Sharlene Kaye & Shane Darke

Non-Fatal Cocaine Overdose and Other Adverse Events Among Injecting and Non-Injecting Cocaine Users

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EXECUTIVE SUMMARY

The use of cocaine has been associated with a range of physical and psychological harms. Many of the adverse effects of cocaine may be short-lived and not associated with long-term consequences for the user's health. Some, however, particularly cardiovascular and cerebrovascular complications, may be fatal. In the US, cocaine has been implicated in a substantial proportion of fatal accidental drug overdoses.

Since the late 1990s, cocaine use has become increasingly prevalent among illicit drug users, particularly injecting drug users, in Sydney, Australia. Recent research has indicated that a substantial proportion of both injecting and non-injecting cocaine users in Sydney have reported serious physical and psychological symptoms associated with their use of cocaine. Moreover, these symptoms are consistent with the documented effects of cocaine and some are indicative of cocaine toxicity or 'overdose'.

Non-fatal cocaine overdose and the adverse events that users attribute to cocaine overdose have not yet been examined in Australia, nor have they been widely studied elsewhere. The aim of the present study was to investigate the prevalence and nature of non-fatal cocaine overdose and, more broadly, cocaine-related adverse events, among injecting and non-injecting cocaine users in Sydney. The study also aimed to examine the circumstances surrounding overdose, responses to overdose in others, and users' risk perceptions of cocaine overdose.

Two hundred cocaine users, including 120 injecting cocaine users (ICU) and 80 non-injecting cocaine users (NICU), were interviewed about their drug use history, cocaine use history, severity of cocaine dependence, history of cocaine-related adverse events, and cocaine overdose history.

Physical (49%) and psychological (42%) adverse events associated with the use of cocaine were prevalent among the sample, with 67% of ICU, and 51% of NICU, reporting at least one such symptom. Among both groups, palpitations, intense sweating and severe nausea/vomiting were the most commonly reported physical problems. The most common

psychological symptoms among ICU and NICU were paranoia, anxiety and panic. These symptoms are consistent with the known effects of cocaine. Age, severity of cocaine dependence, and the extent of polydrug use were significantly associated with more extensive adverse effects.

Thirteen percent of the total sample had overdosed on cocaine. Those who had overdosed had done so on a median of 2 occasions. The prevalence of cocaine overdose was significantly higher among ICU (17% vs 6%) and females (20% vs 9%). Similarly, ICU (2 vs 1) and females (4.5 vs 1) had overdosed on a significantly greater number of occasions. Gender was the only significant independent predictor of cocaine overdose, with females being almost three times as likely as males to have overdosed. The most commonly reported symptoms of cocaine overdose were palpitations, intense sweating and seizures. Other reported symptoms included paranoia, severe agitation, respiratory distress, high body temperature, chest pain, and tremors. These symptoms are consistent with the documented indicators of cocaine overdose.

A substantial proportion of both ICU (13/20) and NICU (3/5) had been using another drug at the time of overdosing on cocaine, with heroin and alcohol, respectively, being the most common drugs used in combination with cocaine. This finding is consistent with the literature regarding fatal cocaine overdose which suggests that the risk of overdose may be increased by the use of heroin and alcohol with cocaine.

Having been present when someone else overdosed on cocaine was more common than having overdosed oneself, with 35% of ICU, and 8% of NICU, reporting that they had witnessed an overdose. Nevertheless, there were substantial proportions of both groups who stated that they would not recognise a cocaine overdose. ICU and NICU differed in terms of the way they responded to a cocaine overdose, with ICU being more likely to call an ambulance or take a person to hospital.

The majority of both ICU and NICU believed that the primary reason for cocaine overdose was using excessive amounts of cocaine, and that it was unlikely that they would overdose in

the future. Substantial proportions of both groups thought, however, that it was likely that other cocaine users would overdose at least once in their lifetime.

Overall, the findings of the current study suggest that cocaine can induce serious symptoms in the context of various patterns of use, but particularly among older, more dependent polydrug users. They also highlight the importance of educating cocaine users about the possibility and nature of overdose and making them aware that cocaine overdose can occur irrespective of dose, frequency and method of use. Furthermore, users need to be aware of the potential danger of combining cocaine with other drugs, such as heroin and alcohol.

1.0 INTRODUCTION

The harms associated with the use of cocaine have been well-documented, with a wide body of literature detailing the adverse effects of acute and chronic cocaine use on physical and psychological health (Chen, Scheier, & Kandel, 1996; Estroff, 1987; Julien, 1998; Karch, 2002; Marsden et al., 1998; Platt, 1997; Warner, 1993; Washton & Gold, 1987). Many of the physical complications of cocaine use appear to be mediated by the drug's vasoconstrictive effects, which are manifested in several of the body's physiological systems. Consequently, cocaine can cause a wide range of problems including: cardiovascular (e.g. chest pain, cardiac arrhythmias, myocardial infarction and ischemia, and cardiomyopathy); neurological (e.g. cerebrovascular accidents, i.e. strokes, seizures, and headaches); gastrointestinal (e.g. abdominal pain, vomiting, colitis, and bowel infarction); and respiratory symptoms (e.g. exacerbation of asthma, rapid and/or irregular breathing, respiratory collapse, pulmonary oedema, and bronchitis). Cocaine can induce hyperthermia as a result of increased metabolism, peripheral vasoconstriction, and an impairment of the thalamus to control body temperature and can also cause obstetric complications, such as irregularities in placental blood flow, premature labour, and low neonate birth weights (Blum, 1984; Brands, Sproule, & Marshman, 1998; Crandall, Vongpatanasin, & Victor, 2002; Friedman et al., 1996; Henry, 2000; Lange & Hillis, 2001; Marzuk et al., 1998; McCann & Ricaurte, 2000; Platt, 1997; Warner, 1993).

Some of the adverse physical effects of cocaine are specific to the route of administration (Cregler & Mark, 1986; Yeager et al., 1987). Intranasal cocaine use is associated with a number of nasal symptoms, such as congestion, rhinitis, bleeding, ulceration and perforation of the nasal septum, as well as a loss of the sense of smell. The specific effects of smoking cocaine relate to pulmonary and respiratory complications, such as coughing, the production of bloody or black sputum, chest pain, wheezing, and shortness of breath (Platt, 1997). Injecting cocaine use is associated with the problems related to injecting drug use *per se*, such as vascular damage, abscesses, bacterial infections (e.g. endocarditis - an infection of the heart and its valves), and a greater risk of contracting blood-borne viruses such as hepatitis and HIV (Chaisson et al., 1989; Cherubin, 1967; Cherubin & Sapira, 1993; Julien, 1998;

Ostor, 1977; Schoenbaum et al., 1989; Stone, Stone, & MacGregor, 1990; Yeager et al., 1987).

Due to the higher frequency of injecting that is associated with cocaine use, the injection-related problems noted above are more prevalent among cocaine injectors than among injectors of other illicit drugs, such as heroin (Chaisson et al., 1989; Schoenbaum et al., 1989; Bux, Lamb, & Iguchi, 1995; Darke, Kaye, & Topp, 2002a; McKetin, Darke, & Godycka-Cwirko, 1999; van Beek, Dwyer, & Malcolm, 2001). In the US, for example, injecting cocaine use has been associated with higher levels of needle-sharing, increased sexual risk-taking, and a higher HIV seroprevalence than injecting heroin use (Chaisson et al., 1989; Schoenbaum et al., 1989; Bux et al., 1995). Studies conducted in Europe (Torrens et al., 1991) and Australia (Darke, Baker, et al., 1992) have also reported an association between cocaine injecting and higher levels of HIV risk-taking behaviours. More recent Australian research has found that injecting cocaine users report a greater number of injection-related problems (e.g. vascular damage, abscesses, and infections) than other injecting drug users (IDU) (Darke et al., 2002a; McKetin et al., 1999; van Beek et al., 2001).

While there are certainly serious problems related to route of administration, two of the most serious adverse effects of cocaine use, i.e. cardiovascular and cerebrovascular complications, can occur regardless of administration route (Cregler, 1991; Cregler, 1994; Cregler & Mark, 1986; Isner et al., 1986; Klonoff, Andrews, & Obana, 1989; Lange & Hillis, 2001; National Institute on Drug Abuse [NIDA], 1999). Indeed, chest pains, palpitations and seizures are among the most common complaints among cocaine users presenting to emergency departments in the US (Derlet & Albertson, 1989; Kontos et al., 2003; Lange & Hillis, 2001; McCann & Ricaurte, 2000). Although cocaine-induced strokes may be less common than seizures, their prevalence has increased in the US since the early 1980s as cocaine use has become more prevalent (Klonoff et al., 1989). In a study examining risk factors for stroke, Petitti et al. (1998) found that cocaine users were 14 times more likely than non-users to have suffered a stroke. Cocaine use was associated with a greater risk of stroke than amphetamine use, amphetamine users being 4 times more likely than non-users to have had a stroke.

