

Overview of amphetamine-type stimulant mortality data (UK, 1997-2007)

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Abstract

Background/Aims: Despite being amphetamine derivatives, MDMA and its analogues show a number of clinical pharmacological differences with respect to both amphetamine (AMP) and methylamphetamine (METH). We aimed here at reporting and analysing information relating to the socio-demographics and clinical circumstances of the amphetamine-type stimulant related deaths for the whole of the UK.

Methods: Data (1997-2007) were taken from the National Programme on Substance Abuse Deaths (np-SAD) database, collecting information from UK Coroners/procurators fiscal. To calculate rates of fatalities per 100,000 users, appropriate AMP/METH and ecstasy users' numbers were taken from the 2001-2007 British Crime Survey.

Results: Overall, 832 AMP/METH- and 605 ecstasy- (mostly MDMA and methylenedioxyamphetamine/MDA) related deaths were respectively identified. In comparison with AMP/METH victims, the ecstasy ones were more likely to be: younger (28.3 vs 32.7 years; $p < .0001$) and less likely to be known as drug users (PR=1.9; CI: 1.5-2.6). Ecstasy was more likely to be identified on its own than AMP/METH ($p=0.0192$). Contributory factors were more frequently mentioned by Coroners in the 'AMP/METH only' (106 cases) group than in the 'ecstasy only' (104 cases) one ($p=0.0043$). Both poly-drug and mono-drug AMP/METH fatalities per 100,000 16-59 year old users were significantly more represented than ecstasy fatalities (respectively: 17.87 +/- 4.77 deaths vs 10.89 +/- 1.27; $p=0.000$; 2.09 +/- 0.88 vs 1.75 +/- 0.56; $p=0.0096$). However, mono-intoxication ecstasy fatalities per 100,000 16-24 years old users were significantly more represented than AMP/METH fatalities (1.67 +/- 0.52 vs 0.8 +/- 0.65; $p=0.0007$).

Conclusion: With respect to AMP/METH, ecstasy was here more typically identified in victims who were young, healthy, and less likely to be known as drug users. AMP/METH high mortality rates may be explained by users' high levels of physical co-morbidity; excess ecstasy-related fatality rates in young users may be a reason of concern. Although the Coroners' response rate was of 90-95%, study limitations include both reporting inconsistency over time and lack of routine information on drug intake levels prior to death.

Key words: amphetamine, methylamphetamine, ecstasy, MDMA, MDA, MDEA, PMA, mortality, drug misuse

Introduction

In the second part of the '90s, a global trend of escalating amphetamine-type stimulant (ATS; a group including amphetamine, methylamphetamine, ecstasy and the ecstasy-type drugs) use was observed [1]. Despite being amphetamine derivatives, MDMA and MDMA-like drugs clearly show a number of clinical pharmacological differences with respect to both amphetamine and methylamphetamine. MDMA and other phenethylamine drugs (including: methylenedioxyamphetamine/MDA/'love drug'; methylenedioxyethylamphetamine/MDEA/'eve', paramethoxyamphetamine/PMA; and – methylthioamphetamine/4-MTA/'flatliners') occupy an intermediate position between stimulants and hallucinogens, making up the distinct class of 'entactogens' [2]. In contrast with amphetamine and its immediate derivatives, which can be prescribed for a number of clinical conditions [3], MDMA/ecstasy and the remaining entactogens do not have any recognized therapeutic use so far.

The risk of ecstasy 'overdose' has been described in the UK since the early 1990s [4]; ecstasy price fluctuations over the years are inversely correlated with levels of ecstasy availability and numbers of related deaths [5]. In England and Wales, in parallel with increased surveillance, a steady and constant increase of ecstasy-related fatalities has been observed in the time frame August 1996–April 2002, when a total of 202 related deaths were recorded [6]. It is of concern that significant number of ecstasy related deaths occur at doses associated with recreational use [4]; both individual drug polymorphisms and polydrug abuse ingestion itself may act as confounding factors [7]. It seems that not all entactogens show similar overdose risks. In fact, although MDA, MDEA and MBDB show acute toxicity levels comparable to MDMA [5], PMA has been associated with a much higher rate of lethal complications than MDMA [8, 9]. Similarly, Carmo et al [10] suggested that 4-MTA in humans has been associated with severe intoxications and several deaths.

Data related to amphetamine/methylamphetamine (AMP/METH) deaths in the UK (1990–2002) have previously been commented on as well [11], but no studies have described so far the possible similarities and differences between the AMP/METH-related and the entactogen-related fatalities.

Given the very large numbers of consumers involved in the use of amphetamine-type stimulants across both the EU and the UK [12], the main aims of this study were to report and analyse information relating to the socio-demographics and clinical circumstances of all recorded ATS-related deaths for the whole of the UK, both when the index drugs were taken on their own and when in combination with other drugs. To provide a better understanding of the relative toxicity risk of AMP/METH and MDMA/ecstasy, rates of related deaths over the years were also assessed whenever possible whilst taking into account number of consumers of AMP/METH and MDMA/ecstasy, respectively.

