

Oxycodone Involvement in Drug Abuse Deaths: A DAWN-Based Classification Scheme Applied to an Oxycodone Postmortem Database Containing Over 1000 Cases*

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Abstract

An oxycodone postmortem database was created from 1243 solicited cases from Medical Examiner and Coroner (ME/C) offices in 23 states in the United States over the period from August 27, 1999, through January 17, 2002. The request for cases was specific to only those cases in which the ME/C opined that the death involved oxycodone. Each case was evaluated to determine the role of oxycodone and the specific drug product OxyContin[®] tablets in the death. Oxycodone identification was based on toxicology testing, and OxyContin identification was based on evidence found at the scene, credible witness reports, or identification of tablets in gastrointestinal contents. A system of case categorization was developed for this study based on the Drug Abuse Warning Network (DAWN) system for reporting drug abuse mortality data in the United States, using the same standardized, well-understood terminology. Of the 1243 cases, 79 cases were incomplete and could not be evaluated. There were an additional 150 cases submitted in which oxycodone was not identified by the originating ME/C. Of the remaining 1014 cases, 919 (90.6%) were related to drug abuse, whereas 95 (9.4%) cases were categorized as not involving drug abuse. Only 30 (3.3%) of the drug abuse cases involved oxycodone as the single reported chemical entity; of these, 12 cases had OxyContin identified as a source of oxycodone. Of the 919 drug abuse cases, the vast majority ($N = 889$, 96.7%) were multiple drug abuse deaths in which there was at least one

other plausible contributory drug in addition to oxycodone. The most prevalent drug combinations were oxycodone in combination with benzodiazepines, alcohol, cocaine, other narcotics, marijuana, or antidepressants. Using the DAWN definitions, drug abuse cases were further categorized as drug-induced or drug-related. A total of 851 (92.6%) cases met the criteria for classification as being drug-induced, and the remaining 68 (7.4%) cases were categorized as drug-related. Cause of death (COD) statements from the originating ME/C indicated a general recognition of the role of abuse of multiple drugs in causing fatalities. Approximately 70% of the 889 cases in the multiple-drug-induced categories were listed in the COD or contributing COD statements as multiple-drug deaths. A variety of terms were employed in the COD statements to indicate multiple drug involvement such as "polydrug toxicity", "polypharmacy", "multiple drug poisoning", and "polypharmaceutical overdose". The system for death classification employed in this study recognizes the problems inherent in COD attribution when multiple drugs are involved. Use of this new system for reporting mortality data in future studies involving opioids is recommended.

Introduction

Narcotic analgesics and narcotic analgesic combinations were among the most frequently mentioned central nervous system (CNS) agents in medication-related emergency department visits (ED) in the 2001 Drug Abuse Warning Network (DAWN) report (1). From 1998 to 2000, the period during which most of the deaths included in this study occurred, hydrocodone ED mentions increased by 48%, oxycodone increased by 108%,

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and methadone increased by 63% (1). Abuse of oxycodone, which is available in immediate-release combination products (Percocet®, Tylox®, etc.), immediate-release single-entity prod-

ucts (Roxicodone®, OxyIR®, OxyFast®, etc.), and controlled-release formulations (OxyContin tablets), has been reported by the media, particularly in the eastern United States. OxyContin became available following its approval by the Food and Drug Administration on December 12, 1995. Although OxyContin tablets are safe and effective when taken intact and as recommended by the manufacturer for the treatment of moderate to severe, ongoing pain, abusers have discovered that crushing the tablets defeats the controlled-release mechanism and makes much of the oxycodone immediately available, which can then be ingested or administered by intranasal or intravenous routes, sometimes with fatal outcome.

Although opioid overdose is a known risk to drug abusers, there appears to be under-appreciation of the added risks of concomitant use or abuse of other central nervous system depressant drugs. When combined with opioids, self-administration of other depressant drugs can substantially increase the likelihood of a fatal outcome (2). Numerous studies have documented multiple drug use in fatal heroin overdose cases (3–15). Polydrug abuse is also apparent in overdose cases involving oxycodone (16).

Unfortunately, the reporting of opioid-related deaths has not been systemized. Medical Examiners and Coroners (ME/C) fre-

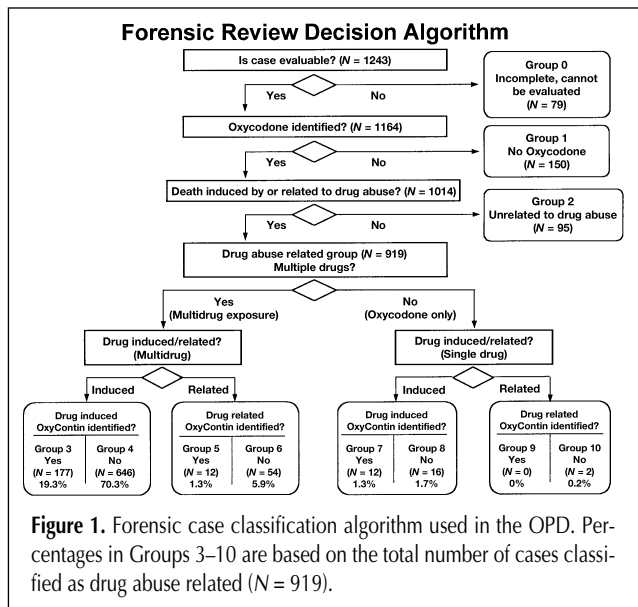


Figure 1. Forensic case classification algorithm used in the OPD. Percentages in Groups 3–10 are based on the total number of cases classified as drug abuse related (N = 919).

Table I. Questions for Categorization of Mortality Cases

Question #	Question	Response	Comment
1	Was oxycodone present?	Yes or No	Yes—If oxycodone is specifically reported as detectable or present in any biological specimen. No—If oxycodone is not detected, evaluation is complete. If there is no toxicology report, continue evaluation.
2	Was OxyContin identified?	Yes or No	Yes—If OxyContin is specifically mentioned anywhere in the case report form (i.e., scene investigation, identified in stomach contents, etc). No—If OxyContin is not mentioned.
3	Can the case be evaluated?	Yes or No	Yes—If there is a minimum of a partial autopsy report or a statement of COD, and specific toxicology findings. No—If there are no specific toxicology findings, or if there is no autopsy report or a statement of COD.
4	Was the death associated with drug abuse?	Yes or No	Yes—If there is any indication of drug abuse in the originating ME/C COD or contributing COD statement, a history of drug abuse, evidence at the scene, physical examination evidence (track marks, nasal septal perforation, etc.), or positive toxicology results for an illicit drug of abuse or ethanol > 0.02 g/dL. No—If there is no evidence of drug abuse or if the death is rated as a homicide by the ME/C.
5	Were other contributory drugs present?	Yes or No	Yes—If contributory drugs were identified in any body specimen. Contributory drugs include: ethanol > 0.02 g/dL, illicit drugs or metabolites, other CNS actives. No—If there is no evidence of contributory drugs based on toxicology testing of body specimens. Drugs not considered contributory included: acetaminophen, alcohol ≤ 0.02 g/dL, antibiotics, oral contraceptives, caffeine, local anesthetics, nicotine, and salicylates.
6	Was the death drug-induced or drug-related?	Induced or Related	Induced—If death was directly caused by the drug (or drugs) based on the ME/C COD or contributing COD including suicide by overdose. Related—If drug was a contributing factor, but not the immediate or sole cause.