The above complications are potentially fatal and can occur among young, healthy users without any previous risk factors (Cregler, 1991; Lange & Hillis, 2001; Pavon-Jimenez, Garcia-Rubira, & Calderon-Leal, 1999; Platt, 1997; Vasica & Tennant, 2002; Wickes, 1993). Moreover, there is no specific combination of conditions under which such outcomes can be predicted. While dose and frequency of use undoubtedly interact to influence the likelihood of adverse reactions to cocaine, the thresholds over which these potentially fatal reactions occur can vary widely between individuals. Toxic reactions to cocaine can occur irrespective of dose, frequency of use, or route of administration and have been reported with small amounts of cocaine and on the first occasion of use (Cregler, 1994; Estroff, 1987; Jenkins et al., 1999; Karch & Stephens, 1991; Karch, Stephens, & Ho, 1998; Lange & Hillis, 2001; Platt, 1997; Washton & Gold, 1984).

Cocaine can cause myocardial ischemia and infarction via several mechanisms: an increase in myocardial oxygen demand, vasoconstriction of the coronary arteries, and coronary thrombosis (Friedman et al., 1996; Hollander et al., 1997; Kontos et al., 2003; Lange & Hillis, 2001; Rump, Theisohn, & Klaus, 1995; Wilson, 1998). Although cocaine can induce such cardiovascular complications in users with normal coronary arteries (Karch & Stephens, 1991; Lange & Hillis, 2001; Minor et al., 1991; Mittleman et al., 1999; Vasica & Tennant, 2002; Williams, Restieaux, & Low, 1998), underlying atherosclerotic coronary artery disease has been demonstrated in a number of studies of cocaine users, both living and deceased (Dressler, Malekzadeh, & Roberts, 1990; Hollander et al., 1997; Karch, 2002; Kontos et al., 2003; Mittleman et al., 1999; Pavon-Jimenez et al., 1999; Vasica & Tennant, 2002; Wilson, 1998). A more recent study examining cardiac pathology among cocaine-related fatalities has also found high levels of coronary pathology, particularly coronary artery atherosclerosis (Darke, Kaye, & Duflou, 2003). Moreover, coronary artery disease has been found not only among cocaine users presenting with myocardial infarction or among fatal overdose cases, but among young chronic cocaine users who are asymptomatic (Roldan, Aliabadi, & Crawford, 2001). This premature and accelerated development of coronary artery atherosclerosis, which increases the risk of an acute event such as cocaine-related myocardial infarction, has been associated with the chronic use of cocaine (Benzaquen, Cohen, & Eisenberg, 2001; Friedman et al., 1996; Hollander et al., 1997; Kontos et al., 2003; Lange & Hillis, 2001; Mittleman et al., 1999; Wilson, 1998). Chronic cocaine use has also been

associated with such cardiovascular pathology as left ventricular hypertrophy (i.e. increased mass and wall thickness of the left ventricle), a condition which can predispose the individual to cocaine-induced myocardial ischemia and/or arrhythmia (Benzaquen et al., 2001; Brickner et al., 1991; Friedman et al., 1996; Om et al., 1993).

A definition of the psychological sequelae of cocaine use is necessarily complex, as the psychological effects of cocaine are subject to variation according to dose, route of administration, context in which the drug is taken, and individual characteristics and experience (American Psychiatric Association, 2000; Johanson, 1986). Although cocaine can produce feelings of pleasure or euphoria, it can also produce aversive psychological symptoms, such as anxiety, panic, dysphoria, severe depression, paranoia, hallucinations, delirium, and violent agitation, particularly in high doses and during withdrawal (American Psychiatric Association, 2000; Friedman et al., 1996). Binge use of cocaine typically induces such symptoms and can lead to a state known as "cocaine psychosis". Cocaine psychosis is essentially a schizophreniform paranoid psychosis where the user experiences paranoid delusions, mania, delirium, and hallucinations. It has been described as a cocaine-induced psychiatric syndrome that is typically comprised of four successive stages that progress as the dose and frequency of use increases - euphoria, dysphoria, hallucinosis, and psychosis (Estroff, 1987).

Although cocaine is regarded as a harmful, and potentially lethal, drug, irrespective of the frequency and method of use (Cregler & Mark, 1986; Dackis & O'Brien, 2001; Isner et al., 1986; Klonoff et al., 1989; NIDA, 1999; Platt, 1997; Rodriguez, 1989), these factors may play a role in determining the likelihood of the occurrence of adverse events following cocaine use, as well as the severity of symptoms. Using cocaine at high doses or during binges, for instance, can increase the risk of serious physical and psychological complications (Cregler & Mark, 1986; Platt, 1997), and chronic cocaine use, in addition to inducing the aforementioned forms of cardiovascular disease, is commonly associated with problems such as anxiety, paranoia, aggression, depression and weight loss, not to mention dependence (American Psychiatric Association, 2000). Moreover, injecting cocaine use has been associated with a greater risk of physical and psychological symptomatology than either intranasal use (Hando, Flaherty, & Rutter, 1997; Washton & Gold, 1987) or smoking (Lexau,

Nelson, & Hatsukami, 1998). In turn, smoking cocaine is associated with a higher prevalence of physical and psychological symptoms than intranasal use (Ferri & Gossop, 1999; Washton & Gold, 1987).

Cocaine has been implicated in a significant proportion of fatal accidental drug overdoses in the US. Tardiff et al. (1996), for example, found that almost three-quarters of deaths due to drug overdose in New York between 1990 and 1992 were caused by cocaine, often in combination with opiates and alcohol. More recently, Coffin et al. (2003) looked at accidental drug overdose deaths in New York from 1990 to 1998 and found that cocaine was a cause of death in 70% of cases, with cocaine and opiates the most frequently observed drug combination.

As cocaine toxicity can involve multiple organ systems and, as such, may manifest as a variety of acute physical and psychological effects, the presentation of a cocaine overdose can vary among individuals. The physical symptoms of a cocaine overdose include nausea and vomiting, chest pain, tremors, increased body temperature, increased heart rate, rapid, irregular and shallow breathing, and seizures. Psychological symptoms such as anxiety, panic, extreme agitation, paranoia, hallucinations, and delirium are also indicative of a cocaine overdose.

The acute effects of cocaine, albeit intense, are generally short-lived, due to the short half-life of cocaine (45-90 mins) (Lange & Hillis, 2001). As such, many cocaine overdose victims recover spontaneously or respond successfully to medical intervention, though, as discussed above, chronic use may accelerate the development of serious cardiac pathology. As noted above, however, cocaine overdose can be fatal. Cocaine-related deaths are typically caused by seizures, cardiac arrhythmias, or respiratory failure (Brands et al., 1998; Cregler & Mark, 1986, Jacobs & Fehr, 1987), with cardiovascular complications accounting for the majority of cocaine-related deaths (Advisory Council on the Misuse of Drugs, 2000; Vasica & Tennant, 2002). Fatal cocaine overdose has also occurred due to brain haemorrhage, stroke and kidney failure (Australian Drug Foundation, 2003; Brands et al., 1998). Hyperthermia may also contribute to cocaine-related mortality, with previous research demonstrating an increase in cocaine overdose fatalities during hot weather (Marzuk et al., 1998). As noted

above, cocaine toxicity or overdose is not dose-specific. The lethal dose of cocaine is highly variable due to individual differences in sensitivity among users. Although deaths have been reported after a single dose of a few hundred milligrams, there are cases in which a dose of several grams has not proved fatal (Brands et al., 1998; Jacobs & Fehr, 1987; Jenkins et al., 1999; Karch & Stephens, 1991; Karch et al., 1998; Lange & Hillis, 2001). Moreover, overdose can occur regardless of the administration route, although the risk of overdosing, as well as the likelihood that an overdose will be fatal, increases when cocaine is administered in a way that causes a rapid increase in brain levels of the drug, and that it is this factor that may be more important than the absolute dose administered (Jacobs & Fehr, 1987; Pottieger et al., 1992; Wetli & Wright, 1979). Thus, injecting cocaine is likely to pose the greatest risk of overdose, followed by smoking, and then intranasal use (Pottieger et al., 1992).

