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Review

Mortality among cocaine users: A systematic review of cohort studies☆

Louisa Degenhardt[a,e,f,*], Jessica Singleton[a], Bianca Calabria[a], Jennifer McLaren[a], Thomas Kerr[b], Shruti Mehta[c], Gregory Kirk[c], Wayne D. Hall[d]

[a] National Drug and Alcohol Research Centre, University of New South Wales, Sydney, New South Wales 2052, Australia
[b] British Columbia Centre for Excellence in HIV/AIDS, University of British Columbia, Vancouver, British Columbia V6Z1Y6, Canada
[c] School of Public Health, Johns Hopkins University, Baltimore, MA 21205, United States
[d] School of Population Health, University of Queensland, St. Lucia, Queensland 4006, Australia
[e] Burnet Institute, GPO Box 2284, Melbourne, Victoria 3001, Australia
[f] Murdoch Children's Research Institute, Royal Children's Hospital, Flemington Road, Parkville, Victoria 3052, Australia

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ABSTRACT

Aims: To conduct a systematic review of mortality among cohort studies of cocaine users.
Methods: Three electronic databases were searched (EMBASE, Medline and PsychINFO); other online databases were searched using online libraries and repositories of reports and literature in the drug and alcohol field, with requested contributions from trained librarians and experts. Searches and extraction were undertaken using protocols and cross-checking of decisions by two authors. Additional data were requested from study investigators where studies did not report relevant data.
Results: 1911 articles and 2 reports were identified from searches, with data from another four studies located from review articles. Seven cohorts of "problem" or dependent cocaine users reported data that permitted mortality rates to be estimated. Crude mortality rates ranged from 0.53 (95% CI: 0.10–1.58) to 6.16 (95% CI: 5.21–7.11) per 100PY. Standardised mortality ratios (SMRs) reported in four studies suggested that mortality was four to eight times higher among cocaine users than age and sex peers in the general population.
Conclusions: There are limited data on the extent of elevated mortality among problematic or dependent cocaine users and it is unclear how generalisable the results of these studies may be to other populations of problematic cocaine users. Greater attention to both the method of recruitment, and the characteristics of cocaine users, would enhance our understanding of the mortality risks of problematic cocaine use.

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* Corresponding author at: National Drug and Alcohol Research Centre, University of New South Wales, Sydney, NSW 2052, Australia. Tel.: +61 2 9385 0230; fax: +61 2 9385 0222.
E-mail address: l.degenhardt@unsw.edu.au (L. Degenhardt).

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1. Introduction

Globally, cocaine use is thought to be concentrated in Western Europe and the Americas, but its use is thought to be spreading geographically (United Nations Office on Drugs and Crime, 2009). In the latest World Drug Report, the United Nations Office on Drugs and Crime (UNODC) reported that although cocaine consumption may have levelled off in North America, use has increased in Europe over the past decade and perhaps in some West African countries (United Nations Office on Drugs and Crime, 2009). Cocaine may be used as powder or "crack" cocaine: the powder form can be snorted (taken intranasally), injected or inhaled when in the form of freebase. Crack cocaine can be injected or smoked, but is rarely snorted – snorting tends to cause nosebleeds for this form of cocaine, and is generally avoided as a route of administration.

Regular cocaine use is associated with a range of adverse consequences that potentially increase mortality. These include the risk of: developing dependence, experiencing cardiovascular complications (most commonly acute myocardial infarctions but also significant arrhythmias), psychotic episodes and panic attacks, and acquiring blood-borne viral infections, particularly among users who inject the drug. Cocaine use is among the leading causes of acute drug-related deaths in the United States (Brody et al., 1990; Harruff et al., 1991; Hood et al., 1990; Ruttenber et al., 1997; Tardiff et al., 1995; Wysowski et al., 1993).

Despite these mortality risks, there has never been a systematic review of prospective studies quantifying crude and excess mortality risk among people who are problematic or dependent cocaine users. This paper reviews the mortality risk of problematic or dependent cocaine use derived from a systematic search of prospective cohort studies of mortality of regular, injecting or dependent cocaine users. This approach has been used in multiple other systematic reviews of mortality among drug users (Calabria et al., 2010; Degenhardt et al., in press; Hulse et al., 1999; Singleton et al., 2009; Wilcox et al., 2004). We focus upon this study design rather than registries of poisonings, overdose or population registers where cocaine is mentioned or detected post mortem for several reasons. First, many causes of death among drug users, although often directly or indirectly drug-related, are not due to acute intoxication (Darke et al., 2006). Second, many deaths may not be identified post mortem as drug-related deaths. Third, they may not be recorded as deaths that have occurred among people who have used the drug. These data therefore underestimate mortality among cocaine users. This is even more marked since in many countries, suspected drug-related deaths are not necessarily subject to toxicological testing, and even fewer countries routinely report these data. Even acute deaths directly related to cocaine use are likely to be underestimated in population mortality registers.

