

Increases in Methadone-Related Adverse Events: Is it pills or liquid?

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The data on methadone formulations and adverse events are limited. This research brief reports data on methadone exposures as reported by the Addiction Research Institute and the RADARS[®] System.

Methadone comes in three different formulations: 5mg and 10mg pills for pain, 40mg wafers or diskettes which, as of the time of this brief, are available for pain and for narcotic treatment, and liquid syrup, which can only be used by narcotic treatment programs.

The data from the Addiction Research Institute include statistics presented at the 2007 meeting of the College on Problems of Drug Dependence and the July 2007 Center for Substance Abuse Treatment (CSAT) Methadone Mortality Meeting. These data include admissions to treatment programs as reported by the Substance Abuse and Mental Health Services Administration's (SAMHSA) Treatment Episode Data Set (TEDS), the Drug Enforcement Administration's (DEA) Automation of Reports and Consolidated Orders System (ARCOS), data on adverse human exposures from the Texas Poison Control Centers, data on deaths of clients in Texas methadone programs as reported to the Texas Department of State Health Services (DSHS), and mentions of methadone on Texas death certificates obtained from DSHS.

The Researched Abuse, Diversion and Addiction Related Surveillance (RADARS[®]) System is a surveillance network utilizing six signal detection systems to monitor prescription opioid abuse, misuse, and diversion throughout the United States. Drugs of interest include buprenorphine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, and tramadol. These are the signal detection systems:

- Drug Diversion
- Key Informants

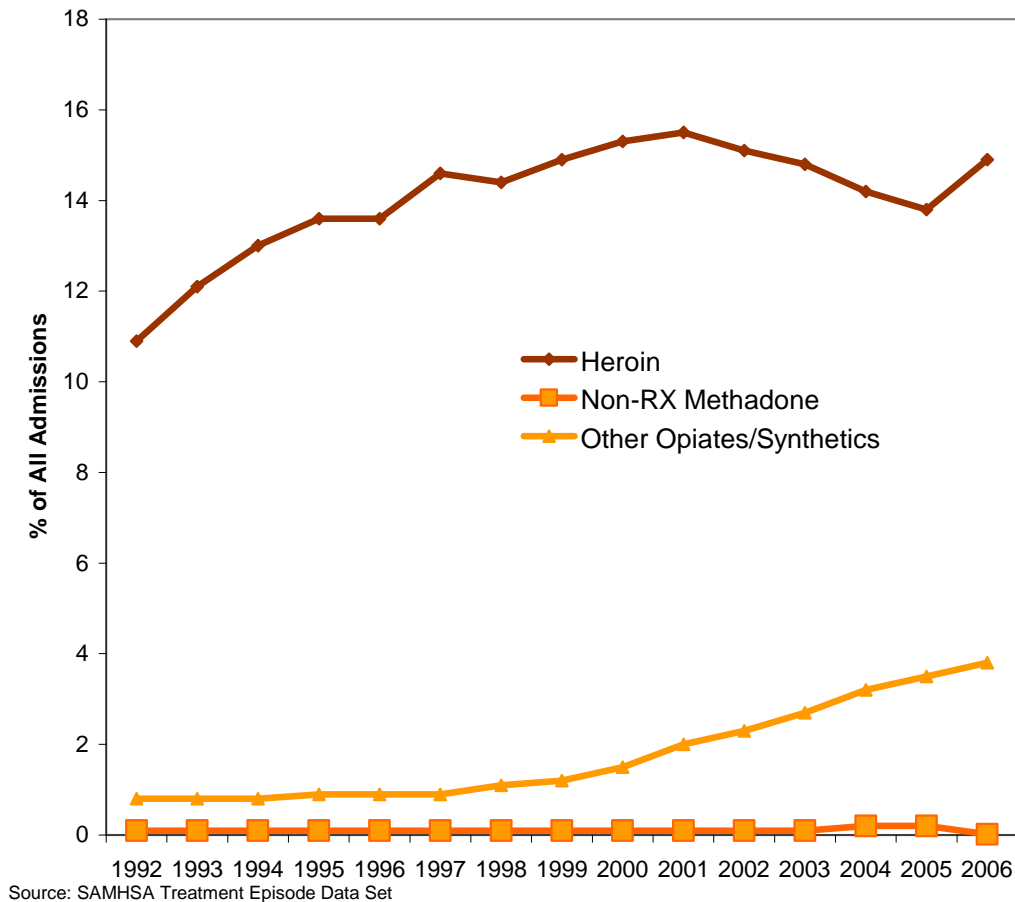
- Opioid Treatment Programs
- Poison Centers
- Impaired Health Care Workers
- College Surveys

However, only the Poison Center Signal Detection System captures data on the medical outcomes associated with the exposure.

