Surveillance of methadone-related adverse drug events using multiple public health data sources

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Abstract

Healthcare safety and quality surveillance is increasingly conducted by public health agencies. We describe a biomedical informatics method that uses multiple public health data sources to perform surveillance of methadone-related adverse drug events. Data from Utah medical examiner records, vital statistics, emergency department encounter administrative data and a database of controlled substances prescriptions are used to examine trends in state-wide adverse events related to methadone. From 1997 to 2004, population-adjusted methadone prescriptions increased 727%, with evidence to suggest the rise in the methadone prescription rate is for treatment of pain, not addiction therapy. During the same period of time, population adjusted, accidental methadone-related deaths in medical examiner data increased 1770%. Population adjusted methadone-related emergency department encounters rose 612% from 1997 to 2003. Our results suggest that the increase in methadone prescription rates from 1997 to 2004 was accompanied by a concurrent increase in methadone-related morbidity and mortality. Although patient data is not linked between data sources, our results demonstrate that utilizing multiple public health data sources captures more cases and provides more clinical detail than individual data sources alone. Our approach is a successful biomedical informatics approach for surveillance of adverse events and utilizes widely available public health data sources, as well as an emerging source of public health data, controlled substance prescription registries.

Keywords: Methadone; Adverse drug events; Patient safety

1. Introduction

Unintentional fatalities due to prescription medications are an increasing problem in the United States and Utah [1]. For the years 1999–2003, unintentional deaths due to prescription medications were the fourth-leading cause of death in 25–54 year olds in Utah (Barry Nangle, PhD. Personal communication, 8/31/2004). A recent study of Utah medical examiner data found deaths of unintentional or undetermined intent caused by prescription medications increased from 1.5/100,000 residents (1991–1998) to 4.4/100,000 residents (1999–2003). Methadone was the most common drug identified by the Utah medical examiner as causing or contributing to accidental deaths for 2003–2005. Notably, while deaths of unintentional or undetermined intent caused by prescribable narcotics nearly tripled, cases of self-inflicted harm (suicide) with those drugs remained stable from 1991 to 2003 [2]. In addition to the medical examiner data, retail supply data from the United States Drug Enforcement Administration (DEA) shows a sharp increase in the amount of methadone distributed in Utah since 1999 [3]. The medical examiner and DEA data suggest methadone prescription rates and methadone-related deaths are both rising in Utah, but more research is necessary to confirm this finding.

Methadone may be prone to cause serious harm and death for several reasons. Historically, methadone has been used to treat chronic abuse of opiates such as heroin.
However, in recent years methadone has become increasingly prescribed for acute and chronic pain [4]. Methadone may pose patient safety concerns because of its highly variable half life, 16–100 h, and variable potency with chronic opiate users. Additionally, methadone may be more likely to cause harm than other pain medications due to physician inexperience titrating a safe, effective dose; lack of clear evidence for appropriate use; and the risk of delayed overdose [4,5].

To study methadone-related harm in Utah, we adopt an informatics approach that utilizes data from multiple public health data sources to examine concurrent trends in methadone-related morbidity and mortality and methadone prescription rates. Our first objective is to determine whether broader examination of available public health data corroborate the finding from medical examiner and DEA data that methadone-related deaths and prescriptions are trending upward for the past eight years. We also seek to determine trends in serious methadone-related adverse events requiring an emergency department encounter; i.e., those cases in which death is not the initial medical presentation. Our second objective is to demonstrate the value of utilizing commonly available public health data sources for surveillance of adverse events, though the patient data is not linked between sources.

Public health surveillance of adverse events differs from patient-level clinical surveillance. Both seek to quantify, analyze and ultimately prevent adverse events; however, clinical informatics surveillance focuses on the individual and has ready access to data not always available to public health practitioners. The clinical informatics literature has documented the value of utilizing multiple data sources to capture the largest fraction of actual adverse events and the most information about those patient-level events. Published data sources for clinical informatics surveillance of adverse drug events include inpatient pharmacy data, laboratory data and natural language understanding examination of provider notes [6]. We examine the utility of extending a multiple data source surveillance approach to commonly available public health data sources and focusing on population-level data rather than individuals.