A common pattern of use among polydrug injectors is to inject a mixture of cocaine/crack and heroin - the resultant combination is known as a "speedball" (Marsden et al., 1998; NIDA, 1999; Platt, 1997). As the respiratory depression caused by heroin may be further exacerbated by cocaine, speedballing may be a highly risky practice (Friedman et al., 1996; Platt, 1997). After the combination of cocaine and alcohol, cocaine and heroin was the second most prevalent drug combination among those admitted to emergency rooms in the US during 1992 (Platt, 1997). Indeed, heroin has been present in a substantial proportion of cocaine-positive deaths in the US (Coffin et al., 2003; Community Epidemiology Work Group [CEWG], 1999; Tardiff et al., 1996). The injection of speedballs has been associated with a greater risk of overdose, with speedball injectors in a study of overdose among IDU in San Fransisco being 2.6 times more likely than other IDU to report having overdosed (Ochoa et al., 2001). Speedballing has also been associated with increased HIV risk and seroprevalence due to the combined immunosuppressive effects of cocaine and heroin, as well as increased needle-sharing and a greater likelihood of developing skin and soft-tissue abscesses (Mendelson & Mello, 1996; Murphy et al., 2001; Platt, 1997).

There has been relatively little research on the prevalence and correlates of non-fatal overdose among cocaine users, and no such research conducted in Australia. In a study of cocaine/crack users in Miami, 40% had overdosed on cocaine at least once (Pottieger et al.,

1992). Those who had injected cocaine had more extensive overdose histories than users who had used cocaine intranasally (snorted) or smoked crack cocaine. Specifically, 40% of users who had injected cocaine in the past had overdosed on the drug via that route of administration, and they had done so a median of 3 times. In comparison, 29% percent of those who had snorted cocaine had overdosed from intranasal use, with a median of 2 past overdoses, and 19% of past crack smokers had overdosed on crack on a median of one occasion. A more recent study of cocaine users in Brazil by Mesquita et al. (2001) found that 20% of cocaine users had experienced one or more overdoses and 50% reported knowing one or more other cocaine users who had died of an overdose. Given, however, that Mesquita and colleagues defined overdose as losing consciousness following the use of a drug, these figures may be a conservative estimate of the true prevalence of cocaine overdose among the sample in question.

Cocaine use in Australia differs from that in countries such as the US, UK and Europe in that cocaine powder (cocaine hydrochloride) is overwhelmingly the predominant form of cocaine used in Australia. To date, there has been no evidence that crack is widely available to users in Australia, and very few people have reported using it (Darke et al., 2002a; Roxburgh et al., 2003). Hando et al. (1997) identified two distinct groups of cocaine users in Sydney – a group with a higher socio-economic status (SES) who typically administered the drug intranasally, and another with a lower SES who injected cocaine. The lower SES users were more likely to be unemployed or, in the case of females, working in the sex industry, had lower levels of education, were more criminally active, and more likely to be enrolled in a methadone maintenance program.

To date, cocaine injecting in Australia has most commonly occurred among regular heroin injectors, for whom polydrug use is the norm. Between 1996 and 2001, the Illicit Drug Reporting System (IDRS) (Hando, O'Brien, et al., 1997) detected a progressive increase in both the prevalence and frequency of cocaine use and injecting among IDU in Sydney. In 1996, 41% of Sydney IDU surveyed for the IDRS had used cocaine in the previous six months (Hando, O'Brien, et al., 1997). By 2001, however, this figure had risen to 84% (Darke, Kaye, & Topp, 2002b). Moreover, the median number of use days in the past six months increased from 3 days in 1996 to 96 days in 2001, with the proportion of those using

daily during this period increasing from 2% to 35% (Darke et al., 2002b). Cocaine use has also become prevalent among non-injecting drug users in Sydney, with over half of the ecstasy users surveyed for the IDRS in 2000 (53%) (Topp & Darke, 2001) and 2001 (57%) (Topp et al., 2002) having used cocaine in the preceding six months.

Given that cocaine has become more widely used in Australia, the harms associated with its use warrant investigation. A recent Australian study of cocaine-related harm found that serious physical and psychological symptoms associated with cocaine use were commonly reported by both injecting and non-injecting cocaine users (Kaye & Darke, in press). Non-fatal cocaine overdose and the adverse events that users attribute to cocaine overdose, however, have not been examined in Australia, nor have they been widely studied elsewhere. The aim of the present study was to investigate the prevalence and nature of non-fatal cocaine overdose and, more broadly, cocaine-related adverse events, among injecting and non-injecting cocaine users in Sydney. The study also aimed to examine the circumstances surrounding overdose, responses to overdose in others, and users' risk perceptions of cocaine overdose.

1.1 Study Aims

The specific aims of the present study were as follows:-

1. To determine the prevalence and nature of cocaine-related adverse events among injecting and non-injecting cocaine users in Sydney;
2. To determine the prevalence of non-fatal cocaine overdose;
3. To examine the nature of cocaine overdose by ascertaining the signs and symptoms of cocaine overdose, as well as determining the associated risk factors;
4. Examine the circumstances, responses to, and risk perceptions of cocaine overdose.

2.0 METHOD

2.1 Procedure

All subjects were volunteers who were paid A$30 for their participation in the study. Recruitment took place between July 2002 and February 2003, via advertisements placed in needle and syringe programs, dance club magazines, rock magazines, local newspapers and by word of mouth. Respondents approached the researcher at the agency, or contacted them by telephone, at which time the respondent was screened for eligibility to be included in the study. To be eligible for participation the respondent had to have used cocaine within the preceding 12 months. Among the ICU sample, it was a requirement that the primary route of cocaine administration during the preceding 12 months was by injection, and, among NICU, that the primary route of cocaine administration during this period was non-parenteral. Frequency of cocaine use was not an inclusion criterion as cocaine-related adverse events and overdose associated with a range of use patterns was under investigation.

All subjects were guaranteed, both at the time of screening and interview, that any information they provided would remain strictly anonymous and confidential. Interviews were conducted by a member of the research team and took approximately 30 minutes to complete.

2.2 Structured Interview

A structured interview that addressed demographic characteristics, drug use history, cocaine use history, severity of cocaine dependence, history of cocaine-related adverse events, and cocaine overdose history was developed.

2.2.1 Demographic characteristics

Demographic information obtained included: age, gender, level of secondary and tertiary education, employment status, drug treatment history, and prison history.

2.2.2 Drug use history

Drug use history was ascertained by asking about past and recent (i.e. preceding 6 months) use and injection of the following drug classes: heroin, methadone/buprenorphine, other opiates, amphetamines, cocaine, hallucinogens, ecstasy, benzodiazepines, cannabis, anti-depressants, inhalants, alcohol, and tobacco. Frequency of use of each drug class over the preceding six months was also obtained.

2.2.3 Cocaine use history

The ages at which subjects first used and first regularly used (i.e. at least monthly) cocaine were obtained, as were the initial and recent routes of cocaine administration. Cocaine use in the preceding month was measured using the Opiate Treatment Index (OTI) (Darke, Hall, et al., 1992). OTI scores of 1 equate to one use episode a day, greater than 1 to more than daily use, and less than 1 to less than daily use.

2.2.4 Cocaine dependence

Cocaine dependence was measured using the Severity of Dependence Scale (SDS) (Gossop et al., 1995). A diagnostic cut-off score of 3 (i.e. a score of 3 or more) on the SDS has previously been determined, via ROC analysis, as indicating cocaine dependence (Kaye & Darke, 2002).

2.2.5 Cocaine-related adverse events

History of cocaine-related adverse events was assessed by asking subjects if they had ever suffered any adverse effects after or while using cocaine. If so, they were asked to indicate which symptoms, from a list of known physical and psychological effects of cocaine, they had experienced. Reported symptoms not otherwise specified were recorded separately.

2.2.6 Cocaine overdose

Cocaine overdose history was ascertained by asking subjects if they had ever overdosed on cocaine, and if so, which symptoms from the aforementioned list they identified as indicators of previous overdose. Subjects were asked how often they had overdosed on

cocaine, when they first and last overdosed, and whether medical intervention occurred. The circumstances of their most recent cocaine overdose were also ascertained, as was beliefs about the primary reason for this overdose. Overdose in others was also investigated by asking subjects how they would recognize a cocaine overdose in others, whether and how many times they had been present when someone else had overdosed on cocaine, how they responded, and circumstances of the last cocaine overdose they had witnessed. Risk perceptions of cocaine overdose were assessed by asking subjects to give a primary reason for cocaine overdose and to estimate how likely it was that they and others would overdose on cocaine in the future.

2.3 Statistical Analyses

For continuous variables t-tests were employed. Where distributions were highly skewed, medians were reported, and Mann-Whitney U tests conducted. Categorical variables were analysed using chi-square. In order to determine the factors that were independently associated the extent of cocaine-induced adverse events, simultaneous multiple regressions were conducted. Multiple logistic regressions were conducted in order to determine the factors that were independently associated with having overdosed on cocaine. All analyses were conducted using SPSS for Windows, Version 11.0 (SPSS Inc., 2001).

