

Unintentional methadone-related overdose death in New Mexico (USA) and implications for surveillance, 1998–2002

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ABSTRACT

Aims To determine death rates from methadone over time, to characterize methadone-related death and to discuss public health surveillance of methadone-related death.

Design We analyzed medical examiner data for all unintentional drug overdose deaths in New Mexico, USA, between 1998 and 2002.

Measurements Age-adjusted death rates for methadone-related death, logistic regression models for likelihood of methadone-related death among all unintentional drug overdose deaths and bivariate comparisons within methadone-related death.

Findings Of 1120 drug overdose deaths during this period, there were 143 (12.8%) methadone-related deaths; the death rate decreased over the time period, averaging 1.6 per 100 000. Of 143 methadone-related deaths, 22.4% were due to methadone alone, 23.8% were due to methadone/prescription drugs (no illicit drugs), 50.3% were due to methadone/illicit drugs and 3.5% were due to methadone/alcohol. These groups were significantly different in demographics, health history and circumstances of death. Of 79 decedents (55.2%) with a known source of methadone, 68 obtained methadone through a physician prescription (31 for methadone maintenance treatment (MMT), 27 for managing pain and 10 had unknown reason for prescription).

Conclusions Methadone-related death rates and the proportion of methadone-related death among all drug overdose deaths decreased in New Mexico from 1998 to 2002. It is important for surveillance of methadone-related death to assess multiple drug causes, not just underlying cause. Also, methadone for pain management must be examined alongside MMT and when possible, methadone co-intoxication should be described in the context of other drugs causing death.

KEYWORDS Death, drug overdose, medical examiner, methadone, methadone-related death, surveillance.

INTRODUCTION

Methadone is the most accepted and established opiate substitute for treating heroin dependence worldwide, but recent controversy has emerged due to reports of increased overdose death due to methadone (Cairns *et al.* 1996; Lehder *et al.* 2002; Sorg &

Greenwald 2002; Ballesteros *et al.* 2003; Florida Department of Law Enforcement 2003). Some US states have reported a rise in methadone-related death in recent years, but most news reports describe incidents where methadone is present in toxicology and the extent of involvement is not well characterized.

There are numerous studies of methadone-related death among patients in methadone maintenance treatment (MMT) (Caplehorn *et al.* 1996; Appel, Joseph & Richman 2000; Zador & Sunjic 2000; Buster, van Brusel & van den Brink 2002), but the focus has shifted. Since 1998 there has been a rapid increase in the distribution of solid methadone formulation (pill, diskette) through pharmacies in the United States, now surpassing that of liquid formulation, the mainstay of dispensing in MMT programs (USDHHS 2004a). As a result of a growing number of physicians prescribing methadone for pain management, it is important to examine methadone-related death in the general population as well.

Two scientific studies used medical examiner data to evaluate methadone-related death in the United States. Ballesteros *et al.* (2003) investigated an increase in unintentional drug overdose deaths in North Carolina from 1997 to 2001. They found that the rate of death due to methadone increased from 0.16 per 100 000 persons in 1997 to 0.98 in 2001, an increase from 12 to 80 deaths during this time period. On the contrary, Bryant *et al.* (2004) in New York City found that deaths caused by methadone from 1990 to 1998 remained relatively stable over time, and also found a lower likelihood of methadone-related death among decedents with positive toxicology for illicit drugs.

Historically, a high prevalence of drug use has been observed in New Mexico (Goldstein & Herrera 1995). New Mexico has led the nation in drug-related death since the 1990s and the drug-related death rate in New Mexico of 15.0 per 100 000 persons in 2001 was twice the national rate of 7.6 (USDHHS 2004b). New Mexico reached its highest drug-related death rate of 16.7 per 100 000 persons in 2002, a total of 302 deaths. A high rate of premature death from drug overdose has been found among heroin users, similar to other studies worldwide (Joe & Simpson 1987; Goldstein & Herrera 1995; Orti *et al.* 1996; Hall *et al.* 1999; Hulse *et al.* 1999; Preti *et al.* 2002; Hickman *et al.* 2003), and roughly 70% of all illicit drug overdose deaths in New Mexico are caused by heroin. Given the drug overdose epidemic and growing need for increasing the percentage of opiate-dependent persons in MMT, it is of utmost importance to clarify the relative contribution of methadone in drug overdose death.

