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An Investigation of Medical Examiner Cases in Which Methadone Was Detected, Harris County, Texas, 1987–1992

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ABSTRACT: In 1991, media reports of an increase in the number of deaths attributed to methadone toxicity in Harris County, Texas, raised public concern about the safety of methadone. This concern was heightened by publicity surrounding the closure of three Harris County methadone maintenance treatment programs due to their poor compliance with federal methadone regulations. In response to this concern, the Texas Department of Public Health requested that the Centers for Disease Control and Prevention (CDC) assist in an epidemiologic study to determine the extent of methadone-related mortality in Harris County during 1991 and to determine the role of methadone maintenance treatment in these deaths.

We reviewed cases investigated by the Harris County Medical Examiner's Office from 1987 through 1992 in which methadone was detected by postmortem drug testing. The autopsy reports for cases occurring in 1991 were also reviewed by three independent forensic pathologists who were asked to determine the role of methadone in the death. In addition, we attempted to document Harris County methadone maintenance treatment program enrollment for each decedent.

We identified 91 decedents in whom methadone was detected at the time of death, with the largest number of cases occurring in 1991 (n = 27). Other substances, including alcohol, were detected in 85% of the cases. The Harris County Medical Examiner attributed 11 of the deaths to methadone toxicity. No more than three cases per year from 1987 through 1992 were attributed to methadone toxicity. In contrast, 34 deaths were attributed to polydrug toxicity, the largest number occurring in 1991 (n = 11). There was good agreement between the results of the independent review and the opinions of the Harris County Medical Examiner. Only 20% of the decedents were found to have been enrolled in a Harris County methadone maintenance treatment program at the time of death. Four people died of drug toxicity shortly after enrolling in a methadone maintenance treatment program.

We found an increase in the number deaths occurring in Harris County, Texas, in 1991 in which methadone was detected. We also found that methadone blood levels were higher among decedents identified for 1991 and 1992 than among those identified in the previous years studied. However, we did not find evidence that the cause of these deaths could be attributed solely to methadone toxicity. Instead, for all years studied, the use of multiple drugs was the leading cause of death among people in whom methadone was detected. This finding points out the difficulties involved in determining the role of methadone as a cause of death.

KEYWORDS: forensic science, methadone, mortality, death, drug abuse, opiate abuse, forensic pathology, forensic toxicology

Methadone maintenance treatment of opiate addiction reduces illicit drug use, lowers mortality rates, and reduces the spread of human immunodeficiency virus among intravenous opiate users (1–7). However, concerns about the safety of methadone persist. Most often cited is concern that methadone may be illegally diverted from treatment programs for recreational use, with potentially fatal results (8).

Several studies of deaths attributed to methadone toxicity illustrate the difficulty in establishing the role of methadone as a cause of death (8–14). In most instances involving methadone toxicity, death results from gradual central nervous system and respiratory depression and is often accompanied by nonspecific pathologic and autopsy findings (9,11–13,15). In addition to methadone, other substances, especially benzodiazepines and alcohol, are commonly found on postmortem drug testing. These findings, along with individual variations in opiate tolerance, often make postmortem blood methadone levels difficult to interpret (16).

Other studies have documented the deaths of patients shortly after their enrollment in methadone maintenance treatment (8,11). This finding suggests that patients are at particularly high risk for fatal methadone toxicity during the induction phase of treatment (that is, during the initial treatment when the methadone dose is increased gradually to a therapeutic maintenance dose) (8,11). During the induction phase, blood methadone level can rise rapidly; death may result if the patient has not developed a sufficient tolerance to the toxic effects of opiates (15,17).