quently rely on toxicology analysis with a focus on drug concentration in the biological fluids as a key determinant of the cause of death. Such practices ignore the contribution of other drugs present at lower concentrations, pharmacological issues such as toxic drug-drug interactions, antemortem development of tolerance to the respiratory depression effects of opioids, and postmortem drug redistribution.

Darke and Zador (2) have proposed a "polydrug use" theory that takes into account the depressant effect of other drugs when used or abused in combination with heroin. Consistent with this approach, the DAWN system for classification of drug-abuse deaths does not attribute cause of death (COD) to a single drug entity when multiple drugs that could contribute to death are identified in toxicological analysis (17). The difficulty of assigning COD to a single drug entity when multiple drugs are present is well understood by many ME/Cs and forensic toxicologists (18). Fatalities involving only a single opioid represent a minority of overdose cases. The presence of other drugs (primarily CNS depressants) is commonly encountered in toxicological analysis accompanying autopsy proceedings (2). Fatalities attributed to overdose are likely to have opioid concentrations no higher than those found in regular opioid abusers, abusers who died from other causes (2), or patients who have been compliant with therapy and died from other causes. Concomitant co-administration of other depressant drugs, however, is common practice among opioid abusers. This practice substantially increases the likelihood of a fatal outcome because of potentiation of the respiratory depressant effects of opioids.

The objective of this study was to classify mortality reports in a large oxycodone postmortem database (OPD), recently collected from 23 states, by means of standardized terminology used in the DAWN reporting system. This method of classification differentiates cases into categories involving drug-abuse and non-drug-abuse cases, differentiates single-drug deaths from multiple-drug deaths, differentiates drug-induced deaths from drug-related deaths, and differentiates abuse of a specific drug product, OxyContin (oxycodone hydrochloride controlled-release) tablets (Purdue Pharma L.P., Stamford, CT), from other oxycodone products.

Methods

OPD

In response to a written request from Purdue Pharma L.P. (Purdue), a total of 1419 mortality reports in which oxycodone or OxyContin was considered in the opinion of the originating ME/C to have played a role in the death of the individual were received. Requests were mailed to selected jurisdictions based on news media or other reports (e.g., Purdue's adverse events reporting system) of oxycodone or OxyContin overdose deaths. The 1419 cases had dates of death from August 27, 1999, to January 17, 2002. Requests were made for autopsy reports and toxicology test results for each case. Some jurisdictions did not respond and some responded partially. Materials were received from a total of 279 ME/C offices in 23 states. The re-

sponding states and corresponding number of cases were as follows: AL, 42; AZ, 1; CA, 28; CT, 29; FL, 351; GA, 142; HI, 23; IL, 1; IN, 1; KY, 87; LA, 41; ME, 12; MD, 43; MI, 4; NC, 1; OH, 326; OK, 1; PA, 121; SC, 1; TN, 57; VA, 102; WI, 1; and WV, 4. A board-certified forensic pathologist and a board-certified forensic toxicologist reviewed each case file independently. Information on each case was summarized on a Postmortem Case Evaluation Form. The completed form contained information on subject demographics, originating ME/C COD, contributing COD, manner of death (MOD), information from police and ME/C investigations, medical and psychiatric history, drug abuse history, ME/C rationale for COD, source of drugs, signs and symptoms from administration of the drug(s) to death, and toxicology findings.

Each of the 1243 cases making up the OPD was categorized into a group according to the algorithm shown in Figure 1. Following the extraction of case data by the forensic toxicologist and pathologist, two more reviewers performed independent assessments of each case based on responses to the six questions described in Table I. Concordance between these independent reviews was 93.5%. Following completion of their independent assessments, the two final reviewers resolved these few discordant results.

Information received on 176 of the 1419 reports of death was insufficient (lack of autopsy and/or toxicology results) to permit any evaluation. The remaining 1243 cases were entered into the OPD (Purdue Pharma L.P.).

Terminology for categorizing mortality data involving oxycodone drug abuse deaths

The system for categorizing mortality data involving oxycodone drug abuse deaths was developed based on terminology utilized by the DAWN system (17). The following specific terms were abstracted from the DAWN 2001 report:

- Drug abuse: "The nonmedical use of a substance for any of the following reasons: psychic effect, dependence, or suicide attempt/gesture."
- Drug-induced death: "A death directly resulting from drug abuse or other substance abuse, such as drug overdoses or the interactive effects of drug combinations."
- Drug-related death: "A death in which the abuse of the drug is a contributing factor, but is not the sole cause of death. Such cases include drug abuse that exacerbates a pre-existing physiological condition; drug abuse in combination with an external physical event (e.g., a fall or automobile accident); or a medical disorder that was itself caused by drug abuse (e.g., hepatitis contracted through injection drug abuse)."
- Single-drug death: "A single-drug death is that in which only one drug was involved."

Additional terminology employed in the model, but not specifically defined by DAWN, was as follows:

- Multiple-drug death: A death in which oxycodone or OxyContin was identified in combination with other plausible contributory drugs (e.g., ethanol > 0.02 g/dL, benzodiazepines, opioids, etc.). Drugs not considered contributory included: nicotine, ethanol ≤ 0.02 g/dL, caffeine, antibiotics, and oral contraceptives. Salicylates and acetaminophen were also not considered contributory for purposes of classification so that in-

dividuals who only abused a combination oxycodone product (e.g., Percocet) would not be classified as a multiple-drug death.

