



ARTICLES

UNIFORM STANDARDS AND CASE DEFINITIONS FOR CLASSIFYING OPIOID-RELATED DEATHS: RECOMMENDATIONS BY A SAMHSA CONSENSUS PANEL

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Deaths involving prescription and illicit opioids are on the rise, which is an issue of increasing concern to health care professionals, policymakers, and the public. However, because medical examiners, coroners, and other practitioners do not use uniform standards and case definitions in classifying such drug-related deaths, the incidence and prevalence data are challenging to analyze and difficult to interpret, and thus form a poor basis for crafting effective responses. To address this situation, the Substance Abuse and Mental Health Services Administration convened a Consensus Panel and charged it with devising uniform standards and case definitions that can assist medical examiners, coroners, public health officials, and others in consistently distinguishing between deaths that were caused by a certain opioids and deaths in which such a drug was detected but was not a major cause of or contributor to the death. The consensus statement presented here incorporates the panel's recommendations in four key areas.

KEYWORDS. Drug-related deaths, death classification, case definitions

INTRODUCTION

Deaths involving prescription and illicit opioids are on the rise, which is an issue of increasing concern.^{1,2} To better understand these phenomena, the Substance Abuse and Mental

Health Services Administration (SAMSHA) of the Department of Health and Human Services convened multidisciplinary groups of experts in 2003, 2007, and 2010. At those meetings, participants concluded that the lack of

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uniformity in classifying opioid-related deaths on the part of medical examiners, coroners, and other practitioners results in data that are challenging to analyze and difficult to interpret. In particular, they concluded that coroners and medical examiners appear to not use common definitions in classifying deaths caused by opioids and that their definitions may not be the same as those used on death certificates.^{1,3,4}

Therefore, a recommendation from all three meetings was that uniform standards and case definitions be established to assist medical examiners, coroners, and other persons or entities who create and use such data in consistently distinguishing between deaths that were caused by a certain drug and deaths in which the drug was detected but was not a major cause of or contributor to the death.^{1,3,4}

To develop such uniform standards and case definitions, SAMHSA convened a panel of medical examiners, coroners, toxicologists, epidemiologists, and other public health officials to examine the research literature and current practices and to formulate a consensus-based document. The panel included representatives of organizations and agencies that share a commitment to assuring the safety and effectiveness of opioid addiction treatment. Panel members had backgrounds in addiction medicine, opioid pharmacology, methadone maintenance treatment, and medical education. Ex officio members represented government health care, drug safety, and regulatory agencies (Appendix A).

METHODS

In support of the panel's efforts, a comprehensive literature search was performed via MEDLINE and Embase (1970 through 2012) for research articles and clinical guidelines addressing various aspects of death classification and case definitions. English-language articles were reviewed, as were official guidelines published in the United States, Canada, and the United Kingdom, as well as relevant reports produced by government agencies. Based on their review of the articles, members of the Consensus Panel prepared a preliminary report that was circu-

lated to experts in the field for review. Input obtained through that review was incorporated in the consensus statement presented here.

DISCUSSION AND RECOMMENDATIONS

The Expert Panel agreed that standardizing approaches in four areas would help produce more uniform and reliable data on drug-related deaths: scene investigation, toxicologic testing and analysis, case definitions, and determination and documentation of causality. Each of these is discussed and the Panel's recommendations are presented.

Scene Investigation

The investigation of a death should include a complete inspection of the scene, as well as photographic documentation and collection of all evidence related to the potential exposure to a drug or drugs, including a history provided by family members or other bystanders. The drugs should be inventoried to determine or estimate the amount ingested.

In deaths involving controlled prescription drugs, the death investigator should request the records of the decedent from the state Prescription Drug Monitoring Program (PDMP), where one exists, to establish prescription history and to evaluate evidence of use of such drugs without a prescription, because this information is important to help determine the level of tolerance. The investigator also can use the PDMP to identify health care providers from whom the decedent's medical history can be obtained. In cases involving methadone or buprenorphine, the investigator or medical examiner/coroner should contact local opioid treatment programs to determine whether the decedent was receiving drugs from them, if it is possible to obtain such information in the jurisdiction.