In Texas, concerns about the safety of methadone maintenance treatment were fueled by media reports of an increase in the number of deaths attributed to methadone toxicity in Harris County during 1991. This concern was heightened by publicity surrounding the closure of three Harris County methadone maintenance treatment programs (MMTPs) in 1992 due to their poor compliance with federal methadone regulations (18–22). An investigation conducted by the National Institute on Drug Abuse (NIDA) of the 1991 Harris County Medical Examiner death records identified 25 decedents

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who had methadone detected by postmortem toxicologic testing. This study could not determine the role of methadone in causing these deaths and suggested that further studies be done to determine whether the decedents were enrolled in MMTPs.

The objectives of our investigation were to 1) determine whether the number of deaths attributed to methadone toxicity in Harris County, Texas, in 1991 was different from such deaths in previous or subsequent years; 2) determine the role of methadone in the cause of death; and 3) determine whether the deaths were associated with enrollment in a MMTP. Because computerized toxicologic records were available from the Harris County Medical Examiner for calendar years 1987 through 1992, we investigated deaths in those years.

Methods

Harris County, Texas, is a large metropolitan county (1990 population = 2,818,199) that includes the city of Houston and surrounding areas. Medical examiners at the Joseph A. Jachimczyk Forensic Center investigate deaths occurring in Harris County. We defined a "methadone-detected" medical examiner case as a death investigated by the Harris County Medical Examiner (ME) from January 1, 1987 through December 31, 1992, in which methadone was detected by postmortem drug testing in any body fluid or stomach contents. We identified methadone-detected cases from computerized toxicologic records maintained at the Joseph A. Jachimczyk Forensic Center. For each methadone-detected case we abstracted demographic information, pathologic diagnoses, circumstances and cause of death, and toxicologic findings from the investigation and autopsy report. Quantitative methadone levels were not available for all decedents. In some cases, the toxicology report only indicated that the sample was "positive" for methadone or that a "trace" amount of methadone was found. In some cases the result of the blood test was negative for methadone, but methadone was detected in another body fluid.

We grouped the methadone-detected cases by cause of death (as determined by the Harris County ME) into three categories: natural, trauma-related, and toxicity-related. We subdivided the toxicity-related category into three subcategories: methadone toxicity, polydrug toxicity, and "other" toxicity. We considered a death to be caused by methadone toxicity if the Harris County ME had listed methadone toxicity as the cause of death on the autopsy report. Cases where methadone and at least one other substance (including alcohol) were listed as the cause of death were categorized as polydrug toxicity deaths. The "other" toxicity category included deaths attributed to a single substance other than methadone. We included deaths attributed to carbon monoxide poisoning in this "other" toxicity category.

We categorized blood methadone levels into five groups: 1) $<$ 0.02 mg/dL, 2) 0.02 mg/dL to $<$ 0.06 mg/dL, 3) 0.06 mg/dL to $<$ 0.10 mg/dL, 4) $\geq$ 0.10 mg/dL, and 5) undetected blood methadone. Blood methadone results reported as "positive" or "trace" were placed in the $<$ 0.02 mg/dL group. "Negative" blood methadone results were categorized as "Undetected Blood Methadone." Drugs other than methadone were categorized only as present or absent.

To obtain an independent assessment of the role of methadone in the cause of death, we conducted an independent review of the 1991 methadone-detected cases. We provided three board-certified forensic pathologists with the autopsy report, toxicologic data, and a summary of the investigation for each case. The pathologists were asked to determine the likelihood that methadone toxicity caused or contributed to death using the following categories:

A. Definitely the primary cause of death;
B. Definitely a contributory cause of death;
C. Probably the primary cause of death;
D. Probably a contributory cause of death;
E. Possibly a contributory cause;
F. Probably not a contributory cause; or
G. Definitely not a contributory cause.

The pathologists were asked to assign each case to only one category; they used their own criteria for determining the role of methadone toxicity in each death.

We analyzed the results of the independent autopsy review by collapsing the above categories into three groups: 1) methadone was the primary cause of death (Categories A and C); 2) methadone was a contributing cause of death (Categories B, D, and E); and 3) methadone was unrelated to death (Categories F and G). We assigned a case to one of these three groups only if it had been placed in that group by at least two of the three reviewers.