A previous study linking medical examiner data and vital statistics records determined that the centralized medical examiner in New Mexico captures at least 95% of unintentional drug overdose deaths in the state (Landen *et al.* 2003) and is a timely, detailed source of data that can be used to assess the contribution of methadone to drug overdose death over time. Using this data source, the purposes of this investigation were to: (1) examine methadone-related death among unintentional drug overdose

deaths in New Mexico from 1998 to 2002 and (2) compare characteristics of methadone-related death and non-methadone-related death among all unintentional overdose deaths.

METHODS

All cases of unintentional drug overdose death involving methadone were identified in New Mexico from 1998 to 2002 using data provided by the Office of the Medical Investigator (OMI) and the Toxicology Bureau of the Scientific Laboratory Division (SLD), New Mexico Department of Health.

The OMI is authorized to investigate all deaths in New Mexico that are sudden, unexplained, suspicious, violent or unattended, with the exception of those that occur on federal or tribal jurisdictions (i.e. Indian reservations and military installations). However, the OMI is contracted to investigate most of those deaths as well. For all deaths suspected of being due to the effect of drugs or poisons, a full autopsy and toxicological evaluation is carried out. OMI pathologists consult with the toxicologists of the SLD in case evaluations. Positive screening tests were confirmed using gas chromatography with mass spectrometry. When individuals die from toxic substances after a period of hospitalization, the OMI procures antemortem specimens when available from the health care facility for toxicological testing.

Classification of cause of death is determined by OMI board-certified forensic pathologists and is not simply a determination of the presence or absence of a drug in a toxicological screen. The diagnosis of a methadone-related death is dependent on the circumstances of death, scene and medical background investigation, and the presence of a lethal level of methadone blood concentration, either alone or in combination with other drugs, as determined by the pathologist. Accordingly, OMI pathologists classify an unintentional overdose death as an illicit or prescription drug death based on the findings from a complete investigation and full autopsy.

Statistical analyses and covariates

Analyses included all unintentional drug overdose decedents who were residents of and died in New Mexico from 1998 to 2002. Overdose deaths in which methadone was cited as a cause of death, alone or in combination with another drug (illicit and/or prescription), were classified as methadone-related deaths. The total number of methadone-related deaths and rates were calculated for each year from 1998 to 2002. Trends for proportion of methadone-related death among all unintentional drug overdose deaths were estimated using the

Cochrane–Armitage test for trend. Population denominators for rate calculations were 2000 US census data for 2000 and intercensal estimates for the other years (consistent with both the 1990 and 2000 census enumerations) (US Bureau of the Census 2004). Rates were expressed per 100 000 persons and age-adjusted to the 2000 US standard population.

For all unintentional drug overdose death, we examined covariates of interest such as gender, age, race/ethnicity, decedent residence, type of overdose as determined by OMI, drugs causing death and year of death. Drugs that caused death were not mutually exclusive (i.e. a death can be attributed to methadone and heroin and/or cocaine). Decedent residence was categorized by current Metropolitan Statistical Area (MSA) regions for New Mexico: Albuquerque (Bernalillo, Sandoval, Valencia and Tarrant Counties), Las Cruces (Dona Ana County), Santa Fe (Santa Fe County), Farmington (San Juan County) and outside any MSA. Logistic regression was used to examine bivariate and multivariate associations between decedent characteristics and the likelihood of dying from methadone, among all unintentional drug overdose deaths. Covariates of interest with statistical significance at levels $\alpha=0.10$ in bivariate models were entered into the multivariate model.

