

AN EPIDEMIOLOGY PUBLICATION OF THE OREGON DEPARTMENT OF HUMAN SERVICES

METHADONE DEATHS (AND DISTRIBUTION) ON THE RISE

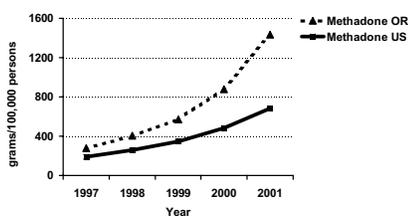
ALTHOUGH methadone has been around for half a century, recently it has been catching the attention of public health officials. A *New York Times* headline on February 9, 2003 read "Methadone, Once the Way Out, Suddenly Grows as a Killer Drug."¹ Methadone deaths are on the rise in Maine, North Carolina, Florida... and Oregon. Who is dying and how? What can be done to prevent these deaths?

BACKGROUND

Methadone is a long-acting synthetic opiate that was approved by the Food and Drug Administration (FDA) in 1947 for analgesic and antitussive uses and in 1972 for the treatment of opiate addiction.* More recently, methadone has been widely used to control chronic pain, including cancer pain.

From 1997–2001 methadone distribution increased 3.5-fold in the US and 5-fold in Oregon (figure, below left). Oregon now ranks 5th among the states in the amount of methadone distributed per 100,000 people.² Methadone's low cost (about eight cents per pill) and its use in place of OxyContin (a newer, more expensive long-acting opiate that can be abused and that has caused a number of deaths) may have contributed to its increasing use for chronic pain.

Methadone distribution Oregon vs. US, 1997–2001



*From Automation of Reports and Consolidated Orders System of Drug Enforcement Administration

* Although a provider registered with the Drug Enforcement Administration (DEA) can prescribe methadone for pain, only those physicians specifically registered with the DEA and FDA can prescribe methadone for opiate addiction treatment. There is a new program to dispense buprenorphine for office-based treatment of opioid dependence: contact www.buprenorphine.samhsa.gov or 1-866-287-2728 for more information.

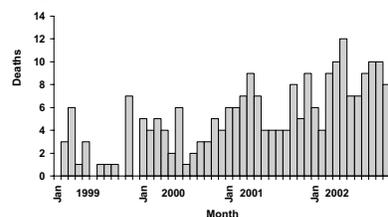
Although we do not know for sure why methadone use has increased more in Oregon than in the rest of the country, an increased focus on adequate pain management here, particularly for patients with terminal diseases, may have contributed.

METHADONE-RELATED DEATHS

The Oregon Medical Examiner's (ME) office recently noted an increase in the number of deaths related to methadone among ME cases. To determine if an increase in deaths related to methadone had occurred in the population as a whole, and to better characterize methadone-related deaths in Oregon we reviewed the ME records for 1999–2002. Over this period there were 245 methadone-related deaths[†] of which 103 (45%) occurred in 2002 alone. The number of methadone-related deaths has increased annually at least since 1999 (figure, below center), with a 4-fold rise in these deaths since 1999.

Among the 245 people who died a methadone-related death between 1999–2002, 58% were male, 91% were white, the mean age was 45 years (range 15–72), and the median year of school completed was 12th grade. Methadone deaths were not just an urban phenomenon; 46% of these deaths occurred outside of Multnomah and Lane counties. According to the ME report 43% of

Methadone-related deaths by month, Oregon, 1999–2002



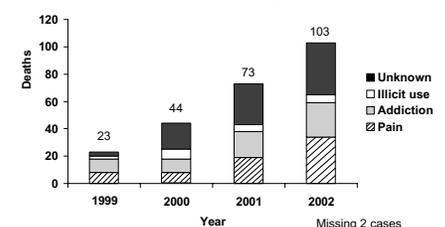
† Deaths were identified for possible inclusion in this study if methadone overdose was listed as a cause of death, methadone was noted as a significant finding on the death certificate, or the ME had identified a blood methadone level ≥ 0.2 mg/L. Each of these deaths was then reviewed by an ME and an epidemiologist to determine whether the death was methadone-related.

the decedents reported chronic pain (e.g., backache, headache, fibromyalgia), 38% had a history of using heroin (60% had a history of abusing illegal drugs or alcohol) and 37% had a history of mental illness (note that a single decedent could be counted in more than one category). Although we were not able to quantify this factor reliably, many of these decedents were reported to have been snoring loudly or difficult to arouse before their deaths, suggesting that excessive sedation contributed to their demise.