2. Data sources

For our analysis, we use methadone prescription data from Utah’s controlled substances registry, methadone-related death data from vital statistics and medical examiner data and methadone-related emergency department encounters from the Utah Emergency Department Encounter Database (Table 1).

2.1. Utah Controlled Substances Database

The Utah Controlled Substances Database (CSDB) is a registry enacted by legislative mandate (Utah Code Section 57-37-7.5) to track all outpatient prescriptions for Schedule II–V drugs dispensed in Utah and by Utah providers. In use since 1995, Utah’s registry is the oldest controlled substances registry in the United States. All retail, institutional and mail order pharmacies in Utah that dispense prescriptions for Schedule II–V drugs are required to report; however, inpatient facilities do not submit data [7]. The Division of Occupational and Professional Licensing within the Utah Department of Commerce maintains the CSDB.

Pharmacies report seventeen variables to the CSDB from pharmacies: pharmacy identification number, name, address, birth date and sex of prescription holder, date filled, prescription number, new/refill code, metric quantity of drug, days supply of drug, National Drug Code Number, prescriber identification number, date the prescription was written and number of refills authorized.

2.2. Utah medical examiner data

Utah has a state-wide, centralized medical examiner system that has statutorily mandated jurisdiction over all deaths thought to be drug-related [8]. Case information for methadone-related deaths is taken from the Office of the State Medical Examiner’s (ME) database. The ME database contains 113 variables including demographic information about the decedent, toxicological, laboratory and autopsy examination results. Cause of death ascertainment is supervised by a physician examiner using all

Table 1

<table>
<thead>
<tr>
<th>Data source</th>
<th>Years examined</th>
<th>Coding ontology</th>
<th>Case selection criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controlled substances database</td>
<td>1997–2004</td>
<td>Drug data is encoded with National Drug Code number and ingredient Free text</td>
<td>Prescription for methadone</td>
</tr>
<tr>
<td>Medical examiner data</td>
<td>1997–2004</td>
<td></td>
<td>Deceased from Utah with methadone included as a drug causing or contributing to death AND manner of death is not suicide Deceased from Utah with secondary cause of death code due to methadone AND primary cause of death is not suicide Patients with diagnosis code(s) for methadone-related harm AND no code(s) for intentional harm to self</td>
</tr>
<tr>
<td>Death certificate data</td>
<td>1999–2004</td>
<td>Primary and secondary cause of death are encoded with ICD-10(^a)</td>
<td></td>
</tr>
<tr>
<td>Emergency department</td>
<td>1997–2003</td>
<td>Diagnosis data is encoded with ICD-9-CM(^b)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) World Health Organization’s International Classification of Diseases, Revision 10.

\(^b\) Centers for Medicaid and Medicare’s International Classification of Diseases, Revision 9, Clinical Modification.
available clinical information, including manner of death, circumstances of death, physical examination, laboratory data, and medical records.

2.3. Utah vital statistics data

Death certificate data is a component of vital statistics information maintained by the Office of Vital Records and Statistics at the Utah Department of Health (UDOH). Each death certificate has a primary cause of death field and up to nine contributing diagnosis fields. Deaths for 1997 and 1998 are coded using the World Health Organization’s International Classification of Diseases, Ninth Revision (ICD-9). ICD, Tenth Revision (ICD-10) is used for deaths after 1998. ICD-9 differs substantially from ICD-10. ICD-10 has approximately twice as many codes, allows greater specificity and does not have one-to-one matches with all ICD-9 codes. Thus, comparing mortality trends from years utilizing different versions of the ICD coding system is challenging and must be done cautiously [9,10]. In addition to concerns with cross-walking between ICD-9 and ICD-10, there are technical difficulties with the 1997–1998 data that limit analysis. Therefore, death certificate data from the years 1997–1998 are excluded from our analysis.

2.4. Utah emergency department encounter database

The Emergency Department Encounter Database (EDED) is a repository of all emergency department patient encounters in Utah and is maintained by the Bureau of Emergency Medical Services at the UDOH. Utah administrative rule R426-1-7 mandates that all licensed Utah hospitals report information on emergency department patient encounters to the EDED. The database contains complete administrative (claims) data for each encounter including diagnosis codes, procedure codes, patient demographic information, services received and hospital charges. For 1997–2003, diagnosis and procedure information is encoded with the Centers for Medicare and Medicaid Services’ International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) [11]. Data from 2004 is not available for this study.