The RADARS System Poison Center data presented within this brief were first presented at the July 2007 Center for Substance Abuse Treatment (CSAT) Methadone Mortality Meeting.

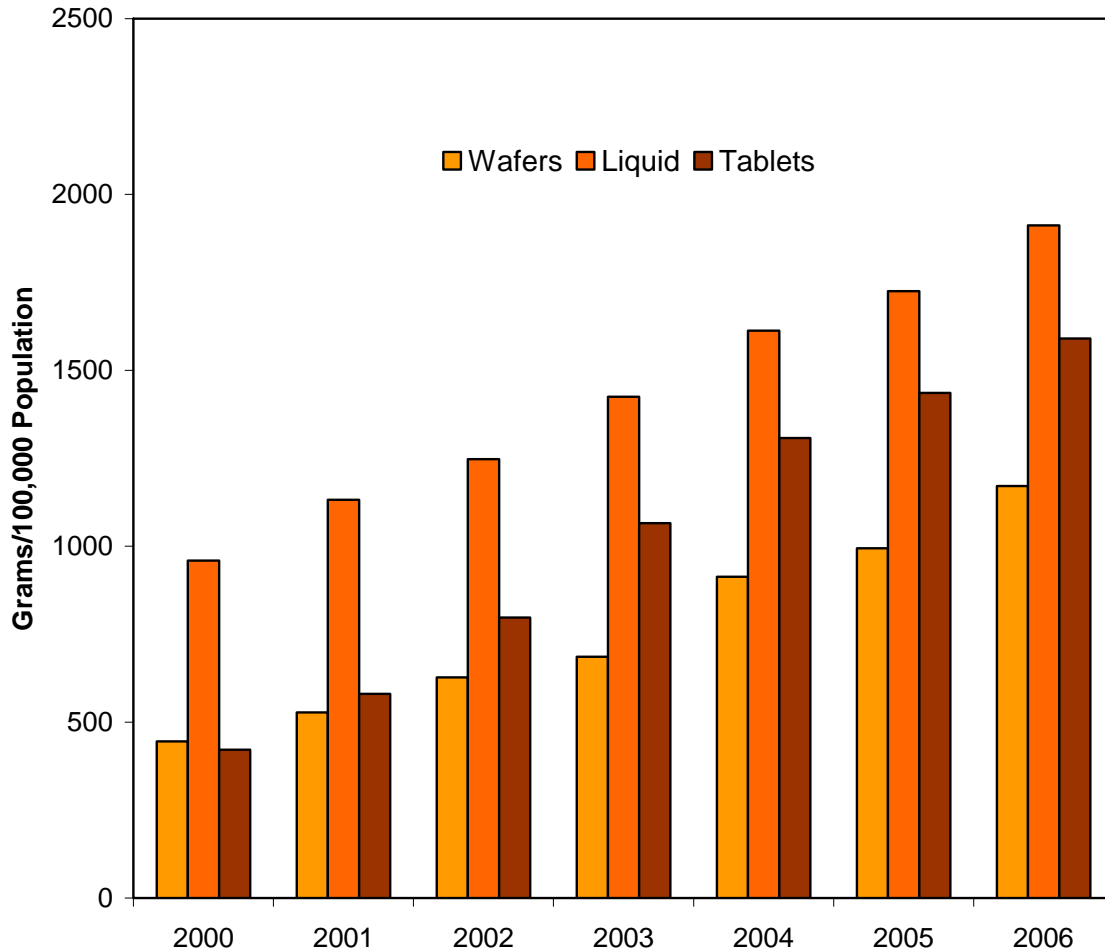
- These data are medical outcomes of death associated with methadone exposures.
- Data reported are from 1st quarter 2003 through 2nd quarter 2007.
- 11 of 60 US poison centers (18%) participated in 1st quarter 2003. (population covered = 59,612,144; 21% of US population).
- 43 of 60 US poison centers (72%) participated in 2nd quarter 2007 (population covered = 193,472,082; 69% of US population).
- For the purpose of this brief, these data previously presented at the CSAT meeting were updated to represent data through the most recent quarter (2nd quarter 2007).

U.S. Treatment Admissions by Primary Substance: 1992-2006



This chart shows that while the proportion of clients entering with a primary problem with other opiates (hydrocodone, oxycodone, etc.) has increased from 1% in 1992 to 4% in 2006, the proportion of clients entering with a primary problem with “street” or illicitly-obtained methadone has remained stable (less than 0.2% of all drug and alcohol treatment admissions).

