

Obtaining Adequate Data to Determine Causes of Opioid-Related Overdose Deaths

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Abstract

Current data collected by medical examiners and coroners are incomplete and inadequate to evaluate the factors that lead to fatalities involving prescription opioids. Determining cause of death is critically important. Two methods are proposed to improve consistency and accuracy in the collection and analysis of decedent data in opioid-related poisoning deaths. First, an improved death certificate is needed to collect evaluative data, including: extent to which opioids were judged to 1) cause, 2) contribute to, or 3) be present in investigated deaths; extent to which opioids as a cause of death were found 1) alone, 2) combined with other prescription drugs, 3) combined with alcohol, or 4) combined with illicit drugs; the time of death; the presence or absence of a valid prescription; and the estimated quantity of opioids taken proximal to death. Patient characteristics for analysis include age, gender, race/ethnicity, geographic area (particularly whether urban or rural), body mass index, duration of opioid usage and daily average dose during the last 2 weeks of life, and histories of chronic pain/medical conditions, substance abuse, and mental illness/psychiatric diagnoses. Second, expanding the scope of opioid toxicology categories used to classify and code cause-of-death data reported by death investigators would improve identification of individual drugs and classes most often associated with overdose deaths. Formulation-specific codes should be added to facilitate consistent recording of

findings by death investigators and entry into national vital statistics databases.

Key Words. Opioids; Overdose Deaths; Medical Examiner; Mortality; Death Investigations; ICD Codes

Introduction

To reverse the trend of annually increasing poisoning deaths associated with prescription opioids, it is necessary to systematically collect and study those factors involved in the deaths. However, inconsistent data collection, reporting, and cataloging methods employed by medical examiners and coroners (MEs/Cs) nationwide impede this goal.

Consider, for example, that people who overdose on opioids and subsequently die may be nonmedical users who consume toxic amounts of opioids in the absence of medical need, or they may be medical patients who consume toxic amounts of opioids in an effort to escape pain, self-treat a comorbid condition, or follow inappropriate prescribing directions. This type of information is critical because nationally proposed interventions will vary dramatically depending on the motives for overuse (see, for example, articles within this supplement that address motives stemming from psychiatric or personality disorders [1] and suicidality [2]).

In addition, collection methods fail to illuminate the specific drugs, classes of drugs, and important related issues involved with the death. As a result, many recorded causes of death reflect only medical opinion. Currently, proposed interventions—even regulations and laws—are based on national vital statistic reports on causation of overdose deaths, a situation that calls for caution until better data are available to inform such decisions.

We propose two methods to improve consistency and accuracy in the collection and analysis of decedent data in opioid-related poisoning deaths. First, improving the death certificate would assist in collecting discrete data relevant to analyzing the deaths. Second, expanding the opioid toxicology categories used to classify and code cause-of-death data reported by death investigators would improve identification of individual drugs, formulations, and classes most often associated with overdose deaths.

To obtain better information to study root causes, we must first acknowledge that the data are collected for administrative purposes; despite our reliance upon it, the system is not designed to collect research grade data. Coroners at the local level may not be trained to assess all the dimensions needed for meaningful overdose assessment. Shrinking state budgets may result in fewer autopsies and less thorough toxicology panels. The next generation of toxicology coding must be designed with these circumstances in mind, offering a flexible system that allows for hierarchically more detailed data when available but that acknowledges the limited resources of available personnel time and materials. While overdoses present a serious public health problem, in making the case for better overdose reporting, we recognize that we are competing with other diseases for the limited time of under-resourced MEs/Cs, nosologists, and state health department statisticians. It is within this context that we propose plausible solutions to collect better data and, it is hoped, to help save lives.

Current Data Collection

It bears closer examination how death certificate data arise, although each state has a slightly different process. In general, each US death triggers a registration of the death and is subsequently appended with a death certificate listing the cause(s) of death. This pair of documents provides the starting point for research on patterns of causation among overdose deaths. The initial registration of death is a mandated administrative task for the purposes of collecting vital statistics; determination of the cause of death may be done by local MEs/Cs, attending physicians, or state medical examiners, with a few state-specific exceptions. Findings of autopsies and other investigation may take months before the cause(s) of death can be determined. In many states, this process is still conducted using paper forms and records. Once the cause(s) of death has been determined, the death record is then appended with the literal line mention (i.e., the words used to describe the cause of death), which may occur many months after the issuance of the original certification of death. The literal line listings and death records are submitted by medical examiners to state vital statistics agencies, whereupon the literal cause listings are converted by nosologists to codes using the International Classification of Diseases, 10th Revision (ICD-10) [3]. State vital statistics offices, in turn, send their data to the National Center for Health Statistics at the Centers for Disease Control and Prevention (CDC). This process can take up to 4 years with timeliness often dependent on whether electronic record keeping is available.