Methods

Established in 1997, the National Programme on Substance Abuse Deaths (np-SAD) [13] collects all information pertaining to drug related deaths from the UK Coroners' and procurators' fiscal jurisdictions, as well as data collated by the Scottish Crime & Drug Enforcement Agency from Scottish police forces. An np-SAD case is defined as a relevant death where any of the following criteria are met at a completed inquest, fatal accident inquiry or similar investigation: a) one or more psychoactive substances directly implicated in death; b) history of dependence or abuse of psychoactive drugs; c) presence of controlled drugs at post mortem; or d) cases of deaths directly due to drugs but with no inquest. More

specifically, np-SAD database deaths here included were those in which one or more ATS drugs were either directly implicated in death and/or were identified during necropsy.

The response rate from Coroners in England and Wales is typically in the region of 90-95% [13]. In line with Schifano et al [5], we defined here deaths related to *ecstasy* as a Coroner's report including 'ecstasy', 'XTC', 'MDMA', 'MDA', 'MBDB', and 'MDEA'. Although presenting with different toxicity levels [10, 9], we tried to identify here as well possible mentions of 'PMA' and '4-MTA', since Coroners may at times include these entactogens in the broader 'ecstasy-type' group. Conversely, deaths identified as *amphetamine/methylamphetamine* (AMP/METH) included the text 'amphetamine', 'methylamphetamine', 'methamphetamine' and 'amphetamine salts'. Data shown here refer to analysis of the whole of the np-SAD database, from 1 July 1997 to 15 April 2009. In this way, the range of data extends from 1997 to 2007. In fact, it is argued here that by mid-April 2009 the vast majority of Coroners' inquests related to deaths occurring in 2007 were already completed and included in the database. Mono-substance deaths were defined as the index drug was found at post mortem on its own or the index drug was the sole drug implicated and there was no other substance found at post mortem.

Apart from the raw number of ATS-related fatalities observed over the years, to better interpret the available data number of AMP/METH and MDMA/ecstasy fatalities will be respectively analyzed whilst taking into account both the total number of substance-related deaths reported to np-SAD and the total number of the index ATS consumers as denominators. In particular, to calculate number of AMP/METH and MDMA/ecstasy consumers over the years, data from the British Crime Survey (BCS; England and Wales) were taken into account. The BCS offers regular estimates of last year use for amphetamines and ecstasy, although this is only available from 2001 onwards [14 – 20].

Descriptive statistics were used for data sources; probability ratios (PR) and 95% confidence intervals (95% CI) were reported. The Mann-Whitney U test was used to calculate age differences in the two groups and the chi square test to analyse categorical variables. Rates of deaths per 100,000 users were calculated using BCS for last year use and np-SAD cases reported by coroners in England and Wales for the relevant age groups. The data were analysed using SPSS™ for Windows version 15.

Results

Figure 1 shows the rates of AMP/METH and ecstasy-related deaths reported to the np-SAD over the years. The number of AMP/METH deaths peaked first in 1998, fell steeply in 2000 but since then have increased to a higher peak in 2007; rates of ecstasy fatalities peaked first in 2001 and fell slightly afterwards before rising to a new peak in 2006.

Insert figure 1 around here

Overall, 832 AMP/METH- and 605 ecstasy-related deaths were respectively identified (see table 1). In the so called 'ecstasy' group, during the study period 1997-2007 the following drugs were mentioned at post mortem: MDMA 564; MDA 117; MDEA 4; PMA 1 (in a number of cases, more than one entactogenic drug was identified).

With respect to the AMP/METH polydrug victims (see table 1), the ecstasy polydrug ones were more likely to be younger (28.3 vs 32.7 years; $p < .0001$) and less likely to be known as drug addicts/users (PR=1.9; CI: 1.5-2.6). In the polydrug cases (see table 1), both alcohol (PR=1.5; CI: 1.3-1.8) and cocaine (PR=1.8; CI: 1.4-2.2) were more frequently identified in

the ecstasy group, whilst both methadone (PR=1.9; CI: 1.4-2.5), heroin/morphine (PR=1.6; CI: 1.3-1.8), and other opiates/opioid analgesics (PR=1.4; CI:1.0-1.9) were more likely to be reported in the AMP/METH group.

Although most AMP/METH and ecstasy victims died of polydrug abuse ingestion, ecstasy was more likely to be identified on its own (104 cases out of 605) than AMP/METH (106 cases out of 832; Fisher's exact test; two-tailed P value= 0.0192; see table 2). In these mono-intoxication groups, the index ATS drug was either the sole drug found at post mortem or the sole drug implicated and no other substances were identified at post mortem. Similarly to what was identified in comparing multiple drug misuse fatalities, in comparison with the AMP/METH only victims the 'ecstasy only' ones turned out to be younger (23.9 vs 32.0 years; $p < .0001$) and less likely to be known as drug addicts/users (PR=2.8; CI: 1.5-5.5). Furthermore, suicide trended towards significance in ecstasy only-related deaths (PR=1.5; CI: 0.4-5.3; see table 2).

Insert tables 1 and 2 around here

In the 'ecstasy only' group, no contributory factors/suicidal intent were identified in 90 out of 104 (86.5%) cases, with only ecstasy and its well-known acute medical consequences (Schifano, 2004) having been mentioned as the cause of death (see table 3). Conversely, the presence of contributory factors (74 cases out of 106 cases; 69.8%) was more frequently mentioned by Coroners in the group of 'AMP/METH only' fatalities (Fisher's exact test; two-tailed $p=0.0043$). Similarly (see table 3), the proportion of deaths directly attributed to toxicity related to the index ATS drugs out of the total number of fatalities in which the index drug (either on its own or in combination) was implicated in death was found to be higher for the ecstasy only group with respect to the AMP/METH only group (90/605 vs 74/832; Fisher's exact test; two-tailed $p=0.0005$).