System for categorization

Autopsy reports and toxicology results were categorized by use of standardized questions (Table I). Terminology consistent with the DAWN 2001 report was utilized in all cases. The questionnaire facilitated determination of the following aspects of each case: whether it involved oxycodone or OxyContin; whether it was sufficiently complete for evaluation; whether death was associated with drug abuse and, if so, whether the death was drug-induced or drug-related; and whether contributory drugs in addition to oxycodone or OxyContin were present. Drug identification was based on toxicological analysis at a concentration greater than or equal to the limit of detection (LOD) by a specific chromatographic assay. Nearly all assays involved drug identification by gas chromatography–mass spectrometry. Immunoassay results were not considered sufficiently specific for inclusion. Identification of the specific drug product OxyContin was based on either evidence obtained at the scene; a credible witness; identification of OxyContin tablets; or the presence of OxyContin “ghost tablets” (tablet matrix after active ingredients have dissolved) in the gastrointestinal tract. Cases were evaluated if they contained at a minimum: a partial autopsy report or a statement of COD, plus specific toxicological findings. Determination that the death was associated with drug abuse was based on any of the following: the COD or contributing COD statements mentioned drug abuse, a history of

drug abuse was cited in the autopsy report or the investigator's report, there was evidence of drug abuse at the scene, physical examination of the body revealed evidence of drug abuse (e.g., track marks, etc.), or toxicology results from any body specimen were positive for an illicit drug or ethanol > 0.02 g/dL. The presence of contributory drugs was based on confirmed toxicology results of any drug(s) that might potentially contribute to the depressant effects of opioids.

Eleven groups were created based on responses to the six questions that allowed disaggregation of mortality cases into specific groups as follows: Group 0, incomplete, cannot be evaluated; Group 1, no oxycodone reported; Group 2, death unrelated to drug abuse; Group 3, multiple drug-induced death involving OxyContin; Group 4, multiple drug-induced death involving oxycodone with no evidence of OxyContin; Group 5, multiple drug-related death involving OxyContin; Group 6, multiple drug-related death involving oxycodone with no evidence of OxyContin; Group 7, OxyContin drug-induced death; Group 8, oxycodone drug-induced death (OxyContin not identified); Group 9, OxyContin drug-related death; and Group 10, oxycodone drug-related death (OxyContin not identified). Characteristics of each category are listed in Table II. The algorithm for categorization of death cases is illustrated in Figure 1.

Statistics

Statistical analyses were conducted to compare various combinations of groups. Group differences of categorical variables (e.g., gender, race, COD, MOD) were assessed using Fisher's Exact test. Because of the large differences in group sizes, continuous variables (e.g., age and weight) were assessed using the non-parametric Wilcoxon Rank-Sum test.

Results

Categorization and general demographics of the OPD

Of the entire dataset in the OPD, 823 (66.2%) were male, 408 (32.8%) were female, and 12 (1.0%) had no gender specified on the available materials from the ME/C. Of the 1183 cases with age specified, the average age (years \pm SD), median, and range were 40.3 \pm 11.8, 41.0, 1–92, respectively. The average weight (kg \pm SD), median, and range were 86.2 \pm 24.7, 84.4, and 10.7–204.1, respectively ($N = 1006$). The ethnic distribution was as follows: white, 1082 (87.0%); black, 51 (4.1%); Hispanic, 5 (0.4%); Asian (non-Japanese), 3 (0.2%); Japanese, 2 (0.2%); Native American, 1 (0.1%); and Unknown, 99 (8.0%). COD and contributing COD statements were categorized as follows: Drug involvement [specific reference in COD statement to drug abuse or drug(s) as a contributing factor], 993 (79.9%); External trauma, 62 (5.0%); Disease, 107 (8.6%); and Unknown, 81 (6.5%). MOD statements were categorized as follows: Suicide, 196 (15.8%); Natural, 108 (8.7%); Accident, 628 (50.5%); Homicide, 4 (0.3%); Undetermined, 305 (24.5%); and Other, 2 (0.2%).

Cases not evaluated (Group 0)

Of the 1243 cases entered in the OPD, 79 (6.4%) failed to meet minimum criteria and were classified as Group 0 (incomplete,

Table II. Categorization of Case Reports in the Oxycodone Postmortem Database

Group	Description
0	Incomplete; case lacked autopsy report or COD statement, or lacked specific toxicology results
1	No oxycodone identified by toxicology tests specific for oxycodone
2	Death was unrelated to drug abuse, e.g., cancer death
3	OxyContin was identified by evidence at the scene, credible witness, or by analysis of stomach contents; other contributory drugs were identified by toxicology tests; death was drug-induced
4	Oxycodone was identified by toxicology tests; no evidence of OxyContin; death was drug-induced
5	OxyContin was identified; other contributory drugs were identified by toxicology tests; death was drug-related
6	Oxycodone was identified by toxicology tests; no evidence of OxyContin; other contributory drugs were identified by toxicology tests; death was drug-related
7	OxyContin was identified; no other contributory drugs were identified by toxicology tests; death was drug-induced
8	Oxycodone was identified by toxicology tests; no evidence of OxyContin; no other contributory drugs were identified by toxicology tests; death was drug-induced
9	OxyContin was identified; no other contributory drugs were identified by toxicology tests; death was drug-related
10	Oxycodone was identified by toxicology tests; no evidence of OxyContin; no other contributory drugs were identified by toxicology tests; death was drug-related

cannot be evaluated). Seventy reports did not contain an autopsy report or a COD statement, and 14 reports did not contain toxicology results (some reports did not contain either; therefore, the total deficiencies do not equal 79). The 79 cases were reviewed, based on available information, to determine if oxycodone or OxyContin were mentioned in the autopsy report or detected by toxicological analysis. There were 75 mentions of oxycodone and 4 mentions of OxyContin in this group.

Cases not involving oxycodone (Group 1)

Despite the nature of the request to ME/Cs to forward only those cases in which oxycodone or OxyContin were involved,

there were 150 cases in the OPD classified as Group 1 (not involving oxycodone or OxyContin). The COD or contributing COD from the originating ME/Cs for this group indicated drug involvement in 117 cases, external trauma in 19 cases, disease in 5 cases, and unknown causes in 9 cases. There was one mention of oxycodone and no mentions of OxyContin. Review of toxicology results for the single case in which oxycodone was mentioned as a contributing COD indicated that oxycodone was below the quantitation limit for the reporting laboratory. The MOD distribution and percent for this group were as follows: Suicide, 31 (20.7%); Natural, 5 (3%); Accident, 64 (42.7%); Homicide, 3 (2%); Undetermined, 45 (30%); and Other, 2 (1.3%).