Death certificates have the potential to help researchers understand the causes of overdose. However, while a determination of cause is made for each individual death, in aggregate, the information collected is insufficient to aid in understanding the root causes of many opioid-related overdose deaths. The US Substance Abuse and Mental Health Services Administration (SAMHSA) called attention to this problem by identifying barriers to the analysis of

methadone mortality, including the lack of common toxicological nomenclature and standards in death reporting [4]. A standardized form to facilitate greater consistency in collection and analysis by death investigators could greatly ease the study of opioid-decedent data and assist in finding solutions.

Proposal to Expand Death Certificate Data

The Opioid Treatment Program Mortality Report Form published by the SAMHSA [5] was reviewed with the goals of adapting its format and adding data points needed to analyze opioid-related overdose poisoning deaths. The result is the document in Table 1, which is presented as a proposal for a standardized form to facilitate the collection of greater detail in deaths due to overdose. Once the data are collected, the CDC can then record the results with enough detail to allow epidemiologists and researchers to better analyze factors giving rise to harm from therapeutic opioids.

In the absence of such a standardized form, the current methods to systematically study opioid-decedent data pose several difficulties. First, it is difficult to determine a cause of death from postmortem opioid blood levels alone. Postmortem blood concentrations of methadone vary widely [6], and heroin decedents are likely to have morphine levels no higher than those who survive [7]. Furthermore, lethal levels of opioids may vary depending on a decedent's degree of opioid tolerance, the rapidity of drug metabolism, the severity of chronic pain, and the action of polydrug combinations, among other factors. Opioid-poisoning decedents frequently have ingested multiple substances whose individual or collective contributions to the death are unclear. Also, bias may exist toward assigning an opioid as the cause of death whenever it is present in a toxicology report.

The analysis of death data is further complicated in that serum levels of opioids typically reported as a cause of death may actually be therapeutic in some chronic pain patients on long-term therapy [6]. Deaths may be connected to a patient's dosing schedule (including time of the last dose of the day in relation to the onset of sleep); the presence of sleep apnea; the degree of adherence to medical direction, particularly whether prescribed doses have been escalated; and the presence and timing of use of alcohol or central nervous system-depressant medications such as benzodiazepines.

To help researchers gain greater insight into preventative measures to reduce opioid-related mortality, several pieces of information are necessary. Some of these points of information can be denoted using existing ICD-10 codes but others would require novel data collection. Death investigators are asked to consider collecting specific data points, including:

- Extent to which one or more opioids were judged to 1) cause death, 2) contribute to death, or 3) be present in the decedent.

Table 1 Proposal for standardized form to collect drug-related decedent data

Prescription Overdose Mortality Report

Note: This form will assist in the regulatory agency review of patients who die from prescription drug-related overdoses. The goal is to standardize reporting to better understand the factors contributing to overdose. **Please print all information clearly.**

A. Background Information

Date of Birth: ____/____/____ **Date of Report:** ____/____/____
Sex: Female ____ Male ____ **Date of Death:** ____/____/____ (e.g., mm/dd/yyyy)
Face/ethnicity: _____ **ZIP Code of Death:** _____
Presence of Sleep Apnea: _____ **Time of Death:** _____
 Yes ____ No ____ Unknown ____ **BMI:** ____ lbs.
Height: ____ ft. ____ in.

Health Insurance: Yes ____ No ____ **If yes, what kind:** Medicaid ____
 Medicare ____ Commercial ____ Workers' Comp ____ Other ____

B. Description of Event (detailed description of the factors related to the patient's death, including where the death occurred, if others were involved, how the death was discovered, if decedent was previously familiar with the setting of death). If more space is needed, use a continuation sheet, as described in the general instructions accompanying this form.

