increase in mortality has not occurred among recent recruits to heroin use. Rather, the rate of increase in overdose mortality has been steepest among adults in the 35 to 44 age group, those who initiated their heroin use in the late 1970s and early 1980s.

4.3. Increased purity of heroin

The popular explanation in the media is that the rise in opioid overdose deaths is the result of an increase in average heroin purity. Opioid overdose deaths that are clustered in time and space are usually attributed to unusually potent or "killer" heroin. Such an explanation has the advantages of plausibility since the higher the heroin dose used the easier it will be to overdose.

There is reasonable evidence that purity increased in the period 1992 to 1995. Reports from the Australian Bureau of Criminal Intelligence (ABCI) suggest that there was a rise in the purity of heroin seizures during this period (ABCI, 1996) and the average purity of samples collected in Sydney by the NSW Bureau of Criminal Statistics and Research in 1993-1995 was 60%, two to three times that reported earlier in the decade (Weatherburn & Lind, 1995). Additional evidence of an increase in average heroin purity is the doubling between 1992 and 1995 in the average blood morphine levels in fatal heroin overdoses in south western Sydney (Darke et al, 1997). It is therefore likely that heroin users are now able to use larger quantities of purer heroin than users a decade ago.

Increased heroin purity has, in all probability, made a contribution to the increase in opiate-related mortality. Nonetheless, there are a number of reasons why heroin purity is unlikely to be the major explanation of the increase. First, mortality increased throughout the study period, rather than being confined to the last three or so years of the period. Second, retrospective analyses of overdose fatalities in 1995 found that it was still the case that a large proportion of fatalities had blood morphine levels that were below the conventionally accepted fatal range, and polydrug use

was a feature of half of these cases (Darke et al, 1997). The average blood morphine level doubled but the proportion of users who had used heroin in combination with other respiratory depressants, such as, alcohol and benzodiazepines, was unchanged (50% in both years).

Third, if increased heroin purity was the explanation of the rise in overdose deaths one would expect most of the increase to be among new recruits who have the lowest tolerance for opioid drugs and are the least experienced in using street drugs. But deaths among young, inexperienced users were less common than among older experienced heroin users. Instead, the typical overdose fatality towards the end of the study period was a 30 year old male with a 12 year history of dependent heroin use. The rate of the increase in mortality rate among adults in the 15 to 25 year age group was also much less than that among older adults aged 25 to 44 years.

A more plausible hypothesis is that increased heroin purity has amplified the risks of using other CNS depressants in combination with heroin. A substantial increase in heroin purity would increase the risk of respiratory failure when users combine heroin with the use of other CNS depressant drugs. The 120% increase in the number of south western Sydney fatalities in a three year period, while the prevalence of polydrug use and the mean blood alcohol level among fatalities remained the same, is consistent with this hypothesis.

4.4. An increased number of methadone-related deaths

It has been claimed in the media that there has been a marked increase in methadone-related deaths in the early 1990s among heroin users. These included deaths among persons who were enrolled in methadone maintenance programs as well as heroin users who were not enrolled in methadone treatment who used diverted methadone. This hypothesis deserves further study as the number of heroin users enrolled in methadone treatment increased over the study period from approximately 2000 in 1985 to an estimated 20,000 in 1996, and the rate of increase was highest in New South Wales (Hall, 1996a). There is also some evidence that oral methadone syrup is being injected by Sydney heroin users enrolled in methadone programs, and that diverted methadone is being injected by heroin users who are not enrolled in methadone programs (Darke et al, 1996c).

Unfortunately, this hypothesis cannot be tested on these mortality data because no distinction is made by the ABS in coding the cause of death between deaths attributed to heroin use and those attributed to the use of opioids like methadone. There are a number of reasons why this explanation is unlikely to wholly explain the increase in opioid overdose mortality. First, Zador et al's (1996) data on opioid deaths in 1992 found that 80% of opioid related deaths were due to heroin. Second, Zador and Sunjic's (1996) analysis of data on deaths among patients in the NSW methadone program has found that after induction into treatment methadone maintenance has a substantial protective effect on mortality from overdose. Mortality from all causes among those in methadone treatment was 25% that of heroin users who were not in methadone maintenance treatment, a finding that is consistent with the literature (e.g. Caplehorn et al, 1994). Zador and Sunjic also found that there was no increase in the *mortality rate* among methadone program participants between 1990 and 1995. Further research is necessary to estimate the contribution that methadone-related deaths may have made to the increased rate of opioid overdose mortality.

4.5. Changes in opioid user behaviour

Another possibility is that the increase in opioid overdose deaths is the result of changes in patterns of opioid and other drug use among opioid users between 1979 and 1995. There are at least three such possible changes in patterns of drug use that could contribute to an increased rate of opiate overdose deaths.