For methadone-related death only, the circumstances of death and the decedent's medical and drug use history (if present) were collected by abstractors using standard data collection forms, in addition to the above-listed covariates. Data for circumstances of death included location of overdose, day of the week death was pronounced, evidence of injecting drug use (IDU) at the scene (presence of track marks or syringe at scene), source of methadone and reason for ingestion (pill bottle with decedent's name, medical records), and methadone blood concentration (mg/l). Data for history of drug use were collected when available from medical records and family history. History of drug use included illicit drug use, non-medical use of prescription drugs, IDU and previous overdose. Medical history included chronic pain and other known medical conditions, grouped as the following: drug abuse, alcohol abuse, cardiovascular diseases, mental illness (bipolar disorder, schizophrenia, depression, anxiety disorder, post-traumatic stress disorder), hepatitis C or B virus (HCV/HBV) and chronic obstructive pulmonary disease (COPD)/emphysema. Data on the form of methadone (liquid, diskette, pill) ingested were not available for many decedents and not collected for this study.

Methadone-related death was classified into three groups for comparison: (1) death from methadone alone, (2) death from co-intoxication of methadone and prescription drugs [i.e. other opioids/narcotics, central nervous system (CNS) depressants, stimulants, psychotherapeutics], in the absence of illicit drugs (heroin,

cocaine or methamphetamine) and (3) death from co-intoxication of methadone and any illicit drugs, where prescription drugs could have been contributory to death. OMI pathologists were consulted on difficult cases during this process. χ^2 tests or exact tests were used to compare categorical covariates and Wilcoxon's rank-sum tests were used to analyze continuous covariates.

Among methadone co-intoxication deaths, five overdose deaths were caused by methadone and alcohol and were excluded from analyses for co-intoxication death because we lacked a large enough sample for comparison.

RESULTS

Of a total of 1120 unintentional drug overdose deaths occurring in New Mexico and among New Mexico residents between 1998 and 2002, 143 overdose deaths were attributed to methadone. The age-adjusted death rate due to unintentional methadone overdose decreased from 2.3 per 100 000 persons in 1998 to 1.5 per 100 000 persons in 2002 (Fig. 1). Deaths due to methadone represented 18.4% of unintentional drug overdose deaths in 1998 and then decreased over time to 10.3% of unintentional drug overdose deaths in 2002 (test for trend, $P=0.016$). Over the 5-year period, 12.8% of all unintentional overdose deaths were due to methadone.

Of the 1120 unintentional drug overdose deaths, 77.4% of decedents were male, 52.5% were Hispanic, 42.0% were white non-Hispanic and 5.5% were American Indian, black or Asian, and the median age of decedents was 40.0 years (1st, 3rd interquartile range (IQR): 34, 47) (Table 1). From the OMI, 75.6% of unintentional overdose deaths were due mainly to illicit drugs. A large proportion of decedents lived in the Albuquerque MSA (56.4%) and 32.8% of all decedents were pronounced dead on Saturday or Sunday. Heroin was commonly present as a drug causing death (51.4%), as was cocaine (37.5%) and alcohol (29.3%).

Table 1 also shows the bivariate and multivariate correlates of methadone-related death. In bivariate analyses, covariates associated significantly with an increased likelihood of methadone-related death compared to non-methadone drug overdose deaths were being white non-Hispanic, death due to prescription drugs, absence of heroin as a cause of death, absence of alcohol as a cause of death and year (where methadone-related death was more likely in 1998 relative to following years). In the multivariate model, the only covariates associated significantly with methadone-related death were heroin as a cause of death [OR = 0.24 (95% CI: 0.15–0.40)] and year of death, wherein methadone-related death was more likely in 1998 relative to following years