C. Immediate Cause of Death: _____

Underlying Cause(s) of Death: _____

D. Manner of Death: (Check one) Accident ____ Suicide ____ Homicide ____
 Natural ____ Indeterminate ____ Pending ____

E. List of Known Over-the-Counter and Prescription Medications at the Time of Last Visit:

F. Formulation of Prescriptions (e.g., tablets, liquids, patch, controlled release, immediate release):

H. Amount of Prescription Remaining at Time of Death:

J. Source of Opioid:
 Legitimate Prescription ____ Theft ____ Forgery ____ Obtained from Family or Friend ____ Other ____

L. Specialty of Prescribing Physician: _____

G. Amount of Last Prescription: _____
Date of Last Prescription: ____/____/____
I. Prescription Frequency Instruction (e.g., twice daily, three times daily)
K. Reason for Use (Check all that apply)
 Pain ____ Recreation ____ Anxiety ____ Other ____
Reason Obtained From
 Family/Physician/Other _____

M. Awareness of Risk by Relatives and Friends: Yes ____ No ____

N. Blood Levels of All Concomitant Medications (particularly benzodiazepines and sleep aids):

O. Extent to Which Opioids Were Found:

- 1) Alone _____
- 2) Combined with Other Prescription Drugs _____
- 3) Combined with Alcohol _____
- 4) Combined with Street Drugs _____

P. Enrollment in Prescription Monitoring Program: Yes ____ No ____
 If yes, number of providers prescribing scheduled medication: _____

Number of pharmacies filling scheduled medication: _____

Q. History of Substance Abuse:

Yes ___ No ___

If yes, what type (check all that apply):

Alcohol ___ Cocaine ___ Heroin ___

Methamphetamine ___ Prescription Opioids ___ Other _____

Substance Abuse Treatment:

Yes ___ No ___

If yes, what type most recently:

Hospital ___ Outpatient Program ___ Inpatient Resident ___ Office Based ___ Oral substitution therapy ___ Other _____

Days since release or termination of treatment _____

R. History of Mental Illness/Psychiatric Problems: Yes ___ No ___

If yes, what diagnosis (e.g., depression, bipolar disorder, generalized anxiety disorder, attention deficit disorder): _____

History of Mental Health Treatment: Inpatient ___ Outpatient _____

<6 months ___ 0.5-1 years ___ 1-3 years ___ 3-5 years ___ 5-10 years ___ >10 years ___

S. History of Chronic Pain (medical conditions, surgeries, and accidents)

Pain type: Neuropathic ___ Nociceptive ___ Functional ___ Inflammatory ___

Mixed _____

Severity: Mild ___ Moderate ___ Moderate-to-Severe ___ Severe ___

Location: Spine ___ Muscle ___
Nerve ___ Abdomen ___ Extremities _____

T. Other Relevant Medical History (for example, allergies, pregnancy, preexisting medical conditions): _____

U. Recent Release from Prison, Jail, or Other Detention: Yes ___ No ___

If yes, days since release: _____

V. Medical Examiner's/Coroner's Contact Information (if known): _____

BMI, body mass index.

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- Extent to which an opioid as a cause of death was found 1) alone, 2) combined with other prescription drugs, including benzodiazepines, 3) combined with alcohol, or 4) combined with illicit drugs.
- The time the death occurred.
- Whether or not the decedent had a valid prescription for all medications ingested.
- The fill date of each prescription and amount of prescribed opioid remaining at the time of death.
- The opioid milligrams taken (as nearly as can be determined from prescription data or interviews with family and friends).
- The amount and timing of ingestion of concomitant medications.
- Blood levels of concomitant medications, particularly benzodiazepines.
- Whether the decedent had health insurance and, if so, what type.

This last piece of data could help analyze whether or not cost issues are driving opioid choices.

Patient characteristics for analysis include those on the following list. Many MEs/Cs already collect some of these data. Our request would be for greater detail pertaining to relevant factors such as mental health and substance use disorders and for database handlers of vital statistics to ensure that pertinent variables such as body mass index (BMI) are recorded.

- Age
- Gender
- Race/ethnicity
- Geographic area (particularly whether urban or rural)
- History of chronic pain/medical conditions
- History of substance abuse
- History of mental illness/psychiatric problems
- BMI
- Experience with opioids to determine whether the patient was opioid tolerant or naïve.
- Duration of experience with opioids and average daily use during last 2 weeks of life (by known history or best estimate by prescription use data)

Proposal to Expand Opioid Toxicology Codes

Once more detailed information is collected and reported on death certificates, it should be classified more specifically than in the past by the CDC. The current ICD codes group together drugs and drug classes and do not specify individual drugs or formulations. This creates a significant limitation to understanding the frequency with which any specific drug or formulation is associated with deaths. Most postmortem toxicology reports are unclear whether an opioid death involving oxycodone, for example, is due to a modified-release formulation, an immediate-release formulation, or both. Because of the lack of specificity, an oxycodone-related death could have an underlying cause of death coded F19, X42, or Y14 with T40.2, T40.6, T50.9 listed as contributing causes of death (Table 2) [3]. The Food and Drug Administration (FDA) proposes to reduce

