

London audit of drug-related overdose deaths: characteristics and typology, and implications for prevention and monitoring

Matthew Hickman^{1,2}, Sandra Carrivick^{2,3}, Susan Paterson⁴, Neil Hunt², Deborah Zador⁵, Linda Cusick^{2,6} & John Henry⁷

Department of Social Medicine, University of Bristol,¹ Centre for Research on Drugs and Health Behaviour, LSHTM, London,² Royal College Nursing Institute,³ Toxicology Unit, Imperial College, London,⁴ Centre for Addiction Research and Education, University of Dundee, Scotland,⁵ School of Social Sciences, University of Paisley, Scotland⁶ and Accident and Emergency (A&E), Imperial College, London, UK⁷

ABSTRACT

Objectives To describe the circumstances and draft a typology of drug-related overdose deaths. **Setting** London, 2003. **Methods** An audit of 148 drug overdose deaths (involving heroin, methadone, dihydrocodeine, cocaine, amphetamine or MDMA) investigated by coroners during 2003. Information extracted on toxicology, pathology and circumstances were used to identify drug(s) implicated in the death. **Results** Poly- or multiple drug use was detected in the majority of deaths with at least 69 different combinations, including 66% for heroin and 42% for cocaine. Six categories of death were identified involving an opiate (100, 68%); cocaine (14, 9%); other controlled drug (five, 3%); mixed drug overdose (18, 12%); other prescribed drug (five, 3%); and other causes (seven, 5%). A witness was present and the death was not instantaneous in 92 (61%) cases, although evidence in the coronial file suggested that in the majority of cases the overdose went unnoticed until too late to intervene. In all, 15 (one in 10) of the deceased were released from prison within 3 months of death; and 37 (one in four) were reported as in receipt of a methadone prescription. **Conclusions** Perhaps for the first time in the United Kingdom cocaine was detected in more drug overdose deaths than methadone. However, reducing heroin use is central to the prevention of drug-related deaths. We recommend that overdose prevention encompasses strategies to encourage a 'mutual duty of care' among problem drug users, and in the United Kingdom further investigation of the relationship of methadone treatment failures on overall trends in drug-related deaths is merited.

Keywords Audit, cocaine, drug misuse, mortality, opiate, prevention.

Correspondence to: Matthew Hickman, Social Medicine, University of Bristol, Canynge Hall, Whiteladies Road, Bristol BS8 2PR, UK. E-mail: matthew.hickman@bristol.ac.uk

Submitted 19 October 2005; initial review completed 27 February 2006; final version accepted 25 September 2006

INTRODUCTION

Reducing drug overdose deaths, one of the UK government's drug policy targets, could improve the health of the overall population [1,2]. Heroin users in many cities in Europe and other developing countries have an annual risk of mortality of approximately 1%, often 15 times or more higher than the young adult (15–44) general population, and potentially contribute more than 10% of young adult mortality [3–6].

In England and Wales the number of drug overdose deaths has increased dramatically. Since 1970 the number of deaths certified as opiate overdose death

increased 100-fold; during the 1990s the number of deaths involving a controlled drug doubled from 805 in 1993 to 1593 in 2000; and after a decline in the number of drug-related deaths from 2001 to 2003 the number increased in 2004 [7–9]. In the United Kingdom, as in other countries, it is unclear to what extent these trends are dictated purely by changes in the population of drug users or, crucially, whether other factors, such as changes in availability of substitution treatment, prison policy or drug consumption have had an impact on mortality risk [9].

In Australia, the number of drug-related deaths fell dramatically following a 'heroin drought', which may

have been due to reductions in both the prevalence of injecting and risk of death [10]. In Switzerland, increased availability of methadone occurred at the same time as a decline in overdose deaths, although other trends suggest that the population of heroin users also has declined [11,12]. In Vienna, an increase in heroin deaths was observed, but not associated with any change in drug quality [13]. In New York, changes in the pattern of multiple drug consumption between alcohol, cocaine and heroin were identified as key drivers to trends in drug-related deaths [14]. In Italy, a range of treatments were shown to reduce the risk of overdose, but the period immediately following treatment dropout or discharge substantially increases the risk of death [Davioli *et al.*, unpublished data]. Similarly, in the United Kingdom the month following prison release has been shown to increase overdose risk [15,16] compared to other periods, and unsupervised methadone consumption has been identified as a contributory cause in some drug-related deaths [17,18]. Audits of drug-related deaths in Australia suggested that the majority of deaths were among dependent older users, and that the events involved multiple drugs, occurred several hours after last consumption and in the presence of other people [5,19–22]. We conducted an audit of drug-related overdose deaths in London to inform prevention priorities and interpretation of drug trends—reporting on the characteristics and toxicology and seeking to identify the principal drug(s) that may have caused the death towards drafting a typology of overdose death.