Table III. Demographics, Cause of Death (COD), and Manner of Death (MOD) for Deaths Involving Drug Abuse (Drug-Induced or Drug-Related, Groups 3–10) Compared to Those Unrelated to Drug Abuse (Group 2)

	Drug-Abuse Deaths (Groups 3–10) (% Group)	Non-Drug-Abuse Deaths (Group 2) (% Group)	Group Comparisons Statistics
N	919 (100)	95 (100)	
Gender			
Female	300 (32.6)	38 (40.0)	NS*,†
Male	617 (67.1)	57 (60.0)	
Unknown	2 (0.2)	0 (0)	
Mean age (SD), years	39.7 (10.6)‡	47.7 (17.0)‡	< 0.0001§
Median age, years	40.0‡	47.0‡	
Age range, years	9–88	1–85	
Mean weight (SD), kg	85.7#	89.2#	NS§
Median weight, kg	84.4#	85.1#	
Weight range, kg	30.4–183.7	10.7–204.1	
Ethnicity			
White	853 (92.8)	82 (86.3)	0.0409†,**
Black	30 (3.3)	10 (10.5)	
Hispanic	2 (0.2)	2 (2.1)	
Asian (non-Japanese)	2 (0.2)	0 (0)	
Japanese	2 (0.2)	0 (0)	
Native American	1 (0.1)	0 (0)	
Not known	29 (3.2)	1 (1.1)	
COD/Contributing COD			
Drug involvement	855 (93.0)	2 (2.1)	N/A††
External trauma	12 (1.3)	31 (32.6)	
Disease	43 (4.7)	59 (62.1)	
Unknown	9 (1.0)	3 (3.2)	
MOD			
Suicide	141 (15.3)	20 (21.1)	NS†
Natural	52 (5.7)	51 (53.7)	< 0.0001†
Accident	538 (58.5)	15 (15.8)	< 0.0001†
Homicide	0 (0)	1 (1.1)	
Undetermined	188 (20.5)	8 (8.4)	< 0.0014†

* NS = nonsignificant.

† Fisher's Exact Test.

‡ Mean and median ages were based on an N = 903 cases for Groups 3–10 and an N = 93 for Group 2.

§ Wilcoxon Z Score (normal approximation).

Mean and median weights were based on an N = 793 cases for Groups 3–10 and an N = 88 for Group 2.

** Compares white versus all other groups.

†† N/A = not applicable; no statistical test was conducted as drug involvement was inherent in defining groups.

Table IV. Demographics, Cause of Death (COD), and Manner of Death (MOD) for the Multiple Drug Abuse Group (Groups 3–6) Compared to the Oxycodone/OxyContin Only Groups (Groups 7–10)

	Multiple Drug Abuse Deaths (Groups 3–6) (% Group)	Oxycodone/OxyContin-Only Deaths (Groups 7–10) (% Group)	Group Comparisons Statistics
N	889 (100)	30 (100)	
Gender			
Female	290 (32.6)	10 (33.3)	NS*,†
Male	597 (67.2)	20 (66.7)	
Unknown	2 (0.2)	0 (0)	
Mean age (SD), years	39.7 (10.6)‡	39.1 (11.6)‡	NS§
Median age, years	40.0‡	41.0‡	
Age range, years	9–88	15–58	
Mean weight (SD), kg	85.5 (23.0)#	92.4 (23.2)#	NS§
Median weight, kg	84.4#	90.0#	
Weight range, kg	30.4–183.7	62.1–136.1	
Ethnicity			
White	826 (92.9)	27 (90.0)	NS†,**
Black	28 (3.1)	2 (6.7)	
Hispanic	2 (0.2)	0 (0)	
Asian (non-Japanese)	2 (0.2)	0 (0)	
Japanese	2 (0.2)	0 (0)	
Native Indian	1 (0.1)	0 (0)	
Not known	28 (3.1)	1 (3.2)	
COD/Contributing COD			
Drug involvement	826 (92.9)	29 (96.7)	NS†
External trauma	12 (1.3)	0 (0)	
Disease	42 (4.7)	1 (3.3)	
Unknown	9 (1.0)	0 (0)	
MOD			
Suicide	134 (15.1)	7 (23.3)	NS†
Natural	51 (5.7)	1 (3.3)	
Accident	522 (58.7)	16 (53.3)	NS†
Undetermined	182 (20.5)	6 (20.0)	NS†

* NS = nonsignificant.

† Fisher's Exact Test.

‡ Mean and median ages were based on an N = 874 for Groups 3–6 and an N = 29 cases for Groups 7–10.

§ Wilcoxon Z Score (normal approximation).

Mean and median weights were based on an N = 767 cases for Groups 3–6 and an N = 26 for Groups 7–10.

** Compares white versus all other groups.

Comparisons of drug-abuse deaths (Groups 3–10) and non-drug-abuse deaths (Group 2) involving oxycodone

The remaining 1014 cases in the OPD were classified as either being induced by or related to drug abuse, or as unrelated to

Table V. Twenty Most Frequently Mentioned "Contributory" Drugs to Death (in Addition to Oxycodone/OxyContin) in Groups 3–6*

Drug	Mentions	Relative Frequency
Diazepam	304	1
Hydrocodone	255	2
Ethanol (> 0.02 g/dL)	232	3
Cocaine	184	4
Alprazolam	162	5
Propoxyphene	109	6
Marijuana	104	7
Heroin/morphine	101	8
Amitriptyline	93	9
Meprobamate	90	10
Diphenhydramine	87	11
Nortriptyline	84	12
Temazepam	81	13
Carisoprodol	80	14
Promethazine	70	15
Codeine	59	16
Oxazepam [†]	56	17
Methadone	52	18
Fluoxetine	48	19
Cyclobenzaprine [‡]	38	20
Sertraline [‡]	38	20

* Acetaminophen, which was considered "non-contributory", was present in 246 cases.
[†] Oxazepam could be present from use of specific drug product or as a result of metabolism of related benzodiazepines.
[‡] Cyclobenzaprine and sertraline occurred in equal frequency, i.e., 38 mentions for each drug.

drug abuse. On the basis of this classification, there were 919 (90.6%) cases (Groups 3–10) that involved drug abuse and 95 (9.4%) cases (Group 2) that were categorized as being unrelated to drug abuse. The demographics, COD, and MOD distribution for these groups are shown in Table III. The major differences between the drug-abuse groups and the non-drug-abuse group were age and MOD distributions. For MOD, there was a lower frequency of natural deaths and a higher frequency of accidental and undetermined deaths for the drug-abuse groups

Table VI. Comparison of Cause of Death (COD) and Manner of Death (MOD) Statements from the Originating ME/C for Drug-Induced Deaths (Groups 3, 4, 7, 8) versus Drug-Related Deaths (Groups 5, 6, 9, 10)

	Drug-Induced Deaths (Groups 3, 4, 7, 8) (% Group)	Drug-Related Deaths (Groups 5, 6, 9, 10) (% Group)	Group Comparisons Statistics*
COD/Contributing COD			
N	851 (100)	68 (100)	
Drug involvement	842 (98.9)	13 (19.1)	< 0.0001
External trauma	1 (0.1)	11 (16.2)	< 0.0001
Disease	2 (0.2)	41 (60.3)	< 0.0001
Unknown	6 (0.7)	3 (4.4)	< 0.05
MOD			
N	851 (100)	68 (100)	
Suicide	135 (15.9)	6 (8.8)	NS [†]
Natural	9 (1.1)	43 (63.2)	< 0.0001
Accident	528 (62.0)	10 (14.7)	< 0.0001
Undetermined	179 (21.0)	9 (13.2)	NS

* Fisher's Exact test.
[†] NS = not significant.