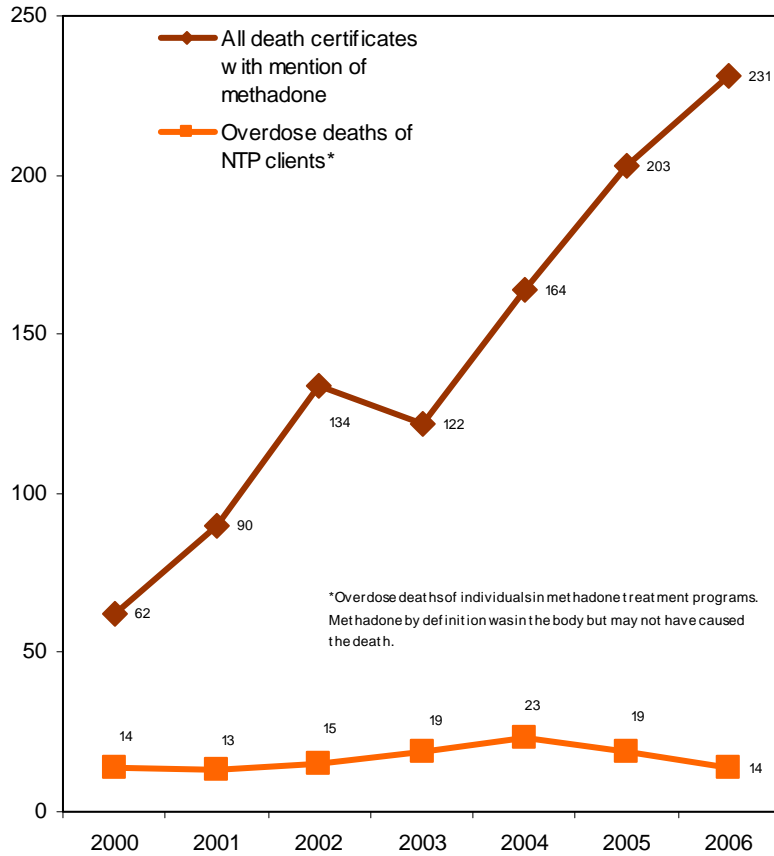
Distribution of Methadone in U.S. by Formulation: 2000-2006



Source: DEA's ARCOS

This chart shows that while more grams of methadone liquid per 100,000 population are distributed each year, there has been a greater increase in the amount of methadone tablets and wafers distributed. Between 2000 and 2006, the grams of liquid methadone per 100,000 distributed increased by 99%, while the amount of 40 mg wafers increased by 163% and the amount of 5 and 10 mg tablets increased 277%.