3.0 RESULTS

3.1 Sample characteristics

The sample consisted of 200 illicit drug users who, in accordance with the aforementioned inclusion criteria, had used cocaine at least once in the 12 months preceding interview. Subjects who had injected cocaine during the preceding 12 months (n=120) were classified as injecting cocaine users (ICU), while those who had employed non-injecting routes of cocaine administration (n=80) were classified as non-injecting users (NICU).

The mean age of the sample was 30.1 years (SD 7.9; range 18-54 yrs), with 65% being male. The mean length of school education was 10.4 years (SD 1.7; range 5-12 yrs), with 23% having completed a trade or technical course, and 19% having completed a university course. Nearly two-thirds (60%) of the sample were unemployed at the time of interview, with 18% in full-time employment, 17% in part-time or casual employment, 4% in full-time study, and 1% who performed home duties. Nine percent of the sample reported that they were currently engaged in sex work. A third of the sample (33%) were in treatment for drug dependence at the time of interview and had been so for a median of 12 months (range 1-180 mths). The majority of those in treatment (50/67) were enrolled in a methadone maintenance program on a median dose of 75 mg. The remainder of those in treatment were on buprenorphine (n=13), on a detox program (n=1), attending Narcotics Anonymous (NA) meetings (n=1), or receiving counselling for drug use (n=2). A third of the sample (33%) had a prison history.

3.2 Demographics and drug use histories of ICU and NICU

As Table 1 illustrates, ICU were significantly older, had less education, and were more likely to be male than NICU. They were also more likely to be unemployed, engaged in treatment for drug dependence, and to have a prison history than NICU.

Heroin was the nominated drug of choice for half of the ICU group, with cocaine and cannabis the drugs of choice for 30% and 10% of ICU, respectively (Table 2). Ecstasy and

cannabis were the drugs of choice for equal proportions (26%) of NICU, with cocaine being nominated as the drug of choice by 21% of this group.

ICU had used a greater number of drug classes than NICU in their lifetime (10.6 vs 7.4, t_{198}=7.12, p<.001), as well as in the preceding six months (8.7 vs 5.8, t_{190}=6.36, p<.001) (Table 2). Although NICU had not injected cocaine in the 12 months preceding interview, 21% (n=17) had injected a drug in the past and 6% (n=5) had done so in the previous six months. Not surprisingly, ICU had injected a greater number of drug classes than NICU in their lifetime (4.8 vs 0.6, t_{198}=17.88, p<.001) and in the previous six months (3.1 vs 0.9, t_{141}=22.12, p<.001).

Table 1: Demographic characteristics of ICU and NICU

	ICU (n=120)	**NICU (n=80)**
Age (mean yrs)	32.3	26.7 *
% Male	72	54 *
Yrs of School (mean yrs)	9.6	11.5 *
Level of Education		
% Trade/technical	20	28
% University/college	4	41 *
Employment		
% Unemployed	84	23 *
% Sex work	15	0
Drug Treatment		
% Methadone	42	0
% Buprenorphine	11	0
% Detox	1	0
% Narcotics Anonymous	1	0
% Drug Counselling	0	3
% Prison History	53	1 *

Table 2: Drug use histories of ICU and NICU

	ICU (n=120)		NICU (n=80)	
Primary drug of choice	Heroin	50%	Ecstasy	26%
	Cocaine	30%	Cannabis	26%
	Cannabis	10%	Cocaine	21%
Mean no. of drug classes used				
Ever	10.6		8.7*	
Last 6 mths	7.4		5.8*	
Mean no. of drug classes injected				
Ever	4.8		0.6	
Last 6 mths	3.1		.09	

3.3 Cocaine use histories and current cocaine use patterns of ICU and NICU

Although ICU first used cocaine at a later age than NICU (21.8 vs 19.9, $t_{189}=2.68$, $p<.01$) there was no significant difference between the groups in age of first regular use of cocaine (23.9 vs 22.5) (Table 3).

Injection was the most common primary route of cocaine administration among ICU (92%), however there were cocaine injectors who had also snorted cocaine in the preceding 12 months (6%). A minority of ICU (2%) reported that they had injected and snorted cocaine on an equal number of occasions during this period. Among NICU, snorting was the most common route of administration (93%), although there were also reports of swallowing (1.5%) and smoking (1.5%) cocaine. A small proportion of NICU (4.5%) reported that they had snorted and either swallowed or rubbed cocaine on their gums with equal frequency during this time.

Table 3: Cocaine use histories of ICU and NICU

	ICU (n=120)	**NICU (n=80)**
Age first used cocaine	21.8	19.9 *
Age regular use	23.9	22.5
Primary route of administration (last 12 mths)		
Injecting	92	0
Snorting	6	92.5
Swallowing	0	1.5
Smoked	0	1.5
Mean OTI-Q scores	1.43	0.28 *
% used in last month	68	36 *
% used at least once/day in last mth	29	9 *
Mean days of use in last 6 mths	51.9	8.4 *
Mean SDS scores	5.2	1.4 *
Cocaine dependence (SDS)	67	21 *

Cocaine use in the month preceding interview, as indicated by mean scores on the OTI, was significantly more frequent for ICU than for NICU (1.43 vs 0.28, t_{141}=3.36, p<.01) (Table 3). The proportion of ICU that had used cocaine at all in the preceding month (68% vs 36%, χ^2=18.94, p<.001), and that had used at least daily (29% vs 9%, χ^2=12.06, p=.001), was higher than that of NICU. ICU had also used cocaine on a significantly greater number of days in the preceding six months than NICU (51.9 vs 8.4, t_{141}=7.38, p<.001).

As Table 3 illustrates, mean SDS scores were significantly higher among ICU than NICU (5.2 vs 1.4, t_{192}=7.58, p<.001), as was the proportion of users who exceeded the SDS cut-off for cocaine dependence (67% vs 21%, χ^2=39.64, p<.001).

3.4 Adverse effects of cocaine use

Subjects were asked if they had ever suffered any acute adverse effects either while or after using cocaine. Two-thirds of ICU (67%) and over half of NICU (51%) reported that they

had experienced at least one serious physical or psychological symptom as a result of using cocaine, this difference being statistically significant (χ^2=4.77, p<.05) (Table 4). The proportions of subjects who had experienced an adverse effect from using cocaine did not significantly differ according to gender (males: 62%; females: 58%), nor were there any significant differences between male and female users with respect to the proportions that had suffered physical (47% vs 52%) or psychological symptoms (40% vs 47%).

3.4.1 Physical effects

Over half of the ICU group (52%) and forty four percent of the NICU group reported having experienced adverse physical effects from using cocaine, this difference between proportions failing to attain statistical significance (Table 4). Among both groups, palpitations (ICU:28%; NICU:19%), intense sweating (ICU:20%; NICU:20%) and severe nausea/vomiting (ICU:19%; NICU:21%) were the most commonly reported problems. Other reported problems included severe headache (13%), high body temperature (10%), dizziness (10%), chest pain (8%), and seizures (7%).

Of those who reported physical effects of cocaine use, the median number of symptoms was 3 among ICU and 2 among NICU.

3.4.2 Psychological effects

Almost half (48%) of the ICU group and over a third (34%) of the NICU group reported having experienced adverse psychological effects from using cocaine (χ^2=3.73, p=.05) (Table 4). Among both ICU and NICU, paranoia (ICU:30%; NICU:19%), anxiety (ICU:25%; NICU:18%) and panic (ICU:18%; NICU:11%) were the most commonly reported psychological symptoms. Confusion (12%), increased sensitivity to sound (11%), auditory hallucinations (10%), severe agitation (10%), visual hallucinations (8%), and depression (7%) were some of the other psychological problems reported by the sample.

Of those who reported psychological effects of cocaine use, the median number of symptoms was 3 among ICU and 2 among NICU.

Table 4: Adverse physical and psychological effects of cocaine use

	ICU (n=120)	NICU (n=80)	TOTAL (N=200)
% Ever experienced adverse physical effect of cocaine use	52	44	49
Most common adverse physical effects:-			
Palpitations	28	19	24
Intense sweating	20	20	20
Nausea/vomiting	19	21	20
% Ever experienced adverse psychological effect of cocaine use	48	34 *	42
Most common adverse psychological effects:-	30	19	26
Paranoia	25	18	22
Anxiety	18	11	15
Panic			
% Ever experienced either physical or psychological adverse effect of cocaine use	67	51 *	61

3.4.3 Factors associated with adverse effects of cocaine

In order to determine the factors that were independently associated the extent of cocaine-induced adverse events, simultaneous multiple regressions were conducted. Variables entered into the model predicting the number of physical and psychological adverse effects were: age, gender, group, the number of days on which heroin, cocaine and ecstasy had been used in the preceding six months, SDS scores, and the number of drug classes used in the previous six months. Current age and the number of years elapsed since the first use of cocaine were collinear. Thus, only age was entered into the regression model. Age (β=0.16, $p<.05$), severity of dependence (β=0.30, $p<.001$), and the extent of polydrug use in the preceding six months (β=0.17, $p<.05$) were all significantly associated with the extent of the adverse effects of cocaine use. Thus, being older, more dependent on cocaine, and having used more drug classes in the previous six months was associated with having experienced a greater number of adverse effects. The model was significant ($F_{8,191}$=4.12, $p<.001$) and accounted for 15% of the variance.