3. Methods

Our study concurrently analyzes the CSDB for methadone prescriptions and the remaining three data sources for methadone-related morbidity and mortality. However, we do not link data across the four data sources for legal, political and technical reasons. Access to study the CSDB was granted to UDOH researchers only after lobbying the Utah legislature to amend the CSDB statute. Our study is a prudent first use of the CSDB data and we aim to demonstrate the potential value of additional informatics work to link CSDB prescription data to morbidity and mortality data. A technical limitation to record matching is the lack of a single patient identifier across all the data sources. However, some combinations of data sources have linking identifiers and all data sources have demographic data that can be used by record matching algorithms. For this reason, linking patient records across all four data sources is viable in the future, though the usual concerns with record matching algorithm accuracy will apply [12,13].

3.1. Methadone prescription rates and demographic characteristics of prescription recipients

We use all CSDB records from 1997–2004 and group the data by calendar year. We identify methadone prescription records by searching the ‘ingredient name’ field for entries that include the character string ‘methadone.’ We report the total number of methadone prescriptions per year, since the number of individual patients and prescribers cannot be identified due to incompleteness of the CSDB data and the de-identified data set used for this study. Methadone prescription records are analyzed for patient age and sex, as well as temporal and geographic variables. For all data sources, we define urban according to the UDOH convention: residence in Salt Lake, Davis, UT or Weber counties. Significance testing for differences in demographic characteristics between data sources is done using the unpaired t-test.

3.2. Medical examiner methadone-related death rates and demographic characteristics

We use ME database records from 1997 to 2004 for Utah residents with drug poisoning listed as cause of death. The manner of death is classified by the medical examiner as intentional (i.e., suicide or homicide); unintentional (i.e., accidental or natural deaths); or of undetermined intent. From this larger group of drug poisoning deaths, we select only cases with methadone included as a drug causing or contributing to death and exclude cases classified as intentional injuries (suicides). We exclude suicides because self-inflicted injuries involve a separate approach to evaluation and prevention. We determine the annual numbers and rates of drug-poisoning deaths, trends in methadone-related deaths over time and the demographic characteristics of the patients.

3.3. Vital statistics methadone-related death rates and demographic characteristics

Our study draws on complete, state-wide death certificate data for the years 1999–2004, during which time ICD-10 encodes causes of death. We select cases with ICD-10 code T40.3, ‘Poisoning by Methadone,’ as a cause of death. Since ICD-10 ‘T’ codes cannot be a primary cause of death, all cases have the T40.3 code in one of the contributing cause of death fields. We exclude cases with suicide listed as the primary cause of death (ICD-10 codes
X62 and X64). We group the cases by calendar year and determine the number of deaths per year, trends in methadone-related deaths over time, demographic characteristics of the decedents and the primary causes of death associated with methadone-related deaths.

3.4. Emergency department encounters with methadone-related diagnoses

We use EDED data for the years 1997–2003 and identify records with ICD-9-CM codes specific for methadone-related harm using the following codes: 965.02, ‘poisoning by methadone;’ E850.1, ‘accidental poisoning by methadone;’ and E935.1, ‘methadone causing adverse effects in therapeutic use.’ We select cases in which one or more of the three methadone-related codes are present and self-inflicted harm is not coded in the primary or secondary diagnoses fields. The EDED records are grouped by calendar year and we determine trends in methadone-related visits, demographic characteristics of patients, patient discharge status, charges associated with the encounter and the primary payor (insurer).

3.5. Institutional review board approval

Institutional Review Board approval was granted to conduct this study at the UDOH (#104, approved January 20, 2005) and the University of Utah (#15641, approved December 1, 2005). Our study was deemed exempt from human subject regulatory oversight.

4. Results

Our investigation shows a parallel increase in methadone prescriptions and methadone-related morbidity and mortality for the study period (Fig. 1; note: the y-axis for the graph of prescription data differs from the graphs of death and emergency department data). The number of prescriptions and harmful methadone-related events rises out of proportion to the growth of the Utah population in all data sources (Table 2).