METHODS

Drug overdose deaths

The cases comprised deaths involving heroin or other opiates, cocaine, amphetamine and MDMA determined through toxicological or other evidence investigated by coroners in 2003. Seven of the eight coroners in London agreed to participate in the study. These deaths would appear in routine mortality statistics as 2003 registrations, comprising more than 75% of drug overdose deaths in London and one in six in England and Wales [Clare ariffiths, Office for National Statistics (ONS)]. Cases were identified by hand-searching coronial files. Cross-validating these against a list of drug-related overdose deaths—with the same list of drugs—generated by the ONS did not identify any additional cases for 2003. Potential or other drug-related deaths that did not involve one of the opiate or controlled drugs were excluded (for example, prescription or over the counter drugs only), or were certified as natural causes and drugs were incidental (for example, death due to AIDS with toxicological evidence of cocaine use prior to death).

A combined quantitative and qualitative survey instrument was used to extract information on socio-

demographic characteristics, place of death, drug history, toxicology, presence of witnesses and evidence of substitute prescribing from the coronial files. Prison and arrest history were determined through record linkage, using name, gender and date of birth, with the Offenders Index. Prescription and contact with treatment services were extracted from the coronial file.

Toxicology and typology

Finally, two of the authors (S. P. expert in toxicology, and J. H. expert in poisons and emergency medicine) reviewed the evidence (including toxicology, pathology and events prior to death) in order to assess which, if any, substance(s) could be ascribed as the underlying reason for the death. In other words, would the subject have more than likely survived if they had not taken one or more substance(s)? We acknowledge potential problems in the interpretation of toxicology, and therefore used the other information (for example, known dependent drug user, signs of respiratory depression) to assess whether there was a consistent picture. First, the therapeutic, toxic and potentially fatal levels can overlap and vary considerably between individuals because of individual tolerance [23–26]. Secondly, there is currently no means of quantifying the degree of tolerance to any drug in a given individual, nor can the scale of any interaction between drugs that may interact adversely with each other be quantified (such as combining opiates, benzodiazepines and alcohol) [27]. Thirdly, the majority of deaths occur some hours after ingestion, during which time metabolism of the drugs would continue, diluting the correlation between toxicity and concentration of the drug measured in *post-mortem* blood [28].

RESULTS

Sample characteristics

In total, 148 drug overdose deaths were identified: 116 (78%) were certified as injury (accident or misadventure) and the remaining certified as open (18, 12%), suicide (13, 9%) and one as natural causes. We included the latter because the toxicological evidence showed clearly that the death was due to a drug overdose. Evidence for the pattern of drug use was recorded in 131 cases: 92% showing evidence of drug dependence and 70% injecting drug use. Cocaine, where identified in the coronial file, was taken mainly in the form of crack. The key personal socio-demographic characteristics of the sample were as follows: 80% male; median and mean age 34 and 35.8 years, respectively, with 31% aged under 30, 37% aged 30–39 and 32% aged 40+; 83% white, 8% black minority ethnic group, 5% other and 4% unknown ethnic group; 68% lived in house/flat, 10% in hostel/hotel, 5%

street homeless, 9% roofless/living with friends and 8% unknown place of residence; 28% working, 21% receiving benefits and 52% unknown income or occupation; 28% were in a relationship, 52% unattached or single and 20% unknown marital/relationship status.

Toxicology

Table 1 shows the number of cases grouped by drug, detected by toxicology. Two deaths had no toxicology because the subject had been found some time after the time of death, but were classified as drug-related because of the presence of paraphernalia. Approximately two-thirds (66%) of the deaths had positive toxicology for heroin/morphine, 42% cocaine, 32% methadone, 12% dihydrocodeine, 11% MDMA/amphetamine, 56% alcohol and 41% benzodiazepines. Table 1 also shows the considerable overlap between drugs; for instance, 45% and 25% of deaths positive for heroin were also positive for cocaine and methadone, respectively; and 73% and 32% of deaths positive for cocaine were positive for heroin and methadone, respectively. In addition, 18 (12%) of the cases were positive for cannabis and 48 (32%) deaths were positive for a range of other drugs, mainly antidepressants. Among the 146 deaths, there were at least 69 different combinations of drugs detected (data available on request). In only 16 (11%) deaths was a single drug detected, and the average was more than three drugs detected. Alcohol or benzodiazepines were present in the majority of deaths.