We then compared the cause of death as determined by the Harris County ME with the conclusions of the independent review, using the three classifications described above. That is, for the Harris County ME opinions, a death was defined as being primarily caused by methadone toxicity if methadone toxicity was listed as the cause of death. Methadone was considered a contributing cause of death if toxicity from more than one substance was listed as the cause of death (polydrug toxicity). All other causes of death were classified as being unrelated to methadone.

To ascertain which of the decedents in whom methadone was detected had been enrolled in methadone maintenance treatment, we provided the 18 MMTPs operating in Harris County at the time of this investigation with a list of the methadone-detected cases. We asked each MMTP to identify decedents who had ever been enrolled in their treatment program and to provide the dates of treatment. We were unable to obtain data from three Harris County MMTPs that were closed in 1992.

Results

Harris County ME Data

We identified 91 deaths investigated by the Harris County ME from January 1987 through December 1992 in which methadone was detected by postmortem drug testing. The decedents were predominantly male (77%) and white (85%). Their ages ranged from 19 to 65 years (median = 35 years). The greatest number of decedents in whom methadone had been detected occurred in 1991, with 27 decedents identified in that year (Table 1).

There were slight increases in the number of views and autopsies performed and in the number of drug screens conducted by the Harris County ME during the years investigated (Table 1). The percentage of decedents screened for drugs ranged from 63% in 1987 to 72% in 1989. In all years studied, the percentage of drug screens testing positive for methadone was 1% or less.

Table 2 shows the causes of death, as determined by the Harris County ME, for the 91 methadone-detected cases. Toxicity-related causes of death were listed most frequently, accounting for 59% of the deaths. Polydrug toxicity was listed as the cause of death for 37% of the decedents, whereas methadone toxicity was listed for 11% of the decedents. Deaths were determined to be the result of natural causes for 22% of the decedents and the result of trauma for 19% of the decedents.

Among these decedents, the number of methadone toxicity cases was relatively constant for each of the years studied,

TABLE 1—*Total number of decedents examined, number of drug screens performed, and number of decedents in whom methadone was detected by the Joseph A. Jachimczyk Forensic Center, Harris County, Texas, January 1, 1987–December 31, 1992.*

Year	Total decedents*	Total drug screens	Percentage of decedents screened	Methadone-detected deaths	Percentage of total drug screens positive for methadone
1987	3254	2046	62.9	14	0.68
1988	3647	2513	68.9	6	0.24
1989	3672	2650	72.2	14	0.53
1990	3882	2685	69.2	20	0.74
1991	3981	2640	66.3	27	1.02
1992	3668	2458	67.0	10	0.41
Total	22,104	14,992	67.8	91	0.60

*Figures for total decedents represent number of autopsies and views performed at the Joseph A. Jachimczyk Forensic Center by year.

TABLE 2—*Distribution of decedents in whom methadone was detected by year of death and primary cause of death as determined by the Harris County Medical Examiner, Harris County, Texas, January 1, 1987–December 31, 1992*

Primary cause of death	Year						Total	
	1987	1988	1989	1990	1991	1992	Number	Percentage
Toxicity								
Polydrug toxicity*	8	1	2	9	11	3	34	37.4
Methadone toxicity	1	0	2	3	2	3	11	11.1
Cocaine toxicity	0	0	0	1	4	2	7	7.7
Alcohol toxicity	0	0	0	0	1	0	1	1.1
Carbon monoxide poisoning	0	0	1	0	0	0	1	1.1
Subtotal	9	1	5	13	18	8	54	59.3
Natural								
Coronary artery disease	2	2	1	2	2	0	9	9.9
Pulmonary infectious disease	0	0	1	1	1	0	3	3.3
Cerebral vascular accident	0	0	1	0	1	0	2	2.2
AIDS	0	0	0	0	0	1	1	1.1
Cirrhosis	0	0	0	0	1	0	1	1.1
Gastrointestinal hemorrhage	0	0	0	0	1	0	1	1.1
Other liver disease	0	0	0	1	0	0	1	1.1
Pulmonary disease	0	1	0	0	0	0	1	1.1
Seiure disorder	1	0	0	0	0	0	1	1.1
Subtotal	3	3	3	4	6	1	20	22.0
Trauma								
Gunshot wound	0	1	3	1	2	1	8	8.8
Motor vehicle accident	0	1	3	1	1	0	6	6.6
Blunt trauma	2	0	0	1	0	0	3	3.3
Subtotal	2	2	6	3	3	1	17	18.7
Total	14	6	14	20	27	10	91	100.0