4.1. Methadone prescriptions

The annual number of population-adjusted methadone prescriptions in the Utah CSDB rose from 256.5 (1997) to 2,120.1 (2004) per 100,000 population (Fig. 1), a 727% increase. The total number of prescriptions rose from 5385 (1997) to 52,350 (2004) (Table 2). Of note, these figures represent total prescriptions filled, not the number of individuals with prescriptions; however, no change in prescription regulations or reporting guidelines occurred during study period to explain the dramatic increase. For 1997–2004, the mean age and gender distribution of individuals with methadone prescriptions varied little (age range = 49.2–50.1 years); the percentage of prescriptions to females ranged from 52.8 to 56.1%; and the percentage of prescriptions for residents of urban counties was 80.7–84.4% (Table 3).

4.2. Medical examiner deaths

In medical examiner data, the number of methadone-related non-suicide deaths per 100,000 Utah population rose from 0.24 (1997) to 4.45 (2004) (Fig. 1), a 1770% increase. The total number of deaths increased from 5 (1997) to 110 (2004) (Table 2). The mean age of decedents ranged from 34.2 to 42.0 years; the percentage of female decedents ranged from 31.3 to 60.0%; and the percentage of decedents from urban counties was 70.0–85.7% (Table 3).
4.3. Vital statistics death certificates

In death certificate data, the number of non-suicide records where methadone was a contributing factor rose from 0.78 (1999) to 4.33 (2004) per 100,000 Utah population (Fig. 1). The absolute number of methadone-related deaths increased from 17 (1999) to 107 (2004) (Table 2). During the same time period, the mean age of decedents ranged from 35.4 to 40.2 years; the percentage of female decedents ranged from 29.4 to 44.0%; and the percentage of decedents from urban counties was 67.9–81.1% (Table 3). In 97.4% of cases, the primary ICD-10 diagnosis code was drug poisoning (accidental or undetermined intent) or mental/behavioral disorder related to prescribable medications or illicit drugs. In 2.6% of the cases, a non-drug-related cause of death (e.g., obesity or cardiac myopathy) was the primary diagnosis.

4.4. Emergency department encounters

Emergency department encounters with non-suicide methadone-related diagnoses increased from 1.0 (1997) to 7.1 (2003) per 100,000 Utah population (Fig. 1), a 612% increase. The absolute number of emergency department encounters rose from 21 (1997) to 172 (2003); 2004 data not available (Table 2). The mean age of patients with emergency department encounters from 1997 to 2003 ranged from 31.0 to 43.4 years; the percentage of female patients varied from 46.0 to 70.0%; and the percentage of encounters with patients from urban counties was 61.9–82.5% (Table 3).

For methadone-related encounters, the patient disposition was most commonly discharged to home (76.9–100%); admission to the hospital or other healthcare facility was the next most frequent disposition (0–20.3%); and death in the emergency department occurred rarely (0–5.0%). The primary type of payor was a private insurer in 25.0–48.9% of cases, Medicare, Medicaid, or other government source was the primary payor in 23.8–50.9% of cases. Average hospital charges for methadone-related emergency department encounters rose from $622 in 1997 to $6622 in 2003; the average hospital charges in the EDED for all 2003 ED visits were $1970. The sum of all costs for