The aims of this review are to systematically review prospective studies of cocaine users to examine: (1) crude mortality rates; (2) excess mortality; (3) the causes of mortality across studies; and (4) mortality according to HIV status. Our intent was to locate studies of dependent users of cocaine to enable comparisons with mortality studies of problem opioids users. All cohorts where cocaine users were examined were included in this review. We note the way in which cocaine users were identified and defined in each of the studies located.

2. Method

2.1. Identifying studies

A systematic literature review identified peer-reviewed articles and other sources of data describing mortality related to cocaine use published between 1990 and 2008. After consultation with librarians, tailored search strings were devised and used to search three electronic databases: EMBASE, Medline and PsycINFO (see Appendix A for database information) to provide the most complete coverage of catalogued literature. Search strings contained keywords and database specific terms (MeSH headings, EMTREE terms and explode terms). Search strings were developed for four themes: *cocaine*, *drug use*, *mortality epidemiology* and *cohort studies* (see Appendix B for search strings). Multiple variations of the four search themes were combined to produce a single set of results (see Appendix C for search combinations).

The database search set was reviewed and the combination of *cocaine + mortality epidemiology* was selected for review. This search was the most comprehensive of the combinations and it produced a total of 1911 papers (once the duplicates were removed). We also identified literature held outside these peer-reviewed literature databases (referred to as "grey literature") that included technical reports and monographs that reported on mortality among cocaine users. The latter was identified using online databases, library databases and general online searches (the complete list of websites reviewed can be in (Calabria et al., 2008)). Two researchers (JS and LD) independently reviewed these studies to compile a shortlist of relevant articles and reports. The shortlists were compared and any differences in the inclusion or exclusion of data were resolved by consensus.

2.2. Included studies

We included cohort studies that reported raw data on mortality related to the problematic use of or dependence on cocaine. The final list of relevant articles was distributed to experts in drug research who were asked to identify any studies or data sources we had been missed. Further contacts were made with study authors where additional data or further information was needed.

2.3. Excluded studies

Several criteria were grounds for excluding papers: not reporting on a cohort study; not reporting on mortality among cocaine users, not reporting primary research data, and only reporting case studies of cocaine-related deaths (without permitting analysis of the denominator of the number of problem cocaine users).

2.4. Data extraction

The data extraction process followed the recommendations outlined in the Strengthening the Reporting if Observational Studies in Epidemiology (STROBE) guidelines (Vandenbroucke et al., 2007; von Elm et al., 2007) that parallel the CONSORT guidelines for reporting on randomized trials (Mohler et al., 2001). Data were extracted by two researchers into a Microsoft Excel® spreadsheet, with bibliographic information and study specific details were recorded. Study details recorded were the location, country and region; and sample characteristics such as, age structure and sex were recorded. Mortality estimates reported in the study (e.g. crude mortality rate (CMR), odds ratios, hazard ratios, standardised mortality ratios (SMRs)) and causes of death were recorded along with methodological aspects of the research, including the way in which cocaine use or dependence was ascertained, and the sampling method used to obtain the cohort. A quality index adapted from (McGrath et al., 2004) was used (see Appendix D for details). Study information pertaining to the quality criteria was extracted into an Excel spreadsheet. Each criterion included a rating scale and the individual scores were tallied to provide an overall quality score, with higher scores indicating a higher quality. After data extraction was complete, the results of the two researchers were compared for consistency. Any differences were discussed and resolved through consensus.