Toxicologic Testing and Analysis

There are significant variations across medicolegal death investigation systems with respect to standards of practice for routine toxicologic tests.⁵ Historically, toxicology laboratories have used thin layer chromatography, immunoassay,

or both to analyze large batches of urine specimens rapidly and cost-effectively. However, as toxicology laboratory analytical methods evolved throughout the 1980s, most laboratories introduced the use of a confirmatory analysis that is more specific and sensitive than the initial test.⁶ Currently, the most common combination of techniques used for the detection of drugs or drug metabolites in urine is immunoassay, followed by confirmation of presumptive-positive specimens by gas chromatography-mass spectrometry.

The principal shortcoming of immunoassays is that they vary in their ability to detect the presence of a drug. For example, many immunoassays do not detect toxicologically significant opiates, especially oxycodone and hydromorphone. In addition, laboratories do not use a standard threshold of detection (the concentration below which detection of an analyte does not occur). The absence of standardized practices may lead to underreporting of prescription opioids in the deceased.

Toxicological measurements also should be evaluated for their ability to distinguish between acute and chronic drug use, as through determination of free and glucuronidated metabolites. Collection of such data on drug-related deaths may provide indicators for the assessment of future cases. Such analyses are more feasible with the current generation of benchtop liquid chromatography-mass spectrometry equipment.

With most drugs, measurable concentrations vary with the site of collection (e.g., central versus peripheral blood vessels) based on route of administration, chronicity of use, time elapsed between drug use and sample collection, time elapsed between death and sample collection, the process used for collection, and other factors. The most reliable specimens are drawn from a peripheral site, such as the iliac or femoral veins, yet the site of sample collection often is not reported. Thus, heart blood, subclavian blood, body cavity fluid, spleen squeeze, blood contaminated by embalming fluid, and the preferred peripheral blood all may be simply reported as "blood" on the forensic report.

Such mixtures of ideal and non-ideal specimens introduce avoidable errors into the forensic toxicology data.

A variety of techniques, including immunoassay, enzyme-linked immunosorbent assay, and thin layer chromatography, qualitatively detect opioids and their metabolites in blood. Quantitative measurement of an opioid or its metabolite in blood requires high-performance liquid chromatography, gas chromatography, liquid chromatography-mass spectrometry, and gas chromatography-mass spectrometry. Quantitation of the drug should be based on a multipoint calibration curve, standard samples, and other good laboratory practices.

A standard of practice for forensic toxicology would include the following:

1. Identification of the site of specimen collection. If possible, samples should be collected from peripheral blood vessels.
2. Collection and testing of admission (as opposed to autopsy) blood and urine specimens when applicable and available.
3. Comprehensive testing for prescription, illicit, and over-the-counter drugs and alcohol.
4. Testing of appropriate specimens with an emphasis on urine as a means to effectively detect drugs and drug metabolites.
5. The use of an immunoassay screen with a defined level of sensitivity and supplemental immunoassays for drugs with poor cross-reactivity.
6. The determination of free and total drug concentrations in blood specimens, at a minimum, and ideally free and individual glucuronide metabolites.
7. Analysis of free and total opiate/opioid concentrations in other tissues as an adjunct to blood concentrations, where appropriate, or where the blood concentrations may be compromised by postmortem artifact.
8. Similar standards for cut-off concentrations for confirmatory gas chromatography-mass spectrometry and liquid chromatography-mass spectrometry analysis.

9. Use of analytical methods that have been appropriately validated and controlled to provide reliable data.

Case Definitions

Panel members agreed on the following case definitions:

1. Drug-Caused Death

Concept: A death that has been certified as resulting from exposure to a drug, either alone or in combination with other drugs or substances. The intent of the individual who used the drug or gave it to another person is irrelevant; therefore, unintentional deaths, suicides, homicides, and deaths of undetermined intent are included.