Table 2
Data source record counts and Utah population data

<table>
<thead>
<tr>
<th>Data source</th>
<th>Record type</th>
<th>1997</th>
<th>1998</th>
<th>1999</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controlled substances</td>
<td>Methadone prescriptions</td>
<td>5,385</td>
<td>8,954</td>
<td>15,752</td>
<td>20,738</td>
<td>26,527</td>
<td>34,481</td>
<td>44,441</td>
<td>52,350</td>
</tr>
<tr>
<td>database</td>
<td>Total controlled substance</td>
<td>2,069,340</td>
<td>2,054,063</td>
<td>2,544,875</td>
<td>2,685,006</td>
<td>2,918,051</td>
<td>3,183,808</td>
<td>3,417,084</td>
<td>3,450,281</td>
</tr>
<tr>
<td>Medical examiner (ME)</td>
<td>Methadone-related deaths</td>
<td>5</td>
<td>7</td>
<td>16</td>
<td>20</td>
<td>35</td>
<td>59</td>
<td>86</td>
<td>110</td>
</tr>
<tr>
<td>Data</td>
<td>Total ME cases</td>
<td>1,825</td>
<td>1,892</td>
<td>1,896</td>
<td>1,760</td>
<td>03</td>
<td>98</td>
<td>55</td>
<td>107</td>
</tr>
<tr>
<td>Death certificates</td>
<td>Methadone-related deaths</td>
<td>5</td>
<td>7</td>
<td>16</td>
<td>20</td>
<td>35</td>
<td>59</td>
<td>86</td>
<td>110</td>
</tr>
<tr>
<td></td>
<td>Total death certificate</td>
<td>5</td>
<td>7</td>
<td>16</td>
<td>20</td>
<td>35</td>
<td>59</td>
<td>86</td>
<td>110</td>
</tr>
<tr>
<td>Emergency department (ED)</td>
<td>Methadone-related encounters</td>
<td>21</td>
<td>19</td>
<td>53</td>
<td>68</td>
<td>92</td>
<td>143</td>
<td>172</td>
<td>4</td>
</tr>
<tr>
<td>encounters</td>
<td>Total ED encounters</td>
<td>504,706</td>
<td>501,348</td>
<td>605,912</td>
<td>631,066</td>
<td>669,698</td>
<td>692,190</td>
<td>715,400</td>
<td>4</td>
</tr>
<tr>
<td>Utah population</td>
<td>Residents</td>
<td>2,099,404</td>
<td>2,141,619</td>
<td>2,193,006</td>
<td>2,246,553</td>
<td>2,305,652</td>
<td>2,358,330</td>
<td>2,413,618</td>
<td>2,469,230</td>
</tr>
</tbody>
</table>

*Excludes self-inflicted injuries and suicides.

Table 3
Demographic characteristics of methadone-related records in Utah Controlled Substances Database (CSDB), Medical Examiner Data (ME), Death Certificates (DC) and Emergency Department Encounter Database (EDED), 1997–2004

| Year | CSDB Age | ME Age | DC Age | EDED Age | CSDB Female | ME Female | DC Female | EDED Female | CSDB Urban | ME Urban | DC Urban | EDED Urban |
|------|----------|--------|--------|----------|-------------|-----------|-----------|-------------|-------------|-----------|----------|-----------|-------------|
| 1997 | 49.6     | 36.2   | 41.0   | 40.4     | 53.6        | 52.8      | 53.6      | 53.6        | 83.6        | 80.0     | 80.0     | 80.0      |
| 1998 | 49.4     | 35.3   | 40.9   | 40.3     | 52.8        | 42.9      | 42.9      | 42.9        | 83.5        | 85.7     | 85.7     | 85.7      |
| 1999 | 49.7     | 38.4   | 38.3   | 41.0     | 55.6        | 31.3      | 29.4      | 29.4        | 84.4        | 81.3     | 81.3     | 81.3      |
| 2000 | 49.6     | 34.2   | 35.4   | 41.0     | 56.1        | 40.0      | 40.0      | 40.0        | 84.4        | 70.0     | 70.0     | 70.0      |
| 2001 | 49.5     | 40.3   | 40.2   | 42.8     | 55.6        | 48.6      | 40.5      | 40.5        | 83.8        | 82.9     | 82.9     | 82.9      |
| 2002 | 49.6     | 37.7   | 38.5   | 43.4     | 54.8        | 33.9      | 34.5      | 34.5        | 83.4        | 74.6     | 74.6     | 74.6      |
| 2003 | 49.8     | 38.3   | 38.3   | 40.7     | 54.2        | 46.5      | 43.2      | 43.2        | 80.8        | 70.9     | 70.9     | 70.9      |
| 2004 | 49.2     | 37.4   | 37.9   | 39.8     | 53.8        | 32.7      | 35.5      | 35.5        | 80.7        | 80.9     | 80.9     | 80.9      |
| Average | 49.1 | 38.4   | 38.1   | 39.3     | 54.6        | 42.0      | 37.9      | 37.9        | 82.8        | 78.3     | 78.3     | 78.3      |

*Data not available.
methylone-related emergency department encounters increased from $13,058 in 1997 to $1,138,953 in 2003 (Table 4).