There were no significant differences in the average level of drug detected and verdict (intentional versus unintentional injury) for heroin, methadone or cocaine; nor were there any significant differences in the mean toxicological value of drugs detected in relation to the number of other drugs detected [29].

Draft typology

Table 2 shows our assessment of the drug(s) that were more than likely to have caused the death (with pathology or other information summarized in the footnote). In all we identified 21 types within six larger categories: opiate (100, 68%); cocaine (14, 9%); other controlled caused by MDMA (five, 3%); mixed (18, 12%); other prescribed (five, 3%); and other causes (seven, 5%). The mixed drugs involved different types of drug and mechanisms of death where a single underlying type of drug or mechanism was not implicated clearly, such as heroin and cocaine, or controlled drugs and antidepressants. Subjects in the 'other prescribed' and 'other injury' category were all positive for a controlled drug and included in the mortality statistics as such, but we considered it likely that a prescribed drug (antidepressant or antineuroleptic) or other mechanism, respectively, was the cause of death.

Table 1 London drug-related deaths audit: toxicology and extent of polydrug use detected.

Drug	Total	Proportion of positive toxicology reports by drug (%) [*]							No. of drugs		
		Heroin	Alcohol	Cocaine	Benzo	Methadone	Dihydrocodeine	MDMA-amphetamine	Other	1	3+
Heroin	97	100	62	45	42	26	7	6	32	5 (5%)	52 (53%)
Alcohol	82	73	100	35	27	7	15	37	0	0	65 (77%)
Cocaine	61	73	47	100	32	5	10	27	6 (10)	6 (10)	45 (73%)
Benzodiazepines	60	70	52	33	45	5	7	22	0	0	55 (92%)
Methadone	46	55	49	43	100	6	9	28	3 (6%)	3 (6%)	37 (79%)
Dihydrocodeine	18	44	38	19	19	100	6	69	1 (6%)	1 (6%)	12 (75%)
MDMA/amphetamine†	16	33	72	33	22	6	100	22	1 (6%)	1 (6%)	12 (67%)

[†]MDMA and amphetamine were combined because there was no evidence of amphetamine injection, and in the absence of opiates or cocaine, the drugs implicated in the death were MDMA in all but one case of MDMA and amphetamine poisoning. ^{*}Proportion of cases positive for other drugs are shown horizontally.

Table 2 London drug-related deaths audit: draft typology.

Typology	Total (%)	
Opiates	100	68
Heroin*	50	34
Heroin and alcohol*	16	11
Methadone*	16	11
Methadone and alcohol*	2	1
Heroin and methadone*	10	7
Heroin and methadone and alcohol*	1	1
Dihydrocodeine*	5	3
Dihydrocodeine and alcohol*	1	1
Cocaine	14	9
Cocaine†	2	1
Cocaine‡	1	1
Cocaine§	11	7
Other controlled: MDMA¶	5	3
Mixed††	18	12
Mixed—heroin and cocaine	11	7
Mixed—methadone and MDMA	1	1
Mixed prescribed and controlled—heroin and other	1	1
Mixed prescribed and controlled—methadone and other	2	1
Mixed prescribed and controlled—dihydrocodeine and other	2	1
Mixed prescribed and controlled—cocaine and other	1	1
Other prescribed	5	3
Other	5	3
Injury‡‡	5	3
Grand total	148	100

Mechanism and signs: *respiratory depression, aspiration pneumonia and acute poisoning; †body packer/stuffer; ‡toxic additive; §pulmonary oedema, myocardial infarction, stroke, excited delirium, aspiration pneumonia; ¶hyponatraemia—excess fluid, serotonin syndrome; ††unable to separate single drug or mechanism of death as cause; ‡‡hanging, drowning, car accident.