The first possibility is that opioid users may have adopted more risky patterns of heroin use, (such as injecting alone, or in the street) which would mean that there was less opportunity to resuscitate a user who overdosed. There is some evidence that risky injecting behaviours have increased in certain locations. Maher (1996) described a group of high risk young street injectors in the south western suburbs of Sydney who typically injected hurriedly on the street to avoid police detection and so were more likely to inject rapidly than if they had injected in a private home. It has been reported in the United Kingdom that street injectors are more likely to overdose than those who inject in people's homes (Klee & Morris, 1995). These findings are consistent with changes observed in the circumstances of fatal overdoses that occurred in the south western Sydney region between 1992 and 1995 (Darke et al, 1997). In 1992, 35% of deaths occurred on the street whereas by 1995 71% did so. It remains to be discovered to what extent these trends have occurred in other areas of Australia, and to what extent they may have been more likely to have occurred among older drug users.

A second possibility is that there has been an increase in polydrug use among opioid users, especially an increased use of CNS depressants that are self-administered in riskier ways. It is well documented that the majority of Australian opioid users have traditionally used a wide range of other drugs, including alcohol and benzodiazepines (e.g. Darke & Hall, 1995). However, there is no evidence that the *prevalence* of polydrug use has increased among persons who have died of opioid overdoses over the study period. In the Darke et al (1997) study of south western Sydney heroin-related fatalities, the proportions of cases in 1992 and 1995 in which alcohol, benzodiazepines and other drugs were detected were the same, as were the blood alcohol levels of alcohol.

A third possibility is that changes in the route of administration of other CNS drugs over the period have increased the risk of opioid overdose deaths. There has been, for example, a trend in New South Wales in recent years for heroin users to inject preparations intended for oral consumption, such as, benzodiazepines tablets (Darke et al, 1995) and methadone syrup (Darke et al, 1996c). Injectors of these substances are more likely to report a drug overdose (Darke et al, 1996a), as would be expected because the peak plasma level of benzodiazepines and methadone is higher when they are injected rather than taken orally. When combined with heroin, the risk of overdose would be considerably increased by the injection of benzodiazepines or long-acting opioids like methadone.

A fourth possibility is that these more risky drug use patterns may be adopted as opioid users age. It could be, for example, that older heroin users find it more difficult to generate the income to sustain a high rate of daily heroin injection. They may use benzodiazepines and alcohol to manage their withdrawal symptoms. Their tolerance for opioids would be reduced and vary more day to day than younger, more regular, heroin users. This would make older users more vulnerable to the respiratory effects of purer heroin, especially when used in combination with alcohol and

other CNS depressant drugs. It is also possible that liver disease in older users (caused by chronic hepatitis) could make them less able to metabolise opioids, alcohol and other drugs, and hence, more vulnerable to polydrug toxicity.

These changes in drug use patterns may have contributed to increased rates of opioid overdose deaths in some locations in New South Wales. The extent of their contribution is difficult to estimate because it is uncertain how widespread the adoption of riskier drug use and injection practices has been. It also remains to be discovered whether there has been an increased resort to polydrug use as the heroin users who initiated their use in the early 1980s have aged.

5.0 Research and Policy responses

5.1 Research Priorities

The available data are insufficient to decide between competing explanations of the increased overdose mortality, or to estimate the magnitude of their respective contributions to the observed increase in deaths between 1979 and 1995. Additional data are therefore needed to evaluate the reasons for the increase. These will need to include the following.

1. Retrospective analyses of recent overdose fatalities should examine trends in blood morphine levels, circumstances of deaths, patterns of polydrug use and history of heroin and methadone use. In such studies, the reasons given in coronial and forensic pathology reports for the certification of specific causes of death should be critically examined. An analysis should also be done of any changes in the use of these diagnoses over time. Such research would be facilitated if a centralised coronial data base enabled researchers to get more timely access to post-mortem toxicological data and to pathologists' diagnoses and coroners' conclusions. At present, there is a two year delay between collection of this data and release of ABS data on causes of death, a delay that prevents the early identification of emerging trends in opioid related deaths. Such a system has been advocated as a way of monitoring trends in youth suicide; it could readily be used to monitor trends in opioid and other drug overdose deaths.

2. Better estimates are needed (preferably in the form of a time series) of the numbers of opioid dependent persons in Australia and in each of a number of different jurisdictions. Given the marked state differences in mortality (and probably in the prevalence of heroin dependence), these jurisdictions should include New South Wales and Victoria which probably have the largest opioid injecting populations. A sample of smaller jurisdictions should also be studied, with preference being given to including at least one state which has, and one which has not, shown a marked increase in overdose mortality. If data confidentiality permit, these estimates should be obtained from corrected capture-recapture methods (e.g. Kehoe et al, 1992; Duque-Portugal et al, 1994). Sensitivity analyses should be performed to evaluate the impact of failures of model assumptions on the estimates. Such estimates will also have other uses for policy purposes, such as, estimating the need and likely demand for treatment among opioid dependent persons.