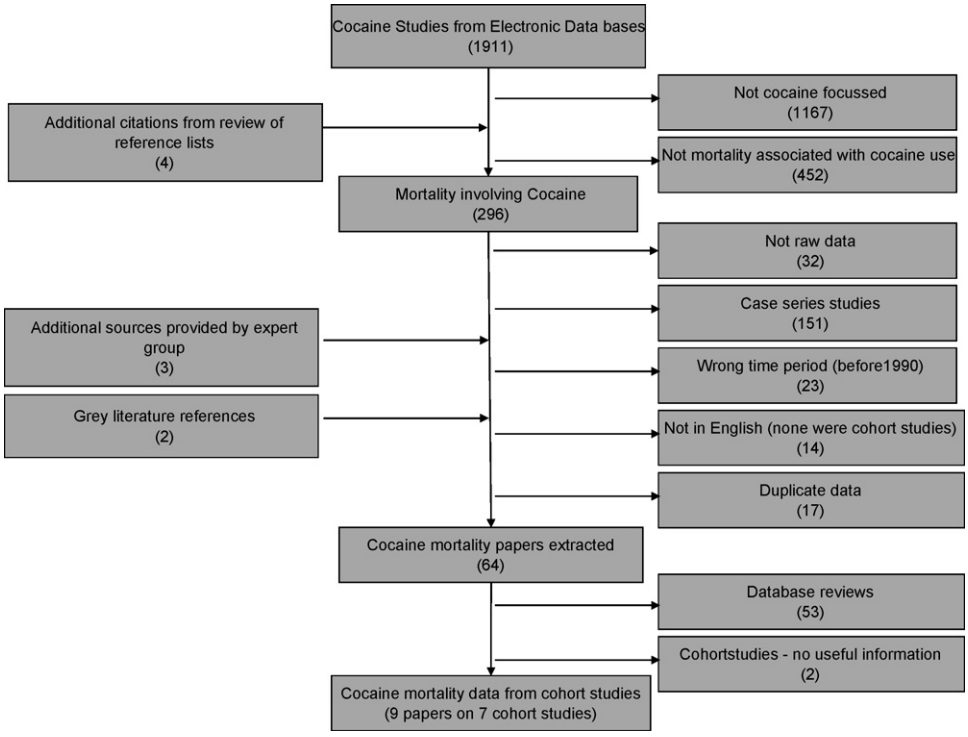

Fig. 1. Flowchart of search strategy to identify articles reporting on mortality associated with cocaine use.

2.5. Reporting of mortality estimates

The reporting of mortality estimates was poor. Most cohort studies ($n = 5$) reported crude mortality rates (CMRs, i.e. the number of deaths per 100 person-years of follow up), and four reported a standardised mortality ratio (SMR, a measure of the mortality relative to *expected* mortality among persons of the same age and sex in the general population of that country). Two only reported case fatality rates (CFRs, i.e. the proportion of cases dying over the entire follow up period). 95% confidence intervals for estimates were also often unreported.

Person years of follow up were not always reported and in some studies it was difficult to estimate the overall years of follow up. In the face of the inconsistencies in the format of the reported data, we calculated summary estimates as follows: reported crude mortality rates were converted to per 100 person years; when person years of follow up were reported, the crude mortality rate was calculated. In studies that only reported the number of deaths and the overall years follow up, we calculated an approximate crude mortality rate by assuming that all deaths occurred exactly half way through the follow up period and so each case contributed half the person years follow up of the survivors. No pooled estimates of mortality were made because of the very limited number of studies, variable nature of the populations studied across countries and the limited reporting of statistics that would have allowed for adjustment for study and population variables.

The limited precision of approximated CMRs, differences in reporting, and variations in sample characteristics and duration of follow up need to be considered when interpreting the estimates presented here. Comparisons of mortality rates across individual cohorts should be cautiously made.

3. Results

The *cocaine + mortality epidemiology* search combination produced 1911 results. An additional 4 references were added after searching review article bibliographies. Three studies from non-peer reviewed sources and two studies with data provided from study coordinators were also included. The abstracts of the articles not in English were reviewed and where possible the full texts were searched for relevant keywords. Only one article (in Spanish) provided relevant data which was not otherwise available in English. Fourteen articles published in languages other than English were excluded; none of them reported mortality in cohort studies. Fig. 1 describes the numbers of studies identified and reasons for exclusion.

1160 of the 1917 articles (61%) were excluded because they did not focus on cocaine use and 452 (24%) because they did not report on mortality among cocaine users. 151 (8%) were case studies, 32 (2%) did not report raw data on mortality, 23 did not contain data for the required time period and 17 were duplicate reports. Seventy-one studies remained, which provided primary data on cocaine-related mortality. Of these, 10 articles/reports reported on nine different cohort studies that examined mortality among cohorts of dependent or problematic cocaine users.

Since 1990, nine prospective cohort studies examined mortality among the cohorts and included cocaine users (Table 1); two were excluded from further discussion because they did not provide sufficient data to permit reliable estimates of mortality among cocaine users (Table 1). The cohorts that were included came from the United States of America (2), Canada, France, the Netherlands, Brazil and Italy.