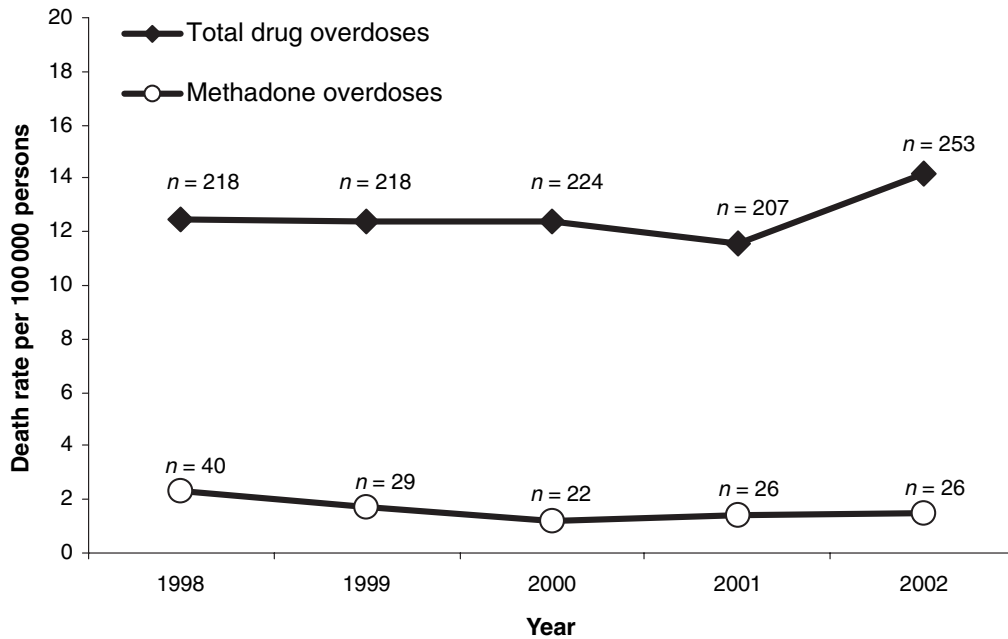


Figure 1 Death rates for unintentional drug overdose and methadone-related death, New Mexico (USA), 1998–2002

[reference: 1998, 1999 OR = 0.60 (95% CI: 0.35–1.04); 2000 OR = 0.39 (95% CI: 0.22–0.70); 2001 OR = 0.43 (95% CI: 0.24–0.76); 2002 OR = 0.39 (95% CI: 0.22–0.68)].

Methadone-related death

Table 2 shows the results of data collected from OMI records for 143 unintentional methadone-related overdose deaths. Of the 143 methadone-related overdose deaths, 74.8% of decedents were male, 54.5% were white non-Hispanic and the median age was 40 years (1st, 3rd IQR: 33, 47). Seventy-one per cent of decedents died in their own residence, 63.6% were pronounced dead on Monday–Friday and 40.6% had evidence of current IDU. Of the 143 methadone-related deaths, cocaine (35.0%), heroin (22.4%) and alcohol (20.3%) were other significant contributors to death. The median methadone blood concentration was 0.46 mg/l (1st, 3rd IQR: 0.23, 0.64). History of illicit drug use (67.1%), IDU (51.7%), non-medicinal use of prescription drugs (31.0%) and chronic pain (40.1%) was determined from the medical examiner investigations.

The source of methadone was available for 79/143 decedents; 68 decedents (47.5%) had a physician prescription for methadone (31 for MMT, 27 for chronic pain and 10 had an unknown reason for prescription) and 11 decedents (7.7%) obtained diverted methadone, meaning purchased ‘off the street’ or obtained from a prescription for someone else. The source of methadone for 64 decedents (44.8%) was not indicated.

Death caused by methadone alone, methadone and prescription drugs only and methadone and illicit drugs

Within methadone co-intoxication death, two groups were identified: (1) persons who died from methadone in combination with prescription drugs in the absence of illicit drugs ($n = 34$) and (2) persons who died from methadone in combination with any illicit drugs, where prescription drugs may have been contributory ($n = 72$).

Table 2 shows a comparison of decedent characteristics between the three categories of methadone-related death. Compared to the other two groups, decedents from methadone alone were significantly ($P < 0.05$) more likely to be white non-Hispanic (84.4% versus 61.8% for methadone and prescription drugs and 37.5% for methadone and illicit drugs) and have a known history of chronic pain (71.9% versus 53.0% for methadone and prescription drugs and 20.9% for methadone and illicit drugs).

Decedents who died from methadone co-intoxication with prescription drugs were significantly more likely to be female (50.0% versus 9.4% for methadone alone and 22.2% for methadone and illicit drugs), be living with a partner or married (44.1% versus 29.0% for methadone alone and 25.0% for methadone and illicit drugs), have a known history of non-medicinal use of prescription drugs (61.8% versus 25.0% for methadone alone and 21.1% for methadone and illicit drugs) and mental illness (50.0% versus 21.9% for methadone alone and 13.9% for methadone and illicit drugs), compared to the other groups.