Heroin, due primarily to respiratory depression or aspiration pneumonia, was the most common mode of death in more than one-third ($n = 50$) of the cases, and was a contributory cause with other respiratory depressants or other combinations of drugs in a further 39 (26%) deaths. Comparing the typology with toxicology suggests that heroin was the principal or contributory cause in 91% of the deaths with a positive toxicology for heroin. In contrast, methadone was the primary cause alone or with alcohol in 18 (12%) deaths and a contributory cause in 14 (10%) deaths (in all 70% of the deaths with a positive toxicology for methadone). Cocaine was a principal or contributory cause in 26 (18%) of the deaths (43% of the deaths with a positive toxicology for cocaine). The 14 (9%) deaths assessed to be caused principally by cocaine were due to a number of mechanisms including: swallowing a fatal amount of cocaine, cocaine cut with

lignocaine as a toxic additive, acute overdose, aspiration pneumonia, cerebrovascular and cardiac arrest and excited delirium leading to a fatal injury. Alcohol was judged to be a contributory cause in 20 of the deaths (24% of the deaths with positive toxicology for alcohol), where it was unclear whether the person would have died from the other drug(s) without also having consumed the alcohol, although they would not have died if alcohol had been the only drug taken. We considered that benzodiazepines, although present in a substantial number of deaths (Table 1), were detected at low levels in contrast to other drugs and may not have contributed to the death.

Circumstances of death

Evidence was reported in the coronial files that more than 80% of cases had had previous contact with either accident and emergency (A&E), general practitioner (GP) or specialist drug treatment services, 36% in the month prior to death. Overall, in 75% of the cases the subject had had contact with friend or family in the 72 hours prior to death; and in 97 (66%) of the deaths at least one witness was present. Ten of the deaths were documented as rapid or instantaneous (within minutes of consumption). An ambulance arrived in more than 90% of the cases, but for the vast majority of occasions (115, 85%) the person was already dead when the ambulance arrived. In 92 (61%) of the deaths there was at least one witness reported as being present and the death was not reported as instantaneous. However, based on the events and evidence contained within the coronial files, we suspect that in one in four of these cases a different outcome could have occurred if the witness had acted more swiftly, commenced cardiopulmonary resuscitation (CPR) and called an ambulance at the first sign of trouble. In the other three-quarters of cases, a far greater change in events would have had to occur as, due to a number of factors (including intoxication of witness, deceased hiding their drug use or deceased 'seemingly' falling asleep and subsequent aspiration of vomit or respiratory depression going un-noticed), by the time any 'signs of trouble' were recognized the subject had died or the situation was irreversible (e.g. Glasgow Coma score of 3 recorded prior to the deceased being pronounced life extinct).

Evidence of recent imprisonment and substitute drug treatment

Table 3 shows that, in all, 101 (68%) subjects were matched to the Offenders Index, identifying nearly 900 previous convictions (mean and median 8.7 and five, respectively). Fifty-nine (40%) of the cases had been in prison previously, of whom 15 (25% of those with a prison history and 10% of the total sample) had been released within 3 months of the death. All but three of

Table 3 London drug-related deaths audit: offending history.

<i>Previous convictions</i>		<i>Prison history</i>	
No	47 (32%)	No	89 (60%)
Yes	101 (68%)	Yes	59 (40%)

<i>Number of convictions</i>		<i>Time before release and death</i>	
Mean	8.7	< 3 months	15
Median	5	3–12 months	4
Minimum	1	1–5 years	14
Maximum	58	> 5 years	26

Table 4 London drug-related deaths audit: substitute treatment history at time of death.

<i>Treatment history</i>	<i>Total</i>	<i>%</i>
Methadone prescribed by GP	15	10%
Methadone prescribed by specialist agency	22	15%
Dihydrocodeine prescribed by GP	2	1%
Dihydrocodeine prescribed by specialist agency	2	1%
No evidence of current script	107	72%
Total	148	100%

those recently released from prison had positive toxicology for heroin, methadone and/or cocaine; 10 of the deaths were assessed as due to an opiate, three mixed heroin and cocaine, one case of MDMA poisoning and one external injury.

Table 4 shows evidence of treatment history within the coronial files, suggesting that 25% ($n = 37$) of the deceased were in receipt of a methadone prescription, and four (2%) of the subjects were prescribed dihydrocodeine. Among the deceased prescribed methadone, 26 also had positive toxicology for methadone and 17 were assessed as deaths where methadone was the principal or contributory cause (Table 4), therefore comprising 55% of the deceased with positive methadone toxicology and 46% of methadone-related deaths. All four of the deceased with a dihydrocodeine prescription were positive for the drug, with two assessed as dying from a dihydrocodeine overdose.