The way in which "cocaine use" was operationalised varied markedly between cohorts. For example, studies largely comprised non-injecting dependent crack cocaine users in the Italian and Brazilian cohorts; the French cohort comprised those arrested for cocaine use/dealing, and the cohorts in North America comprised cocaine injectors and/or crack cocaine smokers. For the purposes of this review, we will refer (when making summary statements) to "*problematic or dependent cocaine users*" because this described the cocaine users in all cohorts, who comprised those who: had legal problems related to their use (French study), were injecting the drug (typically daily) (Dutch, North American studies) or were receiving treatment for dependent cocaine use (Brazilian, Italian studies).

3.1. All-cause mortality

Mortality estimates were reported in a variety of forms that included odds ratios, relative risks, hazard ratios and crude mortality rates (CMRs). Overall CMRs were most common; these are by

Table 1

.

Study	Country	Year	Sample	Quality score	*N*	Person years	Deaths	CMR/100PY (95% CI)		SMR (95% CI)	
1a Cohorts that included cocaine users for which estimates of mortality were reported											
1.	Brazil	1992–1999	Crack dependent people in treatment; 44.3 months of follow up on average	11	131	NR	23	3.51	–	7.60	NR
2.	Canada	1996–2004	VIDUS cohort: cocaine-only IDUs	14	717	2613.2	161	6.16	(5.21,7.11)	4.74	(4.19,5 .29)
3.	Netherlands	1985–1993	HIV seronegative drug users at baseline; primary cocaine IDU sub-sample	11	632	194	9	4.6	–	NR	–
4.	United States	1994–1997	RAVEN study participants	9							
			Daily cocaine IDU		319	319	3[a]	0.53	0.10, 1.58	NR	–
			Daily cocaine non-IDU[b]		52	85	3[a]	3.53	–	NR	–
5.	United States	1988–2005	HIV seronegative IDU (ALIVE study)	9							
			Cocaine-only IDUs		518	3727	175	4.69	4.03, 5.45	NR	–
			Cocaine and heroin IDUs		2439	18023	787	4.37	4.07, 4.68	NR	–
6.	France	1992–1999	Crack or cocaine using/dealing arrestees	15	2212	11496	80	0.69	0.55, 0.87	4.36 (M) 7.70 (F)	NR
7.	Italy	1989–2004	Cocaine dependent people in treatment		347	1289	7 (males) 7 (total)	0.54 0.50	(0.00, 1.07) M (0.22, 0.91) T	4.75 (M)	2.26, 9.96

Study	Country	Year	Sample	Quality score	*N*	Person years	Deaths	CMR/100PY	Notes
1b Cohorts that included cocaine users, but without sufficient information to estimate mortality among cocaine users									
8.	Netherlands	1987–1991	"Experienced non-deviant cocaine users"	1	160	NR	3	N/A	61 out of 160 lost to follow up; No person years, CMRs, SMRs reported
9.	United Kingdom	1995–1999	Crack or cocaine users in treatment	9	247	NR	NR	N/A	Deaths among cocaine users not reported, No person years, CMRs, SMRs reported

Note: IDU, injection drug use; NR, not reported; CMR, crude mortality rate per 100 person years of follow up; SMR, standardised mortality ratio; VIDUS, Vancouver Injection Drug Users Study; RAVEN study, Risk Activity Variables, Epidemiology, and Network study; ALIVE, AIDS Link to Intravenous Experience study. *M* = male, *F* = female, *T* = total sample. 1. Ribeiro et al. (2004, 2006); please note that a more recent paper reported on this cohort and documented a 70% follow up rate, with 4 further deaths (Dias et al., 2008). No person years, crude mortality rates, or standardised mortality ratios were reported at that 12-year follows up so the earlier data (from the 5-year follow up) have been used. 2. Tyndall et al. (2001); personal communication, Thomas Kerr, September 2008. 3. Van Haastrecht et al. (1996); 4. O'Driscoll et al. (2001); 5. Wang et al. (2005); personal communication, Erin Ricketts, September 2008; 6. OFDT (2004); personal communication, Eric Janssen, October 2008; 7. Pavarin (2008). 8. Cohen and Sas (1993); 9. Gossop et al. (2002).

[a] Represented in both injecting IDU group and non-IDU group.

[b] Not independent from the daily cocaine IDU group; presumed to be daily crack smokers.