Insert table 3 around here

For the examination of ATS fatalities within the larger context of drug related fatalities, we calculated rates of deaths for the index drugs compared to all deaths reported to np-SAD over the study period (1997-2007). It appeared (see both table 4 and figure 2) that although average rates of 'AMP/METH only' (0.58%) over the years were comparable to the 'ecstasy only' ones (0.57%), AMP/METH polydrug intoxication fatalities (average value over the years: 4.53%; range: 3.02-6.23%) were more frequently identified than the ecstasy polydrug intoxication ones (average value over the years: 3.29%; range: 1.14-4.32%)

Insert both table 4 and figure 2 around here

In terms of rates of deaths per 100,000 users of AMP/METH and ecstasy (2001-2007 only), if data related to multiple drug intoxication were taken into account (see table 5) it appeared that AMP/METH fatalities were significantly more represented (17.87 +/- 4.77 deaths vs 10.89 +/- 1.27; $p=0.000$) than ecstasy fatalities if the whole of the population (16-59 years old; see figure 3) of users was taken into account. Conversely, if only data related to mono-intoxication fatalities were taken into account (see table 6), it appeared that rates of 16-24 years old (see figure 4) ecstasy fatalities per 100,000 16-24 years old users were significantly more represented than 16-24 years old AMP/METH fatalities per 100,000 16-24 years old users (1.67 +/- 0.52 vs 0.8 +/- 0.65; $p=0.0007$). Conversely, 'AMP/METH only' fatalities per

100,000 users were more represented than ecstasy fatalities if all ages were taken into account (2.09 +/- 0.88 vs 1.75 +/- 0.56; p=0.0096; see table 6).

Insert tables 5 and 6 and figures 3 and 4 around here

Discussion

This report has provided an 11-year, UK-wide, analysis of ecstasy/entactogen (MDMA, MDA, MDEA, MBDB, PMA) and amphetamine/methylamphetamine mortality data set. This may constitute the largest collection of amphetamine-type stimulant fatalities so far, offering both detailed notes of the individual clinical/accidental circumstances contributing to death and direct comparison of data referring to ecstasy on one hand and AMP/METH on the other.

It is interesting to note that number of AMP/METH deaths seemed to have dropped in 2000 to peak once again over the few following years and that rates of MDMA-related fatalities after a drop in 2003 increased over the following few years. Although data to offer a straightforward explanation for this year-on-year change are not available from this data-source, it is intriguing that previous observations have suggested similarly increasing rates of other stimulant- (e.g. cocaine/crack cocaine) related deaths in the UK after 2001-2002 [21]. On the other hand, ATS percent deaths did not show here a substantial and consistent increase over the years. Since ATS fatality figures have indeed increased during the index period, one could wonder if this increase in ATS-related deaths may just be reflecting a more generalized increase in all drug-related deaths over the years. However, recent data may suggest a stabilization instead of an increase in UK drug related deaths during the period 1998-2008 [22]. Of course, changes in fatality rates over time may be related to parallel changes in coroner methods/policies/laws/technology, which would in turn affect surveillance.

Typical ATS victims in this study were young, males (thus confirming previous reports) [23] and white. In comparison with amphetamine, ecstasy seemed here to be both more likely to be identified on its own at post mortem and less likely to be associated with concomitant/contributory factors when taken on its own.

Indeed, most AMP/METH and ecstasy victims died of polydrug abuse ingestion. Ecstasy fatal ingestion seemed here to be most typically identified together with cocaine, and both drugs are frequently associated with the recreational scene [24]. This is consistent with the observation made here that, with respect to the AMP/METH victims, the ecstasy ones were more likely to be without a known history of drug addiction. Co-occurrence of two stimulants (i.e.: MDMA together with cocaine) might increase, in a synergic way, both the dopaminergic and serotonergic stimulation, so that the serotonin syndrome is more likely to occur [7]. Ecstasy was here identified on its own at post mortem in about 1 case out of 6; according to the UK General Mortality Registers (GMRs) figures, ecstasy was the sole drug mentioned in the death certificate in 42% of the total number of related fatalities [5]. The reason for the discrepancy between the np-SAD and the GMRs data may be due to the fact that the np-SAD data capture system allows collection of fairly detailed information from Coroners. As a consequence, a more precise description of the index related death is made possible and this may have decreased, in the present np-SAD dataset, the number of cases in which ecstasy was considered to be involved on its own.

Contributory clinical factors here described at post mortem in ATS fatalities were overall consistent with the existing, mainly anecdotal in nature, literature and reflect a number of

issues, including: the sympathomimetic actions of both AMP/METH and ecstasy [25, 26]; the possible idiosyncratic toxic reactions to these compounds [4]; and the accident-prone behaviour of ATS misusers [4, 27, 28]. The sympathomimetic stimulation may be further exacerbated by the environmental condition which is in turn induced by both the repetitive high frequency rhythm of the techno music itself and by the aggregation in close environments/high ambient temperature [26].