Table 1 Decedent characteristics for total unintentional drug overdose death and bivariate and multivariate associations with methadone-related death, New Mexico (USA), 1998–2002.

	Total drug overdose deaths		Methadone-related overdose death		Non-methadone-related overdose death		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
	n	%	n	%	n	%		
Total	1120	100.0	143	12.8	977	87.2		
Female	253	22.6	36	25.2	217	22.2	1.18 (0.79–1.77)	
Male	867	77.4	107	74.8	760	77.8	1.00	
Race/ethnicity								
White, non-Hispanic	471	42.0	78	54.6	393	40.2	1.78 (1.25–2.54)	1.19 (0.81–1.75)
Hispanic	588	52.5	65	45.4	523	53.5	1.00	1.00
American Indian	22	2.0	0	0	22	2.3	1.00	1.00
Black or Asian	32	2.9	0	0	32	3.3	1.00	1.00
Unknown	7	0.6	0	0	7	0.7	1.00	1.00
Age group (years)								
<15	2	0.2	0	0	2	0.2	1.00	
15–24	76	6.8	13	9.1	63	6.5	1.00	
25–34	234	20.9	33	23.1	201	20.6	0.85 (0.42–1.70)	
35–44	437	39.1	52	36.4	385	39.5	0.70 (0.36–1.35)	
45–54	298	26.7	38	26.6	260	26.7	0.75 (0.38–1.49)	
55–64	51	4.6	4	2.8	47	4.8	0.44 (0.14–1.43)	
65–74	16	1.4	3	2.1	13	1.3	1.19 (0.30–4.77)	
75 +	4	0.4	0	0	4	0.4	Undefined	
Median age (1st, 3rd IQR)	40 (34, 47)		40 (33, 47)		40 (34, 47)			
Type of overdose								
Illicit drug overdose	847	75.6	78	54.5	769	78.7	1.00	1.00
Prescription drug overdose	273	24.4	65	45.5	208	21.3	3.08 (2.14–4.43)	1.37 (0.89–2.12)

Table 2 Unintentional methadone-related overdose death: comparison of decedent characteristics for deaths caused by methadone alone, methadone co-intoxication with prescription drugs and methadone co-intoxication with illicit drugs, New Mexico (USA), 1998–2002.

	Methadone co-intoxication*				P-value
	Total methadone-related death (n = 143)	Methadone alone (n = 32)	Methadone and prescription drug (n = 34)	Methadone and any illicit drug (n = 72)	
		A	B	C	
Male	107 (74.8)	29 (90.6)	17 (50.0)	56 (77.8)	<0.001
Female	36 (25.2)	3 (9.4)	17 (50.0)	16 (22.2)	
Median age (1st, 3rd IQR)	40 (33, 47)	40 (32.5, 48)	44.3 (34, 48.7)	36.9 (31, 44)	0.43
Race/ethnicity					0.039
White, non-Hispanic	78 (54.5)	27 (84.4)	21 (61.8)	27 (37.5)	<0.001
Hispanic	65 (45.5)	5 (15.6)	13 (38.2)	45 (62.5)	
Marital status					0.032
Single	32 (22.4)	8 (25.8)	1 (2.9)	20 (27.8)	0.96
Living with partner/married	43 (30.1)	9 (29.0)	15 (44.1)	18 (25.0)	
Divorced/separated/widowed	21 (14.7)	4 (12.9)	9 (26.5)	8 (11.1)	
Unknown	46 (32.2)	10 (32.3)	9 (26.5)	26 (36.1)	
Decedent residence (MSA)					0.62
Albuquerque	84 (58.7)	20 (62.5)	17 (50.0)	44 (61.1)	0.99
Las Cruces	3 (2.1)	0	1 (2.9)	1 (1.4)	
Santa Fe	10 (7.0)	1 (3.1)	4 (11.8)	5 (6.9)	
Farmington	9 (6.3)	3 (9.4)	4 (11.8)	2 (2.8)	
Outside any MSA	37 (25.9)	8 (25.0)	8 (23.5)	20 (27.8)	
Circumstances of death					0.18
Day death pronounced					0.51
Saturday–Sunday	52 (36.4)	9 (28.1)	15 (44.1)	25 (34.7)	
Monday–Friday	91 (63.6)	23 (71.9)	19 (55.9)	47 (65.3)	
Location of overdose					0.17
Own residence	100 (70.9)	25 (78.1)	31 (91.2)	40 (57.1)	0.09
Friend's residence	15 (10.6)	2 (6.2)	1 (2.9)	12 (17.1)	
Hotel/motel	5 (3.5)	2 (6.2)	0	3 (4.3)	
Hospital	9 (6.4)	1 (3.1)	2 (5.9)	6 (8.6)	
Other	12 (8.5)	2 (6.2)	0	9 (12.9)	