Table 2
Causes of death among cocaine injecting participants in the ALIVE and VIDUS cohorts.

	ALIVE cohort – cocaine + heroin IDUs		ALIVE cohort – cocaine-only IDUs		VIDUS cohort	
	N deaths	% total deaths (95% CI)	*N* deaths	% total deaths (95% CI)	*N* deaths	% total deaths (95% CI)
AIDS	206	26.2 (22.0, 30.4)	62	35.4 (24.4, 46.4)	30	20.0 (12.2, 27.8)
Overdose	134	17.0 (13.8, 20.2)	20	11.4 (6.1, 16.7)	53	35.3 (23.8, 46.9)
Sepsis/endocarditis	81	10.3 (7.9, 12.7)	15	8.6 (4.1, 13.1)	5	3.3 (0.4, 6.2)
Traumatic deaths[a]	60	7.6 (5.6, 9.6)	12	6.9 (2.9, 10.9)	23	15.3 (8.7, 22.0)
Cardiac	54	6.9 (5.0, 8.8)	7	4.0 (1.0, 7.0)	6	4.0 (0.8, 7.2)
Liver/gastrointestinal	50	6.4 (4.6, 8.2)	10	5.7 (2.1, 9.3)	9	6.0 (2.1, 9.9)
Cancer	47	6.0 (4.2, 7.8)	13	7.4 (3.2, 11.6)	3	2.0 (0, 4.2)
Chronic drug-related	46	5.8 (4.1, 7.5)	9	5.1 (1.7, 8.5)	1	0.7 (0, 1.9)
Pneumonia	24	3.0 (1.8, 4.2)	8	4.6 (1.3, 7.9)	3	2.0 (0, 4.2)
Suicide	3	0.4 (0.0, 0.8)	2	1.1 (0, 2.7)	7	4.7 (1.2, 8.1)
Other[b]	82	10.4 (8.0, 12.8)	17	9.7 (4.8, 14.6)	18	12.0 (6.2, 17.8)
Total	787	100	175	100	158	100

VIDUS, Vancouver Injection Drug Users Study; RAVEN study, Risk Activity Variables, Epidemiology, and Network study; ALIVE, AIDS Link to Intravenous Experience study.
[a] In ALIVE: includes homicide, motor vehicle accidents, falls and fires; and in VIDUS, includes homicide, motor vehicle accidents, falls and fires.
[b] In ALIVE: includes renal, pulmonary, neurological, diabetes, hypothermia, bleeding disorder, encephalopathy, chronic alcoholism, pancreatitis, other infections, non-liver gastrointestinal, and unknown; and in VIDUS: includes hypothermia, meningitis, respiratory failure, multiple organ failure, brain haemorrhage, "don't know", "other".

definition unadjusted for variables such as age, sex, HIV status or length of drug use.

One study in the Netherlands that followed-up 632 drug users in 1993 from the original sample of 650 (enrolled between 1985 and 1992) found a CMR of 4.6/100PY among HIV seronegative primary cocaine injectors (Van Haastrecht et al., 1996).

One study reported on a cohort of 131 dependent crack cocaine users recruited from treatment clinics in Sao Paulo, Brazil (Ribeiro et al., 2004, 2006). During 5 years of follow up, the CMR was 3.51/100PY. A 12-year follow up (70% of the original sample were followed-up) reported that a further four cohort participants had died, but no person years, CMRs or SMRs were reported (Dias et al., 2008).

A cohort of injecting drug users (IDUs) in Vancouver, Canada (the VIDUS study), was followed between 1996 and 2004 (Miller et al., 2007; Tyndall et al., 2001). Among the 717 primary cocaine injectors there were 161 deaths over the follow up period, a CMR of 6.16/100PY (95% CI: 5.21–7.11) (Table 1; Thomas Kerr, personal communication, September 2008). In further analyses of mortality according to HIV status, mortality among HIV-positive cocaine IDUs was 9.83/100PY (95% CI: 7.59–12.54), and among those who were HIV-negative, it was 4.91/100PY (95% CI: 3.98–5.99). These rates were significantly different from each other ($p < .001$; Kathy Li, personal communication, October 2008).

In 2001, O'Driscoll et al. (2001) reported on deaths observed in the RAVEN study: a cohort of IDUs in Seattle and King County, Washington State, USA. The overall case fatality rate for "primary" injectors of cocaine was 4.29%. This study reported separate rates according to daily cocaine use by non-injection (crack smoking) and injecting routes (these were not mutually exclusive – some participants used through both routes): those who smoked crack cocaine at least daily had a CMR of 3.53/100PY; those who injected cocaine at least daily had a CMR of 0.53/100PY (95% CI: 0.10–1.58; Table 1).