DISCUSSION

In the London drug-related death audit we sought to describe the characteristics of drug-related overdose deaths, and draft a typology that could prove useful in shaping prevention policies and future monitoring. There were strong similarities between our audit conducted in London and the characteristics of people dying from

drug-related deaths in other countries [5,19,31]. The majority of deaths were among people with a history of dependent drug use and injecting drug use, who had extensive social and other contact prior to death [32]. The deceased were more likely to be male (four-fifths) and older (half over 35) than problem drug users in treatment or prevalence estimates [33].

In theory, there was extensive capacity to intervene prior to the death—more than 60% if defined in terms of a death that was not immediate and with an available witness. Health education and drug-related prevention campaigns in the United Kingdom and elsewhere often focus on alerting fellow users, friends and family to the signs of overdose and encouraging people to call an ambulance and undertake basic first aid. These are important messages. However, we suggest that alone these may have limited success, as we conclude that in the majority of cases the witness's capacity was compromised. In addition, therefore, we need to encourage a stronger, mutual 'duty of care' among users, in order that the 'capacity' for monitoring, identifying and responding to potential overdoses is increased, because the opportunity to intervene so often passed by unnoticed until it was too late.

Substitute prescription, especially methadone, and loss of tolerance following release from prison constitute key protective and risk factors associated with fatal overdose [15,16,34,35]. Increasing the availability of treatment among heroin users in the community and in prison is critical to preventing drug-related mortality. It is a cause of concern that in at least 41 of the cases we found evidence within the coronial files of current substitute prescription, including more than half of the deaths with a positive toxicology for methadone, which was higher than some earlier audits [36]. Unfortunately, our audit could not determine methadone dose, whether the subjects had very recently dropped out of treatment, or report and compare the management of the deceased with living subjects. Increased methadone prescription has been associated with declining overdose deaths in other European cities, and was one explanation for the overall fall in drug-related deaths in England and Wales from 2000 to 2003 [9]. In the United Kingdom there has been a great deal of concern directed towards problems of methadone diversion and the potential for increasing overdose risk, which has largely proved unfounded [17,37]. However, our audit raises other concerns that merit further investigation: specifically, what impact those cases currently in treatment at the time of death (i.e. treatment failures) may have had on trends in drug-related deaths over time.

One in 10 of the drug-related poisonings were in people recently (< 3 months) released from prison. Although slightly lower than audits of overdose deaths in

Glasgow and Scotland [30], this provides a baseline target against which interventions in prison can be measured.

Toxicology, typology and polydrug use

Multiple or polydrug use has been emphasized as a key feature and risk of drug overdose deaths. The toxicological data reveal polydrug use in 90% of the cases, with at least 69 different combinations of drugs in only 148 deaths. However, in our draft typology based on the drug(s) that may have contributed to the death we reduced the number of permutations to six main and 21 potentially different types. Opiate use, primarily heroin, was judged to be a key contributor on its own or in combination with other drugs in nearly 80% of the drug overdose deaths. One clear message is that removing or managing the risk of heroin use must be central to the prevention of drug overdose deaths.

The increase in cocaine and crack use observed in London was also observed among drug overdose deaths [38]. Perhaps for the first time in the United Kingdom, cocaine (taken mainly in the form of crack) was detected in more drug overdose deaths than methadone. However, within our typology—taking into account the mechanism of death and toxicology—cocaine was a contributory cause in approximately one in five deaths, slightly lower than methadone.

In a substantial minority of cases a single drug could not be identified, but the death could have been due to one or more drugs that may act synergistically (such as alcohol and opiates), or have different potential mechanisms of death such that if they do not interact toxicologically, may increase behaviourally the risk of a fatal overdose (such as opiates and cocaine). Other more analytical studies (both biological and epidemiological) are required to explore the impact of the large number of deaths positive for heroin and cocaine or alcohol and other drugs, in order to address the critical public health question of whether changes in the pattern of drug use increase, decrease or have no impact on the risk of a fatal overdose (i.e. on the mortality rate experienced by injecting drug users and problem drug users).