3.5 Personal experience with cocaine overdose

3.5.1 History of cocaine overdose

Seventeen percent of ICU and 6% of NICU reported that they had overdosed on cocaine in the past, the difference between groups being statistically significant (χ^2=4.76, p<.05) (Table 5). There was, however, no significant difference between ICU and NICU in terms of the proportions that had overdosed in the preceding 12 months (9% vs 3%). Similarly, there were no significant differences between ICU (n=20) and NICU (n=5) who had overdosed in the past with respect to the median number of past overdoses (2 vs 1), the median number of months between initiation of cocaine use and the first overdose (60 vs 96), or the median number of months since the last overdose (10 vs 24 mths).

Table 5: Cocaine overdose histories of ICU and NICU

	ICU (n=120)	**NICU (n=80)**	**TOTAL (N=200)**
% Ever overdosed on cocaine	17	6 *	13
% Overdosed on cocaine in past year	9	3	7
No. of past ODs (median)	2	1	2
Time until first overdose (median mths)	60	96	72
Time since last overdose (median mths)	10	24	12

In order to determine whether cocaine overdose histories differed according to gender, comparisons between male and female cocaine users were made. Male and female cocaine users did not significantly differ in their age at the time of interview (30.6 vs 29 yrs). Males, however, first used cocaine at a significantly later age than females (21.6 vs 20.0 yrs, t_{190}=2.25, p<.05) (Table 6). Females scored higher on the SDS (4.6 vs 3.1, t_{114}=-2.21, p<.05). They were also more likely to have overdosed on cocaine in the past (20% vs 9%, χ^2=5.24, p<.05), as well as in the preceding 12 months (11% vs 4%, χ^2=4.12, p<.05), and had overdosed on a greater number of occasions than males (4.5 vs 1, U=35, p<.05). There were no significant differences between males and females with respect to the median number of

months between initiation of cocaine use and the first overdose (84 vs 54 mths), or the median number of months since the last overdose (18 vs 10 mths).

Table 6: Cocaine overdose histories of female and male cocaine users

	Females (n=71)	**Males (n=129)**
Age (mean yrs)	29.0	30.6
Age first used cocaine (mean yrs)	20.0	21.6 *
Mean SDS score	4.6	3.1 *
% Ever overdosed on cocaine	20	9 *
% Overdosed on cocaine in past year	11	4 *
No. of past ODs (median)	4.5	1 *
Time until first overdose (median mths)	54	84
Time since last overdose (median mths)	10	18

3.5.2 Cocaine overdose symptoms

The most common symptoms experienced by those who had previously overdosed on cocaine were palpitations (68%), intense sweating (44%) and seizures (40%) (Table 7). While there were no statistically significant gender differences, a slightly different pattern emerged among females, who most commonly reported palpitations, intense sweating and passing out as symptoms of cocaine overdose. Other symptoms of cocaine overdose reported by the sample included paranoia (32%), severe agitation (32%), respiratory distress (28%), high body temperature (28%), chest pain (28%), and tremors (28%). In around a third of overdose cases an ambulance had been called (36%) or the person had been taken to hospital (32%). Again there were no significant differences between females and males in these respects.

Table 7: Circumstances of past cocaine overdoses

	Females (n=14) %	**Males (n=11) %**	**Total (n=25) %**
Most common overdose symptoms:-			
Palpitations	**79#**	**55**	**68**
Intense sweating	**43**	**46**	**44**
Seizures	29	**55**	**40**
Passing out	**43**	27	36
Ambulance ever attended an overdose	43	27	36
Ever been taken to hospital	29	36	32

Bold font highlights the three most common overdose symptoms

3.5.3 Circumstances of most recent cocaine overdose

Nine out of the 20 ICU (45%) who had overdosed on cocaine had been in treatment (methadone maintenance) at the time that they last overdosed, and 2/20 reported that they had recently come out of prison or residential rehabilitation (Table 8). Conversely, no NICU were in treatment or had recently left prison or rehabilitation when they last overdosed. The majority of both ICU (13/20) and NICU (4/5) were with other people when they overdosed. However, while 7/20 ICU were attended to by an ambulance or were taken to hospital, none of the NICU received any such intervention. When asked if there had been any changes in their amount of cocaine use around the time of their most recent overdose, the most common response from both groups was that their use of cocaine had increased (ICU: 11/20; NICU: 4/5). Similarly, over half of both groups (ICU: 12/20; NICU: 3/5) reported that they had used more cocaine than usual on the day of their last overdose. ICU appeared to differ from NICU in terms of the time of the week at which they overdosed, with 12/20 (60%) ICU overdosing on a weekday and 3/5 (60%) NICU overdosing on a weekend. While the majority of NICU (4/5) overdosed at their home or at a friend's home, the majority of ICU (12/20) had overdosed in a public area or venue, or in a car.

Table 8: Circumstances of most recent cocaine overdose

	ICU (n=20)	NICU (n=5)	TOTAL (n=25)
Treatment when last overdosed:-			
Not in treatment	11	5	16
Methadone	9	0	9
Recently come out of prison/rehab	2	0	2
Alone at time of overdose	7	1	8
Others present	13	4	17
Taken to hospital/ambulance called	7	0	7
Recent changes in cocaine use:-			
Same	5	1	6
Increased	11	4	15
Decreased	0	0	0
Hadn't been using	4	0	4
Last dose preceding overdose compared with usual dose:-			
Same	7	3	10
More	12	2	14
Less	0	0	0
More cocaine used on day of last overdose compared with usual amount?			
Yes	12	3	15
No	8	2	10
Time of week:-			
Weekday	12	1	13
Weekend	5	3	8
Can't recall	3	1	4
Location of overdose:-			
Home	5	2	7
Friend's home	3	2	5
Car	1	0	1
Public location	4	0	4
Shooting gallery	2	0	2
Other	5	1	5

A substantial proportion of both ICU (13/20) and NICU (3/5) had been using another drug at the time of overdosing on cocaine. The most common drug used other than cocaine was heroin among ICU (9/20) and alcohol among NICU (3/5) (Table 9).

Table 9: Other drug use at most recent cocaine overdose

	ICU (n=20)	NICU (n=5)	TOTAL (n=25)
Heroin	9	0	9
Methadone	2	0	2
Other opiates	3	0	3
Benzodiazepines	2	0	2
Amphetamines	0	2	2
Ecstasy	0	1	1
Cannabis	5	1	6
Alcohol	3	3	6
Any other drug	13	3	16

3.5.4 Beliefs about primary causes of cocaine overdose

The primary reason given for the subjects' most recent cocaine overdose was overwhelmingly that the person had used an excess of cocaine, or more cocaine than usual (ICU: 14/20; NICU: 4/5) (Table 10). Whereas the remainder of ICU attributed their last overdose to an increase in purity, a decrease in tolerance or the failure to adequately space out doses, other NICU attributed their overdose to impurities in the cocaine.

Table 10: Primary reasons for most recent overdose

	ICU (n=20)	NICU (n=5)	TOTAL (n=25)
Used more than usual/too much	14	4	18
Impurities	0	1	1
Cocaine stronger than usual	2	0	2
Low tolerance	2	0	2
Didn't space out doses	2	0	2

3.5.5 Factors associated with past cocaine overdose

In order to determine the factors that were independently associated with having overdosed on cocaine, multiple logistic regressions were conducted. Variables entered into the initial model were: age, gender (female=1, male=0), group (ICU=1, NICU=0), the number of days on which heroin, cocaine and ecstasy had been used in the preceding six months, SDS scores, and the number of drug classes used in the previous six months. Gender was the only significant predictor of past cocaine overdose (OR=2.73, χ^2=4.00, df=1, p<.05; 95%CI=1.02, 7.32), indicating that, after taking all other factors into account, females were almost three times as likely as males to have overdosed on cocaine. The model was significant (χ^2=18.65, df=8, p<.05) and had a good fit (Hosmer-Lemeshow χ^2=3.53, df=8, p=.90).

3.6 Cocaine overdose in others

3.6.1 Symptoms of overdose in others

Subjects were asked how they would recognize a cocaine overdose. The more frequently reported symptoms of overdose in others are depicted in Figure 1. Among ICU, seizures (23%), passing out (19%) and palpitations (16%) were the most commonly reported symptoms of overdose, where among NICU, passing out (29%), anxiety (14%) and vomiting (14%) where the most common overdose symptoms reported. Forty one percent of ICU, however, and 50% of NICU, reported that they would not be able to recognize a cocaine overdose. The overwhelming majority of those who stated that they did not know how to recognize a cocaine overdose had never overdosed on cocaine themselves (96%) and had never witnessed a cocaine overdose in others (98%).