Texas Deaths With a Mention of Methadone: 2000-2006



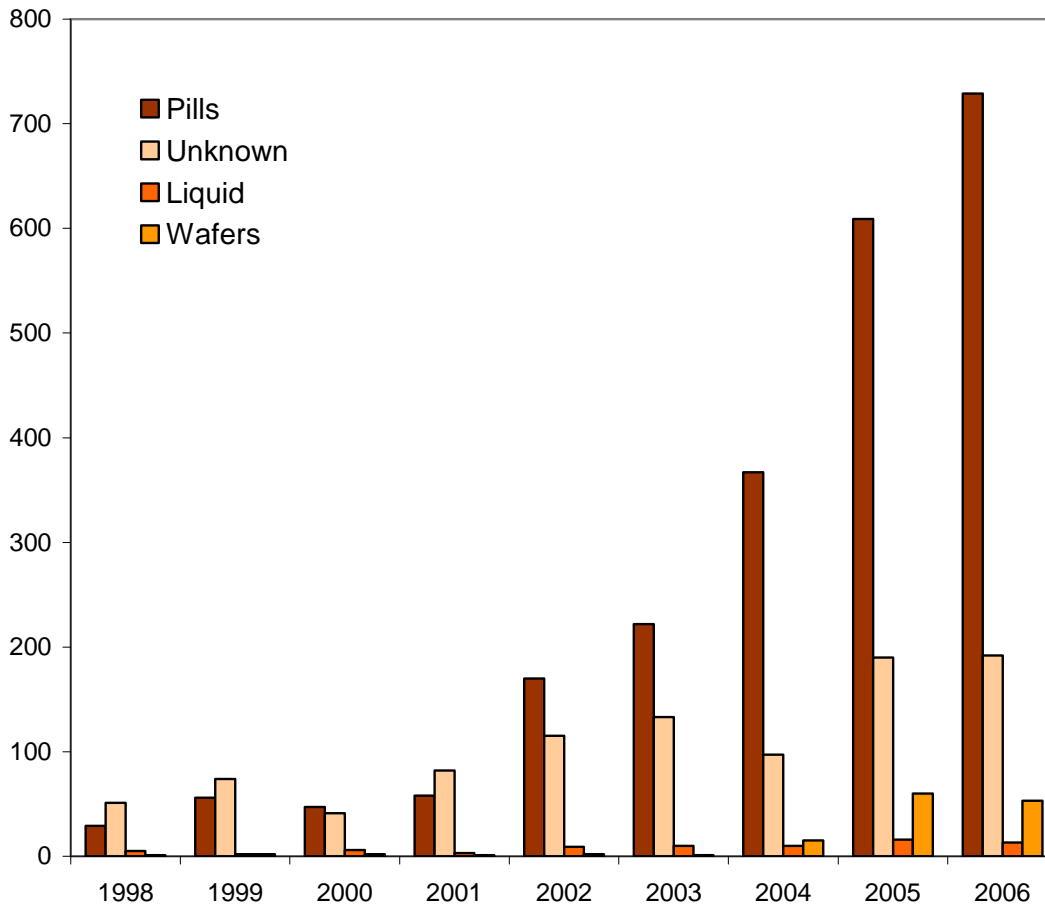
Source: Texas DSHS

This chart shows the increase in the number of death certificates in Texas which included a mention of methadone. The death certificates rarely indicate whether the decedent had taken pills or liquid, so there is no way to determine the methadone formulation involved in these deaths.

Methadone treatment programs are required by the State to report information on every client who dies while in treatment, with 89 deaths in 2006. The leading causes of death were cardiovascular (22 deaths), drug overdose (14 cases), liver disease (13), and unknown (13). Of the 14 overdoses, 7 died of toxic effects of combined drugs, 5 died of acute methadone intoxication, 1 died of cocaine intoxication, and the cause of the overdose was listed as “unknown” in 1 case.

Of the drug overdose deaths, 5 of the 14 clients had been in treatment less than 3 weeks. Of the 14 clients, 7 came in daily for their doses, 4 received weekly take-homes, 2 got take-homes twice a month, and 1 came in every 3 weeks. None were on monthly take-homes. The take-home bottles were recovered in 11 of the cases, which would indicate the liquid had not been diverted to other people.

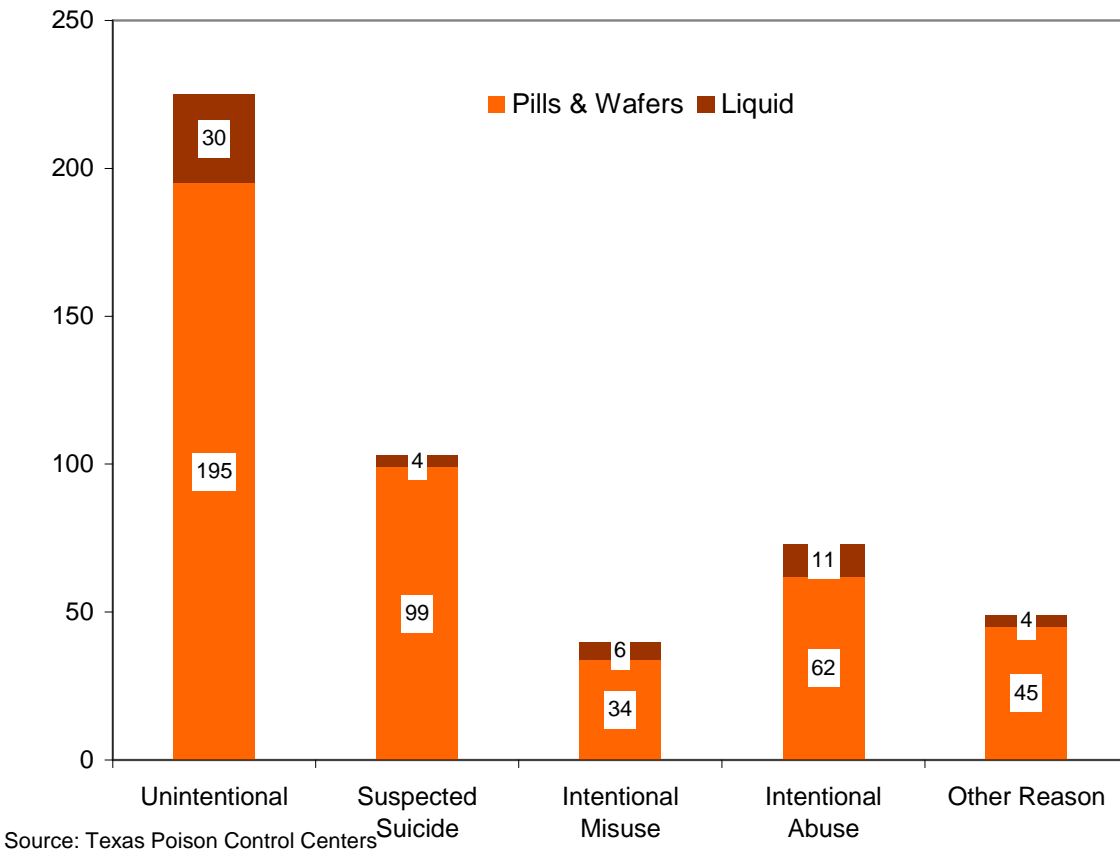
Human Exposure Calls to Texas Poison Control Centers Involving Methadone by Formulation: 1998-2006



Source: Texas Poison Control Centers

The only reliable statistics on methadone formulation are provided by the Texas Poison Control Centers. This exhibit shows the number of human exposure calls received by the centers, and beginning in 2002, the number of calls due to the 5mg and 10mg pain pills outnumber the “unknown” category. Notice that throughout the period of 1998-2006, the number of calls involving liquid methadone were lower than for any other formulation.