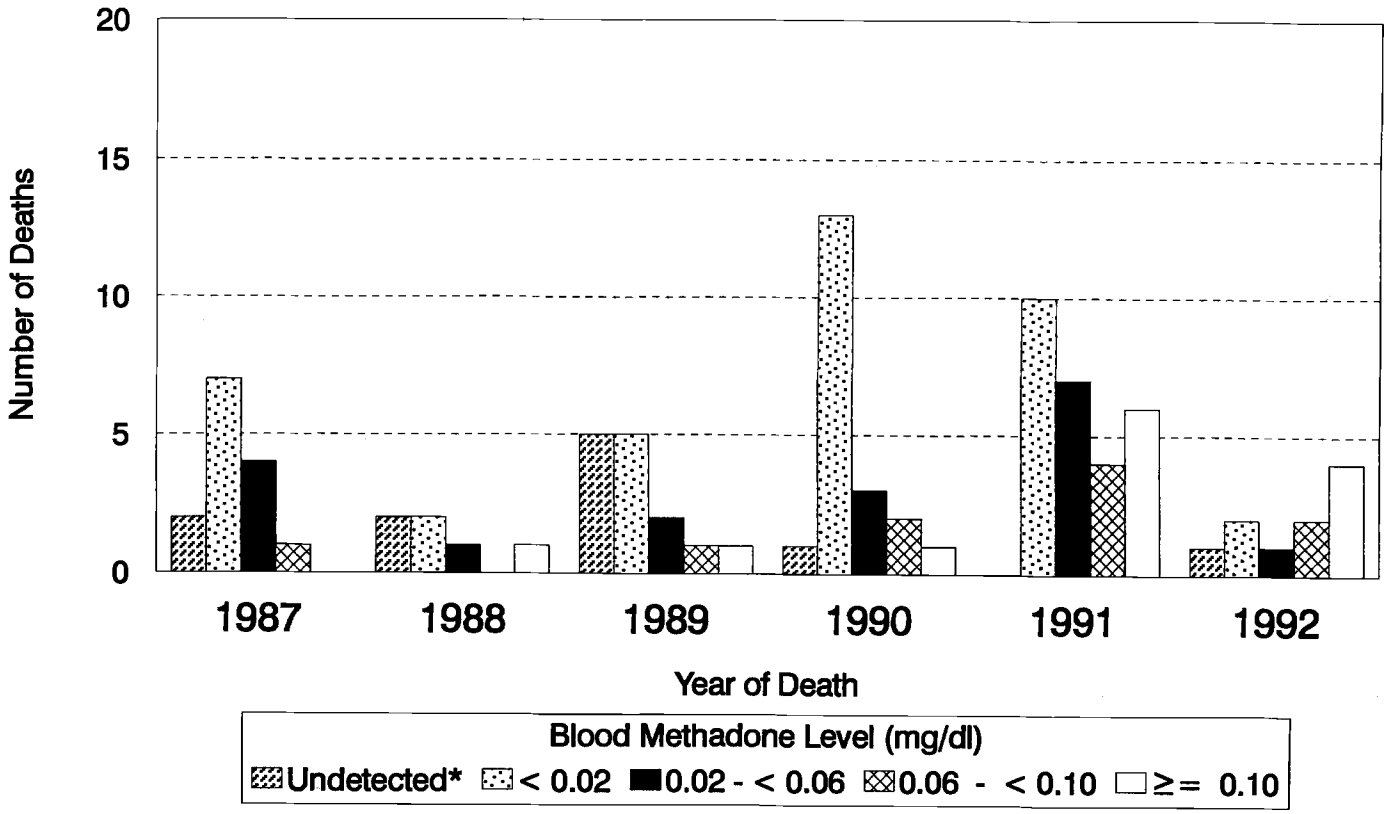
*Polydrug toxicity includes deaths in which more than one substance was listed as the cause of death.