Laboratory Criteria: In most cases, evidence of the drug will be found on postmortem toxicology. However, a death may meet the case definition in rare instances when toxicologic testing is not available or was omitted but circumstantial evidence is sufficient to certify the death as drug-caused.

Includes: Acute drug toxicity, chronic drug effects, adverse drug reactions/effects, legal executions by drugs, terrorist events involving drugs, and mental and behavioral disorders due to drugs.

Excludes: Deaths from infections resulting from drug use such as intravenous drug use. Deaths from congenital anomalies resulting from drug use.

Equivalent Category in Vital Statistics Data: This definition parallels the definition of “drug-induced deaths,” a category developed by the National Center for Health Statistics.⁷ The National Center for Health Statistics considers a death to be “drug induced” if any one of a list of factors identified in specific codes in the tenth revision of the International Classification of Diseases (ICD-10) is the underlying cause of death. The list of codes is included in the National Vital Statistics Report “Deaths, Final Data,” published annually by the National Center for Health Statistics.⁸ This definition also includes deaths involving adverse effects of drugs for therapeutic use.

1-a. Drug Poisoning Death (a proposed subcategory of drug-caused death)

Concept: A death that has been certified as due to acute exposure to a drug, either alone or in combination with other drugs or other substances. This category is intended to be equivalent to the layperson’s concept of a drug overdose. The intent of the individual who used the drug or gave it to another person is irrelevant; therefore, unintentional, suicidal, and homicidal deaths, and deaths of undetermined intent are included.

Laboratory Criteria: In most cases, evidence of the drug will be found in postmortem toxicology. However, a death may meet the case definition in rare instances when toxicological testing is not available or was omitted but circumstantial evidence is sufficient to certify the death as a drug poisoning death.

Includes: Acute toxicity from drugs used recreationally, drugs given or taken in error, drugs taken that were prescribed to another person, and overdose in a medical setting.

Excludes: Deaths from (a) infections resulting from drug use, such as intravenous drug use; (b) congenital anomalies resulting from drug use; (c) chronic drug effects; (d) correct drug properly administered in therapeutic or prophylactic dosage as the cause of any adverse effect; (e) legal executions by drugs; (f) terrorist events involving drugs; and (g) mental and behavioral disorders due to drugs.

Equivalent Category in Vital Statistics Data: This case definition closely parallels the definition of the drug subset of “poisoning by and exposure to noxious substances,” a category of injury used in the ICD-10.⁹ The ICD considers a death to be drug poisoning if any one of the following ICD-10 codes is the underlying cause of death: X40-X44 (unintentional), X60-X64 (suicide), X85 (assault), and Y10-Y14 (undetermined intent).

2. Drug-Detected Death

Concept: A death in which a drug is detected in postmortem testing, regardless of the drug’s role in causing the death. The intent of the person in using the drug or giving the drug to another person is irrelevant, so unintentional, suicidal,

homicidal, and deaths of undetermined intent are included.

Laboratory Criteria: Evidence of the drug must be found on postmortem toxicology. (This definition simplifies the process of reporting such deaths for Coroners Medical Examiners because the data can be pulled from their own laboratory database. They need not have a database that integrates all sources of toxicology data, and they need not select drug levels above specified cutpoints to report.) However, a death may meet the case definition in rare instances in which toxicological testing is not available or was omitted but circumstantial evidence is sufficient to certify the death as a drug poisoning death.

Includes: All deaths, whether natural or the result of trauma, in which a drug is detected, and all drug-caused and drug poisoning deaths, as described above. This category may include deaths from mechanisms of injury other than poisoning, such as motor vehicle crashes and suffocation.

Excludes: Deaths for which the toxicology was performed premortem by staff of a hospital or other medical facility.

Equivalent Category in Vital Statistics Data: This category does not map to any specific set of ICD-10 codes.