Reasons for Calls to Texas Poison Control Centers for Human Exposure to Methadone: 1998-2006



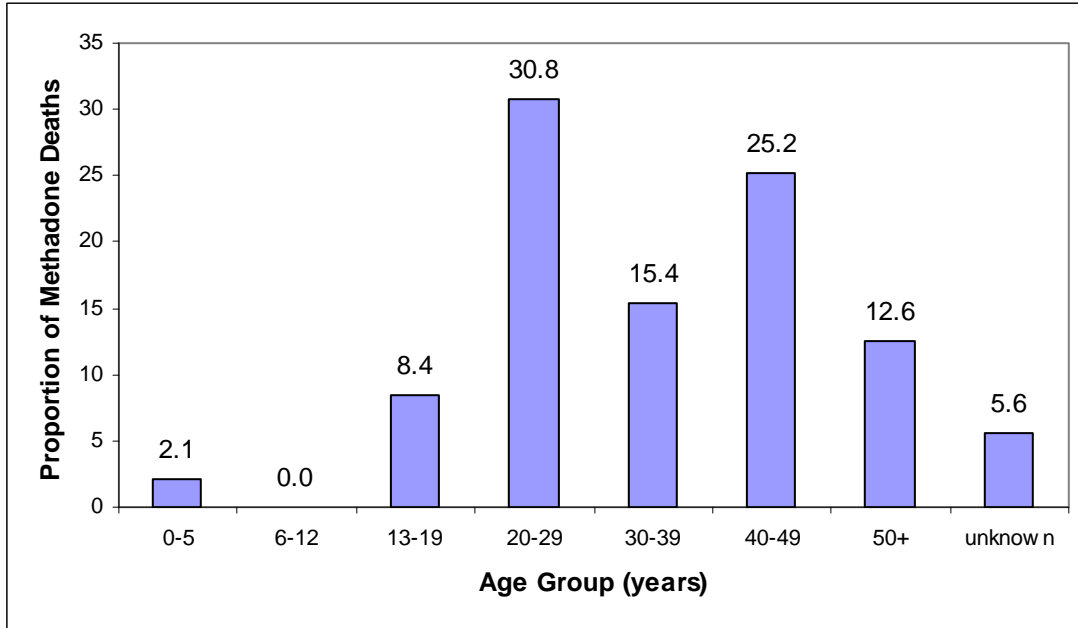
This exhibit shows the reasons for calls to Texas Poison Control Centers. Human exposure calls are not information calls, but calls where the person had actually taken the substance.

As this exhibit shows, 87% of the unintentional exposure calls, 96% of the suicide calls, 85% of the intentional misuse, 85% of the intentional abuse, and 92% of the exposures for other reasons involved 5mg and 10mg pills and 40 mg wafers.

RADARS System Methadone Mortality Data

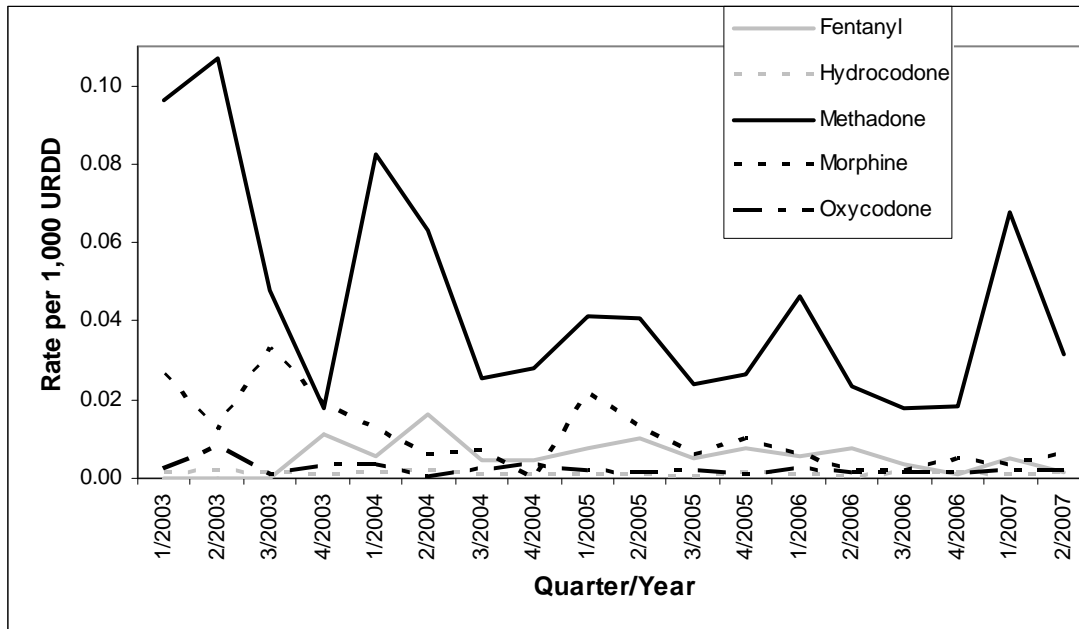
These data are medical outcomes of death associated with methadone exposures. Data reported are from 1st quarter 2003 through 2nd quarter 2007: 143 deaths associated with methadone exposures were reported.