3. Statistical analyses should be conducted on time series data on heroin purity. This should preferably be done in several jurisdictions, with data from Sydney and Melbourne a priority.

4. Priority should also be given to the prospective collection of data on heroin price and purity

to examine relationships between heroin purity and opioid overdoses. These data could also be used to monitor changes in drug availability and to evaluate the impact of law enforcement strategies on drug markets.

5. Consideration should also be given to the collection and analysis of ambulance data on persons who have been resuscitated after opioid overdoses (e.g. by the administration of naloxone). These data would provide more sensitive information on trends in overdoses than data on fatalities, since non-fatal overdoses are much more frequent than fatal ones (Darke et al, 1995). They could also be used in analyses of relationships between heroin purity and opioid overdoses.

6. Changes in polydrug use and risk taking among heroin users should be studied to identify behaviour patterns that increase the risk of overdose. This may be done by analyses of archival data, such as the 1989 ANAIDUS survey and the 1995 ASHIDU data. Prospective studies of such trends could also be conducted as part of the Illicit Drug Reporting System.

7. More detailed studies of opioid overdose fatalities in the larger jurisdictions are needed to assess the contribution that methadone-related deaths have made to the increased opioid mortality rate. Special attention needs to be paid to methadone related deaths among heroin users who are not in treatment.

5.2 Policy Responses

While awaiting the results of this research there are a number of policy options that should be considered (Hall, 1996b). The first priority must be to reduce the frequency of opioid overdoses. We do not need more research to start informing heroin users about the risks of combining heroin with alcohol and other depressant drugs. Heroin users also need to be discouraged from injecting in the streets or alone, thereby denying themselves assistance in the event of an overdose. An evaluation of peer based education on these issues is currently being conducted in South Australia. Recent proposals to establish safe injecting rooms in locations where street injection is common may also be worth serious consideration as a way of reducing overdose deaths caused by these risky practices.

A second priority should be increasing the number of older heroin users who enter treatment. The risk of overdose death is substantially reduced while heroin users are enrolled in methadone treatment (Caplehorn et al, 1994; Zador and Sunjic, 1996). Given the higher risks among older heroin users, a useful strategy for reducing overdose deaths would be to increase the number of older heroin users who are enrolled in methadone maintenance treatment. There has been a substantial increase in the number of heroin users enrolled in methadone maintenance treatment over the past decade (Hall, 1996a). More effort may be needed to enrol older heroin users who have so far found methadone treatment unattractive, e.g. by offering a wider range of alternative opioid maintenance agents, or by reducing the demands made of users (Hall, 1996a).

The third priority must be to reduce the number of overdoses that are fatal by improving users' responses to the overdoses of peers. Heroin users could be taught simple cardiopulmonary resuscitation skills so that they can keep comatose users alive until help arrives. Users also need to be encouraged to call an ambulance sooner than is the case at present (Darke et al, 1996b). Their understandable fears of police involvement need to be addressed, and relations between

ambulance officers and heroin users need to be improved.

A serious analysis also needs to be made of the benefits and costs of either distributing or selling over the counter the opiate antagonist naloxone (Strang et al, 1996). Overdoses often occur in the presence of others who could administer naloxone if it was available, thereby reversing the effects of opioid drugs that are involved in drug overdoses (Darke et al, 1996b).

6.0 Summary and Implications

There was a statistically significant six-fold increase in the rate of opioid overdose mortality in Australia between 1979 and 1995. This increase was more marked among males than females, and older heroin users aged between 25 and 44 years. Much of the increase has therefore occurred among persons who initiated heroin use in the late 1970s and early 1980s.

The factors that have most probably contributed to the increase are increased heroin purity and changes in patterns of polydrug use and injecting behaviour. At present, the specific contributions of these causes to this large increase in overdose mortality are uncertain. Additional research is required in order to determine exactly which of these factors have contributed to the six-fold increase in opioid-related mortality in Australia.

More detailed policy responses to reduce opioid mortality will depend upon the results of further research. In the meantime, it would be desirable to increase the recruitment of older heroin users into treatment and to focus peer education users on persuading drug users of the overdose risks of using heroin in conjunction with other CNS depressants, especially by injection. Serious consideration should be given to a controlled evaluation of the impact of naloxone distribution on overdose fatalities among heroin users.

The current data show that much of the recent increase in opioid overdose mortality has occurred among older heroin users, and so preventive efforts need to focus on this group of heroin users. Efforts also need to be made to prevent a future epidemic of overdose deaths. These should include educational and other policies to reduce rates of initiation of heroin use, and peer education to reduce polydrug use and risky injecting practices among young persons who have initiated heroin use. If the current mortality experience among older heroin users is replicated among new recruits, we will face another epidemic of overdose deaths in 10 to 15 years.