3. Drug

Concept: Any chemical compound that may be used by or administered to humans or animals as an aid in the diagnosis, treatment, or prevention of disease or injury; for the relief of pain or suffering; to control or improve any physiologic or pathologic condition; or for the feeling it causes.

Includes: Illicit drugs such as heroin, cocaine, and hallucinogens; prescription drugs; over-the-counter agents; biological substances, such as vaccinations, veterinary drugs, dietary supplements; and nonmedicinal substances, such as inhaled solvents.

Excludes: Alcohol and tobacco and the toxic effects of other noxious substances eaten as food, such as hallucinogenic mushrooms.

Equivalent Category in Vital Statistics Data: This category corresponds roughly to substances

covered by the ICD-10 code T36-T50, "poisoning by drugs, medicaments, and biological substances."⁹ Note that this code range does not include alcohol or tobacco, which are elsewhere classified as "substances chiefly nonmedicinal as to source."

Determination and Documentation of Causality

Proper and accurate certification of a death that may have resulted entirely or partially from the effects of a drug requires the synthesis of data obtained from multiple sources. Laboratory values cannot be interpreted in a vacuum, but instead require context, such as the circumstances of death, medical and substance use history of the decedent, drug source, and autopsy findings. From these factors, the death investigator may reach a determination as to whether a given postmortem drug concentration in the blood was fatal or if it was toxic in combination with other drugs, which together were fatal.

Issues in Determining Causality: The ME/C needs to determine whether the preterminal events were consistent with the mechanism of action and toxicity of a drug (or combination of substances) and whether the decedent was potentially tolerant to the drug effects. Two circumstances are particularly important in this regard. First, drugs with long half-lives, such as methadone, may accumulate to toxic serum concentrations during the induction period (first few days of treatment) before a steady state is achieved or tolerance develops. Second, individuals whose tolerance declined while they were not taking the drug (e.g., while incarcerated or hospitalized) can overdose if they miscalculate the dosage and resume drug use at past levels.

Deaths involving drugs become more complicated to certify if there are competing or superseding causes of death. These causes may be natural (e.g., hypertension or mental disorders) or external (e.g., a motor vehicle collision or drowning). To certify the death, the causal chain of events leading to death must be inferred from the available evidence and then appropriately recorded on the death certificate.

Mixed intoxications present a special challenge for purposes of death certification. When multiple drugs or alcohol are detected postmortem, each exposure must be considered individually and as a part of the mixture present. Thus, each individual concentration should be assessed as to its toxicity or lethality, after which the combination of drugs must be viewed in terms of the similarity of mechanisms of action and whether the combination is known to have additive or synergistic effects.

Documenting Causality on the Death Certificate: The ME/C must determine which one, or more, of the drugs detected is present in a concentration that is sufficient—by itself or in combination—to be toxic and to be listed as a the cause of death.^{10,11} All drugs that are deemed physiologically significant in causing death should be listed individually in Part I of the cause of death portion of the death certificate. Part II is reserved for preexisting or coexisting conditions that contributed to death but are not the underlying cause of death listed in Part I. For example, hypertension might be a preexisting condition that contributes to a fatal stroke precipitated by cocaine intoxication. In drug-caused deaths that result from the combined effects of multiple drugs on the central nervous system, all drugs that contributed to the underlying cause of death should be listed in Part I of the death certificate. The intention is not to put the most lethal drugs in Part I and the less lethal drugs in Part II, but for the role the drug played in contributing to the death to be the factor that determines whether a drug should be reported in Part I or II.¹²

When postmortem toxicology is not available but the ME/C has concluded from other available evidence that a drug caused the death, that drug should be listed in Part I.

Drugs that did not contribute to the cause of death should not be recorded on the death certificate. (Deaths associated with drugs found postmortem, whether causal or incidental, would be included in the drug-detected category defined above, even though the incidental findings would not be specified on the death certificate.) The field on the death certificate labeled “Describe how injury occurred” pro-

vides additional space to include details of the circumstances of death, and information contained in this box is sometimes used when determining the underlying cause of death. However, the most important information should be recorded in the cause of death section of the death certificate.