Limitations

We acknowledge several important limitations to the audit. First, the study is underpowered to explore significant differences between groups of cases (e.g. toxicological level by verdict or typology of death)—notwithstanding that approximately three-quarters and one in six illicit drug overdose deaths in London and England, respectively, were included. Secondly, the study is descriptive, and without a control sample can only suggest (but not test) factors that may be causally important to the drug-related death. None the less, audits of

drug-related deaths extend our understanding of the characteristics of drug-related deaths beyond data provided by mortality statistics. Thirdly, our draft typology is a judgement-based assessment (albeit made by experts in the field), which may be open to bias in terms of interpretation and incompleteness of information contained within the coronial file. However, we think it important that we move beyond consideration simply of the drugs detected, and that future audits consider generating similar typologies to inform priorities for prevention.

Acknowledgements

We are most grateful to coroners in London for their participation with the audit. We are also most grateful to the help and support of Clare Griffiths (ONS) and Andrew Kalinsky (Home Office). The work was undertaken by the Centre for Research on Drugs and Health Behaviour, funded by the National Treatment Agency (NTA) for Substance Misuse. The views expressed in the publication are those of the authors and not necessarily those of the NTA. Mathew Hickman is funded partly through an NHS public health career scientist award.

References

1. Advisory Council on Misuse of Drugs. *Reducing Drug Related Deaths*. London: Home Office; 2000.
2. Darke S., Hall W. Heroin overdose: research and evidence-based intervention. *J Urban Health* 2003; **80**: 189–200.
3. Bargagli A. M., Hickman M., Davoli M., Perucci C. A., Schifano P., Buster M., Brugal T. Drug related mortality and its impact on adult mortality in eight European countries. *Eur J Public Health* 2006; **16**: 198–202.
4. Hickman M., Carnwath Z., Madden P., Farrell M., Rooney R., Ashcroft R. *et al.* Mortality and fatal overdose risk—pilot cohort study of heroin users recruited from specialist drug treatment sites in London. *J Urban Health* 2003; **90**: 274–87.
5. Darke S., Zador D. Fatal heroin 'overdose': a review. *Addiction* 1996; **91**: 1765–72.
6. Degenhardt L., Hall W., Warner-Smith M. Using cohort studies to estimate mortality among injecting drug users that is not attributable to AIDS. *Sex Transm Infect* 2006; **82**: 56–63.
7. De Angelis D., Hickman M., Yang S. Estimating long-term trends in the incidence and prevalence of opiate/injecting drug use and the number of ex-users: the use of back-calculation methods and opiate overdose deaths. *Am J Epidemiol* 2004; **160**: 994–1004.
8. Brock A., Griffiths C. Trends in the mortality of young adults aged 15–44, England and Wales 1961–2001. *Health Stat Q* 2003; **19**: 22–31.
9. Morgan O., Griffiths C., Hickman M. Fatal poisoning is associated with illicit supplies of heroin and methadone but not methadone treatment: analysis of time trends in England and Wales 1993–2003. *Int J Epidemiol* in press.
10. Degenhardt L., Day C., Dietze P., Pointer S., Conroy E., Collins L. *et al.* Effects of a sustained heroin shortage in three Australian States. *Addiction* 2005; **100**: 908–20.