Table 2 Cont.

	Total methadone-related death (n = 143)	Methadone co-intoxication*			P-value		
		Methadone alone (n = 32) A	Methadone and prescription drug (n = 34) B	Methadone and any illicit drug (n = 72) C			
						A versus B	A versus C
Medical and drug use history							
Illicit drug use							
Yes	96 (67.1)	13 (40.6)	16 (47.1)	63 (87.5)	0.78	<0.001	<0.001
No	16 (11.2)	7 (21.9)	8 (23.5)	1 (1.4)			
Unknown	31 (21.7)	12 (37.5)	10 (29.4)	8 (11.1)			
Non-medical use of prescription drugs							
Yes	44 (31.0)	8 (25)	21 (61.8)	15 (21.1)	0.006	0.80	<0.001
No	5 (3.5)	2 (6.3)	0	3 (4.2)			
Unknown	93 (65.5)	22 (68.7)	13 (38.2)	53 (74.7)			
Injection drug use							
Yes	74 (51.7)	7 (21.9)	10 (29.4)	55 (76.4)	0.72	<0.001	<0.001
No	24 (16.8)	9 (28.1)	10 (29.4)	4 (5.6)			
Unknown	45 (31.5)	16 (50.0)	14 (41.2)	13 (18.1)			
Previous overdose							
Yes	22 (15.4)	3 (9.4)	9 (26.5)	9 (12.5)	0.19	0.84	0.17
No	15 (10.5)	4 (12.5)	4 (11.8)	7 (9.7)			
Unknown	106 (74.1)	25 (78.1)	21 (61.8)	56 (77.8)			
History of pain (n = 137)							
Yes	55 (40.1)	23 (71.9)	18 (53.0)	14 (20.9)	0.05	<0.001	0.003
No	46 (33.6)	1 (3.1)	8 (23.5)	34 (50.8)			
Unknown	36 (26.3)	8 (25.0)	8 (23.5)	19 (28.4)			
Other known health conditions							
Drug abuse	36 (25.2)	9 (28.1)	7 (20.6)	20 (27.8)	0.48	0.97	0.43
Alcohol abuse	32 (22.4)	6 (18.8)	5 (14.7)	19 (26.4)	0.66	0.40	0.18
Cardiovascular diseases	28 (19.6)	10 (31.2)	8 (23.5)	9 (12.5)	0.48	0.022	0.15
Mental illness	34 (23.8)	7 (21.9)	17 (50.0)	10 (13.9)	0.018	0.31	<0.001
HCV/HBV	37 (25.9)	6 (18.8)	4 (11.8)	25 (34.7)	0.43	0.10	0.013
COPD	13 (9.1)	3 (9.4)	5 (14.7)	5 (6.9)	0.51	0.67	0.20

*Excluding five deaths caused by methadone and alcohol.

Decedents who died from methadone co-intoxication with illicit drugs were significantly more likely to be Hispanic (62.5% versus 15.6% for methadone alone and 38.2% for methadone and prescription drugs), have evidence of IDU at scene (62.5% versus 25.0% for methadone alone and 14.7% for methadone and prescription drugs), have a methadone prescription for MMT (75.9% versus 17.6% for methadone alone and 23.8% for methadone and prescription drugs), have a larger proportion of deaths caused by alcohol (29.2% versus 3.1% for methadone alone and 5.9% for methadone and prescription drugs) and have a known history of illicit drug use (87.5% versus 40.6% for methadone alone and 47.1% for methadone and prescription drugs) and IDU (76.4% versus 21.9% for methadone alone and 29.4% for methadone and prescription drugs), compared to the other groups.