ranging from 0 to 3 per year (Table 2). However, there was a substantially higher number of methadone-detected deaths attributed to polydrug toxicity in 1987, 1990 and 1991 than in the other years studied.

On the postmortem drug screen, methadone was found in the blood of 80 decedents; the remaining 11 decedents tested positive for methadone in the urine, bile, or stomach contents but had undetectable levels of methadone in their blood. The distribution of postmortem blood methadone level by year of death is shown in Fig. 1. The highest blood methadone levels were found among people who died in 1991 and 1992. For these two years, 10 decedents were identified with blood methadone levels equal to or above 0.10 mg/dL, a level considered to be toxic by the Harris County ME. Three decedents were identified with blood methadone levels in this range for the previous years.

Table 3 shows the distribution of toxicity-related, natural, and trauma-related deaths by blood methadone level. We found that 20% of the decedents classified by the Harris County ME as having died of natural causes had blood methadone levels in the toxic range ($\geq$ 0.1 mg/dL). A total of 15% of those whose deaths were toxicity-related and 6% of those whose deaths were trauma-related had blood methadone levels in this range. People whose deaths were attributed to methadone toxicity were more likely than those whose deaths were attributed to other causes to have blood methadone levels in the toxic range (27%).

In addition to methadone, at least one other drug was detected in postmortem testing among 85% of the methadone-detected cases (Table 4). The substance detected most frequently was diazepam, which was found in 42% of the cases.



*Methadone not detected in decedent's blood but was present in another body fluid.

FIG. 1—*Number of methadone-detected deaths identified by the Harris County, Texas, Medical Examiner by methadone blood level (mg/dL), January 1, 1987—December 31, 1992.*

TABLE 3—*Percentage of decedents in each blood methadone level category by cause of death, Harris County, Texas, January 1, 1987–December 31, 1992.*

	Cause of Death*											
	Toxicity†											
	Polydrug‡ (*N* = 34)		Methadone (*N* = 11)		Other (*N* = 9)		Subtotal (*N* = 54)		Natural (*N* = 20)		Trauma (*N* = 17)	
Blood Methadone Level (mg/dL)	*N*	%	N	%	N	%	N	%	N	%	N	%
Undetected§	2	5.9	0	0.0	1	11.1	3	5.6	2	10.0	6	35.3
<.02	14	41.2	3	27.3	8	88.9	25	46.3	8	40.0	6	35.3
.02–<.06	10	29.4	2	18.2	0	0.0	12	22.2	3	15.0	3	17.6
.06–<.10	3	8.8	3	27.3	0	0.0	6	11.1	3	15.0	1	5.9
≥.10	5	14.7	3	27.3	0	0.0	8	14.8	4	20.0	1	5.9

*Cause of death based on the opinion of the Harris County Medical Examiner.
†Toxicity includes cocaine toxicity, alcohol toxicity, methadone toxicity, polydrug toxicity, and carbon monoxide poisoning.
‡Polydrug toxicity includes deaths in which more than one substance was listed as the cause of death.
§Methadone not detected in decedent's blood but was present in another body fluid.