Specifying individual drug names on the death certificate is important because death certificates are the source documents for national mortality statistics.¹³ Simply ascribing death to drug intoxication or polypharmacy does not identify which drugs or even which classes of drugs have caused the death, thus preventing any meaningful use of death certificates for epidemiologic purposes. In cases involving specified opioids, particular attention should be given to opioids used in combination with other central nervous system depressants, especially benzodiazepines, other opioids, and alcohol.

In general, it is better to record the parent drug than the drug metabolite whenever that information can be determined. For example, where morphine is detected on postmortem toxicology, and depending on the results of additional toxicologic testing (e.g., 6-AM) or the circumstantial information from the death investigation, the ME/C should specify morphine if it appears that prescription morphine was involved and heroin if it appears that the morphine was a metabolite of heroin (e.g., 6-AM). Otherwise, it is impossible to use death certificate information to determine how many deaths involved prescription agents rather than illicit substances.

Caution should be exercised in selecting the words used to describe the cause of death because such wording determines whether the death is categorized as an acute poisoning injury or a chronic condition in vital statistics (Appendix B).¹⁴ The coding rules specify the wording that qualifies for each code assigned to the underlying cause of death and each contributing cause of death on the death certificate.⁹ For example, the following phrases would be coded with the same ICD-10 category “poisoning (X42) with nature of injury specifying the cocaine involvement (T40.5)”:

acute cocaine intoxication, acute cocaine toxicity, toxic effects of cocaine, cocaine poisoning, and cocaine overdose. In contrast, the following phrases would be coded to the ICD-10 F14 category “Mental and Behavioral Disorders Due to Use of Cocaine”: *cocaine use, cocaine abuse, cocaine snorting, and cocaine addiction.*

Thus, when reporting a death due to the acute toxic effects of a drug, use *toxicity, toxic effects, intoxication, or poisoning* in the Cause of Death portion of the death certificate and avoid the words *use* or *abuse*, which—along with terms such as *dependence* and *disorder*—would be appropriate to use only if the intent is to implicate substance use as the cause of death.

Terms such as *addiction* and *disorder* are appropriately used to describe long-term drug dependence or drug addiction that has caused physiological damage to a point at which a natural death occurred (as through organ failure). It is best to avoid the term *overdose* because it lacks a specific meaning.

Case 1: Multiple Drug Use in a Tolerant Individual. A 40-year-old man with a history of substance use disorder engages in an episode of drug use with friends and goes to sleep. The next day, he could not be awakened. Emergency medical services are summoned, and he is found to be dead. At autopsy, he is found to have pulmonary congestion and edema, with a bladder full of urine, but no indication of a specific disease or injury that caused his death. Toxicologic analysis reveals low-toxic concentrations of oxycodone and diazepam.

Cause of Death, Part I: Acute intoxication by oxycodone and diazepam

Cause of Death, Part II: None

How Injury Occurred: Ingested diazepam and injected oxycodone intravenously

Drug-Caused Death: Yes

Drug Poisoning Death: Yes

Drug-Detected Death: Yes

Comment: This common scenario is consistent with coma and death due to drug intoxication.¹⁵ It is particularly suggestive of severe respiratory depression associated with use of opioids in combination with benzodiazepines.

One must consider the blood concentration of the opioid and the state of drug tolerance of the decedent.

Because of his drug use history, this decedent was expected to be opioid-tolerant and likely would have required a high blood concentration of the opioid or ethanol to produce the ultimately fatal toxicity.¹⁶ During the ensuing coma, he would have metabolized a significant portion of the drug. Therefore, even if the postmortem concentrations are not classically lethal per se, the circumstances are highly compelling for a determination that the death was caused by multidrug intoxication. Note that the diazepam is appropriately listed as a cause of death because it contributed to the respiratory depression, even though, taken in isolation, diazepam is unlikely to cause a fatality.

