

Patterns of Abuse Among Unintentional Pharmaceutical Overdose Fatalities

Aron J. Hall, DVM, MSPH

Joseph E. Logan, PhD

Robin L. Toblin, PhD, MPH

James A. Kaplan, MD

James C. Kraner, PhD

Danae Bixler, MD, MPH

Alex E. Crosby, MD, MPH

Leonard J. Paulozzi, MD, MPH

IN 1997, 2 EXPERT PANELS IN THE United States introduced clinical guidelines for management of chronic pain.^{1,2} Both guidelines encouraged expanded use of opioid pain medications after careful patient evaluation and counseling when other treatments are inadequate. In subsequent years, experts have continued to advocate for improved pain management,³ and the Federation of State Medical Boards has encouraged adoption of model policies to promote more compassionate pain management by clinicians.⁴ States have increasingly complied by enacting new regulations or issuing guidelines or policy statements promoting improved pain management.⁵ In the 10 years (1997-2007) since the guidelines were first published, per capita retail purchases of methadone, hydrocodone, and oxycodone in the United States increased 13-fold, 4-fold, and 9-fold, respectively.⁶

Concurrent with the increase in legitimate sales of opioids, diversion of these drugs to nonmedical uses has also increased. The National Survey on Drug

For editorial comment see p 2672.

Context Use and abuse of prescription narcotic analgesics have increased dramatically in the United States since 1990. The effect of this pharmacoepidemic has been most pronounced in rural states, including West Virginia, which experienced the nation's largest increase in drug overdose mortality rates during 1999-2004.

Objective To evaluate the risk characteristics of persons dying of unintentional pharmaceutical overdose in West Virginia, the types of drugs involved, and the role of drug abuse in the deaths.

Design, Setting, and Participants Population-based, observational study using data from medical examiner, prescription drug monitoring program, and opiate treatment program records. The study population was all state residents who died of unintentional pharmaceutical overdoses in West Virginia in 2006.

Main Outcome Measures Rates and rate ratios for selected demographic variables. Prevalence of specific drugs among decedents and proportion that had been prescribed to decedents. Associations between demographics and substance abuse indicators and evidence of pharmaceutical diversion, defined as a death involving a prescription drug without a documented prescription and having received prescriptions for controlled substances from 5 or more clinicians during the year prior to death (ie, doctor shopping).

Results Of 295 decedents, 198 (67.1%) were men and 271 (91.9%) were aged 18 through 54 years. Pharmaceutical diversion was associated with 186 (63.1%) deaths, while 63 (21.4%) were accompanied by evidence of doctor shopping. Prevalence of diversion was greatest among decedents aged 18 through 24 years and decreased across each successive age group. Having prescriptions for a controlled substance from 5 or more clinicians in the year prior to death was more common among women (30 [30.9%]) and decedents aged 35 through 44 years (23 [30.7%]) compared with men (33 [16.7%]) and other age groups (40 [18.2%]). Substance abuse indicators were identified in 279 decedents (94.6%), with nonmedical routes of exposure and illicit contributory drugs particularly prevalent among drug diverters. Multiple contributory substances were implicated in 234 deaths (79.3%). Opioid analgesics were taken by 275 decedents (93.2%), of whom only 122 (44.4%) had ever been prescribed these drugs.

Conclusion The majority of overdose deaths in West Virginia in 2006 were associated with nonmedical use and diversion of pharmaceuticals, primarily opioid analgesics.

JAMA. 2008;300(22):2613-2620

www.jama.com

Use and Health discovered that an annual average of 4.8% of persons 12 years or older consumed a prescription pain reliever for nonmedical reasons in the previous year during 2002-2005.⁷ Rates of emergency department visits for opioid analgesic overdoses have also increased.⁸ Unintentional drug poisoning deaths increased 68% during 1999-

Author Affiliations: Epidemic Intelligence Service (Drs Hall, Logan, and Toblin) and National Center for Injury Prevention and Control (Drs Logan, Toblin, Crosby, and Paulozzi), Centers for Disease Control and Prevention, Atlanta, Georgia; Division of Surveillance and Disease Control (Drs Hall and Bixler) and Office of the Chief Medical Examiner (Drs Kaplan and Kraner), West Virginia Department of Health and Human Resources, Charleston.

Corresponding Author: Aron J. Hall, DVM, MSPH, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Mailstop A-47, Atlanta, GA 30333 (ajhall@cdc.gov).

2004⁹; the majority of this increase has been attributed to deaths associated with opioid analgesics.¹⁰

During 1999-2004, West Virginia experienced the nation's most substantial increase (550%) in unintentional poisoning mortality.⁹ State vital records indicate that the increase in drug overdose mortality rates continued after 2004. Therefore, we conducted a study to better understand these unintentional drug poisoning deaths. Our objective was to characterize persons dying of drug overdoses in West Virginia in 2006 with regard to potential risk factors and the types of drugs that resulted in their deaths. Because West Virginia has centralized death investigation records maintained by the state medical examiner as well as centralized prescription records maintained by the state's prescription drug monitoring program, we also were able to assess the decedents' prescription histories in the year before their deaths. This information might help practitioners and public health officials understand how prescription drugs involved in fatal overdoses are obtained and might help prevent future overdoses.