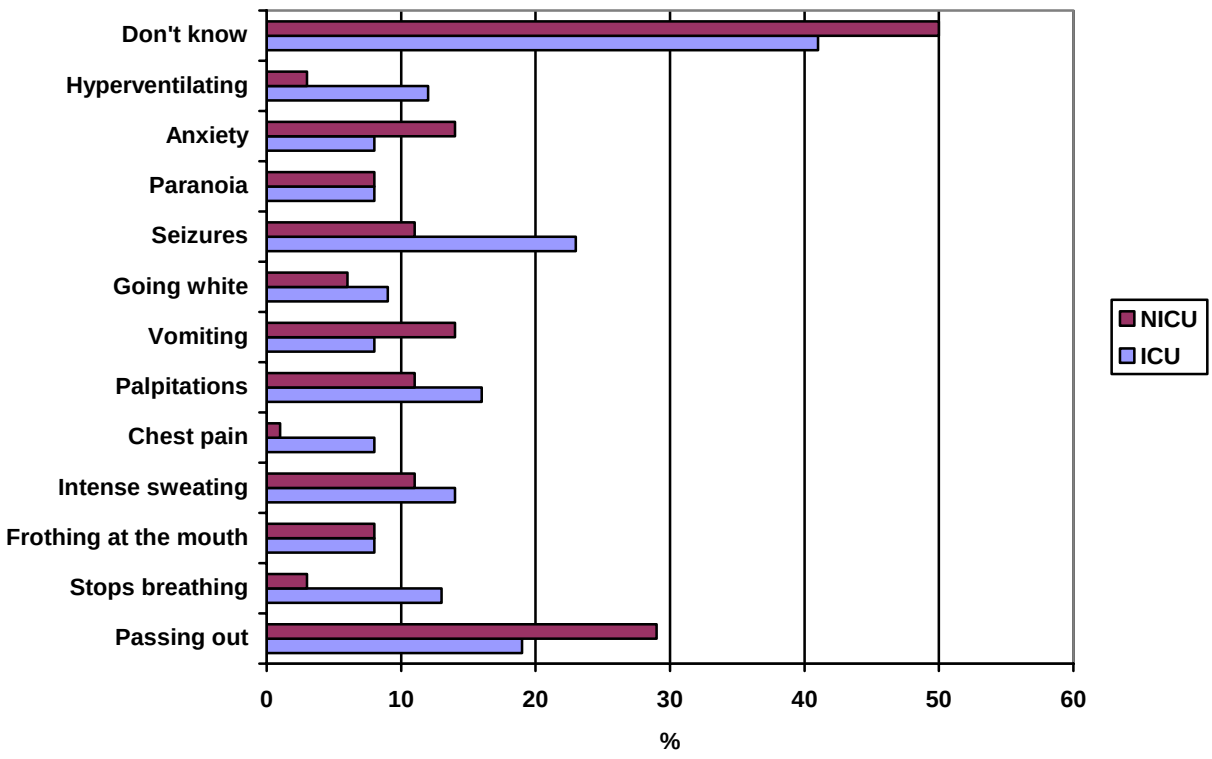

Figure 1: Symptoms of cocaine overdose in others

3.6.2 Prevalence of overdose in others

Over a third of ICU (35%) had witnessed a cocaine overdose, a significantly greater proportion than that of NICU (8%) (χ^2=19.9, p<.001) (Table 11). ICU were also more likely than NICU to have witnessed a cocaine overdose in the preceding 12 months (20% vs 3%, χ^2=13.0, p<.001) and had called an ambulance or taken a person who had overdosed to hospital more often (1 vs 0 median times, U=57.0, p<.05). While a small proportion (5%) of ICU had witnessed a fatal cocaine overdose, no NICU had been present at a fatal overdose.

Table 11: Presence at an overdose

	ICU (n=120)	NICU (n=80)	TOTAL (n=200)
% Ever present	35	8 *	24
% Present in past 12 months	20	3 *	13
No. of times present (median)	2	1	2
Time since last present at an overdose (median mths)	12	27	12
No. of times called an ambulance or taken others to hospital (median)	1	0 *	0
Time since last called ambulance/taken others to hospital (median months)	3	0	0.25
% Witnessed a fatal cocaine overdose	5	0	3

3.6.3 Responses to overdose in others

The ways in which subjects who had witnessed a cocaine overdose in the past responded are presented in Table 12. Almost two-thirds of ICU (64%) responded to an overdose by calling an ambulance or taking the person to hospital, with calling an ambulance being the most common response to overdose among this group (52%). In contrast, no NICU reported taking such courses of action. While ICU had also performed mouth-to-mouth resuscitation and CPR on someone who had overdosed on cocaine (26%), this had not occurred in the NICU group. Giving comfort and reassurance was the most common response to a cocaine overdose by NICU (67%), while a third (33%) had taken no action at all. Overall, 21% of subjects responded to a cocaine overdose by giving the person another drug, which was typically one of the benzodiazepines or heroin.

Table 12: Responses to overdose

	ICU (n=42)	NICU (n=6)	TOTAL (n=48)
Called ambulance	22	0	22
Took person to hospital	5	0	5
Gave person another drug	9	1	10
Performed mouth-to-mouth	6	0	6
Performed CPR	5	0	5
Placed in recovery position	5	0	5
Walked person around	4	0	4
Gave person drink of water	3	2	5
Comforted/reassured	19	4	23
No action taken	5	2	7
Other	13	1	14

3.6.4 Circumstances of most recent overdose witnessed

In the majority of overdoses most recently witnessed by subjects, the identity of the person who overdosed was known to the subject, in that they were a partner (5/48), friend (20/48) or acquaintance (13/48) (Table 13). The most common first response of subjects (11/48) was to comfort and reassure the person, followed by calling an ambulance (10/48). A minority of subjects performed mouth-to-mouth resuscitation (2/48) or placed the person in the recovery position (2/48), while some took no action whatsoever (7/48). There were a variety of other actions taken by a third of the sample (16/48) which included walking the person around, splashing water on the face, calling the person's dealer, and taking the person to a "quieter" and more comfortable area. While it was not necessarily the first response, a significant proportion of the sample (21/48) eventually called an ambulance, with a median time of 3.5 minutes having elapsed between the time it was obvious the person was

overdosing and an ambulance being summoned. It is worthy of note, however, that none of the NICU group called an ambulance. In a minority of cases (4/48) of cases the overdose was fatal. The most commonly reported signs indicating that the person was overdosing were breathing difficulties (19/48), seizures (16/48), and the person turning a different colour (16/48). Other signs of overdose included physical collapse (12/48), eyes rolling back into the head (9/48), intense sweating (8/48), panic (7/48), and frothing at the mouth (5/48).

Table 13: Circumstances of most recent overdose witnessed

	ICU (n=42)	**NICU (n=6)**	**TOTAL (n=48)**
Identity of person:-			
Partner	4	1	5
Friend	16	4	20
Acquaintance	12	1	13
Stranger	10	0	10
First response:-			
No action taken	5	2	7
Called ambulance	10	0	10
Mouth-to-mouth resuscitation	2	0	2
Comforted/reassured	9	2	11
Placed in recovery position	2	0	2
Other	14	2	16
Called an ambulance	21	0	21
Time elapsed before ambulance called (median minutes)	2	-	2
Person died	4	0	4
Signs of cocaine overdose:-			
Breathing difficulties	16	3	19
Seizure	16	0	16
Turned different colour	13	3	16

3.6.5 Beliefs about primary causes of cocaine overdose in others

Subjects were asked why they thought people overdosed on cocaine. The primary reason for overdose given by the majority of both ICU (68%) and NICU (74%) was using more cocaine than usual, or just generally using too much (Table 14). Other reasons given for overdose included a higher purity of cocaine, impurities, the use of other drugs with cocaine, and not spacing out doses.

Table 14: Primary reasons for overdose in others

	ICU (n=120) %	NICU (n=80) %	TOTAL (n=200) %
Used more than usual/too much	68	74	70
Cocaine stronger than usual	13	5	10
Impurities	3	6	5
Other drugs	2	3	2
Low tolerance	1	1	1
Didn't space out doses	1	3	2
Injecting	0	3	1
Other	3	4	3
Don't know	11	3	8

3.7 Risk perceptions of overdose among cocaine users

The majority of both ICU (82%) and NICU (94%) thought it unlikely or very unlikely that they would overdose on cocaine in the future. This was also the case among ICU (75%) and NICU (80%) who had previously overdosed on cocaine. Conversely, a substantial proportion of both groups (ICU: 59%; NICU: 51%) thought that it was likely or very likely that other cocaine users would overdose on cocaine at least once in their lifetime.