Independent Review of 1991 Cases

Of the 27 methadone-detected cases in 1991, at least two of the three independent reviewers agreed that methadone was the primary cause of death for three of the decedents, a contributing cause of death for nine of the decedents, and unrelated to death for 14 of the decedents. (For one case, each pathologist had a different opinion as to the role of methadone in the cause of death.) The degree of inter-rater agreement between the three pathologists, as estimated by the kappa statistic, was 0.4, indicating fair agreement compared to chance. For 78% of the methadone-detected cases identified in 1991, the results of the independent review agreed with the opinions of the Harris County ME regarding the role of methadone in the cause of death (Table 5).

Methadone-Maintenance Treatment Data

We found that 18 (20%) of the decedents in whom methadone was detected were enrolled in a Harris County MMTP at the time of death. Four people died within a week of enrolling in an MMTP. We were able to document only past treatment at a MMTP for 13 (14%) of the decedents and were unable to document any enrollment in a MMTP for 60 (66%) of the decedents. Among decedents in whom methadone had been detected and who had been enrolled

TABLE 4—*Number of decedents in whom methadone was detected who also had substances other than methadone detected by drug screens performed by Harris County, Texas, Medical Examiner, January 1, 1987–December 31, 1992.*

Substance	Number	Percentage
Any other substance*	77	84.6
Any respiratory depressant†	60	65.9
Diazepam	38	41.8
Cocaine	32	35.2
Alcohol	22	24.2
Opiates/morphine	11	12.1
THC	11	12.1
Propoxyphene	5	5.5

*Other substances include diazepam, nordiazepam, alcohol, opiates, morphine, propoxyphene, norpropoxyphene, butalbital, chlordiazepoxide, codeine, hydrocodone, dihydrocodeine, ethchlorvynol, meperidine, meprobamate, cocaine, marijuana, methamphetamine, and phenothiazine.

†Respiratory depressants include diazepam, nordiazepam, alcohol, opiates, morphine, propoxyphene, norpropoxyphene, butalbital, chlordiazepoxide, codeine, hydrocodone, dihydrocodeine, ethchlorvynol, meperidine, and meprobamate.

TABLE 5—*Distribution of agreements between the Harris County Medical Examiner and the independent reviewers on the classification of the role of methadone among the 1991 methadone-detected deaths.*

	Independent reviewer's opinion			
Harris County Medical Examiner's Opinion	Primary Cause	Contributory Cause	Unrelated Cause	Total
Primary* Cause	2	0	0	2
Contributory† Cause	0	8	3	11
Unrelated‡ Cause	1	1	11	13
Total	3	9	14	26

*Deaths due to methadone toxicity.
†Deaths due to polydrug toxicity.
‡Deaths due to all other causes.

in a MMTP for more than seven days before their death, trauma was the leading cause of death (Table 6). None of the deaths among this group was attributed to methadone toxicity. For the other three treatment groups, toxicity was the most frequently cited cause of death.

Discussion

To estimate the extent of methadone-related mortality in Harris County, Texas, between 1987 and 1992, we classified ME cases in which methadone was detected according to the likelihood that methadone toxicity was a cause of death. We found that the number of methadone-detected medical examiner cases in Harris County, Texas, peaked in 1991. Furthermore, the proportion of methadone-detected cases with high postmortem blood methadone levels ($\geq$ 0.10 mg/dL) increased in 1991 and 1992. However, these data do not conclusively point to an increase in deaths due to methadone toxicity in Harris County in 1991.

As with all opiates, methadone toxicity is thought to be the result of respiratory depression due to decreased sensitivity of the brain's respiratory center to the stimulatory effect of carbon dioxide) (15). The respiratory-depressant effect of methadone lasts up to 48 hours after a single dose, whereas the analgesic effect lasts only 4 to 6 hours (23). Experimental studies have suggested that, in addition to the respiratory-depression, opiates also have membrane-stabilizing activity that may depress the cardiac conduction system, thus potentially causing cardiac dysrhythmia (24).

There is disagreement on what constitutes a toxic or fatal blood methadone level. Irey and Froede (25) give a range of toxic levels from 0.02 mg/dL to 0.45 mg/dL, whereas the Harris County Medical Examiner considers the toxic level as falling between 0.1 mg/dL and 0.2 mg/dL. McBay considers the toxic level to be 0.3 mg/dL or greater (16).