Different from ecstasy, AMP/METH drugs were here frequently identified in combination with heroin, methadone, and other opiates/opioid analgesics which are all drugs with high levels of toxicity in overdose and typically associated with the 'hard core' addiction scene [13]. Present data suggested that, within the AMP/METH only fatalities' group, a sizeable proportion of fatalities occurred in a context of physical, and especially cardiovascular, disorders. In amphetamine misusers, deaths are typically associated with acute myocardial necrosis, right ventricle rupture, cardiomyopathy, arrhythmia [29], polytrauma, mechanical asphyxia, and hyperthermia [23]. Conversely, suicide was more likely to be identified here as a cause of death in the ecstasy than in the AMP/METH group. From this point of view, some longitudinal research has been dedicated to the understanding of the association between ecstasy intake and depression [30].

Overall, the present results seem to suggest that proportion of AMP/METH polydrug intoxication fatalities out of all deaths reported to np-SAD were over the years consistently higher than the ecstasy polydrug intoxication ones. This result is likely, however, to be in relation to higher number of consumers of AMP/METH than ecstasy in the UK [12]. In terms of death rates per 100,000 (16-59 years old) users of AMP/METH and ecstasy (2001-2007 only), it appeared that both mono- and poly-drug AMP/METH fatalities were significantly more represented than ecstasy fatalities. However, compared to ecstasy users AMP/METH users were here more likely to be: using opiates/opioids (which are frequently self-administered intravenously and associated with increased inherent risk of lethal accidental overdose); known drug abusers with the related poor living standards; and reporting associated chronic medical co-morbidities. On the other hand, it seems interesting to note that if only the 16-24 years old population was taken into account rates of ecstasy fatalities per 100,000 users were significantly higher than AMP/METH fatalities. This may be partly explained by the fact that the physical co-morbidities linked to both AMP/METH and its related at-risk lifestyle still had to show an impact on the user given the young age/ conceivably relatively short period of use. A further explanation might however be given by the particular susceptibility of youngster to the acute effects of ecstasy [7]. Finally, one could wonder if differences between ecstasy and AMP/METH rates in youngsters may be related to BCS reporting bias. However, although the survey may in fact tend to over-represent older age groups at the expense of younger respondents, BCS may be prone to sampling error only where rare crimes are concerned [31].

The present paper presents with some limitations. In fact, although the np-SAD coverage is excellent (about 90-95%) [22], levels of reporting inconsistency between the different areas have been recorded over time. Furthermore, Coroners' reports do not routinely include either information on levels of drug intake prior to death or post mortem toxicological levels. One could wonder what kind of cases the coronial system would miss. Typically, coroners enquire only into those fatalities reported to them, which include deaths which were sudden, unexpected, violent or unnatural. Indeed, not all deaths are reported to the coroner and in most cases a GP or hospital doctor can issue a medical certificate of the cause of death. From this point of view, one cannot exclude that some people who died due to ATSs, maybe whilst

in hospital for a concurrent medical disease, were not identified by coroners. At present, the np-SAD Programme aims at establishing if all relevant cases are being identified and notified by the coronial system. Finally, the np-SAD has been giving consideration as to how it can further improve both the quality of information collected by coroners, which already include reference to the deceased medical and psychiatric history; comorbid conditions; and history of drug use.

Conclusions

With respect to AMP/METH, ecstasy was here more typically identified in victims who were young, healthy, and less likely to be known as drug users. Although AMP/METH high mortality rates here observed may be explained by users' high levels of physical comorbidity, excess ecstasy-related fatality rates in young users may be a reason of concern.

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Some of the above data have been presented to the Advisory Council on the Misuse of Drugs review of MDMA/ecstasy; London, September 26th, 2008

References

1. UNODC: 2008 World Drug Report. 26 June 2008. Vienna, Austria: United Nations Office on Drugs and Crime, 2008. Available from: http://www.unodc.org/documents/wdr/WDR_2008/WDR_2008_eng_web.pdf (accessed on: November 18th, 2008)
2. Gouzoulis-Mayfrank E, Hermle L, Kovar KA, Sass H: Entactogenic drugs; the widely used recreational drugs 3,4-methylenedioxymethylamphetamine derivatives. A new class of substances among illegal designer drugs? *Nervenarzt* 1996; 67: 369-380.
3. Advisory Council on the Misuse of Drugs (ACMD): Methylamphetamine review, 2005. Available from: <http://drugs.homeoffice.gov.uk/publication-search/acmd/ACMD-meth-report-November-2005?view=Binary> (accessed on: November 18th, 2008)
4. Henry JA, Jeffreys KJ, Dawling S; Toxicity and deaths from 3,4-methylenedioxymethylamphetamine ("ecstasy"). *Lancet* 1992; 340: 384-387.
5. Schifano F, Corkery J, Deluca P, Oyefeso A, Ghodse AH; Ecstasy (MDMA, MDA, MDEA, MBDB) consumption, seizures, related offences, prices, dosage levels and deaths in the UK (1994-2003). *J Psychopharmacol*, 2006; 20: 456-463.
6. Schifano F, Oyefeso A, Corkery J, Cobain K, Jambert-Gray R, Martinotti G, Ghodse AH; Death rates from ecstasy (MDMA, MDA) and polydrug use in England and Wales 1996-2002. *Hum Psychopharmacol Clin Exp* 2003; 18: 519-524.
7. Schifano F; A bitter pill? Overview of ecstasy (MDMA; MDA) related fatalities. *Psychopharmacol (Berlin)* 2004; 173: 242-248.
8. Byard RW, Gilbert J, James R, Lokan RJ; Amphetamine derivative fatalities in South Australia-is "Ecstasy" the culprit? *Am J Forensic Med Pathol* 1998; 9:261-5.