11. Perret G., Deglon J.-J., Kreek M. J., Ho A., La Harpe R. Lethal methadone intoxications in Geneva, Switzerland, from 1994 to 1998. *Addiction* 2000; **95**: 1647–53.
12. Nordst C., Stohler R. Incidence of heroin use has declined dramatically in Zurich, Switzerland. *Lancet* 2006; **367**: 1830–4.
13. Risser D., Uhl A., Stichenwirth M., Honigschnabl S., Hirz W., Schneider B. *et al.* Quality of heroin and heroin related deaths from 1987 to 1995 in Vienna, Austria. *Addiction* 2000; **95**: 375–82.
14. Coffin P. O., Galea S., Ahern J., Leon A. C., Vlahov D., Tardiff K. Opiates, cocaine and alcohol combinations in accidental drug overdose deaths in New York City, 1990–98. *Addiction* 2003; **98**: 739–47.
15. Bird S., Hutchinson S. Male drugs-related deaths in the fortnight after release from prison: Scotland 1996–99. *Addiction* 2003; **98**: 185–90.
16. Seaman S. R., Brettle R. P., Gore S. M. Mortality from overdose among injecting drug users recently released from prison: database linkage study. *BMJ* 1998; **316**: 426–8.
17. Oliver P., Keen J. Concomitant drugs of misuse and drug using behaviours associated with fatal opiate-related poisonings in Sheffield, UK, 1997–2000. *Addiction* 2003; **98**: 191–7.
18. Seymour A., Black M., Jay J., Cooper G., Weir C., Oliver J. The role of methadone in drug-related deaths in the west of Scotland. *Addiction* 2003; **98**: 995–1002.
19. Darke S., Ross J., Zador D., Sunjic S. Heroin related deaths in New South Wales, Australia, 1992–96. *Drug Alcohol Depend* 2000; **60**: 141–50.
20. Sunjic S., Zador D. A. Methadone syrup related deaths in New South Wales, Australia, 1990–95. *Drug Alcohol Rev* 1999; **18**: 409–15.
21. Zador D. A., Sunjic S., Darke S. Heroin related deaths in New South Wales, 1992: toxicological findings and circumstances. *Med J Aust* 1996; **164**: 204–7.
22. Zador D. Circumstances and users' perceptions of heroin overdose at the time of event and at one-week follow-up in Sydney, Australia: implications for prevention. *Addict Res Theory* 2001; **9**.
23. Darke S., Sunjic S., Zador D., Prolov T. A comparison of blood toxicology of heroin-related deaths and current heroin users in Sydney, Australia. *Drug Alcohol Depend* 1997; **47**: 45–53.
24. Tagliaro F., De Battisti Z., Smith F. P., Marigo M. Death from heroin overdose: findings from hair analysis. *Lancet* 1998; **351**: 1923–5.
25. Baselt R. C. *Disposition of Toxic Drugs and Chemicals in Man*, 7th edn. Foster City, CA: Biomedical Publications; 2004.
26. Uges D. R. A. Therapeutic and toxic drug concentrations list. Available at: <http://www.tiaft.org> (updated September 2004).
27. White J. M., Irvine R. J. Mechanisms of fatal opioid overdose. *Addiction* 1999; **94**: 961–72.
28. Isenschmid D. S., Levine B. S., Caplan Y. H. A comprehensive study of the stability of cocaine and its metabolites. *J Anal Toxicol* 1989; **13**: 250–6.
29. Gossop M., Stewart D., Treacy S., Marsden J. A. A prospective study of mortality among drug misusers during a 4-year period after seeking treatment. *Addiction* 2002; **97**: 39–47.
30. Zador D., Hutchinson S., Kidd B., Hickman M., Taylor A., Fahey T. *et al.* National investigation into drug related deaths in Scotland 2003. Substance Misuse Research, Scottish Executive, August 2005.
31. Warner-Smith M., Darke S., Lynskey M., Hall W. Heroin overdoses: causes and consequences. *Addiction* 2001; **96**: 1113–25.
32. Jones R., Gruer L., Gilchirst G., Symour A., Black M., Oliver J. Recent contact with health and social services by drug misusers in Glasgow who died of a fatal overdose in 1999. *Addiction* 2002; **97**: 1517–22.
33. Hickman M., Higgins V., Hope V., Bellis M., Tilling K., Walker A. *et al.* Injecting drug use in Brighton, Liverpool, and London: best estimates of prevalence and coverage of public health indicators. *J Epidemiol Commun Health* 2004; **58**: 766–71.
34. Hulse G. K., English D. R., Milne E., Holman D. J. The quantification of mortality resulting from the regular use of illicit opiates. *Addiction* 1999; **94**: 221–9.
35. Capelhorn J. R. M., Dalton M. S. Y. N., Haldar F., Paterenas A. M., Nisbet J. G. Methadone maintenance and addicts' risk of fatal heroin overdose. *Subst Misuse* 1996; **31**: 177–96.
36. Cook S., Moeschler O., Michaud K., Yersin B. Acute opiate overdose. *Addiction* 1998; **93**: 1559–65.
37. Hickman M., Madden P., Henry J., Baker A., Wallace C., Wakefield J. *et al.* Trends in drug overdose deaths in England and Wales 1993–98: methadone does not kill more people than heroin. *Addiction* 2003; **98**: 419–26.
38. Hope V. D., Hickman M., Tilling K. Capturing crack-cocaine use: estimating the prevalence of crack-cocaine use in London using capture–recapture with covariates. *Addiction* 2005; **100**: 1701–8.