7.0 References

- ADERJAN, R., HOEMANN, S., SCHMITT, G. & SKOPP, G. (1995) Morphine and morphine glucuronides in serum of heroin consumers and in heroin-related deaths determined by HPLC with native fluorescence detection. *Journal of Analytical Toxicology*, 19, 163-168.
- ANTHONY, J.C. & HELZER, J.E. (1991) Syndromes of drug abuse and dependence. In L.N. Robins & D.A. Regier (eds). *Psychiatric Disorders in America: The Epidemiologic Catchment Area Study* (New York, The Free Press).
- ANTHONY, J.C., WARNER, L.A. & KESSLER, R.C. (1994) Comparative epidemiology of dependence on tobacco, alcohol, controlled substances and inhalants: basic findings from the National Comorbidity Study. *Clinical and Experimental Psychopharmacology*, 2, 244-268.
- AUSTRALIAN BUREAU OF CRIMINAL INTELLIGENCE (1996) *Australian Illicit Drug Report, 1995-96* (Canberra, Commonwealth of Australia).
- AUSTRALIAN NATIONAL AIDS AND INJECTING DRUG USE STUDY (1991) Neither a Borrower Nor A Lender Be: First Report of the ANAIDUS, 1989 data collection (Sydney, ANAIDUS).
- BRECHER, E.M. (1972) *Licit and Illicit Drugs*. (Boston, Little Brown and Company).
- CAPLEHORN, J.R.M., DALTON, S.Y.N., CLUFF, M.C. & PETRENAS, A.M. (1994) Retention in methadone maintenance and heroin addicts' risk of death. *Addiction*, 89, 203-207.
- COMMONWEALTH DEPARTMENT OF HUMAN SERVICES AND HEALTH (1994) *Statistical Update, Issue 3, March 1994*.
- COTTRELL, D., CHILDS-CLARKE, A. & GHODSE, A.H. (1985) British opiate addicts: an 11-year follow-up. *British Journal of Psychiatry*, 146, 448-450.
- 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., ROSS, J. & HALL, W. (1995) Benzodiazepine use among injecting heroin users. *Medical Journal of Australia*, 162, 645-647.
- DARKE, S., ROSS, J. & HALL, W. (1996a) The injection of methadone syrup in Sydney, Australia. *Drug and Alcohol Dependence*, 43, 191-198.
- DARKE, S., ROSS, J. & HALL, W. (1996b) Overdose among heroin users in Sydney, Australia: I. Prevalence and correlates of non-fatal overdose. *Addiction*, 91, 405-411.
- DARKE, S., ROSS, J. & HALL, W. (1996c) Overdose among heroin users in Sydney, Australia: II. Responses to overdoses. *Addiction*, 91, 413-417.

DARKE, S. & ZADOR, D. (1996) Fatal heroin overdose: A review. *Addiction*, 91, 1757-1764.

DARKE, S., ZADOR, D. & SUNJIC, S. (1997) Toxicological findings and circumstances of heroin-related deaths in south western Sydney, 1995. *National Drug and Alcohol Research Centre Technical Report No. 40*.

DUQUE-PORTUGAL, F., MARTIN, A.A. & TAYLOR, R. (1994) Mark-recapture estimates of injecting drug users in Sydney. *Australian Journal of Public Health*, 1994, 18, 201-204.

ENGLISH, D., HOLMAN, C.J.D., MILNE, E., WINTER, M.G., HULSE, G.K., CODDE, J.P., CORI, B., DAWES, V., DE KLERK, N., KNUIMAN, J.J., LEWIN, G.F. & RYAN, G.A. (1995) *The quantification of drug caused morbidity and mortality in Australia 1995 edition* (Canberra, Commonwealth Department of Human Services and Health).

ENGSTROM, A., ADAMSSON, C.M., ALLEBECK, P. & RYDBERG, W. (1991) Mortality in patients with substance abuse: a follow-up in Stockholm County, 1973-1984. *International Journal of the Addictions*, 26, 91-106.

ESKILD, A., MAGNUS, P., SAMUELSON, S.O., SOHOLBERG, 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, 315-320.

FARRELL, M., NEELEMAN, J., GRIFFITHS, P. & STRANG, J. (1996) Suicide and overdose among opiate addicts. *Addiction*, 91, 321-323.

FEACHEM, R.G.A. (1995) *Valuing the Past ... Investing in the Future* (Canberra, Commonwealth of Australia).

FRISCHER, M., BLOOR, M., GOLDBERG, D., CLARK, J., GREEN, S. & MCKEGANY, N. (1993) Mortality among injecting drug users: A critical reappraisal. *Journal of Epidemiology and Community Health*, 47, 59-63.