9. Refstad S; Paramethoxyamphetamine (PMA) poisoning; a 'party drug' with lethal effects. *Acta Anaesthesiol Scand* 2003; 47:1298-9.
10. Carmo H, Remião F, Carvalho F, Fernandes E, de Boer D, dos Reys LA, de Lourdes Bastos M; 4-Methylthioamphetamine-induced hyperthermia in mice: influence of serotonergic and catecholaminergic pathways. *Toxicol Appl Pharmacol* 2003; 190: 262-71.
11. Schifano F, Corkery JM, Cuffolo G; Smokable ("ice", "crystal meth") and non smokable amphetamine-type stimulants: clinical pharmacological and epidemiological issues, with special reference to the UK. *Ann Ist Super Sanita* 2007; 43: 110-5.
12. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA); Annual Report 2008. The state of drug problems in Europe. 2008. Luxembourg: Office for Official Publications of the European Communities.
13. Ghodse AH, Corkery J, Oyefeso A, Schifano F; Drug related deaths in the UK. Annual Report 2008. 2008. International Centre for Drug Policy, St George's, University of London (UK).
14. Aust R, Sharp C, Goulden, C; Prevalence of drug use: key findings from the 2001/2002 British Crime Survey. Home Office Findings 182. 2002. London: Home Office Research Development and Statistics Directorate. Available at: <http://www.homeoffice.gov.uk/rds/pdfs2/r182.pdf>
15. Condon J, Smith N; Prevalence of drug use: key findings from the 2002/2003 British Crime Survey. Home Office Findings 229. 2003. London: Home Office Research Development and Statistics Directorate. Available at: <http://www.homeoffice.gov.uk/rds/pdfs2/r229.pdf>
16. Chivite-Matthews N, Richardson A, O'Shea J, Becker J, Owen N, Roe S, Condon J; Drug Misuse Declared: Findings from the 2003/04 British Crime Survey. Home Office Statistical Bulletin 04/05. 2005. London: Home Office Research Development and Statistics Directorate. Available at: <http://www.homeoffice.gov.uk/rds/pdfs05/hosb0405.pdf>
17. Hoare J, Flatley J; Drug Misuse Declared: Findings from the 2007/08 British Crime Survey: England and Wales. December 2007. Home Office Statistical Bulletin 13/08. London: Home Office Research Development and Statistics Directorate. Available at: <http://www.homeoffice.gov.uk/rds/pdfs08/hosb1308.pdf>
18. Murphy R, Roe S; Drug Misuse Declared: Findings from the 2006/07 British Crime Survey: England and Wales. Home Office Statistical Bulletin 18/07. December 2007. London: Home Office Research Development and Statistics Directorate. Available at: <http://www.homeoffice.gov.uk/rds/pdfs07/hosb1807.pdf>
19. Roe S; Drug Misuse Declared: Findings from the 2004/5 British Crime Survey. Home Office Statistical Bulletin 16/05. 2005. London: Home Office Research Development and

Statistics Directorate. Available at:

<http://www.homeoffice.gov.uk/rds/pdfs05/hosb1605.pdf>

20. Roe S, Man L; Drug Misuse Declared: Findings from the 2005/06 British Crime Survey England and Wales. Home Office Statistical Bulletin 15/06. 2006. London: Home Office Research Development and Statistics Directorate. Available at: <http://www.homeoffice.gov.uk/rds/pdfs06/hosb1506.pdf>
21. Schifano F, Corkery J; Cocaine/crack cocaine consumption, treatment demand, seizures, related offences, prices, average purity levels and deaths in the UK (1990-2004). *J Psychopharmacol* 2008; 22:71-79.
22. Ghodse AH, Corkery J, Oyefeso A, Schifano F, Ahmed K, Naidoo V; Drug related deaths in the UK. Annual Report 2009. August 2009. International Centre for Drug Policy, St George's, University of London (UK).
23. De Letter EA, Piette MH, Lambert WE, Cordonnier JA; Amphetamines as potential inducers of fatalities: a review in the district of Ghent from 1976-2004. *Med Sci Law* 2006; 46:37-65.
24. Winstock A, Schifano F; Disorders relating to the use of ecstasy, other 'party drugs' and khat; in: Gelder M, Andreasen N, Lopez-Ibor JJ, Geddes J (eds): *New Oxford Textbook of Psychiatry*. Oxford, Oxford University Press, 2009
25. Green AR, Marsden CA, Fone KCF; MDMA as a clinical tool: a note of caution. A response to Sessa and Nutt. *J Psychopharmacol* 2008; 22: 929-31.
26. Parrott AC; Human psychopharmacology of Ecstasy (MDMA): a review of 15 years of empirical research. *Hum Psychopharmacol Clin Exp* 2001; 16: 557-577.
27. Oyefeso A, Schifano F, Ghodse H, Cobain K, Dryden R, Corkery J; Fatal injuries while under the influence of psychoactive drugs: a cross-sectional exploratory study in England. *BMC Public Health* 2006; 6: 148.
28. Webb L, Oyefeso A, Schifano F, Cheeta S, Pollard M, Ghodse AH; Cause and manner of death in drug-related fatality: An analysis of drug-related deaths recorded by Coroners in England & Wales in 2000. *Drug Alcohol Depend* 2003; 72: 67-74.
29. Jacobs W; Fatal amphetamine-associated cardiotoxicity and its medicolegal implications. *Am J Forensic Med Pathol* 2006; 27: 156-60.
30. Falck RS, Wang J, Carlson RG; Depressive symptomatology in young adults with a history of MDMA use: a longitudinal analysis. *J Psychopharmacol* 2008; 22:47-54.
31. National Digital Archive of Datasets. Series details: CRDA/2; British Crime Survey. Available from: <http://www.ndad.nationalarchives.gov.uk/CRDA/2/detail.html>
32. Hendrickson H, Laurenzana E, Owens SM; Quantitative Determination of total methylamphetamine and active metabolites in rat tissue by liquid chromatography with tandem mass spectrometric detection. *AAPS Journal* 2006; 8: E709-E717.