Methadone Deaths by Age Group: 2003-2007



The largest number of methadone deaths occurred in individuals 20 – 29 years old. Three deaths occurred in young children 0 – 5 years old.

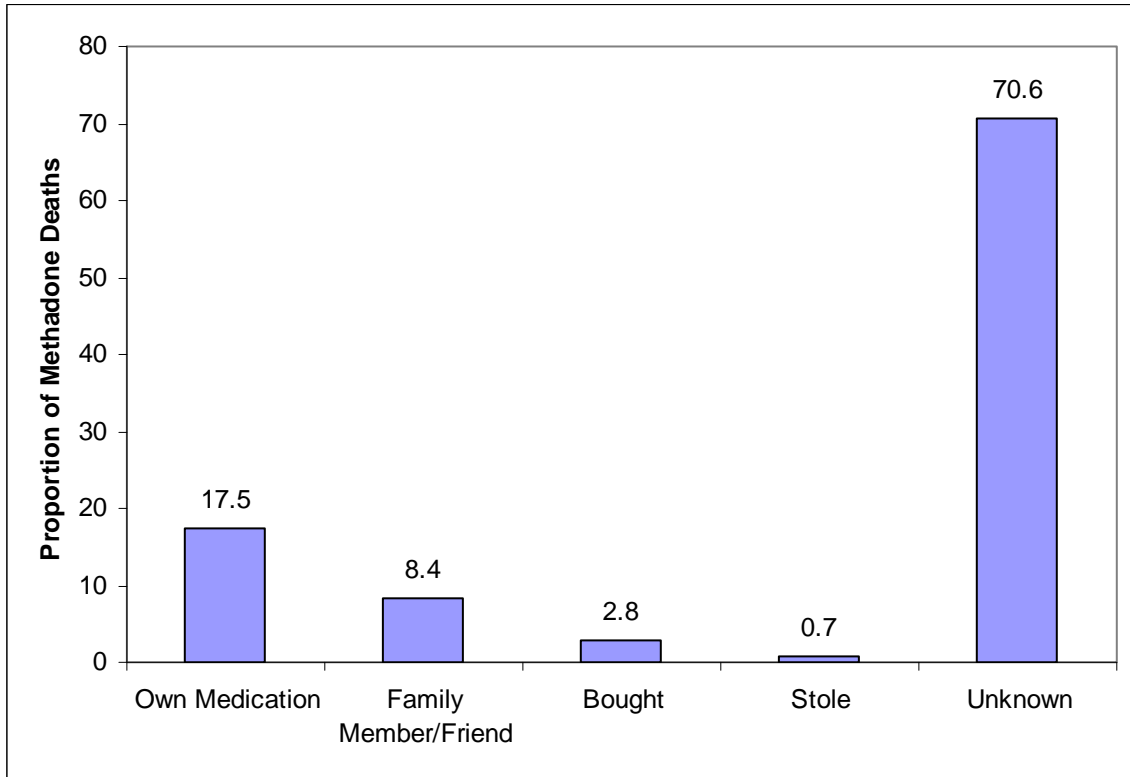
Death Rates per 1,000 Unique Recipients of Dispensed Drug (URDD): 2003-2007



As reported by RADARS System poison centers, methadone has the highest death rate per 1,000 Unique Recipients of Dispensed Drug (URDD). (URDD represents each unique patient who fills a prescription for a drug of interest during the quarter of interest, accounting for refills. This technique is used as a proxy for drug availability in a community.)