When possible, the specific type of drug should be identified. For example, in the case described above, the cause of death statement should be written as “Acute intoxication by oxycodone and diazepam.” Also, in the “How Injury Occurred” section of the death certificate, if known, the route of administration should be specified. In the above case, such a statement might read “Ingested diazepam and injected oxycodone intravenously.”

Case 2: Single Drug Use in a Non-Tolerant Individual. A 45-year-old woman is found dead in bed. She has no history of a substance use disorder but has been treated for years with various opioid analgesics for fibromyalgia. Her physician prescribed methadone 4 days earlier. Autopsy reveals a methadone concentration that would be toxic to a non-tolerant individual, but no other evidence of injury or disease.

Cause of Death, Part I: Acute intoxication by methadone

Cause of Death, Part II: History of chronic pain

How Injury Occurred: Ingested methadone

Drug-Caused Death: Yes

Drug Poisoning Death: Yes

Drug-Detected Death: Yes

Comment: In this case, the death was solely due to drug intoxication in an individual who was not tolerant to the drug’s effects.¹⁷

Case 3: Homicide with a History of Drug Use. Police are called to a known drug-dealing location because of the sound of gunshots. When they arrive, they find a 22-year-old man with multiple gunshot wounds to the head. He is pronounced dead at the scene. Multiple witnesses confirm that the decedent was selling cocaine at the time he was shot. Autopsy reveals two contact entrance gunshot wounds to the back of the head, with perforations of the brain and exit wounds of the forehead. Toxicologic analysis reveals a lethal concentration of a drug.

Cause of Death, Part I: Gunshot wounds to the head

Cause of Death, Part II: None

How Injury Occurred: Shot with [type of weapon] by other(s) while selling cocaine.

Drug-Caused Death: No

Drug Poisoning Death: No

Drug-Detected Death: Yes

Comment: The gunshot wounds are clearly lethal injuries that would cause death, irrespective of any drug intoxication. The individual had the drug in his system at a potentially lethal concentration, but an independent intervening process caused his death. Thus, the drug should not be included in the cause of death statement.

However, the presence of the drug may be significant circumstantially in explaining why the individual was in the situation where he was shot, as well as for the collection of statistics concerning illicit controlled drug use in that jurisdiction. This demonstrates the importance of identifying drug-detected deaths, even though the drug did not itself cause or contribute pathophysiologically to the death.¹⁸

Case 4: Drug Poisoning with a Contributing Medical Condition. A 52-year-old man with a history of high blood pressure smoked crack cocaine. Shortly after doing so, he complained of severe headache, collapsed, and died. Toxicology indicated acute cocaine intoxication and presence of alcohol and alprazolam. Autopsy indicated hemorrhage in the brain in a location typical of hypertensive hemorrhages.

Cause of Death, Part I: (Line A) Intracerebral hemorrhage

(Line B) Due to acute cocaine toxicity

Cause of Death, Part II (Other Significant Conditions): Hypertension

How Injury Occurred: Smoked crack cocaine, thereby exacerbating underlying hypertension

Comment: Typically, even if underlying natural disease is significant, if an acute intoxication exacerbates that disease and causes about death, preference is given to the non-natural manner of death (in this case, accidental). The hypertension is a preexisting or coexisting condition that contributed to death but did not contribute to the underlying cause of death. Therefore, it is reported in Part II. Note that multiple drugs were found on toxicology, but only cocaine toxicity is listed as a cause of death.¹⁹ The alprazolam likely did not contribute the death.

CONCLUSIONS

Comparison of data from various epidemiologic databases and studies of opioid-related deaths is made more difficult by the fact that medical examiners, coroners, and others do not use uniform terminology and standards for defining and classifying cause of death. Accordingly, the SAMHSA convened an Expert Panel to review the literature and any extant guidelines and to use that information to develop uniform standards for case definitions and classification of opioid-related deaths. Concise, scientifically accurately, universally accepted case definitions like those presented here can address the critical distinction between deaths caused by methadone and deaths in which methadone is a contributing factor or merely present. Adoption of more uniform standards will improve the quality of data on which health professionals, policymakers, and the public must depend on in identifying and developing solutions to public health problems such as the apparent increase in opioid-related deaths.