Table VII. Comparison of Cause of Death (COD) and Manner of Death (MOD) for Groups 3–10

	Multiple Drug-Induced (OxyContin Identified) Group 3 (% Group)	Multiple Drug-Induced (Oxycodone Identified) Group 4 (% Group)	Multiple Drug-Related (OxyContin Identified) Group 5 (% Group)	Multiple Drug-Related (Oxycodone Identified) Group 6 (% Group)	OxyContin-Induced Group 7 (% Group)	Oxycodone-Induced Group 8 (% Group)	OxyContin-Related Group 9 (% Group)	Oxycodone-Related Group 10 (% Group)
COD/Contributing COD								
N	177	646	12	54	12	16	0	2
Drug Involvement	173 (97.7)	641 (99.2)	2 (16.7)	10 (18.5)	12 (100)	16 (100)	0 (0)	1 (50.0)
External trauma	0 (0)	1 (0.2)	2 (16.7)	9 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)
Disease	1 (0.6)	1 (0.2)	8 (66.7)	32 (59.3)	0 (0)	0 (0)	0 (0)	1 (50.0)
Unknown	3 (1.7)	3 (0.5)	0 (0)	3 (5.6)	0 (0)	0 (0)	0 (0)	0 (0)
MOD								
N	177	646	12	54	12	16	0	2
Suicide	40 (22.6)	88 (13.6)	2 (16.7)	4 (7.4)	4 (33.3)	3 (18.8)	0 (0)	0 (0)
Natural	2 (1.1)	7 (1.1)	10 (83.3)	32 (59.3)	0 (0)	0 (0)	0 (0)	1 (50.0)
Accident	104 (58.8)	409 (63.3)	0 (0)	9 (16.7)	7 (58.3)	8 (50.0)	0 (0)	1 (50.0)
Undetermined	31 (17.5)	142 (22.0)	0 (0)	9 (16.7)	1 (8.3)	5 (31.3)	0 (0)	0 (0)

compared to the non-drug-abuse group. Suicide and homicide frequencies were approximately equivalent. Differences that reached statistical significance are indicated in Table III.

Comparisons of multiple drug-abuse deaths involving oxycodone (Groups 3–6) and oxycodone-only drug-abuse deaths (Groups 7–10)

Of the 919 cases in the OPD that were classified as deaths induced by or related to drug abuse, 889 (96.7%) cases involved multiple drug abuse deaths (Groups 3–6) where oxycodone was combined with other drugs considered as plausible contributors to COD, and 30 (3.3%) cases involved oxycodone or OxyContin as the single drug entity identified (Groups 7–10). The demographics, COD, and MOD distribution for these groups are shown in Table IV. There were no major differences between the oxycodone/OxyContin-only groups and the multiple drug abuse groups. The 20 most frequently occurring contributory drugs identified by toxicology testing for Groups 3–6 are shown in Table V. Acetaminophen, which was considered as a non-contributory drug for the purposes of this classification, was present in 246 cases. For Groups 3–6, the average number (\pm SD), and maximum number of other contributory drugs (in addition to oxycodone) were as follows: Group 3 (multiple drug-induced, OxyContin identified), 3.5 (\pm 1.8), maximum = 8; Group 4 (multiple drug-induced, no OxyContin identified), 3.6 (\pm 2.0), maximum = 13; Group 5 (multiple drug-related, OxyContin identified), 3.8 (\pm 2.4), maximum = 10; and Group 6 (multiple drug-related, no OxyContin identified), 2.8 (\pm 1.5), maximum = 6.

Comparisons of drug-induced deaths (Groups 3, 4, 7, 8) and drug-related deaths (Groups 5, 6, 9, 10) involving oxycodone

Of the 919 cases in the database that were classified as deaths induced by or related to drug abuse, 851 (92.6%) cases were classified as drug-induced (Groups 3, 4, 7, 8) and 68 (7.4%) were classified as drug-related (Groups 5, 6, 9, 10). The COD and MOD classifications for these groups are shown in Table VI. Drug involvement was listed as the COD by the originating ME/C in 98.9% of the cases we deemed to be drug-induced, whereas disease was the predominant COD in the drug-related

cases (60.3%). Oxycodone was mentioned in COD for 50.3% of the drug-induced cases and 4.4% of the drug-related cases. For MOD, accident was the predominant MOD in the drug-induced cases (62.0%), whereas natural causes was the predominant MOD in the drug-related cases (63.2%).

Comparison of cases involving OxyContin (Groups 3, 5, 7, 9) and oxycodone (Groups 4, 6, 8, 10)

Of the 919 cases in the cohort that were classified as deaths induced by or related to drug abuse, 12 cases were classified as solely OxyContin-induced (Group 7) and none of the drug-related deaths involved OxyContin alone (Group 9). OxyContin was identified in a total of 201 (21.9%) cases (Groups 3, 5, 7, 9). Of these, 73 were identified on basis of evidence at the scene, 42 were based on analysis of stomach contents and 12 reported both evidence at the scene and identifiable tablets in the gastrointestinal contents. OxyContin was identified in the remaining 74 cases based on additional evidence (e.g., autopsy report). Additional oxycodone products were also identified in Group 3 ($N = 20$, 11.3%) and Group 4 ($N = 32$, 5.0%) based on evidence at the scene and autopsy reports. These products included Endocet[®], Endodan[®], OxyIR[®], Percocet, Percodan[®], Roxicet[®], Roxicodone[®], and Roxilox[®]. The prevalence of acetaminophen and/or salicylates (based on toxicological testing) in Groups 3 and 4 was 21.5% ($N = 38$) and 31.3% ($N = 202$), respectively. The remaining 718 (78.1%) were cases in which oxycodone was present, but OxyContin was not identified (Groups 4, 6, 8, 10).