DISCUSSION

Amid an epidemic of drug overdose death in New Mexico, methadone-related overdose death actually decreased from 1998 to 2002, with an average death rate of 1.6 per 100 000 persons and accounting for 12.8% of unintentional drug overdose deaths. It is probable that methadone prescribed for pain management has become a larger proportion of the total methadone consumed in the United States and abroad. In New Mexico, the retail distribution of methadone increased more than 300% from 4561 g in 1998 to 14 318 g in 2002, representing an increase from 22.3 g of methadone sold per registrant to 52.6 g (USDOJ 2004). It is noteworthy that although methadone distribution in the state has rapidly increased in the past 5 years, the death rate due to methadone overdose decreased from 2.3 per 100 000 persons in 1998 to 1.5 in 2002, the peak year of drug overdose deaths in New Mexico.

We found distinct characteristics within methadone-related death for decedents in New Mexico. Persons dying from methadone alone were mostly white non-Hispanic and had history of chronic pain. Persons dying from methadone and prescription drugs were more likely than the other groups to have been female, married or living with a partner and had a history of non-medicinal prescription drug use. Persons dying from methadone co-intoxication with illicit drugs were largely Hispanic, used multiple illicit drugs at the time of death and often had a history of illicit drug use. The role of Hispanic ethnicity is interesting, as studies have shown higher overdose death rates among Hispanics than whites (Harlow 1990; Galea *et al.* 2003), and situational factors, such as differential likelihood of activating emergency medical response, may explain the higher overdose death rates observed

among Hispanics (Galea *et al.* 2003). Accordingly, overdose prevention and intervention measures should be directed to the demographics and circumstances of methadone use whenever possible.

We were able to capture the methadone source for 55% of the deaths caused by methadone. A physician prescription for the decedent was the source of methadone for 86% of decedents for which the source was determined, compared to 75% in North Carolina. Another avenue for obtaining methadone is diversion, where methadone may become available from someone else who was prescribed methadone. Diversion was determined as the decedent's source for only 8% of methadone-related death in this study and 13% in North Carolina (Ballesteros *et al.* 2003).

There are three notable findings for decedents who obtained methadone through physician prescription for MMT or pain management, both of which can result in medicinal and non-medicinal use of methadone. It is interesting to note that a considerably larger proportion of decedents with a physician prescription were prescribed methadone for MMT in New Mexico compared to North Carolina, 45% versus 8% (Ballesteros *et al.* 2003). Unfortunately, additional data on the drug treatment status of the decedent were not available. A second important finding for decedents with a physician prescription was that 70% of decedents who obtained methadone for MMT died from methadone co-intoxication with illicit drugs, suggesting the high risk of death among persons who continued use of illicit drugs during the methadone regimen. It is known that patients enrolled in MMT may use illicit drugs while taking methadone (Strug *et al.* 1985; Kidorf & Stitzer 1993), but drug overdose is addressable and preventable through training and education in the MMT program setting. Lastly, 85% of decedents who obtained methadone for chronic pain management died from methadone alone or co-intoxication with other prescription drugs. There was a high prevalence of chronic pain history in these groups, yet non-medicinal drug use was also high (44%). This underscores the need to train physicians more effectively in pain management of populations with and without a history of drug use (Rosenblum *et al.* 2003), an obvious reality in New Mexico.