Table 15: Risk perceptions of cocaine overdose

	ICU (n=120)	NICU (n=80)	TOTAL (n=200)
	%	%	%
Likelihood of oneself overdosing on cocaine			
Very unlikely	63	68	65
Unlikely	19	25	22
Not sure	12	4	9
Likely	3	3	3
Very likely	4	1	3
Likelihood of others overdosing on cocaine			
Very unlikely	3	14	7
Unlikely	10	28	17
Not sure	29	8	21
Likely	31	36	33
Very likely	28	15	23

4.0 DISCUSSION

4.1 Major Findings

The experience of physical and/or psychological adverse events associated with the use of cocaine was prevalent among cocaine users, with nearly two-thirds of the sample reporting at least one such symptom. While there was no significant difference between the proportions of ICU and NICU that had experienced adverse physical effects of cocaine, a greater proportion of ICU reported adverse psychological effects. Age, severity of dependence, and extent of polydrug use were all significantly associated with more extensive adverse effects.

A history of cocaine overdose was reported by more than 1 in 10 cocaine users, and was more common among ICU. The prevalence of past and recent cocaine overdose among females was over twice that among males. The number of past cocaine overdoses was greater among ICU than among NICU, with females reporting a greater number of overdoses. After taking all other factors into account, females were almost three times more likely to have previously overdosed on cocaine than males

The most commonly reported symptoms of cocaine overdose were palpitations, intense sweating and seizures. Other reported symptoms included paranoia, severe agitation, respiratory distress, high body temperature, chest pain, and tremors. Approximately one third of those who had overdosed on cocaine had been attended by an ambulance or taken to hospital.

Having been present when someone else overdosed on cocaine was more common than having overdosed oneself, with approximately a third of ICU, and 1 in 10 NICU, reporting that they had witnessed an overdose. There were substantial proportions of both groups, however, who stated that they would not recognise a cocaine overdose.

The majority of both ICU and NICU believed that the primary reason for cocaine overdose was using excessive amounts of cocaine, and that it was unlikely that they would overdose in

the future. Substantial proportions of both groups thought, however, that it was likely that other cocaine users would overdose at least once in their lifetime.

4.2 Cocaine-Related Adverse Events

Nearly two-thirds of the total sample had experienced physical and/or psychological adverse events related to the use of cocaine. Adverse events were reported by 2 out of 3 ICU and just over half of NICU. Among both groups, palpitations, intense sweating and severe nausea/vomiting were the most commonly reported physical problems. Other reported problems included severe headache, high body temperature, dizziness, chest pain, and seizures. The most commonly reported psychological symptoms were paranoia, anxiety and panic. Confusion, increased sensitivity to sound, auditory hallucinations, severe agitation, visual hallucinations and depression were also reported.

The adverse physical and psychological symptoms reported by cocaine users in this study are consistent with the known effects of cocaine (American Psychiatric Association, 2000; Brands et al., 1998; Friedman et al., 1996; McCann & Ricaurte, 2000; Platt, 1997). The fact that cardiovascular effects, symptoms of psychosis, and indicators of hyperthermia were the most prevalent adverse effects reported demonstrates not only that the harm attributed to cocaine in the present study parallels that typically associated with cocaine, but that it is the more severe effects of cocaine that are more commonly experienced. While heroin and ecstasy were more commonly nominated than cocaine as the participants' primary drug of choice, the frequency at which these drugs were used was not a significant predictor of the degree of physical and psychological symptomatology reported. Thus, the symptoms that users in this study associated with cocaine do not appear to be attributable to the effects of other such drugs.

Age, severity of cocaine dependence, and the extent of polydrug use were significantly associated with more extensive adverse effects of cocaine. Thus, being older, more dependent on cocaine, and having used more drug classes in the previous six months were associated with having experienced a greater number of adverse effects. It is not surprising that older ages were associated with more cocaine-related symptoms, as older users had a longer history of cocaine use and, thus, a greater number of opportunities to experience such

symptoms. Indeed, an association between an increase in age and an increase in the severity of cocaine-related problems is evident from the Drug Abuse Warning Network data obtained from US emergency room records (Substance Abuse and Mental Health Services Administration [SAMHSA], 2003). Likewise, the finding that a greater severity of cocaine dependence was predictive of a greater degree of adverse symptomatology was not unexpected, as with heavier more frequent use of cocaine the chance of experiencing an adverse event is likely to increase. Moreover, this association has been demonstrated in previous research (Kaye & Darke, in press; Kaye, Darke, & McKetin, 2000; Kaye, Darke, & Topp, 2001). Nevertheless, the frequency of cocaine use in itself was not significantly associated with the degree of adverse symptomatology, indicating that cocaine-related harm can and does occur in the context of occasional use. While the degree to which cocaine users had experienced physical and psychological problems was also unrelated to their frequency of use of drugs other than cocaine, it was associated with the extent of polydrug use in the preceding six months. This finding may reflect a relationship between the high risk behaviour implied by the use of multiple drug classes and risky, e.g. high dose and repetitive, cocaine use. Previous overdose research, however, suggests that is the use of other drugs in combination with cocaine, particularly heroin and alcohol, which increases the harm associated with cocaine use (Coffin et al., 2003; Escobedo et al., 1991; Ochoa et al., 2001; Tardiff et al., 1996). The contribution of polydrug use to overdose is demonstrated in a study investigating fatal drug overdose trends in New York between 1990 and 1998, which found that most of the variation in overdose death rates was accounted for by changes in the rates of overdose attributed to combinations of opiates, cocaine and alcohol, particularly opiates with cocaine (Coffin et al., 2003). The role of other drugs in cocaine overdose will be discussed in more detail below.

4.3 Prevalence of Cocaine Overdose

Almost 1 in 5 ICU reported that they had previously overdosed on cocaine, as had 6% of NICU. ICU had also overdosed on cocaine more often than NICU. Cocaine overdose in the preceding 12 months was less prevalent, being reported by almost 1 in 10 ICU and 3% of ICU, and not significantly more likely among ICU than NICU. The prevalence of cocaine

overdose among females was more than twice that of males, both in the past and in the previous 12 months, and females had overdosed on significantly more occasions than males.

The higher prevalence of cocaine overdose among ICU is consistent with previous studies (Mesquita et al., 2001; Pottieger et al., 1992), in which injecting cocaine use was more likely than snorting or crack smoking to be associated with overdose. In accordance with the gender difference observed in the present study, these studies also demonstrated higher rates of cocaine overdose among females.

The prevalence of witnessing someone else overdose on cocaine was twice that of having overdosed oneself, and was higher among ICU. Thus, exposure to cocaine overdose, particularly among injectors, was not uncommon. While the overdoses witnessed were typically non-fatal, 1 in 20 ICU had witnessed a fatal cocaine overdose, suggesting that cocaine-related deaths may not be as rare as some users believe.

It should be noted that the prevalence of adverse events such as palpitations, intense sweating, and severe nausea/vomiting was higher than the prevalence of cocaine overdose. Given that these adverse events are actually symptoms of a cocaine overdose it is likely that the occurrence of cocaine overdose was under-reported, due to subjects not realising that what they had experienced was actually an overdose and just reporting the symptoms as "adverse events".

4.4 Factors Associated with Cocaine Overdose

Although univariate analysis revealed that cocaine overdose was more prevalent among ICU than NICU, this relationship failed to remain significant once other factors were taken into account. Upon subsequent multivariate analysis, it was found that the only significant independent predictor of having overdosed on cocaine in the past was being female, such that females were almost three times as likely as males to have experienced a cocaine overdose. Mesquita et al. (2001) also found that being female was significantly and independently associated with past cocaine overdose, however it is unclear why this would be the case. Whether such findings reflect gender differences in the development of tolerance to cocaine or whether they are due to differences in the way males and females

attribute causality with respect to cocaine-related adverse events cannot be determined from the research to date.

The fact that frequency of cocaine use, severity of cocaine dependence and route of administration were not significant predictors of having overdosed on cocaine supports the notion that cocaine overdose is an unpredictable event and can occur irrespective of these factors (Cregler, 1994; Estroff, 1987; Jenkins et al., 1999; Karch & Stephens, 1991; Karch et al., 1998; Lange & Hillis, 2001; Platt, 1997; Washton & Gold, 1984).