FRISCHER, M., GOLDBERG, D., RAHMAN, M. & BERNEY, L. (1997) Mortality and survival among a cohort of drug injectors in Glasgow, 1982-1994. *Addiction*, 92, 419-427.

FUGELSTAD, A. (1994) Heroin deaths in Stockholm, 1986-1991, *Paper presented to the Fifth International Conference on the Reduction of Drug Related Harm*, Toronto, 1994.

GOLDBERGER, B.A., CONE, E.J., GRANT, T.M., CAPLAN, Y.H., LEVINE, B.S. & SMIALEK, J.E. (1994) Disposition of heroin and its metabolites in heroin-related deaths. *Journal of Analytical Toxicology*, 18, 22-28.

GUTIERREZ-CEBOLLADA, J., de la TORRE, R., ORTUNO, J., GARCES, J. & CAMI, J. (1994) Psychotropic drug consumption and other factors associated with heroin overdose. *Drug and Alcohol Dependence*, 35, 169-174.

- HAARSTRUP, S. & JEPSON, P.W. (1988) Eleven year follow-up of 300 young opioid addicts. *Acta Psychiatrica Scandinavia*, 77, 22-26.
- HALL, W. (1995) *The demand for methadone maintenance treatment in Australia*. Technical Report Number 28 (Sydney, National Drug and Alcohol Research Centre).
- HALL, W. (1996a) Methadone maintenance treatment as a crime control measure. *Crime and Justice Bulletin*, Number 29, 1-12.
- HALL, W. (1996b) How can we reduce the number of heroin "overdose" deaths? *Medical Journal of Australia*, 164, 197-198.
- HALL, W., BELL, J. & CARLESS, J. (1993) The history of criminal convictions among applicants for an Australian methadone maintenance program. *Drug and Alcohol Dependence*, 31, 123-129.
- HSER, Y.I, ANGLIN, D. & MCGLOTHIN, W. (1987) Sex differences in addict careers. 1 Initiation of use. *American Journal of Drug and Alcohol Abuse*, 13, 33-57.
- KEHOE, L., HALL, W. & MANT, A. (1992) Estimates of the number of injecting drug users in a defined area. *Australian Journal of Public Health*, 16, 232-237.
- KESSLER, R.C., MCGONAGH, K.A., ZHAO, S., NELSON, C.B., HUGHES, M., ESHLEMEN, S. WITTCHEN, U. & KENDLER, K.S. (1994) Lifetime and 12-month prevalence of DSM-II-R psychiatric disorders in the United States. *Archives of General Psychiatry*, 51, 8-19.
- KINTZ, P., MANGIN, P., LUGNIER, A.A. & CHAUMONT (1989) Toxicological data after heroin overdose. *Human Toxicology*, 8, 487-489.
- KLEE, H. & MORRIS, J. (1995) Factors that characterise street injectors. *Addiction*, 90, 837-841.
- MAHER, L. (1996) *Illicit Drug Reporting System (IDRS): Ethnographic component*. National Drug and Alcohol Research Centre Technical Report No. 36 (Sydney, National Drug and Alcohol Research Centre).
- MANDERSON, D. (1993) *From Mr Sin to Mr Big: A History of Australian Drug Laws* (Melbourne, Oxford University Press).
- MANNING, F.J. & INGRAHAM, L.H. (1983) Drug "overdoses" among U.S. soldiers in Europe, 1978-1979. I. Demographics and toxicology. *International Journal of the Addictions*, 18, 89-98.
- MONFORTE, J.R. (1977) Some observations concerning blood morphine concentrations in narcotic addicts. *Journal of Forensic Sciences*, 22, 718-724.
- O'DOHERTY, M. & FARRINGTON, A. (1997) Estimating local opioid addict mortality. *Addiction Research*, 4, 321-327.