Table 1: Overview of amphetamine/methylamphetamine - and ecstasy-associated fatalities as reported to the National Programme on Substance Abuse Deaths - np-SAD (UK: 1997-2007)

	Amphetamine/methylamphetamine (*)	Ecstasy (**)	PR/significance levels	95% CI
No of reported deaths (1997-2007)	832	605		
Male gender	80.2%	85.0%	1.1	1.0-1.1
Less than 34 years at death	60.9%	79.5%	1.6	1.5-1.8
Age at death (years) mean median Semi-interquartile range	32.7 31.9 6.7	28.3 27.0 5.5	Mann-Whitney U test= 179664, p <.0001 (2-tailed)	
Died in hospital	31.3%	39.2%	1.2	1.1-1.4
Known drug addiction	91.7%	82.1%	1.9	1.5-2.6
Cause of death; accidental	71.9%	72.2%	1.0	0.9-1.1
Cause of death; suicide	3.1%	4.1%	1.3	0.8-2.3
Index drug on its own	12.7% (106/832 deaths where amphetamine was identified on its own)	17.2% (104/605 deaths where ecstasy was identified on its own)	Fisher's exact test; two-tailed P value= 0.0192	
Other drugs implicated; alcohol	20.4%	31.6%	1.5	1.3-1.8
Other drugs implicated; cocaine	12.6%	22.3%	1.8	1.4-2.2
Other drugs implicated; heroin/morphine	39.3%	25.3%	1.6	1.3-1.8
Other drugs implicated; methadone	17.4%	9.3%	1.9	1.4-2.5
Other drugs implicated; other opiates/ opioid analgesics	13.7%	9.9%	1.4	1.0-1.9

(*): METH was identified in 14 cases only; in all of these cases, the post mortem toxicological examination identified the presence of amphetamine as well. Since AMP is one of the metabolites of METH [32], it is not possible to conclude from here if the 14 METH deaths were actually a mono-drug intoxication or just an AMP/METH combined intoxication.

(**): There were 98 cases where both ecstasy-type drugs and amphetamines were implicated in death.

Table 2: Overview of amphetamine/methylamphetamine- and ecstasy-associated mono-intoxication* acute poisoning fatalities as reported to the National Programme on Substance Abuse Deaths - np-SAD (UK: 1997-2007)

	Amphetamine/methylamphetamine (*) 106 cases	Ecstasy (*) 104 cases	PR/significance levels	95% CI
Male gender	68.9%	78.8%	1.1	1.0-1.3
Less than 34 years at death	55.7%	85.6%	1.6	1.3-1.9
Age at death (years) mean median Semi-interquartile range	34.2 32.0 8.3	25.9 23.9 4.5	Mann-Whitney U test= 2939, p <.0001 (2-tailed)	
Died in hospital	44.3%	62.5%	1.4	1.1-1.8
Known drug addiction	87.8%	65.4%	2.8	1.5-5.5
Cause of death; accidental	70.8%	84.6%	1.2	1.0-1.4
Cause of death; suicide	3.8%	5.8%	1.5	0.4-5.3

(*): Sole drug found at post mortem or sole drug implicated and no other substance found at post mortem.

Table 3: Presence of contributory factors associated with either amphetamine or MDMA/ecstasy mono-intoxication acute poisoning – np-SAD (UK: 1997-2007)