One reason for the difficulty in determining a toxic blood methadone level is drug interaction. A given blood methadone level may or may not be toxic, depending on the presence of other drugs which may augment or counteract the toxic effects of methadone. Many drugs are known to accelerate methadone metabolism through the induction of hepatic microsomal enzymes. For example, rifampin, phenytoin, and disulfiram can precipitate opiate abstinence syndrome through this mechanism (26–28). It is unclear whether drugs such as benzodiazepines (especially diazepam) and alcohol, which are often used by people in methadone-maintenance treatment (29,30), affect methadone metabolism directly; however, benzodiazepines or alcohol may augment the sedation and respiratory depression caused by methadone (11). A toxic interaction between alcohol and opiates that is independent of slowed opiate metabolism from alcohol-induced liver disease has been postulated. Case data from morphine-involved deaths demonstrate that

TABLE 6—*Autopsy and toxicological findings and demographic variables by treatment status for decedents in whom methadone was detected, Harris County, Texas, January 1, 1987–December 31, 1992.*

	Treatment Status								
	No Identified Treatment (N = 60)		Past Treatment (N = 13)		In Treatment More Than 7 Days at Time of Death (N = 14)		In Treatment 7 Days or Less at Time of Death (N = 4)		
Cause of Death†	N	%	N	%	N	%	N	%	p*
Toxicity‡	37	61.7	9	69.2	4	8.6	4	100.0	0.03
Polydrug Toxicity§	22	36.7	6	46.2	3	21.4	3	75.0	0.22
Methadone Toxicity	7	11.7	3	23.1	0	0.0	1	25.0	0.26
Natural	15	25.0	1	7.7	4	28.6	0	0.0	0.34
Trauma	8	13.3	3	23.1	6	42.9	0	0.0	0.06

*Probability values are based on uncorrected chi-square results unless the expected value for a cell was less than five, in which case the Fisher Exact Test results are presented.

†Cause of death based on the opinion of the Harris County Medical Examiner.

‡Toxicity includes cocaine toxicity, alcohol toxicity, methadone toxicity, polydrug toxicity, and carbon monoxide poisoning.

§Polydrug toxicity includes deaths in which more than one substance was listed as the cause of death.

death may occur at non-toxic morphine concentrations when high levels of blood alcohol are present (31,32). In one study, a blood alcohol level (BAL) of more than 100 mg/dL was found to be associated with a greatly increased risk for death from heroin toxicity (33,34). However, BAL has not been associated with risk for death from methadone toxicity (9).

Another factor that complicates establishing a toxic methadone level is individual variability in susceptibility to methadone's toxic effects. Opiate tolerance is a major determinant of this variability. Some people who have developed tolerance to methadone do not suffer toxic effects even with blood methadone levels that would be toxic among people who have not developed such tolerance. For example, Wolff and colleagues describe a patient taking high doses of methadone (360 mg per day) who had a peak blood level of 0.28 mg/dL with only mild sedation (35). In contrast, people with no or only partial tolerance may die from a dose of methadone of 50 mg or less (36). Because of the phenomena of drug interactions and tolerance, the therapeutic and toxic blood methadone levels overlap. Therefore, the blood methadone level alone cannot be used to determine whether nor not methadone toxicity is the cause of death.

Because of factors such as the presence of multiple drugs and the possibility of opiate tolerance, establishing the role of methadone as a cause of death in our cases proved to be difficult. We could not rely on postmortem blood methadone levels to make this judgment. In our sample, 85% of the decedents in whom methadone was detected had at least one other substance in addition to methadone detected by postmortem blood testing. Methadone and one or more respiratory depressants were found among 66% of the decedents. Furthermore, we did not have sufficient premortem information about the decedents' drug use to determine whether they were tolerant to opiates.