- 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. *Addiction*, 89, 1299-1308.
- PERUCCI, C.A., DAVOLI, M., RAPITI, E., ABENI, D.D. & FORASTIERI, F. (1991) Mortality of intravenous drug users in Rome: A cohort study. *American Journal of Public Health*, 81, 1307-1310.
- PLANT, M. & PLANT, M. (1992) *Risk-takers. Alcohol, drugs, sex and youth* (London, Routledge).
- PROUDFOOT, A.T. (1988) Diamorphine overdose. In SCOTT, D.B. (Ed) *Diamorphine. Its chemistry, pharmacology and clinical use* (Cambridge, Woodhead-Faulkner).
- RISSE, D. & SCHNEIDER, B. (1994) Drug-related deaths between 1985 and 1992 examined at the Institute of Forensic Medicine in Vienna, Austria. *Addiction*, 89, 851-857.
- ROBINS, L.N. & REGIER D.A. (1991) (eds) *Psychiatric Disorders in America: The Epidemiologic Catchment Area Study* (New York, The Free Press).
- RUTTENBER, A.J. & LUKE, J.L. (1984) Heroin-related deaths: new epidemiologic insights. *Science*, 226, 14-20.
- RUTTENBER A.J., KALTER H.O. & SANTINGA P. (1990) The role of ethanol abuse in the etiology of heroin-related death. *Journal for Forensic Sciences*, 35: 891-900.
- SANCHEZ, J., RODRIGUEZ, B., DEL LA FUENTA, L., BARRIO, G., VICENTE, J., ROCA, J., ROYUELA, L. & THE STATE INFORMATION SYSTEM ON DRUG ABUSE (SEIT) WORKING GROUP (1995) Opiates or cocaine: mortality from acute reactions in six major Spanish cities. *Journal of Epidemiology and Community Health*, 49, 54-60.
- SEGEST, E. MYGIND, O. & BAY, H. (1990) The influence of prolonged stable methadone maintenance treatment on mortality and employment: an eight year follow-up. *International Journal of the Addictions*, 25, 53-63.
- STEENTOFT, A., WORM, K. & CHRISTENSON, H. (1988) Morphine concentrations in autopsy material from fatal cases after intake of morphine and/or heroin. *Journal of the Forensic Science Society*, 28, 87-94.
- STRANG, J., DARKE, S., HALL, W., FARRELL, M. & ALI, R. (1996) Heroin overdose: the case for take-home naloxone. *British Medical Journal*, 312, 1435.
- SUNJIC, S. & ZADOR, S. (1997) Methadone-related deaths in New South Wales. *Medical Journal of Australia*, 166, 54-55.
- TUNVING, K. (1988) Fatal outcome in drug addiction. *Acta Psychiatrica Scandinavia*, 77, 551-566.

WAHBAH, W., WINEK, C.L. & ROZIN, L. (1993) Distribution of morphine in body fluids of heroin users. *Journal of Analytical Toxicology*, 17, 123-124.

WARD, J., MATTICK, R. & HALL, W. (1992) *Key Issues in Methadone Maintenance* (Sydney, University of New South Wales Press).

WEATHERBURN, D. & LIND, B. (1995) *Drug Law Enforcement and Its Impact on the Heroin Market* (Sydney, NSW Bureau of Crime Statistics and Research).

ZADOR, D. & SUNJIC, S. (1996) Methadone-related deaths in New South Wales, 1990-1995. Paper presented to the National Methadone Conference, Melbourne, 1996.

ZADOR, D., SUNJIC, S. & DARKE, S. (1996) Heroin-related deaths in New South Wales, 1992: Toxicological findings and circumstances. *Medical Journal of Australia*, 164, 204-207.

Appendix A: Definition of birth cohorts

Birth Cohort	Years at risk of initiation	Midpoint of risk period
1940-1949	1955-1974	1965
1950-1959	1965-1984	1975
1960-1969	1975-1994	1985
1970-1979	1985-2004	1995

APPENDIX B: Tables

**Table 1: Number of fatal opioid overdoses by sex, 1979-1995,
among persons aged 15-44 years**

Year	Males	Females	Total
1979	51	19	70
1980	45	11	56
1981	71	14	85
1982	69	30	99
1983	116	41	157
1984	118	56	174
1985	176	71	247
1986	149	59	208
1987	174	52	226
1988	266	81	347
1989	236	66	302
1990	247	69	316
1991	189	54	243
1992	258	69	327
1993	285	72	357
1994	323	83	406
1995	440	110	550
Total deaths	3313	957	4170

**Table 2: Standardised mortality rate for opioid overdoses by sex,
1979-1995 among persons aged 15 to 44 years**

Year	Males	Females	Total
1979	15.3	5.9	10.7
1980	13.3	3.4	8.4
1981	20.3	4.2	12.4
1982	25.8	8.8	13.7
1983	32.5	11.9	23.0
1984	32.9	16.3	24.7
1985	48.0	20.2	34.4
1986	40.0	16.6	28.6
1987	45.6	14.4	30.3
1988	67.6	22.0	45.3
1989	58.3	17.6	38.3
1990	60.6	18.3	39.9
1991	46.0	13.6	30.1
1992	62.7	17.6	40.6
1993	68.5	17.7	43.6
1994	77.7	20.4	49.6
1995	104.6	27.9	67.0

**Table 3: Rate (per million persons) of fatal opioid overdoses,
by state for males, 1979-1995**

Year	NSW	VIC	Other
1979	21.5	18.1	7.8
1980	22.8	12.3	5.3
1981	36.9	16.4	9.5
1982	41.1	8.6	7.8
1983	58.3	21.1	17.3
1984	60.7	23.9	13.6
1985	77.7	45.0	23.3
1986	62.7	46.2	14.9
1987	78.7	48.4	12.6
1988	118.4	70.7	24.7
1989	92.1	67.9	26.2
1990	107.9	59.5	23.4
1991	80.2	47.1	20.1
1992	104.5	60.5	33.0
1993	112.8	63.8	46.2
1994	124.2	68.2	56.2
1995	168.1	101.2	75.8