The ALIVE study (AIDS Link to the IntraVenous Experience), in Baltimore, USA, investigated mortality in a cohort of IDUs, 2957 of whom were daily cocaine injectors, and 25% of whom were HIV-seropositive at baseline (Wang et al., 2005). Among cocaine-only IDUs, the CMR was 4.69/100PY, and among cocaine *and* heroin injectors (cocaine + heroin IDUs), the CMR was 4.37/100PY (95% CI: 4.07–4.68; Erin Ricketts, personal communication, September 2008). There were clear differences in mortality according to HIV status. Mortality among HIV-positive IDUs was 7.74/100PY for cocaine + heroin IDUs, and 7.98/100PY for cocaine-only IDUs. Among HIV-negative IDUs, the CMRs were 3.25 per 100py for cocaine + heroin IDUs, and 3.45 per 100py for cocaine-only IDUs (Erin Ricketts, personal communication, November 2008).

One French study reported on a national cohort of 2122 cocaine users who had been arrested for supply and/or possession of cocaine (OFDT, 2004). This was the only study that recruited cocaine users in this way and the only national study in this review. The average age of the cohort was 27 years at baseline. Over 7 years of follow up, the overall CMR was 0.69/100PY (95% CI: 0.55–0.87; Eric Janssen and Abdalla Toufik, personal communication, October 2008).

One Italian study of 347 cocaine dependent users, mostly intranasal users, was located (Pavarin, 2008). The CMR over the follow up period was 0.50/100PY (95% CI: 0.22–0.91); all seven deaths occurred among males (CMR among males 0.54/100PY). Mortality risk was higher among those who were older at first treatment contact, had concomitant alcohol use problems, with less socioeconomic stability and a history of imprisonment (Pavarin, 2008).

Two cohort studies did not provide sufficient data to allow analysis of mortality among cocaine users in their cohorts (see Table 1). The first was a cohort of "experienced non-deviant" cocaine users from the Netherlands (Cohen and Sas, 1993). It was excluded because the high loss to follow up (61 subjects from a total sample of 160) and little reporting of other study details. The second study was conducted in the United Kingdom, and followed a cohort of 1075 drug users in treatment, of whom 247 were dependent cocaine users (Gossop et al., 2002). This study did not report deaths, person years or mortality rates among cocaine users.

Standardised mortality ratios (SMRs) were estimated in four studies: the Brazilian study (Dias et al., 2008; Ribeiro et al., 2004, 2006) reported an SMR of 7.6 at 5-year follow up; the French study reported an SMR of 4.36 among males and 7.70 among females (Eric Janssen, personal communication, October 2008); the Canadian VIDUS cohort of cocaine injectors estimated an SMR of 4.74 (95% CI 4.19, 5.29) among daily cocaine injectors (Thomas Kerry and Kathy Li, personal communication, November 2008); and the Italian study reported an SMR of 4.75 among males (95% CI 2.26–9.96) (Pavarin, 2008).

3.2. Cause-specific mortality

Four studies examined specific causes of death among cocaine users. Ribeiro et al. (2004, 2006) reported that among dependent crack cocaine users in Brazil the most common causes of death were fatal gunshot (44% – 10 deaths) and AIDS-related illnesses (26% – 6 deaths).

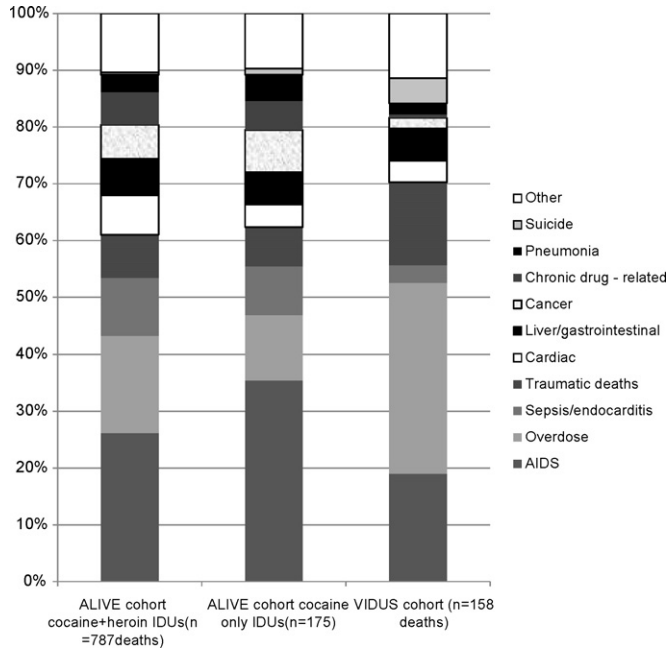

Fig. 2. Comparison of the distribution of causes of death among cocaine users in the VIDUS and ALIVE cohorts.