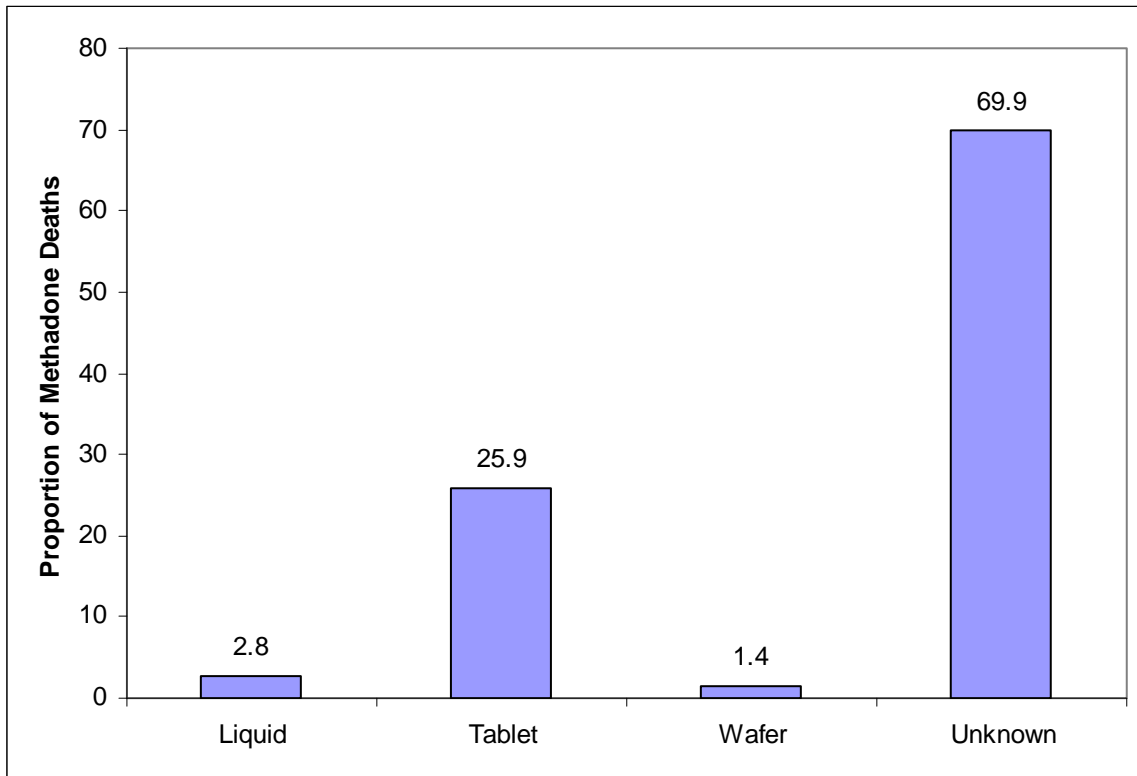
Other drugs which had positive death rates in more than five of the quarters of interest included fentanyl, hydrocodone, morphine, and oxycodone. Buprenorphine, hydromorphone and tramadol are not depicted on the graph because they reported deaths in only one, four and five quarters respectively (of 18 quarters in the time period of interest).

Reported Source of Methadone in Methadone Deaths: 2003-2007



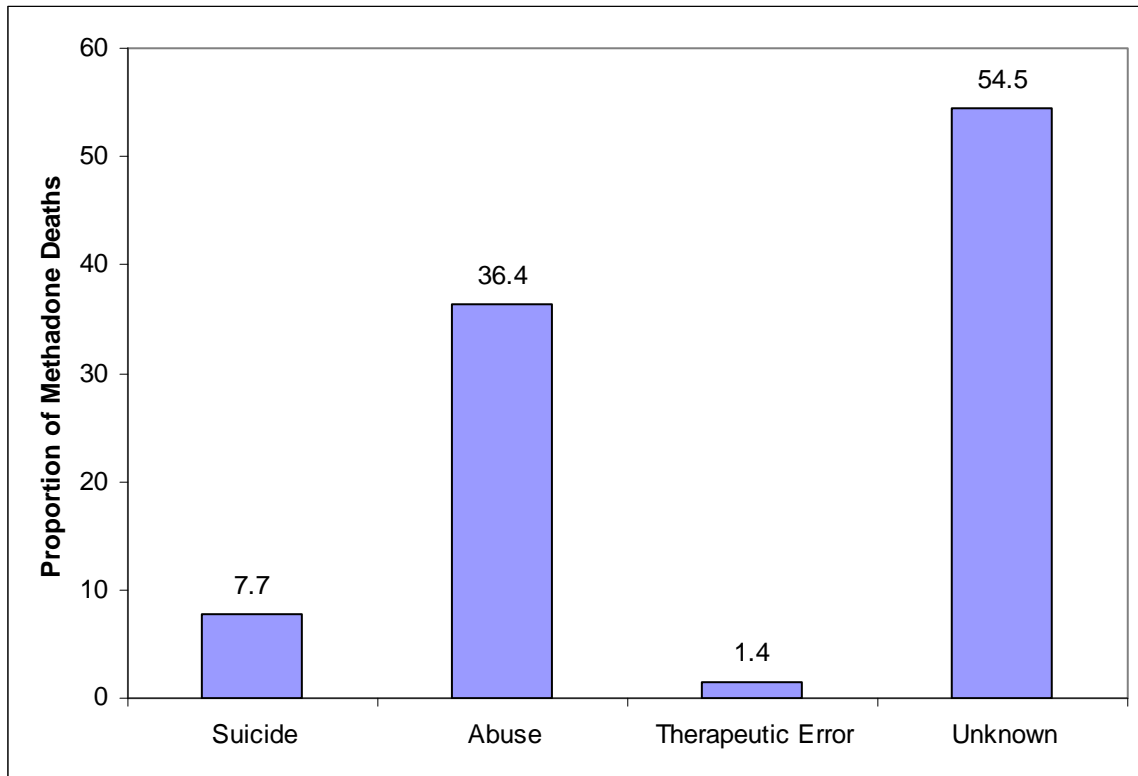
When the reported source of methadone is known, a large proportion of methadone deaths were associated with ingestions of the deceased's own medication.