Amphetamine/methylamphetamine (106 mono-intoxication fatalities)	Ecstasy (104 mono-intoxication fatalities)	Chi-square values
<ul style="list-style-type: none"> • 18 cases: pre-existing cardiovascular /cardiopulmonary issues (e.g.: myocardial fibrosis; ischaemic heart disease; rupture of a berry aneurysm; cardiomyopathy; systemic hypertension; right ventricular dysplasia; emphysema; obstructive pulmonary disease; chronic pulmonary embolus etc) • 8 cases: events possibly related to bizarre/at-risk behaviours whilst on amphetamine (e.g.: hypothermia/immersion in water; drowning; multiple injuries; hanging) • 3 cases: associated infections (e.g.: septicaemia; bronchopneumonia; acute meningitis) • 3 cases: pre-existing chronic medical conditions (e.g. diabetes; liver cirrhosis) <p><i>In the remaining 74 (69.8%) cases, only amphetamines and its well-known medical consequences (cerebral haemorrhage; multiple organ failure; acute hypertensive crisis etc) were mentioned as the cause of death</i></p>	<ul style="list-style-type: none"> • 8 cases: pre-existing cardiovascular issues (e.g.: cardiomegaly, coronary artery atherosclerosis; left ventricular hypertrophy, aortic valve incompetence; aortic aneurysm; dissection of aorta/Marfan's syndrome) • 3 cases: events possibly related to bizarre/at-risk behaviours whilst on ecstasy (e.g.: shock and haemorrhage due to transection of radial arteries; drowning; head/multiple injuries; physical exertion etc) • 1 cases: associated infections (e.g.: glandular fever-Epstein Barr virus) • 1 case: possible epilepsy • 1 case fulminant hepatic failure <p><i>In the remaining 90 (86.5%) cases, only ecstasy with its well-known acute medical consequences (cerebral oedema; hyperpyrexia; DIC/multiple organ failure) were mentioned as the cause of death</i></p>	<p>Total number of fatalities=210; 46 showed presence of contributory factors (e.g. 32 in the amphetamine and 14 in the MDMA/ecstasy group) Fisher's exact test; two-tailed p=0.0043</p>

Table 4: Percentage of amphetamine and ecstasy deaths to all drug deaths, np-SAD data 1997-2007

Year	Amphetamine/methamphetamine polydrug intoxication	Amphetamine/methamphetamine only	Ecstasy polydrug intoxication	Ecstasy only
1997	5.50	0.95	1.14	0.19
1998	6.23	0.87	1.23	0.29
1999	5.48	0.65	2.22	0.26
2000	3.02	0.26	3.08	0.46
2001	3.59	0.51	4.32	0.79
2002	4.47	0.28	3.80	0.55
2003	5.19	0.60	3.46	0.30
2004	3.49	0.44	3.54	0.98
2005	4.30	0.96	3.54	0.71
2006	4.68	0.58	3.90	0.73
2007	5.00	0.58	3.61	0.48
Average 1997-2007	4.53	0.58	3.29	0.57

All cases on np-SAD database

Table 5: Rates of deaths per 100,000 users for amphetamine and ecstasy, including multiple drug use (England and Wales; 2001-2007) (#)

Year	Amphetamine/methamphetamine; young people (16-24) *	Ecstasy; young people (16-24) *	Amphetamine/methamphetamine; all persons (16-59)	Ecstasy; All persons (16-59)
2001	6.03	8.07	12.80	10.44
2002	5.56	6.09	16.46	10.60
2003	7.63	6.01	16.98	9.12
2004	8.37	7.14	16.05	10.61
2005	6.34	5.58	18.31	12.75
2006	7.73	5.88	19.95	10.93
2007	6.49	7.14	27.96	12.55
Average 2001-7	6.85	6.62	17.87	10.89
Standard Deviation	1.04	0.91	4.77	1.27
t-test		t-value of difference: 1.793; df- t: 202 double- sided p- value: 0.0748		t-value of difference: 32.824; df-t: 642 double- sided p- value: 0

*: only 16-24 years old cases were here taken into account

#: Sources:

Death rates: np-SAD datafile – England & Wales cases only

Users' rates:

2001/2 – Findings 182

2002/3 – Findings 229

2003/4 – Statistical Bulletin 04/05

2004/5 – Statistical Bulletin 16/05

2005/6 – Statistical Bulletin 15/06

2006/7 – Statistical Bulletin 18/07

2007/8 – Statistical Bulletin 13/08

Table 6: Rates of deaths per 100,000 users for amphetamine and ecstasy, sole drug use (England and Wales; 2001-2007)

Year	Amphetamines Young people (16-24) *	Ecstasy Young people (16-24) *	Amphetamines All persons (16-59)	Ecstasy All persons (16-59)
2001	0.35	2.60	1.83	1.76
2002	0.46	1.28	1.03	1.47
2003	1.27	0.95	2.07	0.81
2004	0.99	1.70	1.86	2.16
2005	0.98	1.49	3.76	2.59
2006	0.00	1.84	1.66	1.94
2007	1.95	1.59	2.74	1.70
Average 2001-7	0.80	1.67	2.09	1.75
Standard Deviation	0.65	0.52	0.88	0.56
t-test		t-value of difference: - 4.199; df-t: 16 double-sided p- value: 0.0007		t-value of difference: 2.641; df-t: 105 double-sided p-value: 0.0096

*: only 16-24 years old cases were here taken into account

#: Sources:

Death rates: np-SAD datafile – England & Wales cases only

Users' rates:

2001/2 – Findings 182

2002/3 – Findings 229

2003/4 – Statistical Bulletin 04/05

2004/5 – Statistical Bulletin 16/05

2005/6 – Statistical Bulletin 15/06

2006/7 – Statistical Bulletin 18/07

2007/8 – Statistical Bulletin 13/08

Figure 1: Number of amphetamine/methylamphetamine and MDMA/ecstasy deaths reported to np-SAD, 1997-2007