The COD and MOD classifications for Groups 3–10 are shown in Table VII. There was no apparent difference in cases in which OxyContin was identified as a source of oxycodone as compared with cases in which oxycodone was detected, but Oxy-

Table VIII. Incidence of Antidepressant Use, Benzodiazepine Use, and Illicit Drug Use in Multiple-Drug-Induced Cases (Groups 3 and 4)*

	# Cases Multidrug, OxyContin Identified (Group 3) (% Group)	# Cases Multidrug, Oxycodone Detected, No OxyContin Identified (Group 4) (% Group)
N	177	646
Antidepressant(s)	71 (40.1)	225 (34.8)
Benzodiazepine(s)	100 (56.5)	364 (56.3)
Illicit drug(s)	48 (27.1)	227 (35.1)

* Cases in which there were multiple occurrences of drug in the same category were counted only once, e.g., if marijuana and heroin were detected in a single case, it was counted as one case of illicit drug(s) detected.

Table IX. Cause of Death (COD) Statements Identifying Drug as Cause or Contributing Cause of Death

Group(s)	Group N	Oxycodone Mentioned (% Group)	Other Single Specific Drug Mentioned (% Group)	Multiple Drug (Specific and Non-specific) References (% Group)
0	79	5 (6.3)	10 (12.7)	4 (5.1)
1	150	1 (0.7)	40 (26.7)	70 (46.7)
2	95	2 (2.1)	2 (2.1)	0 (0)
3	177	98 (55.4)	38 (21.5)	126 (71.2)
4	646	307 (47.5)	119 (18.4)	491 (76.0)
5	12	1 (8.3)	1 (8.3)	0 (0)
6	54	1 (1.9)	6 (11.1)	3 (5.6)
7	12	11 (91.7)	11 (91.7)	0 (0)
8	16	12 (75.0)	12 (75.0)	3 (18.8)
9	0	0 (N/A)*	0 (N/A)	0 (N/A)
10	2	1 (50.0)	1 (50.0)	0 (0)
Total	1243	439 (35.3)	240 (19.3)	697 (56.1)
3–6	889	407 (45.8)	164 (18.4)	620 (69.7)
7–10	30	24 (80.0)	24 (80.0)	3 (10.0)

* N/A = not applicable.

Contin was not identified. Again, drug involvement was the predominant COD in the drug-induced cases, whereas disease was the predominant COD in the drug-related cases. Prevalence of antidepressant use, benzodiazepine use and illicit drug use for the multiple drug-induced groups (Groups 3 and 4) are shown in Table VIII.

Analysis of COD and contributing COD statements

The COD and contributing COD statements for the 1243 cases in the OPD were evaluated to determine whether oxycodone was specifically mentioned, a single specific drug was mentioned, or multiple drugs (specific and non-specific drug references) were mentioned. The results are shown in Table IX. There were 439 mentions of oxycodone, 240 mentions of other specific single drugs, and 697 references to multiple drugs. References to multiple drug use included both general terms such as "multiple drug overdose" and mentions of specific drugs such as "intoxication with oxycodone, alprazolam, and ethyl alcohol."

Discussion

Although the risk of fatal overdose from opioid abuse has been recognized for many years, there remains little recognition among drug abusers of the added dangers of toxicity from combinations of opioids with other CNS active drugs. There is little doubt that abusing an opioid with another opioid, or with other classes of depressants such as alcohol, antihistamines, sedatives, or minor tranquilizers, can enhance the CNS depressant effects of the opioid, sometimes with a fatal outcome (2,12,13,19–21). Less clear are the risks associated with the combined abuse of an opioid with stimulants, hallucinogens, and other therapeutic agents such as neuroleptics, anticonvulsants, or antidepressants. In the present study of opioid deaths involving oxycodone, 919 of 1014 cases in the OPD that were evaluated were characterized as death being induced by or related to drug abuse. Of the 919 cases, the majority of cases ($N = 889$, 96.7%) involved multiple drugs in which there was at least one additional plausible contributory drug in addition to oxycodone; only 30 (3.3%) cases were found to be associated solely with oxycodone. There were an average of 3.5 additional drugs that plausibly contributed to the fatal outcome in Groups 3–6 (Figure 1), and up to 13 drugs in addition to oxycodone were present. A similar finding for oxycodone-related deaths was reported by Drummer et al. (16), who noted that the majority of cases involved additional drugs in combination with oxycodone. The proclivity for opioid abusers to abuse more than one drug appears to apply to most narcotics. For example, the DAWN 2001 report of mortality data indicates that 92% of deaths involving narcotic analgesics were multiple-drug deaths, as opposed to single-drug deaths (17). Unquestionably, the data presented in this paper indicate there is added risk of fatal overdose to abusers who engage in polydrug abuse.

The most prevalent combinations of other drugs with oxycodone in the current study included benzodiazepines, alcohol, cocaine, other narcotics, marijuana, or antidepressants. There

is, however, scant literature on deaths involving oxycodone for comparison. In a study of nine deaths involving oxycodone, Drummer et al. (16) reported that oxycodone was present in combination with benzodiazepines, alcohol, methamphetamine, or meperidine. A case report by Fu et al. (22) indicated that citalopram in combination with oxycodone, cocaine, promethazine, and propoxyphene resulted in the death of a 47-year-old male with a long history of alcohol and drug abuse. As shown in Table V, the relative frequency of detection of these drugs in combination with oxycodone were as follows: cocaine, 4th; propoxyphene, 6th; promethazine, 15th; and citalopram (not shown), 22nd.

The drug combinations in association with oxycodone appear to be generally the same as those frequently reported in heroin-related deaths. For example, Darke et al. (7) reported 76% of cases involved heroin in combination with other drugs (alcohol, 46%; benzodiazepines, 27%; antidepressants, 7%; and cocaine, 7%). In a review of ME cases reported in the United States, Haberman et al. (13) reported that heroin-positive cases invariably had the highest proportion of positive blood-alcohol results. In eight ME studies, the blood-alcohol-positive proportions for heroin-positive cases ranged from 32% to 70%, with a median of 49%. In the current study, positive alcohol results in combination with oxycodone was the third most prevalent finding after diazepam and hydrocodone. A somewhat lower prevalence of polydrug abuse was noted by Burt et al. (9), who reported that of 57 fatalities with detectable blood morphine, presumably from heroin, 15 (26%) cases were attributed to opioid toxicity, 22 (39%) were attributed to polydrug use that included heroin and/or morphine, and in 20 (35%) cases, the cause of death was not related to opioid use.