Table 2 Current potential International Classification of Diseases, 10th Revision codes used in opioid-related deaths [3]

Code	Description
F19._	Mental and behavioral disorders due to multiple drug use and use of other psychoactive substances
T40.2	Poisoning by other opioids (includes morphine and codeine)
T40.3	Poisoning by methadone
T40.4	Poisoning by other synthetic narcotics
T40.6	Poisoning by other and unspecified narcotics
T42.4	Poisoning by benzodiazepines
T43.0	Poisoning by tricyclic and tetracyclic antidepressants
T43.2	Poisoning by other and unspecified antidepressants
T43.6	Poisoning by psychostimulants with abuse potential
T50.9	Poisoning by other and unspecified drugs, medicaments, and biological substances
X41	Accidental poisoning by and exposure to antiepileptic, sedative-hypnotic, antiparkinsonism, and psychotropic drugs, NEC
X42	Accidental poisoning by and exposure to narcotics and psychodysleptics (hallucinogens), NEC
X44	Accidental poisoning by and exposure to other and unspecified drugs, medicaments, and biological substances
X64	Intentional self-poisoning by and exposure to other and unspecified drugs, medicaments, and biological substances
Y12	Poisoning by and exposure to narcotics and psychodysleptics (hallucinogens) NEC, undetermined intent
Y14	Poisoning by and exposure to other and unspecified drugs, medicaments, and biological substances, undetermined intent

NEC, not elsewhere classified.

harm from modified-release opioid formulations [8], but the goal is impeded by the difficulty, using current death certificates and ICD coding, of discerning which formulation of a particular opioid is responsible for toxicity. Interestingly, the CDC recently added a whole set of new ICD codes for deaths from *terrorism*, which occupies a far smaller data set than overdose deaths, suggesting a willingness to adopt new codes, given ample political will [9].

Another avoidable ambiguity is that ICD codes mix legal and illegal drugs together, making it impossible to attribute causation with any clarity. Intent, whether unintentional overdose or suicide, is also difficult to determine under the current coding system.

That said, the existing ICD-10 coding schema contain enough flexibility to improve coding deaths. For example, ICD-10 codes have enough specificity to differentiate if a drug abuser who died of an overdose was taking opioids long term (i.e., “addict” using F11.2) in contrast to drug taking that was occasional (i.e., “abusers” using F11.0). However, F-codes of this level of specificity are rarely used in the United States. Fundamentally, codes exist within ICD-10 to make many important distinctions, but they are buried deep within the coding structure. MEs/Cs and nosologists may not be aware of them, may not have time to collect the information, or may lack the directives, mandates, or resources to accomplish this in-depth investigation. Furthermore, ambiguous standards for these definitions render the codes unrealistic and the process is unwieldy for busy MEs/Cs to complete in a timely manner.

An expanded, more “user friendly” ICD coding system could help address these deficiencies. Additional codes should allow for formulation classification so that if actual products are miscoded during death investigations, the type of formulation associated with a death still can be examined. To mitigate against single-drug miscodings leading to potentially specious conclusions (and to avoid the necessity of upgrading coding systems every time a new product is released), a prudent categorical approach might be a series of codes that identify variables such as long-acting vs short-acting formulations, oral vs transdermal delivery systems, and so forth. Finally, caution is advised in adding new codes in the absence of the type of accurate decedent-specific data outlined in Table 1. The absence of such data along with a proliferation of drug-specific codes may render accurate analysis more difficult still.

Conclusion

The continued value of opioids as potentially beneficial rather than excessively harmful treatments for chronic pain depends on clarifying the conditions under which they contribute to a rising number of overdose deaths. The contribution of death investigators nationwide will be fundamental in providing some answers. The goals are to reduce the number of preventable deaths and to improve patient safety. For this to occur, we need better data reported to the CDC through an expanded death certificate and ICD codes that allow insight and analysis of the drugs and formulations contributing to the overdoses. With these changes, the FDA and other interested stakeholders could use these data as one measure of effectiveness of new risk management strategies.

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Disclosures

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During the past 3 years, Nabarun Dasgupta, MPH, has served as a consultant for Covidien, Cephalon, King, Neuromed and Reckitt Benckiser; and on the advisory boards for Covidien and King.

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