The study of Italian cocaine dependent treatment entrants examined causes of deaths among the 309 males in the cohort (Pavarin, 2008). The highest SMRs were for vascular diseases (SMR 14.85; CI 4.79–46.04), suicide (SMR 7.07; CI 1–50.16) and overdose (SMR 9.95; CI 1.40–70.61).

The third study was the much larger ALIVE cohort in Baltimore, United States (Wang et al., 2005). Table 4 summarises data on the major causes of death, among cocaine only injectors, and those who injected both cocaine and heroin (Erin Ricketts, personal communication, September 2008). AIDS was the most common cause of death during the follow up period, with a higher proportion among cocaine-only IDU (35%) than among cocaine and heroin IDU (26%). Fatal overdoses were marginally more common among those cocaine IDUs who also injected heroin (17% vs. 11% cocaine only). Infections related to injecting were the next most common cause of mortality in both groups, with traumatic death and suicide accounting for smaller proportions.

Data on specific causes of death were also available from the Vancouver-based VIDUS cohort (Table 2: Kathy Li and Thomas Kerr, personal communication, October 2008). Overdose (35%), HIV and AIDS (20%) and traumatic deaths (15%) were the most common causes of death. Fig. 2 and Table 2 compare the distribution of causes of death in the Baltimore and Vancouver cohorts.

4. Discussion

This systematic review found a limited number of prospective studies of cocaine users that examined all-cause mortality, and even fewer reporting cause-specific mortality. Most studies examined those who used cocaine via injection, or cocaine use among people who inject drugs; two studies examined dependent "crack" cocaine smokers (Brazil) or cocaine snorters (Italy).

The crude mortality rates in the studies identified were high, but varied between cohorts and countries (with CMRs ranging from 0.48 to 6.16 per 100 person years). These differences in CMRs may reflect very large differences between cohorts in general health, routes of administration, the prevalence of HIV infection, access to general and specialist medical care and possibly social disadvantage. Unfortunately, it is impossible to know which and/or how many of these factors contributed to these differences in CMR. Prospective studies of large samples of cocaine dependent users are needed to provide the statistical power to evaluate the role of these potential influences.

Despite the many differences in sampling frames and the way in which cocaine use was operationalised, SMRs were relatively similar in those studies that reported them: the French study estimated an SMR of 4.36 for males and 7.7 for females; the Italian study, 4.6 among males (Pavarin, 2008); the Canadian study estimated an SMR of 4.74, and among Brazilian dependent crack smokers, 7.60 (Ribeiro et al., 2004, 2006). These figures – extremely crudely summarised – suggest that deaths among dependent cocaine users occur between four and eight times more often than in the general population of the same age and sex.

4.1. Limitations

A major limitation of many of the studies is that they recruited and followed-up injecting or treatment-seeking dependent cocaine users, many of who were at higher risk of premature death. There are good reasons to be cautious when generalising this mortality risk to all dependent cocaine users, and especially so to all cocaine users. First, the groups studied largely comprised people who injected cocaine daily, or who were dependent crack cocaine users. No study followed users who only snorted cocaine. It is likely that intranasal cocaine users have much lower mortality and morbidity risks than those who smoke or inject the drug (Kaye and Darke, 2004).

Second, in several of the cohorts, HIV infection was either highly prevalent at baseline and there were high rates of AIDS-related mortality during follow up. HIV prevalence varies greatly across different populations of illicit and injecting drug users (Mathers et al., 2008). HIV infection increased the mortality rates from AIDS in the cohort studies, as seen in the ALIVE and VIDUS studies. In these cohorts, overdose mortality was also significantly higher among people who were HIV-positive compared than those who were HIV-negative, even after adjusting for differences in cocaine and other drug use. A substantial proportion of the increased overdose mortality appeared to be related to liver and other systemic disease among those who were HIV-positive (Wang et al., 2005). Future studies will need to disentangle the impact of HIV serostatus and disease progression on mortality among cocaine users. Furthermore, it was not possible to examine the impact of HAART upon mortality among HIV-positive cocaine users in these cohorts, since no study reported estimates disaggregated by calendar year, nor reported mortality among HIV-positive cocaine users receiving HAART compared to those who were not. Future cohorts need to examine this question, since it is highly likely that access to HAART would have a very substantial and beneficial impact upon AIDS-related mortality.