5. Discussion

Surveillance of healthcare safety and quality is increasingly becoming the domain of public health agencies. In Utah, for example, the legislature mandated that the UDOH publish annual reports on the quality and safety of obstetrical care provided at the state’s healthcare institutions [14]. Public health practitioners have access to a broad range of public health and clinical data resources to draw upon when surveillance is needed. Unfortunately, many of these data sources are in different systems and can lack uniformity in available data, data quality, data completeness, data encoding and cross-system unique identifiers. Information technology tools are available to perform specific types of safety and quality surveillance [15–17], but not all surveillance needs are met by existing tools.

We demonstrate the utility of applying a biomedical informatics approach from patient-level clinical informatics to the public health domain. Concurrently analyzing multiple public health data sources for evidence of morbidity and mortality due to adverse events can be a useful technique for surveillance of population trends, particularly when data linkage between data sources is not possible for technical, financial, temporal or legal reasons. Our multiple data source approach captures a broader range of events and provides more clinical detail than a single data source. Although each data source has limitations, aggregate data analysis can provide more comprehensive morbidity and mortality data.

Our study also demonstrates the value of an important and emerging source of surveillance data, the controlled substance prescription registry. In Utah, pharmacies are required to report outpatient prescriptions filled for controlled substances to the state. Since prescription data are frequently a missing piece of data in surveillance, controlled substance prescription registries offer a powerful source of information for studying controlled substance adverse events. Utah has the oldest such registry, but controlled substance registries were enacted in twenty-six states by the end of 2005, according to the Drug Enforcement Agency, Office of Diversion Control [18]. Our study represents an early model for the effective use of controlled substance prescription data for surveillance of healthcare safety and quality. Concurrent use of controlled substances prescription data and morbidity and mortality data sources has broad applicability since medical examiner, vital statistics and emergency department encounter data are widely available.

We apply this public health informatics surveillance methodology to examine adverse events due to methylone in Utah. Using population adjusted data, methylone prescriptions rose 727% from 1997 to 2004. During the same period of time, population adjusted cases of non-suicide, methylone-related deaths increased 1770% in medical examiner data. Similarly, methylone-related emergency department encounters rose by 612% from 1997 to 2003 (2004 data not available). Death certificate data also showed an upward trend from 1999 to 2004 (1997–1998 data are not available for comparison). Our ecologic study demonstrates parallel trends of increasing methylone prescriptions, increasing accidental methylone deaths and increasing methylone-related emergency department visits. Medical examiner data shows an increase in accidental deaths due to methylone that is substantially greater than the increase in methylone prescriptions.

In Utah, there are several reasons to suspect that the steep rise in methylone prescriptions from 1997 to 2004 is largely due to treatment of pain. The rate of heroin abuse and admissions for opiate addiction to substance abuse treatment facilities in Utah is unchanged during the study period, 1997–2004 [19]. Utah code dictates that physicians may not prescribe methylone for addiction therapy unless they are directly affiliated with an addiction treatment facility. Additionally, methylone data from addiction treatment facilities is not included in retail pharmacy data reported by the DEA and addiction treatment facilities are exempt from reporting data to the Utah CSDB. All of these factors suggest the dramatically increased number of methylone prescriptions and the increased retail supply of drugs are for individuals using methylone for pain therapy, rather than addiction therapy. Our data sources do

Table 4: Descriptive data for methylone-related emergency department encounters in Utah, 1997–2004

<table>
<thead>
<tr>
<th>ED Discharge Status</th>
<th>Primary payor (insurer)</th>
<th>Total charges for ED visit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Healthcare facility</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Home</td>
<td>Death</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>Sum all cases</td>
</tr>
<tr>
<td>1997 (n = 21)</td>
<td>0%</td>
<td>100%</td>
</tr>
<tr>
<td>1998 (n = 19)</td>
<td>10.0%</td>
<td>85.0%</td>
</tr>
<tr>
<td>2000 (n = 68)</td>
<td>14.7%</td>
<td>77.9%</td>
</tr>
<tr>
<td>2001 (n = 92)</td>
<td>13.0%</td>
<td>85.0%</td>
</tr>
<tr>
<td>2002 (n = 143)</td>
<td>20.3%</td>
<td>76.9%</td>
</tr>
<tr>
<td>2003 (n = 172)</td>
<td>19.2%</td>
<td>76.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a Against medical advice, unknown, other.
b Medicare, Medicaid, other government payor.
c Charity, self-pay, unknown.
not allow us to rule out that a segment of our cohort of patients is chronic drug abusers. However, amongst the population of patients using methadone for pain management, a substantial portion of harm and death is likely to be accidental and not associated with chronic drug abuse.