4.5 Symptoms of Cocaine Overdose

The most commonly reported symptoms of cocaine overdose among those who had overdosed on cocaine were palpitations, intense sweating and seizures. Males and females were equally likely to report such symptoms, however, among females, passing out was a more common symptom of overdose than seizures. Other reported symptoms included paranoia, severe agitation, respiratory distress, high body temperature, chest pain, and tremors. Approximately one third of those who had overdosed on cocaine had been attended to by an ambulance or taken to hospital, indicating that the presenting symptoms in such cases were considered by the victim and/or witnesses to be serious enough to warrant medical intervention.

Regardless of whether or not medical intervention was sought, these symptoms are consistent with the known indicators of cocaine toxicity and, as previously discussed, are cause for serious concern. This is particularly the case for cardiovascular and respiratory problems, seizures, and those symptoms indicative of hyperthermia (i.e. intense sweating and high body temperature), which can be fatal. The symptoms subjects reported as present in the most recently witnessed cocaine overdose were also consistent with the known signs of cocaine overdose, e.g. breathing difficulties, seizures, change of skin colour, and physical collapse.

Overall, the results demonstrate that those who stated that they had overdosed on cocaine themselves, or had witnessed a cocaine overdose in someone else, were describing a syndrome that has been well-documented as cocaine "toxicity" or "overdose", and not just a collection of benign or unrelated symptoms.

There were substantial proportions of both ICU and NICU who stated that they would not recognise a cocaine overdose. Almost all of those people had had no experience of cocaine overdose themselves, or in others. This finding is somewhat alarming given that cocaine overdose can occur under a range of circumstances. If cocaine users are unaware that the symptoms they or others are experiencing may be a sign of overdose they may be less likely to seek medical help and, consequently, place themselves or others at risk of severe complications or even death.

ICU and NICU differed in the symptoms they thought were indicative of a cocaine overdose. ICU most commonly reported seizures, passing out and palpitations as overdose symptoms, whereas, among NICU, passing out, anxiety and vomiting were the most often reported signs. Whilst all of these symptoms may indicate a cocaine overdose and should be taken seriously, it appears that, in contrast to the concept of heroin overdose, which is associated with a well-defined and well-known set of symptoms, the term "cocaine overdose" can mean different things to different people. Indeed, as discussed previously, a number of subjects in the current study reported symptoms of a cocaine overdose but did not report having ever actually overdosed on cocaine. As such, cocaine users need to be informed about the various ways in which a cocaine overdose can present.

4.6 Circumstances of Cocaine Overdose

Almost half of ICU who had overdosed on cocaine had been on a methadone maintenance program at the time of their most recent overdose. Furthermore, nearly three-quarters of ICU had also been using opiates at the time they last overdosed on cocaine, with heroin being the most common drug used with cocaine. These findings suggest that the depressant effects of opiates such as heroin and methadone do not, as some have proposed, protect against cocaine overdose. Rather, these results are in accordance with the aforementioned literature in which heroin is implicated as a possible contributor to cocaine overdose (CEWG, 1999; Coffin et al., 2003; Friedman et al., 1996; Ochoa et al., 2001; Platt, 1997; Tardiff et al., 1996). Also consistent with previous research (NIDA, 1999; SAMHSA, 2003) is the finding that, among NICU, alcohol was the most common drug used with cocaine at the time of the most recent overdose. Alcohol use has been proposed as a risk factor for cocaine overdose due to the production of cocaethylene, a metabolite resulting from the

interaction of alcohol and cocaine which is not only more toxic than cocaine itself, but which has a synergistic effect in increasing the toxicity of cocaine (Brookoff et al., 1996; Escobedo et al., 1991; Gottschalk & Kosten, 2002; Julien, 1998; Tardiff et al., 1996). Use of another drug prior to a cocaine overdose was common in the present study, with approximately two-thirds of both groups reporting polydrug use at the time of their most recent overdose. Polydrug use has also been found to be a common feature of fatal and non-fatal heroin overdose (Darke et al., 2000; Darke, Ross, & Hall, 1996; Darke & Zador, 1996).

Information about the actual quantities of cocaine consumed by subjects was not obtained, as it is not possible to ascertain exact dosage, given fluctuations in purity and variations in the mode of administration. Nevertheless, 6 out of 10 cocaine users reported that they had used more cocaine than usual on the day of their most recent overdose. The majority of ICU and NICU had been with other people when they last overdosed on cocaine and over one quarter had been attended to by an ambulance or taken to hospital. The fact that most cocaine users were not alone when they overdosed is encouraging in the sense that using cocaine in the presence of other people should increase the likelihood that medical attention will be sought. If, however, a large proportion of cocaine users do not know how to recognise a cocaine overdose, as the results of this study suggest, there are potentially many situations in which appropriate action may not be taken and the outcome may be more negative than it would otherwise be. A recent study of cocaine-related fatalities found that in 81% of cases there had been no medical intervention prior to death (Darke et al., 2003).

While the majority of ICU had overdosed in a public place or in a car, most NICU had overdosed at home or at a friend's home. In contrast to ICU, who were more likely to overdose on a weekday, NICU were more likely to overdose on a weekend. In conjunction with the generally lower level of cocaine use among NICU and their regular use of ecstasy, the latter finding most likely reflects the use of cocaine by this group as a "party drug" rather than a drug that is used day-to-day.

4.7 Responses to Cocaine Overdose

While almost 2 out of 3 ICU had responded to a cocaine overdose in someone else by calling an ambulance or taking the person to hospital, no NICU had done so. ICU were also more likely to perform CPR or mouth-to-mouth resuscitation on someone who had

overdosed on cocaine. NICU typically comforted or reassured the person, gave them some water, or took no action whatsoever. As noted previously, witnessing a cocaine overdose was a less common event among NICU, as was overdosing themselves. Consequently, NICU may be less likely than ICU to know the appropriate response in the event of a cocaine overdose. Alternatively, the symptoms witnessed by NICU may have been less severe than those witnessed by ICU and, as such, may not have required any further intervention.

One response to cocaine overdose which gives cause for concern is the administering of heroin, as reported by a minority of users. As discussed previously, heroin may contribute to the toxicity of cocaine and, thus, should be contraindicated in cases of cocaine overdose.

4.8 Beliefs About Cocaine Overdose

The majority of cocaine users believed that cocaine overdose was due to using an excessive amount of cocaine, this attribution applying to overdose in themselves as well as in others. As the weight of evidence suggests, this may not always be the case (Cregler, 1994; Estroff, 1987; Jenkins et al., 1999; Karch & Stephens, 1991; Karch et al., 1998; Lange & Hillis, 2001; Platt, 1997; Washton & Gold, 1984). Moreover, irrespective of whether or not they had overdosed on cocaine in the past, most users thought it was unlikely that they would do so in the future. The risk of cocaine overdose among others, however, was estimated to be greater, with over half of the sample believing that it was likely that other cocaine users would overdose at least once in their lifetime. This discrepancy between the attribution of overdose risk to oneself and to others has also been observed among heroin users (Darke & Ross, 1997) and, as Darke and Ross (1997) have suggested, may be due to the fact that overdose is a relatively uncommon event. As such, based on their personal history of overdose, users perceive their own risk of future overdose to be less than that of other users.

4.9 Conclusions

The present study has demonstrated a high prevalence of adverse physical and psychological events related to the use of cocaine among both injecting and non-injecting users. Moreover, these adverse events are consistent in nature with the known negative sequelae of cocaine use. The findings of this study also indicate that cocaine can induce serious symptoms in the

context of various patterns of use, but particularly among older, more dependent polydrug users.

Clinically significant proportions of ICU and NICU had overdosed on cocaine, with overdose being more common among ICU and females. The only significant independent predictor of having overdosed on cocaine, however, was being female. The prevalence of cocaine overdose as reported in the current study may be an underestimate of the true prevalence of what has been medically defined and documented in the literature as a cocaine overdose, as the symptoms of cocaine overdose were more commonly reported than cocaine overdose *per se*.

Those who reported having overdosed on cocaine described symptoms consistent with the documented symptoms of cocaine overdose and, as such, correctly attributed such symptoms to a cocaine overdose. A significant number of users, however, were unable to define the concept of cocaine overdose, with some even asserting that it was impossible to overdose on cocaine. The majority of cocaine users believed that cocaine overdose was primarily dose-related which, as discussed above, is a view that is at odds with the evidence from previous research and which may engender a false sense of security in the user. Moreover, most users believed that their risk of overdosing on cocaine in the future was low, in terms of both absolute risk and risk relative to other users.

Overall, the results of the present study highlight the importance of educating cocaine users about the possibility and nature of overdose and making them aware that cocaine overdose can occur irrespective of dose, frequency and method of use. Furthermore, there is a need to emphasise the potential danger of combining cocaine with other drugs, such as heroin and alcohol. If the trend towards increased cocaine use observed in recent years continues, it is likely that we will see an increase in the prevalence of cocaine overdose and other adverse events in this country. As such, ongoing research and monitoring of the local cocaine market is warranted.

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