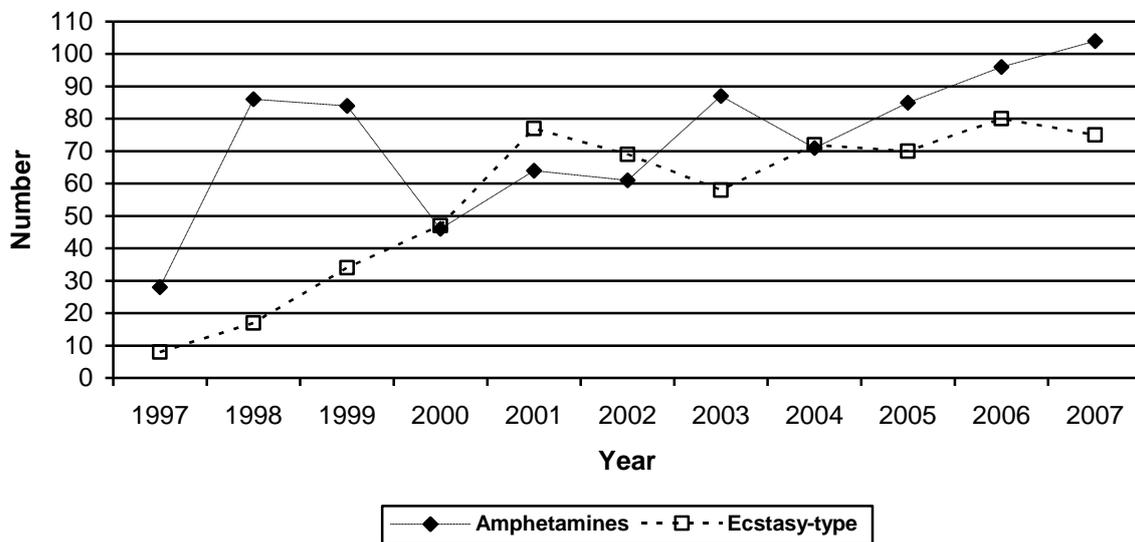
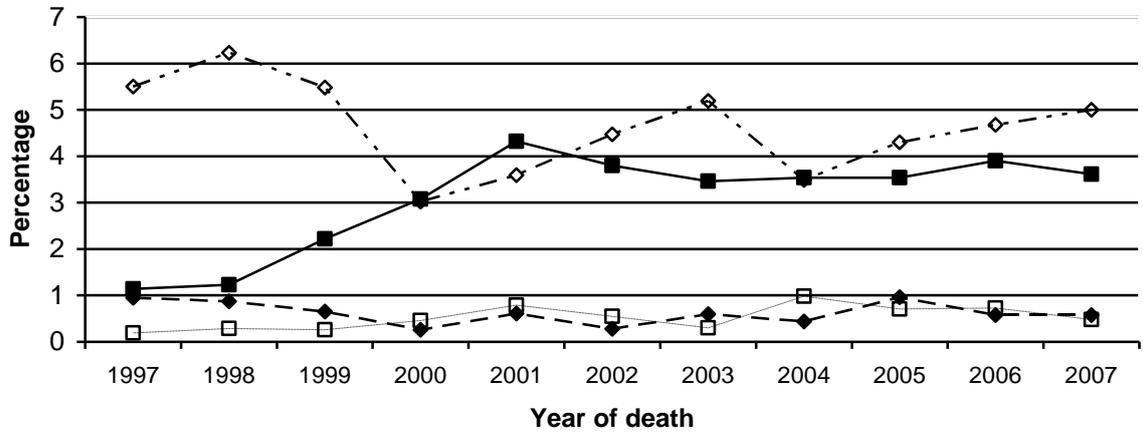


Figure 2: Percentage of amphetamine and ecstasy deaths to all deaths, np-SAD 1997-2007



—◇— Amphetamine polydrug —◆— Amphetamine —■— Ecstasy polydrug —□— Ecstasy

Figure 3: Rate of deaths per 100,000 users aged 16-59, England & Wales (np-SAD and BCS data), 2001-7

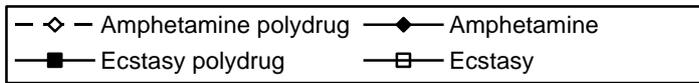
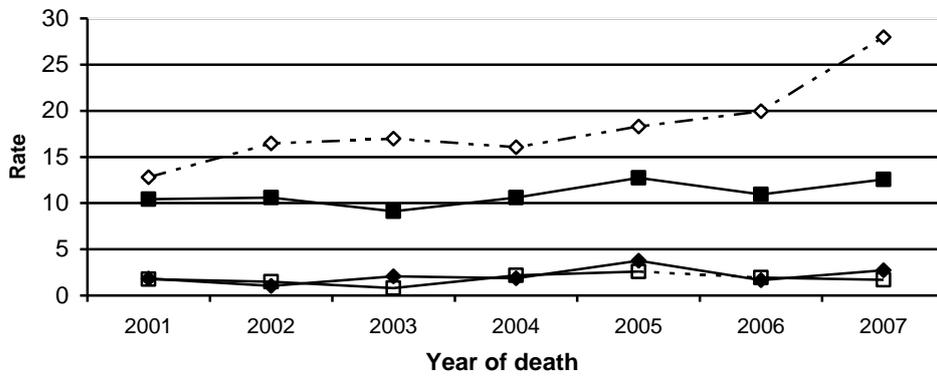


Figure 4: Rate of deaths per 100,000 users aged 16-24, England & Wales (np-SAD and BCS data), 2001-7