The demographic characteristics of individuals harmed by methadone are significantly different from those receiving methadone prescriptions in two ways. First, the mean age of individuals from medical examiner, death certificate and emergency room encounter data ranges from 38.1 to 39.3 years old; in contrast, the mean age of individuals with methadone prescriptions is significantly \( p < 0.01 \) higher at 49.1 years old. Second, the percentage of males dying from methadone-related harm is significantly \( p < 0.01 \) higher than those receiving prescriptions; 58.0% male decedents in the medical examiner data and 62.1% male decedents in the death certificate data. In the controlled substances prescription data, only 45.4% of prescriptions were for males. The younger and predominantly male nature of decedents and the younger age of emergency department encounters may reflect differential health-seeking behaviors of older individuals and female patients. Alternatively, the demographic difference may be due to the subset of our study population who are drug abusers. Drug abusers are more likely to be young and male [19]; they may be more prone to death for a variety of reasons. However, more research is necessary to fully understand the demographic and clinical factors that contribute to the differences in deaths and emergency department visits.

Our data also suggest the cost of healthcare encounters associated with methadone-related harm is rising. Charges associated with methadone-related emergency department encounters show an escalating pattern of cost per patient and total charges for all patients. From 1997 to 2003, both the total cost and average cost per patient increased steadily. The total cost of all methadone-related emergency department encounters increased greater than eighty-fold from $13,058 in 1997 to $1,138,953 in 2003. We do not attempt to capture less serious events that require outpatient management only, the follow-up care required for emergency department visits, or healthcare costs associated with deaths. Thus, our data represent only a fraction of the financial burden caused methadone-related harm, much of which is paid for by government payors.

Our study has some limitations. The ecologic study design does not allow us to designate a causal relationship between increasing methadone prescriptions and harm. Possible confounding factors include the unknown fraction of drug abusers in our population, the unknown portion of individuals who received prescription medication from illicit sources, and the unknown fraction of prescription records that represent unique individuals who received methadone prescriptions. We were unable to utilize 1997–1998 vital statistics data due to technical concerns and the shift in coding terminologies from ICD-9 to ICD-10. Additionally, the controlled substances database, vital statistics and emergency department encounter data sources have inconsistencies in completeness and coding practices over the study period. ICD-9-CM coding is a limiting factor, both for determining the intent of an injury and overall concern with the validity of administrative data for clinical purposes [20].

The next step in examining methadone-related harm is linking patient data across the data sources. Data linkage will allow us to determine if a causal relationship exists between increasing methadone prescription rates and methadone-related morbidity and mortality. The informatics challenges associated with data linkage, however, are substantial. Record-matching across the data sources is technically difficult since there is no unique identifier across all record sources and our investigation shows large gaps in demographic data and completeness of the Utah CSDB necessary for algorithmic record-matching. In addition, access to the controlled substances registry is tightly regulated by Utah statute and politically charged because of concerns with patient privacy. Data linkage efforts will need to carefully balance protecting privacy with gathering the data necessary to further study this issue. Despite the technical and political challenges, data linkage offers great promise to better understand methadone-related adverse events. Critical clinical details such as the time from methadone prescription to harm and the health characteristics of harmed individuals can be better studied. Finally, establishing a definitive relationship between prescribing methadone for pain and harm will shape the public health response. Possible interventions include efforts to educate healthcare consumers and clinicians and, if the evidence warrants, regulatory action to limit methadone prescription privileges to appropriately trained physicians.

6. Conclusion

Concurrent analysis of multiple public health data sources from Utah demonstrates a trend of increasing methadone prescriptions, methadone-related deaths and serious methadone-related events requiring emergency department treatment. Although patient data is not linked between data sources, our results demonstrate that utilizing multiple public health data sources captures more adverse event information and provides more clinical detail than individual data sources alone. Our approach is a widely applicable, successful biomedical informatics approach for surveillance of adverse events and utilizes commonly available public health data sources, as well as an emerging source of public health data, controlled substance prescription registries.

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