**Table 4: Rate (per million persons) of fatal opioid overdoses,
by state for females, 1979-1995**

Year	NSW	VIC	Other
1979	10.7	5.8	3.3
1980	7.0	3.4	1.6
1981	6.0	5.6	2.3
1982	23.4	3.3	0.7
1983	26.5	4.3	6.5
1984	25.3	20.1	6.4
1985	28.9	20.8	11.0
1986	26.9	21.5	5.4
1987	34.1	25.6	7.0
1988	23.9	27.2	5.0
1989	35.5	18.2	4.3
1990	26.4	13.3	4.2
1991	27.0	14.3	12.6
1992	27.0	14.3	12.6
1993	25.6	21.1	13.1
1994	36.5	25.1	8.3
1995	33.4	34.8	22.8

**Table 5: Mean age at death for opioid overdoses by sex, 1979-1995,
among persons aged 15 to 44 years**

Year	Males	Females	Total
1979	24.5	23.5	24.3
1980	24.9	22.9	24.5
1981	25.7	24.4	25.5
1982	26.4	26.9	26.5
1983	26.6	25.8	26.4
1984	25.9	24.6	25.5
1985	27.1	25.9	26.8
1986	26.8	25.2	26.4
1987	27.5	25.6	27.1
1988	28.2	25.1	27.5
1989	29.1	25.9	28.4
1990	29.0	25.8	28.3
1991	29.7	28.6	29.1
1992	29.9	27.9	29.5
1993	30.1	29.5	30.0
1994	29.9	29.3	29.7
1995	30.6	28.0	30.1

**Table 6: Mortality rate (per million) for opioid overdoses 1979-1995,
among males aged 15 to 44 years**

Year	15-24	25-34	35-44
1979	23.2	17.1	1.1
1980	16.9	18.5	1.1
1981	21.2	32.9	2.2
1982	16.5	34.3	4.0
1983	33.6	49.8	7.7
1984	39.4	46.2	5.6
1985	46.6	74.9	14.3
1986	35.8	68.3	8.6
1987	41.9	71.3	16.7
1988	53.7	107.6	34.7
1989	36.5	96.5	39.4
1990	39.1	103.9	34.7
1991	32.0	72.7	31.1
1992	40.5	103.7	40.7
1993	40.0	111.1	53.9
1994	61.6	102.5	68.3
1995	64.1	159.8	90.6

**Table 7: Mortality rate (per million) for opioid overdoses 1979-1995,
among females aged 15 to 44 years**

Year	15-24	25-34	35-44
1979	9.7	6.2	0
1980	5.6	3.4	0
1981	6.3	5.0	0
1982	8.5	13.0	3.2
1983	14.0	15.3	4.1
1984	24.0	19.1	1.0
1985	23.1	29.0	3.7
1986	23.6	19.3	2.7
1987	18.1	19.6	1.7
1988	31.3	24.4	5.0
1989	22.2	22.4	4.0
1990	22.1	25.0	3.1
1991	9.6	22.7	7.0
1992	14.1	30.4	5.3
1993	14.1	23.4	15.0
1994	16.5	28.3	15.6
1995	30.9	33.2	16.0

**Table 8: Opioid overdose mortality rate (per million) males 1979-1995
by birth cohort**

Year	1940-49	1950-59	1960-69	1970-79
1979	7.4	29.2	5.3	0
1980	2.8	31.2	3.0	0
1981	4.7	44.4	7.6	0
1982	6.5	36.9	11.2	0
1983	12.1	54.5	26.1	0
1984	5.6	46.2	39.4	0
1985	15.7	70.1	51.8	0
1986	6.4	52.6	54.4	0.8
1987	8.2	59.0	59.8	4.4
1988	14.5	80.2	98.3	7.4
1989	6.4	75.9	86.7	6.6
1990	10.9	65.7	95.4	13.1
1991	9.1	43.9	79.5	7.9
1992	8.2	60.1	104.1	18.0
1993	15.5	61.6	110.5	32.4
1994	14.6	68.3	102.5	61.6
1995	23.8	79.2	154.0	83.1

**Table 9: Opioid overdose mortality rate (per million) females 1979-1995
by birth cohort**

Year	1940-49	1950-59	1960-69	1970-79
1979	3.0	10.1	3.2	0
1980	0	8.4	0	0
1981	1.0	7.3	3.1	0
1982	3.9	16.1	4.7	0
1983	4.9	17.6	10.8	0
1984	1.0	19.1	23.9	0
1985	2.9	24.5	26.9	1.6
1986	1.0	15.6	28.2	0.8
1987	1.9	12.4	24.2	1.6
1988	1.0	13.8	38.0	7.8
1989	1.0	14.4	26.4	7.7
1990	1.0	13.5	26.8	9.9
1991	0	12.7	20.8	6.1
1992	0	8.9	30.7	9.8
1993	1.0	16.3	22.8	12.8
1994	0	15.6	28.3	16.5
1995	0	14.8	31.6	32.6

APPENDIX C: Statistical Analyses

C.1. Jurisdictional differences in rates of overdose death

Multiple logistic regression analyses were conducted to predict the odds of dying of an opioid overdose from: sex, year (entered as a linear term) and jurisdiction (entered as three categories: New South Wales, Victoria and all other states and territories). Interaction terms between year and state were tested for inclusion in the model to assess whether there were differences between the jurisdictions in the rate of increase of opioid overdoses over the period.