We classified the reasons that decedents had access to methadone into four categories: pain treatment (28%), addiction treatment (34%), illicit use (8%), and unknown (30%). The increase in methadone deaths appears to be related primarily to deaths among those receiving pain and addiction treatment rather than those using methadone illicitly (figure, below right). The proportion of deaths among those treated for pain increased from 18% to 33%. Since we do not know how many persons use methadone for either of these indications, so we cannot calculate the risks attendant to different uses of methadone.

Polypharmacy was common among these decedents, and may have contributed to these deaths by exacerbating the arrhythmogenic or respiratory depressant effects of methadone.³ The majority (87%) of decedents had toxicology tests positive for at least 1 other drug in addition to methadone. Other drugs most commonly present were benzodiazepines (50% of decedents), other opiates (25%), and alcohol (14%).

Reasons for methadone among methadone prescription deaths, Oregon, 1999–2002





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SUMMARY

Although methadone benefits many, the number of methadone-related deaths has recently been increasing in Oregon, in step with the amount of methadone distributed to the state. The increase in deaths has occurred primarily both among those receiving methadone for addiction to heroin or other opiates and among those taking the drug for chronic pain. The majority of decedents had also taken other drugs that can increase the side effects of methadone. Many of these decedents were reported to be difficult to arouse or somnolent before their deaths.

WHAT NOW?

Should you stop prescribing methadone because of these deaths? As for all medical treatments, risks need to be balanced with potential benefits. Methadone is an important treatment modality for heroin addiction, and probably prevents many deaths from heroin overdose as well as attendant problems such as criminal activity undertaken to finance a drug habit, and the suffering of family members related to addicts. It is also an important tool with some unique properties for the treatment of chronic pain.⁴ Untreated chronic pain continues to afflict millions in the US, diminishing their quality of life and causing suffering that could be prevented with proper treatment.

However, when prescribing methadone, particularly for chronic pain, be sure to take steps to educate your patients. The Oregon Board of Medical Examiners requires that you discuss the risks associated with use of a controlled substance, and that you have patients

sign a written notice about these risks.[‡]

Patients should be forewarned that this medication needs time to build to an effective level and that taking too much of this medication or taking it too often can be lethal. Methadone does not produce the same “high” as many other opiates,⁵ and also typically does not produce the same peak in analgesia soon after ingestion that other opiates produce. Also, the half-life can be as long as 150 hours.⁶⁻⁸ These qualities mean that methadone can accumulate insidiously to a fatal level. Similarly, the combination of methadone with other opiates, benzodiazepines, tricyclics, or barbiturates can be fatal.⁹⁻¹¹

In terms of dosing, providers should “start low and go slow.” Experts advise that 5–10 mg/day may be surprisingly effective for chronic pain, and they caution against increasing the dose of methadone more often than weekly.

Providers should assess the history of substance abuse, and incorporate this information into the treatment plan. Also, they should advise family members and others caring for these patients of the need to monitor the patient for somnolence as an early warning sign of toxicity.

This investigation does not support the contention that the increase in methadone deaths can be solely attributed to formulary changes restricting the use of OxyContin, since the increase in deaths began long before those changes were made. However, health systems might consider addressing the problem of methadone deaths through policy changes,

such as developing systems that automatically remind pharmacists or providers about the danger of polypharmacy when methadone is prescribed. Since the effectiveness of these policy approaches is unknown, careful evaluation of their effects might help guide future policy changes.

Additional information on methadone dosing and conversion is available from the May 2003 Drug Utilization Review Board Newsletter at http://pharmacy.oregonstate.edu/drug_policy/newsletter_email.html.

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‡ See OAR 847-015-030, at http://arcweb.sos.state.or.us/rules/OARS_800/OAR_847/847_015.html