Because of the complexities in determining methadone toxicity, consensus among medical examiners regarding how to assess the role of methadone in causing death on the basis of objective toxicologic and pathologic findings is needed. Despite not being able to use blood methadone levels as an objective measure of methadone toxicity, we found relatively good agreement among our independent experts concerning the role of methadone in the cause of death. This agreement may suggest that there is a basis for arriving at a consensus on criteria for defining methadone as a cause of death. If a consensus can be achieved, it would facilitate the development of a case definition for methadone toxicity and assist in the identification of these cases for reporting to systems that monitor methadone-related deaths. To improve geographic coverage, medical examiner participation in existing monitoring systems should be increased. One such system is the Drug Abuse Warning Network (DAWN), an ongoing, multi city, drug-abuse data collection program sponsored by the Substance Abuse and Mental Health Services Administration.

A total of 80% of the decedents in whom methadone was detected in our sample had no documented enrollment in a Harris County MMTP at the time of death, a finding which suggests that they had obtained methadone from other sources, legal or illegal. This finding is also consistent with the findings of several studies of deaths caused by methadone toxicity in which only a minority of people were enrolled in MMTPs at the time of death (9,10,37). In addition, there was a higher proportion of traumatic deaths and a lower proportion of deaths due to drug toxicity among those people enrolled in MMTPs at the time of death than among those not enrolled; studies of heroin addicts have found similar results (2–4). A possible explanation for these observations is that patients who have been stabilized in methadone maintenance treatment may have considerable tolerance to the toxic effects of methadone and other opiates. Alternatively, patients in MMTPs may be less likely to abuse other drugs than are drug users who are not in treatment.

We may have underestimated the proportion of decedents enrolled in MMTPs because of the following reasons: 1) some decedents may have been enrolled in one of the three closed MMTPs (for which we were unable to obtain records) or in MMTPs outside of Harris County; 2) some may have received methadone from other legal sources, including inpatient detoxification programs, retail pharmacies, or cancer treatment facilities that administer methadone for pain relief; and 3) some MMTP staff may have been reluctant to identify decedents in whom methadone was detected as having been enrolled in their program. Because of these limitations, additional information is needed to determine whether diversion of methadone from MMTPs was a problem in Harris County.

Four people died of methadone or polydrug toxicity within a week of starting treatment at a Harris County MMTP. It was not within the scope of this investigation to determine if people being inducted into methadone-maintenance treatment are at an increased risk for death compared with people already established in treatment, as several studies have suggested (8,11). Yet because of the relatively high frequency of polysubstance use in this population and the toxic effect of combining respiratory depressants, deaths due to drug toxicity may occur even when dosage guidelines are followed. Further studies are needed to determine whether existing guidelines for induction dosages are appropriate and if so, whether MMTPs are complying with these guidelines.

As the number of people participating in methadone maintenance treatment increases, it is to be expected that there will be an increase in the numbers of decedents testing positive for methadone. Federal regulations require MMTPs to conduct random urine testing to evaluate compliance with methadone treatment as well as to determine whether or not patients continue to use illicit drugs. To discourage illegal diversion of methadone, MMTPs usually require patients to take their methadone under the direct supervision of clinic staff. However, most MMTPs allow patients with a record of negative results on urine drug screens and good compliance with other program requirements to consume methadone without direct observation by a medical provider.

Efforts should be made to educate the public on the hazards of unsupervised methadone use, including the possibility of adverse interaction between methadone and other drugs. Federal agencies involved in regulating substance use should cooperate to provide information on the safe use of methadone to MMTPs, state drug agencies, state health departments, community-based organizations, and especially to outreach programs working with drug users and other "high risk youth."

In summary, this investigation revealed that although the number of methadone-detected cases in Harris County, Texas, increased in 1990 and 1991, deaths due to methadone toxicity did not increase. Rather, there was an increase in methadone-detected deaths attributed to polydrug toxicity, in which methadone *may* have played a contributory role.

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