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Appendix B. Recommended Terminology

(Note: The term *drug* is used in these definitions to include any drug, medication, or chemical substance to which an individual is exposed by ingestion, injection, inhalation, instil-

lation, or absorption through a mucosal or body surface.)

Medical Examiner and Coroner

Medical Examiner (ME): The government entity responsible for medicolegal death investigations, usually involving deaths that are violent (i.e., caused by any type of injury, including chemical injury) or are sudden and unexplained. In conjunction with investigation and medical examination, the ME certifies deaths (i.e., issues death certificates containing cause and manner of death). MEs are professionally trained forensic pathologists and are appointed positions.

Coroner: The original system of death investigation in the United States, derived from the English system. In the United States, coroners generally are elected or appointed officials, with widely varying qualifications. If not physicians, they must use coroners' physicians to perform autopsies. They typically have the same jurisdiction as defined above for medical examiners; some coroners still retain the power to hold inquests, which are quasi-judicial proceedings.

Drug Effects

Intoxication and Toxicity: In death certification and toxicology, the two terms can be used synonymously to refer to the harmful, noxious, or deleterious effects of a drug or the condition of having/experiencing such effects. This is frequently used to imply the effects of excessive concentration or dose of a drug, although this is not required. Intoxication or toxicity may or may not be fatal.

Intoxication: Dysfunctional changes in physiological functioning, psychological functioning, mood state, cognitive processes, or all of these, as a consequence of consumption of a psychoactive substance; usually disruptive, and often stemming from central nervous system impairment (DSM-IV).

Drug Poisoning

Strictly defined, poisoning means intoxication/toxicity. However, in common parlance it is used to mean intentional administration of a

substance only meant to cause harm or death, without a legitimate pharmacologic or recreational purpose.

Poisoning deaths include those resulting from drug overdose, those resulting from other misuse of drugs, and those associated with solid or liquid biologic substances, gases or vapors, or other substances such as pesticides or unspecified chemicals.

Poisoning subsets can be identified by intent:

Unintentional drug poisoning: (1) an “accidental” overdose of a drug, a wrong drug given or taken in error, or a drug taken inadvertently; (2) accidents involving the use of drugs, medications, and biological substances in medical and surgical procedures; or (3) poisoning, when not specified whether accidental or with intent to harm.

Intentional drug poisoning: (1) poisoning or injury intended to self-harm; or (2) suicide or attempted suicide.

Assault: homicide; injuries inflicted by another person with intent to injure or kill (including homicidal poisoning).

Adverse Drug Reaction: “Any noxious or unintended reaction to a drug that is administered in standard doses by the proper route for the purpose of prophylaxis, diagnosis, or treatment” (Vervloet & Durham, 1998).

Side Effect: An outdated term meaning any unintended response to a drug (i.e., not the desired therapeutic effect); currently, the preferred term is “adverse drug effect.”

Overdose (OD): Common term for intoxication/toxicity, not necessarily fatal. Not recommended for use in death certification.

Narcotism: Chronic abuse of opioids for other than therapeutic purposes and the systemic effects thereof. (Historically, this term was used to describe chronic intravenous heroin abuse. Today, it is outdated and its use is discouraged, but it is seen occasionally and even is imprecisely generalized to mean any substance use disorder.)

Multidrug/Polypharmacy: Literally, the prescription, administration, and use or abuse of multiple drugs. Generally used as an inclusive descriptor of an intoxication caused by multiple

drugs in which there are too many to list conveniently in a cause of death statement or where it is unclear which of the drugs detected actually contributed to death, as in “Multidrug Intoxication” or “Complications of Polypharmacy.” Use of these imprecise and non-specific terms is discouraged because it limits the ability to track specific drugs and emerging patterns of abuse because not all of the drugs identified in the body will be reported. Whenever practical, drugs judged to have exerted a significant effect based on concentrations detected, mechanisms of actions, and drug-drug interactions should be specified.