Third, with the exceptions of one study in Brazil, and three in Western Europe (Italy, France and the Netherlands) these studies were conducted in North America. Countries further from cocaine source countries, with more limited supplies of poorer quality cocaine may have a lower mortality risk. This possibility should be the subject of future research.

Fourth, and very importantly, the cocaine users in most of these studies came from socially disadvantaged settings. It is known that in some developed countries cocaine use is common among very high socio-economic groups, who primarily use cocaine intra-nasally and have a lower pre-existing mortality risks (Chivite-Matthews et al., 2005; Prinzleve et al., 2004; Shearer et al., 2007). Shearer et al. (2007), for example, found socio-economic status differences between better off intranasal users and the lower SES users who were more likely to inject both cocaine and

heroin. Cocaine users from socially disadvantaged settings may also have poorer access to healthcare than cocaine users from higher SES backgrounds. Other systematic differences between these groups that may affect mortality rates include exposure to adverse environmental factors (e.g. violence) and an increased likelihood of engaging in other high risk behaviours. For example, in the Brazilian cohort, the most common cause of death was fatal gunshot injury (Ribeiro et al., 2004, 2006). Shearer et al. (2007) also found that the lower SES Australian cocaine users were more likely to be involved in crime, and had higher risks of blood-borne virus infection than the cocaine users from the higher SES group.

Finally, some studies defined drug use on the basis of the drugs people primarily injected at baseline. Users may switch between injection of different drug types; alter the frequency or route of administration of their drug of choice, or cease drug use altogether. These changes might affect mortality risk in ways that cannot be estimated from the available cohort studies.

4.2. Implications for future research

This review has documented the paucity of research examining mortality among users of cocaine, one of the four most commonly used illicit drug types (United Nations Office on Drugs and Crime, 2010). The lack of studies carefully assessing and following up this group is not unique to cocaine: a similar review focusing upon amphetamines found even fewer studies (Singleton et al., 2009). Many more studies have focused upon regular or dependent opioid users – a recent systematic review located 58 studies in total for that drug type (Degenhardt et al., in press). Although it might be argued that opioids present a greater public health challenge, such a statement is not based on strong data.

We need to increase routine data collections that include cocaine users. These might include data on: arrestees, hospital entrants, harm reduction service attendees, or drug treatment entrants. Identifying cohorts of cocaine users in this way could permit the conduct of large-scale but comparatively low-cost prospective studies of mortality in cocaine, using data linkage with mortality registers. Such study designs (as indicated by the French study cite) have the advantage that they capture a large treated population, rather than a small and possibly unrepresentative subsample of clients from one service.

An additional implication of the review is the necessity to improve reporting of basic epidemiological data such as: person years of follow up, mortality rates, SMRs, and disaggregated mortality, by age and sex. The reporting of simple but irregularly reported information could be improved by following published guidelines on data collection and reporting (Vandenbroucke et al., 2007; von Elm et al., 2007). Furthermore, the precise causes of death need to be classified in line with definitions agreed by experts in the area (see (Randall et al., 2009) for a suggested approach).

5. Conclusions

Despite the relatively widespread use of cocaine and the range of harms that have been documented among problematic users of the drug, there has been surprisingly little prospective research examining mortality risk among cocaine users. The limited extant research has reported extremely high rates of mortality among this group but considerable uncertainties remain. Existing studies have focused on socially disadvantaged, daily or dependent cocaine injectors or crack smokers, who may have a higher mortality risk than regular or dependent cocaine users who snort the drug. Future prospective research on cocaine users should include users from more varied socioeconomic backgrounds to provide more representative estimates of mortality among people who use this drug.

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Contributors

LD and JS managed literature searches and summaries. BC, JM, TK, SM, GK and WH contributed vital information for completion of this manuscript. LD and JS led the drafting of the manuscript. All authors took an active role in commenting upon the manuscript. All authors have seen and approved the final version of the manuscript.

Conflict of interest

None.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.drugalcdep.2010.07.026.

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