Polydrug abuse also appears to be common among living drug abusers. Rooney et al. (3) reported the extensive and serious problem of benzodiazepine abuse by polydrug abusers. They reported a prevalence of 54% dependency on benzodiazepines for patients who co-abused opioids and benzodiazepines. Gossop et al. (18) identified polydrug abuse and, specifically, heavy drinking and abuse of benzodiazepines and amphetamines as risk factors for fatality. In a study of current heroin abusers and amphetamine abusers, Darke and Hall (8) indicated that the occurrence of a "pure" heroin or amphetamine abuser was extremely rare. Heroin abusers ($N = 329$) were more likely to have abused benzodiazepines, whereas amphetamine abusers ($N = 301$) were more likely to have abused hallucinogens. The four most prevalent drugs abused by the heroin group were tobacco (94%), cannabis (84%), alcohol (78%), and benzodiazepines (64%). In the current study, for the purposes of classification, tobacco was not considered a contributor to the death.

Although comparisons of mortality data from different databases are problematic, it appears that the demographics of the drug abusers in the OPD are somewhat different than those found in other studies. For example, Gossop et al. (18) reported a mean age at the time of death of 28.9 years for 32 drug abusers who died of fatal drug overdoses in Nova Scotia with males representing the majority (84.4%) of cases. Hall and Darke (23) noted a trend toward increasing age of opioid overdose deaths. They reported the average age at death for males increased

from 24.5 years in 1979 to 30.6 years in 1995. Darke et al. (7) reported a mean age of 31.0 years for 953 heroin-related deaths in Australia over the period 1992 to 1996. Males represented 85% of the group in that study. In contrast, the mean and median ages for the drug-abuse groups (Groups 3–10, $N = 919$) in the current study were 39.7 years and 40.0 years, respectively, with males representing 67% of the group. Thus, it appears that the drug abusers in the OPD are somewhat older than groups in previous drug overdose mortality cases and that females represent a higher proportion than previously reported.

An evaluation of the COD statements in the OPD for classification into general categories (drug involvement, trauma, disease, and unknown) revealed frequent use of non-standard terminology. COD statements varied from specific drug mentions to vague and general terms such as "narcotic intoxication" and "drug abuse". Others have noted a similar vagueness in COD statements of drug abusers (18,24). Gossop et al. (18) noted that in many cases it may not be possible for the coroner/pathologist/toxicologist to determine with certainty which drugs were a cause of death and suggested that "the accuracy of death certification would be improved by routinely recording all substances detected during toxicological examination". In view of the proclivity of drug abusers to abuse multiple drugs at the same time and the potential for multiple drug-drug interactions, recording all drugs in COD statements would undoubtedly lead to an improved classification system. In the current study, there was noted to be a general recognition in COD statements of the role of multiple drugs. Table IX lists the occurrences of mentions of oxycodone, and other specific drug mentions. As expected, because of bias from requesting only those cases in which oxycodone was thought to be involved, there was a high prevalence of oxycodone mentions for Groups 3, 4, 7, and 8 (drug-induced groups) and a low occurrence in Groups 5, 6, 9, and 10 (drug-related groups). Single specific drugs were also mentioned more frequently for the drug-induced groups compared to the drug-related groups. Of particular note was the high frequency of reference to multiple drug use for Groups 3 and 4 (multiple-drug-induced groups). Approximately 75% of the 823 deaths in these two groups were specified in the COD or contributing COD statements as multiple drug deaths. A variety of terms were employed to indicate multiple drug involvement such as "polydrug toxicity", "polypharmacy", "multiple drug poisoning", and "polypharmaceutical overdose".

There was a high prevalence of illicit drugs used in combination with other drugs. For example, amongst multi-drug abusers (Groups 3–6), cocaine or cocaine metabolites were identified in 184 cases, and marijuana in 104 cases. Of the 101 heroin/morphine cases, 24 could be specifically attributed to heroin use, based on identification of heroin or 6-acetylmorphine in biological specimens.

Although important in monitoring drug abuse trends, the identification of specific opioid products could not be evaluated with a high degree of accuracy in this study. Because many opioid products are marketed in combination with acetaminophen or aspirin, one approach would be to evaluate the presence or absence of acetaminophen or salicylates as a marker for specific products. However, this means of product

identification was not found to be accurate. For example, discrepancies in testing and reporting acetaminophen or salicylates were noted for oxycodone combination products (e.g., Percocet, Percodan). In Groups 3–10, there were 49 cases in which an oxycodone combination product (combination of oxycodone and acetaminophen or aspirin) was identified based on evidence at the scene or autopsy reports. Of these, 20 (40.8%) cases had toxicology results reported without identification of acetaminophen or salicylates. Furthermore, among the 255 cases in which hydrocodone was identified, only 109 (42.7%) cases tested positive for acetaminophen or salicylates and 146 (57.2%) were either not tested or tested negative for acetaminophen or salicylates, despite the fact that the overwhelming majority of hydrocodone products sold in the United States are hydrocodone-acetaminophen combination products. Inconsistency in reporting acetaminophen and salicylates has also been noted by DAWN and by forensic toxicologists performing the analyses. The latest DAWN report (17) states, "...the compounds acetaminophen-oxycodone or aspirin-oxycodone are sometimes reported to DAWN, but it is likely that some mentions of these oxycodone compounds are reported to DAWN simply as oxycodone." Consequently, it is concluded that the presence or absence of acetaminophen or salicylates cannot be used as a reliable means of identification of specific opioid drug products.

Standardization of the system for classification and reporting of mortality data for victims who die of causes involving or related to drug abuse is essential for determining accurate prevalence rates. These data have major impact on public health policies, law enforcement, and pharmaceutical firms whose therapeutic products are misused or abused. The DAWN system is the largest and most standardized system for reporting drug abuse mortality data in the United States. Consequently, the system for classification of cases in the OPD was based on this system. This method of reporting was developed in the early 1970s by the Drug Enforcement Administration and is currently supported by the Office of Applied Studies of the Substance Abuse and Mental Health Services Administration. This system recognizes the potential for multiple drug interactions and has a straightforward approach for reporting mortality data in which abuse of multiple drugs is involved. Up to six of the potentially contributing drugs in mortality cases are reported by DAWN. This is a limitation in the DAWN system in that some abusers exceed this number of drugs in their practice of "polypharmacy". In the current study of deaths involving oxycodone, toxicological testing identified combinations of up to 14 drugs. However, the DAWN system clearly recognizes the danger of drug-drug interactions. The DAWN 2001 Mortality Report (17) states, "When multiple drugs are involved in a single case, the cause of death cannot be attributed to any particular substance." In view of the confusion found in much of the older toxicology literature regarding reporting of such cases, the approach by DAWN in reporting such deaths as "multiple drug deaths" represents an important contribution to how such cases should be interpreted and reported.