Death Certification

Cause of Death: The etiologically specific process (disease or injury) that sets in motion an uninterrupted causal sequence of events culminating in the death of an individual. (The “true” cause of death is the proximate or underlying process; the chain of events initiated by this cause cannot be interrupted by an etiologically independent, intervening cause that supersedes the first process.)

Manner of Death: The (circumstantial) explanation for how the death came about. The choices available on the death certificate are:

Natural: A death caused entirely by natural disease, without any contribution of injury;

Accidental: An unexpected/unforeseen death due to injury; referred to as “unintentional injury” in the International Classification of Diseases and vital statistics.

Homicide: A death caused by the act of another person, either through commission or omission;

Suicide: A death in which the individual intentionally caused himself or herself injury, with the intent to result in death;

Pending investigation: An indefinite classification. If the manner of death is under investigation, the death certificate can be certified as “manner of death pending investigation.”

Could not be determined: A death in which available information is not sufficient to distinguish among accident, self-harm, or assault. Also referred to as an injury of “undetermined intent.”

Mechanism of Death: An etiologically non-specific disorder of anatomy or physiology that is inconsistent with life. In contrast to a proximate cause of death, a mechanism is an immediate cause (i.e., the last step in the sequence of events culminating in death).

Death Certificate: An official document that contains rulings on both the cause and manner of death. The standard death certificate format in the United States provides for the primary cause of death to be entered in a reverse chronological sequence, such that the sequence of events leading to death may be described from the most immediate to the underlying, or proximate, cause, which always should be the “bottom line,” both literally and figuratively.

Part I is used to report a chain of events leading directly to death, with the immediate cause of death (the final disease, injury, or complication directly causing death) on Line A and the underlying cause of death (the disease or injury that initiated the chain of events that led directly and inevitably to death) on the lowest used line.

Part II is used to report all other significant diseases, conditions, or injuries that contributed to death but which did not result in the underlying cause of death given in Part I. The cause-of-death information should represent the certifier’s best medical opinion. A condition can be listed as “probable” even if it has not been definitively diagnosed.

Other Significant Condition: A pre-existing or coexisting condition that contributed to a death but did not lead to the underlying cause of death. Such conditions are included among contributing causes of death when death certificates are coded.

How the Injury Occurred: The section of the death certificate in which the certifier provides a textual description of how the fatal injury occurred, such as “Hanged self with rope” or “Shot by another person(s).”

Appendix C. Sources of Additional Information

Reference Works

DiMaio VJM, Dana SE. Handbook of forensic toxicology, 2nd edition. New York: Taylor & Francis Group, 2007.

Hanzlick R. Death investigation: systems and procedures. Boca Raton: CRC Press, 2007.

Molina DK. Handbook of forensic toxicology for medical examiners: practical aspects of criminal & forensic investigations. Boca Raton: CRC Press, 2009.

National Center for Health Statistics. Medical examiners’ and coroners’ handbook on death registration. Washington, DC: U.S. Department of Health and Human Services, 2003.

Vervloet D, Durham S. Adverse reactions to drugs. *BMJ* 1998; 316 (7143):1514–4.

Web Sites

American Academy of Forensic Sciences: www.aafs.org

American Board of Medicolegal Death Investigators: www.slu.edu/organizations/abmdi/

American Board of Pathology: www.abpath.org
Centers for Disease Control and Prevention—Death Investigation Information: www.cdc.gov/epo/dphsi/mecisp/index.htm

College of American Pathologists: www.cap.org
Coordinating Office for Medical Examiner/Coroner Activities: www.fcmeo.org/COMECA.htm

International Association of Coroners and Medical Examiners: www.theiacme.com/

National Association of Medical Examiners: www.TheNAME.org

National Center for Health Statistics: www.cdc.gov/nchs

Network on Death Investigation Affairs: www.TheNAME.org (click on NODIA on menu bar)