Methadone Formulations in Methadone Deaths: 2003-2007



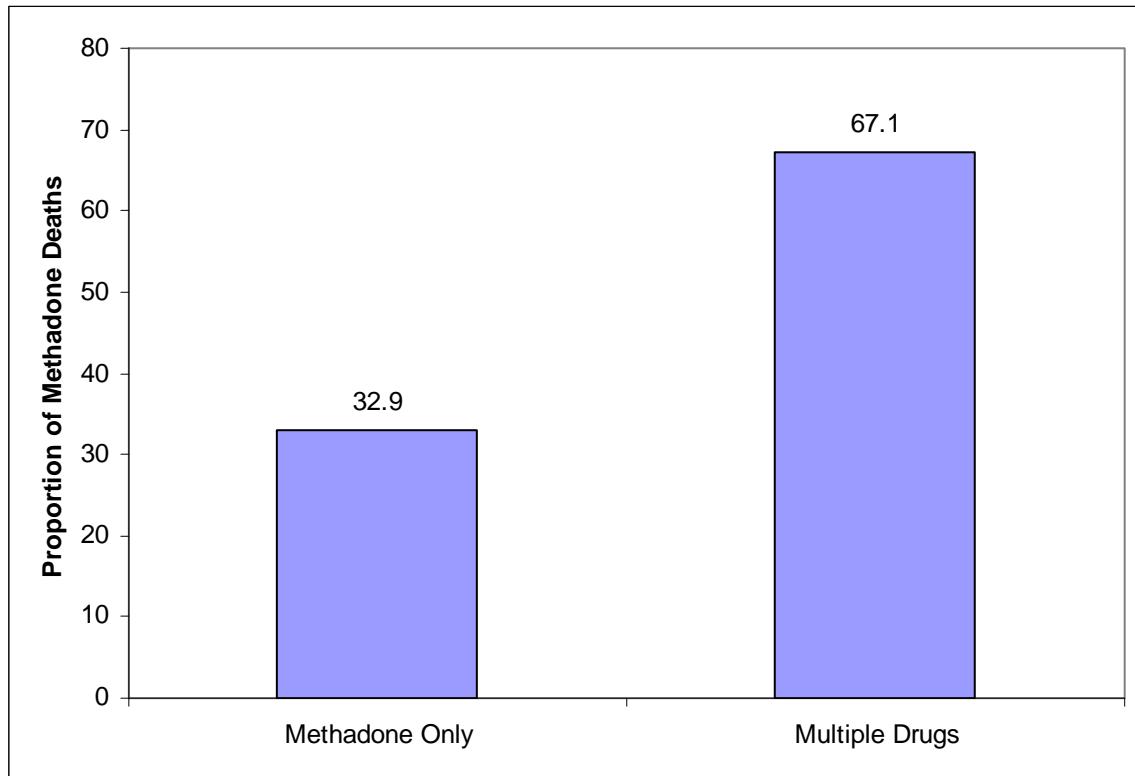
When the methadone formulation is known, the overwhelming majority of methadone deaths were associated with methadone tablets. This is expected, given the amount of tablet and wafer/diskette forms of methadone available by prescription for the treatment of pain.

Reported Exposure Reasons in Methadone Deaths: 2003-2007



When the exposure reason is known, most deaths were associated with exposures with the intent to abuse methadone to achieve a high.

Involvement of Multiple Drugs in Methadone Deaths: 2003-2007



The majority of methadone deaths involved multiple drugs. The most frequently mentioned drugs other than methadone are:

- Benzodiazepine (48% of methadone deaths with multiple drugs involved benzodiazepines).
- Cocaine (11% of methadone deaths with multiple drugs involved cocaine).
- Alcohol and amitriptyline (9% of methadone deaths involved alcohol and another 9% involved amitriptyline).
- SSRI, other type of anticonvulsant, and antidepressant (8% of each of these drugs were involved in methadone deaths).