In the current study, there were 201 cases in which OxyContin was specifically identified. Of these, 12 deaths had both oxycodone as the only drug entity identified on toxicology anal-

ysis and the specific drug product OxyContin implicated as an oxycodone source; the other 189 deaths were induced by or related to a combination of drugs including OxyContin. In some deaths, multiple oxycodone products were identified in combination with other drugs. Among those cases classified as induced by a combination of drugs including OxyContin (Group 3), 56.5% had benzodiazepines identified, 40.1% had antidepressants identified, and 27.1% had illicit drugs identified through toxicological testing. A similar pattern of drug use also occurred in Group 4, deaths induced by oxycodone and other drugs, with no OxyContin identified (see Table VIII). This high frequency of abuse of multiple licit and illicit drugs is clearly the cause of many of the fatal outcomes documented in this report.

The high percentage of decedents testing positive for benzodiazepines and antidepressants does not represent the prescribing patterns of these drugs in the population of persons in pain for whom OxyContin is prescribed. For example, according to the National Disease and Therapeutics Index from IMS Health, the percent of patients with prescriptions for long-acting opioids receiving simultaneous prescriptions for benzodiazepines in 2000 and 2001, respectively, were as follows: OxyContin (3.6%, 3.7%), MS Contin® (5.7%, 3.4%), and Duragesic® (3.7%, 2.5%). The figures for the specific antidepressants identified in this study were as follows: OxyContin (3.1%, 2.4%), MS Contin (3%, 2.3%), and Duragesic (0.5%, 4.8%) (cited with permission, *data on file*). Similarly, methadone, which was identified in 5.8% of the cases from Groups 3–6, comprised only 0.7% of the analgesic prescriptions in the U.S. in 2001 (cited with permission, IMS Health's National Disease and Therapeutics Index (NDTI), *data on file*, Purdue Pharma L.P.). Because some patients with pain do have benzodiazepines, antidepressants, or methadone prescribed along with a long-acting opioid, one interpretation of these data would be that those patients are over-represented in this study, that is, compliant patients in whom these combinations are co-prescribed are at risk of accidental overdose. This interpretation, however, is refuted by the fact that in order for a case to be classified into Group 3 through 10, there had to be unequivocal evidence of drug abuse, as indicated in the Methods section.

The findings in this report are subject to some of the same limitations as those recognized in the DAWN system of reporting. Counts of drug-related deaths do not represent the United States as a whole, and should not be considered as representative of the entire country, as the cases were solicited from areas that had media reports of overdose deaths involving OxyContin. Although nonparametric statistics were applied to demographic data for the different groups of cases, variance estimates may underestimate true variance. Submission of cases from Medical Examiners, Coroners, and other death investigators was entirely voluntary, and several jurisdictions that had reported deaths in the media refused to provide any cases for this study. The focus of this investigation was on deaths in which oxycodone was involved. However, as noted, the majority of deaths involved multiple drugs. Some cases were submitted in which oxycodone was not detected or not reported on the COD. In a number of cases ($N = 108$, 8.7%), the MOD was classified by the ME/C as due to natural causes. Despite the inherent limi-

tations of the DAWN system of reporting mortality data, a slight modification of this system enabled recording and classification of oxycodone and other substances involved in deaths listed in the OPD in a standardized manner. The use of a glossary of terms developed by DAWN enhanced the accuracy and consistency of classification. Expansion of this system of classification and reporting of drug abuse deaths involving other drug classes would be valuable as a means of enhancing our understanding of the public health issues of drug abuse.

Conclusions

Analysis of 1243 cases in the OPD revealed that drug abuse involving multiple drugs was the primary cause of death. A total of 919 deaths were classified as either being induced by or related to drug abuse. However, only 30 deaths were identified that solely involved abuse of oxycodone. Of these, 12 deaths could be identified involving the specific drug product OxyContin. The cases in the OPD involved the abuse of an average of 3.5 drugs in addition to oxycodone. Combinations of oxycodone with other opioids, benzodiazepines, alcohol, cocaine, and antidepressants were most commonly found. Clearly the risk of a fatal overdose is substantially increased when opioids are abused in combination with other CNS active drugs. The patterns seen in the OPD are not consistent with customary, accepted drug regimens used in the treatment of pain.

The system of categorization was based on the DAWN system for reporting mortality data. Use of this system allowed objective grouping of cases into categories not involving drug abuse, into single drug and multiple drug categories, and into drug-induced and drug-related categories. Use of standardized terminology and group classifications based on the DAWN system is recommended. Adoption of this system would enhance future evaluations of opioid involvement in drug abuse death evaluations and allow more meaningful comparisons between studies.

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Commentary

The challenge of the medical examiner/coroner (ME/C) in determining cause and manner of death is both complex and individualized. In some cases, the cause is relatively simple (e.g., gunshot wound, severe trauma), whereas in others it may be much more difficult (e.g., drug-related/induced). In the latter, an individual's medical history and autopsy findings must be evaluated along with the report of drugs used, both licit and illicit. The experience of the ME/C needs to be integrated with systematic inductive reasoning to achieve a supportable outcome that serves the public.

The current study provides an excellent means of classifying deaths thought to be drug related. Deaths involving oxycodone were examined in a very thorough manner. Only culled and reliable case data were incorporated into the study's final results. A forensic pathologist reviewed each case so that natural disease processes were considered in determining if they caused or contributed to the death. The review of information from investigations by police and ME/C investigators is a necessary part of the assessment of each case in order to determine what formulation of oxycodone might be involved.

There is a need to standardize the terminology for reporting the cause of death in cases involving opioid abuse and the abuse of other drugs. The DAWN terminology employed by the authors is very useful and is to be recommended. It forces a focus on the decision-making and thinking about whether the death is drug-induced or drug-related and whether a single drug or multiple drugs are involved. The person making the cause of death and manner of death decisions is forced to consider drug interactions (additive-synergistic-potentiating effects) and the overlapping of therapeutic, toxic, and fatal levels of some drugs. The concept of class definitions incorporated into the 11 groups allows disaggregating death cases into their proper categories. The algorithm presented and utilized for these cases to arrive at a specific category relating oxycodone to the death is a useful instrument that could have broad applicability to the classification and reporting of deaths involving other drugs.

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