There are findings for methadone-related death in New Mexico that are similar to findings in other locales. First, the absence of heroin was predictive of methadone-related overdose death, meaning that persons dying from unintentional methadone-related death in New Mexico were less likely to be using heroin at the time of death. This relationship was also found for alcohol in unadjusted analyses. This result supports findings in New York City from 1990 to 1998, where there was a lower likelihood of methadone-related death in persons who had

positive toxicology for illicit drugs or alcohol (Bryant *et al.* 2004). This finding suggests that compared to deaths caused by a drug other than methadone, the reason for methadone ingestion among methadone-related deaths was more likely for medicinal use as opposed to polydrug use and diversion associated with non-medicinal drug use. Secondly, although distribution of methadone increased in New Mexico, there was no increase in methadone-related death; in fact, the rates decreased. Similarly, there was no increase in methadone-related deaths observed in New York City, Western Australia and the United Kingdom during the 1990s, despite a backdrop of increased prescribing (Ernst *et al.* 2002; Oliver *et al.* 2002; Bryant *et al.* 2004). The proportion of methadone-related death among all unintentional drug overdose deaths was also similar in New Mexico and New York City: 12.8% and 13.7%, respectively.

The most important finding in New Mexico that is different from other studies is the larger proportion of methadone-related death among all unintentional drug overdose death in North Carolina (18%) and Maine (26%) than in New Mexico (13%), from 1997 through 2002. The death rate due to methadone also increased in these other states and is projected to continue rising. Even though the death rate due to methadone over time decreased in New Mexico and increased more than five-fold in North Carolina, the death rate in New Mexico remained higher than that of North Carolina (1.4 versus 1.0 per 100 000 persons in 2001) (Ballesteros *et al.* 2003).

The lack of association between decedent residence and likelihood of methadone-related death means that within all unintentional drug overdose deaths since 1998, decedents from urban regions were no more likely to die from methadone overdose than decedents from non-urban regions or vice versa. An association between methadone-related death and decedent residence would be of particular interest in New Mexico because nearly 40% of the population resides outside a metropolitan area. Persons travel long distances for medical care and to receive MMT doses. We are not aware of any peer-reviewed studies in the United States that examine methadone-related death and urban versus non-urban decedent residence. Understanding that MMT prescribing practices vary world-wide, it would be interesting to identify any patterns or trends in methadone usage and overdose death across levels of urbanization in other locales.

There are limitations to this study. We analyzed methadone-related overdose when it was designated as the cause of death by the OMI. Variability among medical examiners is possible, leading to misclassification of the drug causing death among some decedents analyzed in this study.

Also, because of the small sample and missing or unknown data for some covariates, we lacked statistical power to detect significant differences for comparisons within methadone-related death. Particularly, we were not able to determine the source of methadone and reason for use among 45% of decedents. The medical examiner investigators should make every effort to collect data on source of methadone in order to promote the formulation of prevention measures and enhance surveillance. The direction of association for decedent comparisons within methadone-related death provides valuable insight, however, and more data over time will clarify this relationship.

Lastly, there is the issue of generalizability of findings to populations outside of New Mexico. The pattern of drug use in New Mexico is unique and there are communities where illicit drug use is endemic and accepted. Research among drug users in New Mexico suggests high degrees of intergenerational drug use, strong family ties and relatively stable life-style despite sustained criminal activity and periods of incarceration (Goldstein & Herrera 1995). Nonetheless, these data can contribute to understanding patterns of methadone overdose death among a diverse population burdened by drug-related death, spanning urban and non-urban settings.

In conclusion, the medical examiner system is a valuable source of data for epidemiological surveillance of drug overdose deaths, as noted in other studies (Graitcer *et al.* 1987; Poulin *et al.* 1998). We could determine promptly that while the use of methadone has increased greatly and has been under tremendous global scrutiny, rates of methadone-related death decreased in New Mexico. It is important that public health surveillance of methadone-related death should be able to assess multiple drug causes as 78% of methadone-related death in New Mexico was methadone co-intoxication with other drugs. If underlying cause alone were used to assess the contribution of methadone among unintentional overdose death, only 22% of methadone-related deaths would be captured, an apparent underestimate. Also, death from methadone co-intoxication should be described in the context of the other type(s) of drugs that caused death considering that half of unintentional methadone-related deaths in New Mexico involved lethal levels of cocaine and/or heroin, often combined with 'incidental' or low levels of methadone (Karch & Stephens 2000). Lastly, we found similar numbers of deaths originating from physician prescription for MMT and chronic pain management among all methadone-related deaths.

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