These analyses indicated that there was a marked difference between states in overdose mortality, with New South Wales having the highest rate across the whole study period. The odds were 1.67 times [95% CI 1.55, 1.79] greater than in Victoria and 3.3 times [95% CI: 3.00, 3.51] than in all the other states. Attempts to fit a model which included interactions between state and year produced estimation problems. The estimation procedure failed to converge and produced parameter estimates with extremely large standard errors. These problems reflected the low frequency with which opioid overdose deaths occurred among females in the smaller states. Simplification of the state variable to a contrast between New South Wales and all other states marginally improved estimation of the model but the standard errors for some terms in the model were still unacceptably large. Fitting separate models for men and women reduced but did not resolve the problems of estimation.

Appendix C.2. Multiple regression analysis of age at death

A multiple linear regression analysis was conducted on age at death with year and sex as the predictor variables. Year was entered as a both linear and quadratic term and a interaction between sex and year was also included. The final model (which is shown in Table C.2) included the variables sex and age as a linear term. There were no statistically significant interaction terms. These results indicate that age at death was linearly related to the year in which death occurred (increasing by 4 months per year) and that males were 21 months older on average than females at death.

Table C.2: Unstandardised regression weights (and 95% confidence intervals) for year and sex as predictors of age at death

Variable	Unstandardised Beta weight	95% Confidence Interval
Year	0.36	0.32, 0.40
Sex	-1.79	-2.21, -1.37

$$R^2 = 0.08$$

$$F(2, 4167) = 187.09 \quad p < 0.001$$

C.3. Logistic regression analysis of opioid overdose rate

Multiple logistic regression analyses were conducted to examine trends in opioid overdose mortality between 1979 and 1995, after adjusting for sex and age-group (entered as three categories: 15-24 years, 25-34 years and 34-44 years). Year was entered as a linear term to simplify the analysis. Interaction terms (between year and age group, year and sex, and year, sex and age group) were tested for inclusion in the model by backward elimination.

Table C.3: Odds (and 95% confidence intervals) of an opioid overdose per year 1979-1995 within each age group for males and females

Age Group	Males	Females
15-24 years	1.02 (0.98, 1.07)	1.00
25-34 years	1.10 (1.06, 1.14)	1.06 (1.01, 1.11)
35-44 years	1.33 (1.26, 1.40)	1.32 (1.20, 1.45)

The final model selected included interaction terms between age group and year, and year and sex, indicating that the rate of change in overdose rates over the period varied between age groups and males and females. In order to simplify the presentation of the results, the increase in the odds of an opioid overdose with each year is shown in table C.3 for men and women in each of the three age groups (with interactions between year and age and between sex and age included in the final model). These results suggest that the rate of increase in the odds of an overdose death was greatest among men and women who were 35 years or older at the time of their death.

C.4. Logistic regression analysis by age cohort.

Multiple logistic regression analyses were conducted to examine differences in trends in opioid overdose mortality between 1979 and 1995 in men and women in the two birth cohorts with sufficient numbers of deaths throughout the study period to warrant analysis, namely, those born between 1950-1959 and 1960-1969. As in the previous analyses, year was entered as a linear term and interaction terms (between year and sex, year and cohort and sex, year and cohort) were tested for inclusion in the model by backward elimination.

Table C.4 Odds per year of an overdose death in each age cohort for males and females

Age Cohort	Males	Females
1950-1959	1.06 (1.01, 1.11)	1.00
1960-1969	1.27 (1.21, 1.32)	1.17 (1.11, 1.23)

The best fitting model proved to be one that contained interactions between sex, cohort and year. The presence of these interaction terms indicated that the rate of change in overdose mortality over the study period varied between males and females and age cohorts. In order to simplify the presentation of the results, the increase in the odds of an opioid overdose with each year is shown in table C.3 for men and women in each age cohort. These are derived from the full model (with interactions between year and age cohort, sex and age cohort, and sex, age cohort and year included in the model). These results suggest that the rate of increase in the odds of an overdose death was greater among men than women, greater among those born between 1960 and 1969 than those born between 1950 and 1959 and greatest for males born between 1960 and 1969.