METHODS

Case Finding

We identified all state residents who died of unintentional drug overdose in West Virginia in 2006. Decedents were included if their death certificates listed the underlying cause of death to be unintentional drug poisoning (*International Classification of Diseases, 10th Revision [ICD-10] codes X40-X44*). All cases were initially identified by searching an electronic database of vital records at the Health Statistics Center of the West Virginia Department of Health and Human Resources using the appropriate *ICD-10* codes. Identifying information was cross-referenced with the case logbook and electronic database of the investigations of the Office of the Chief Medical Examiner (OCME) to identify decedent records. We excluded cases certified by county coroners or physicians without benefit of

autopsy and decedents whose only toxicology tests were performed by an admitting hospital. We then focused our analyses on overdoses that involved prescription pharmaceuticals by excluding those overdoses due exclusively to nonpharmaceuticals (ie, illicit drugs such as cocaine and heroin), over-the-counter products, or alcohol. Human subjects review by the Centers for Disease Control and Prevention determined this study to be a public health investigation; as such, institutional review board approval was not required.

OCME Toxicology and Death Certification Protocol

In West Virginia, the state medical examiner system imposes uniform death investigation and certification practices over a statewide jurisdiction and maintains a central registry of case files pertaining to all deaths investigated and certified by that system. The OCME routinely screens all decedents suspected of drug overdose for illicit drugs and pharmaceuticals, including narcotics (eg, heroin and opioid analgesics), marijuana, stimulants (eg, cocaine and amphetamines), depressants (eg, benzodiazepines and barbiturates), and other pharmaceuticals (eg, antidepressants and antihistamines). Blood (or in unusual circumstances urine or other matrices) is screened using automated enzyme immunoassay. Positive findings are confirmed and quantitated using gas or liquid chromatography with mass spectrometry detection.

Specimens are also screened for alcohol and other volatile compounds using gas chromatography with flame ionization detection. Case toxicology testing is preferentially performed using peripheral blood samples collected from subclavian, iliac, or femoral sites. The autopsy protocol also includes assessment and sampling of gastric contents, as well as collection of urine, vitreous fluid, and liver tissue. For cases in which peripheral blood or urine is not available, liver tissue is most often used for toxicology testing.

West Virginia OCME death certification protocol requires that a scene-of-death investigation report be prepared for all cases by trained and certified death investigators, with subsequent case investigation directed by OCME forensic pathologists' initial peer review. Following receipt of all investigative reports and records deemed necessary, including board-of-pharmacy records, medical records, police investigative reports, and toxicology reports, each case receives final peer review to determine which factors, including drugs, are contributory to death.

The manner of death (ie, unintentional vs intentional) is also established through this process. The manner of death, referring to the general circumstances surrounding drug overuse (ie, "accidental," inferring recreational or other unintentionally fatal drug overuse, vs intentionally fatal drug overuse, described as "suicide," "homicide," or "undetermined manner") is also established through this process, which requires final overall case review and cosignature by a senior staff pathologist and is based on toxicology and autopsy results; death investigation findings, including routes of drug administration; status of drug prescription access; witnessed-death circumstances; and other considerations. Multiple drugs may be deemed contributory to death if they are present at therapeutic levels or greater and have potentially deleterious physiological effects (eg, respiratory depression). Drugs found through toxicology testing can be considered contributory to death only if they meet these criteria.

Data Sources

In late 2007, we abstracted information from autopsy reports, toxicology reports, death-scene investigation reports, death certificates, and copies of medical records in OCME files. The West Virginia Board of Pharmacy also provided decedent prescription histories from the state's Controlled Substances Monitoring Program (CSMP), which maintains electronic records of all Schedule II, III, and IV controlled

substances (as defined by the Controlled Substances Act¹¹) dispensed by West Virginia pharmacies since 2003. Furthermore, all 8 opiate treatment programs (OTPs) in West Virginia provided information concerning whether any of the decedents were enrolled in outpatient substance abuse treatment for opiate addiction at the time of death. These are the only facilities in the state that can dispense methadone for long-term treatment of addiction. Decedents were linked to their CSMP and OTP records using name, date of birth, and date of death, where applicable.

Demographic information regarding decedents (eg, sex, age, marital status, highest education level, and county of residence) was collected from death certificates. Office of the Chief Medical Examiner death-scene investigation reports and medical records provided information that might indicate that the overdose was related to substance abuse (eg, whether the decedent had a history of drug overdoses and whether the decedent used a pharmaceutical by a nonmedical route of administration such as snorting, inhalation, or injection). Medical records, death-scene investigation reports, and autopsy reports from OCME files were also used to determine past medical histories and comorbid conditions, including cardiovascular disease, pulmonary disease, mental illness, and pain. Contributory drugs were identified based on medical examiner conclusions stated in the autopsy report and categorized on the basis of the drug reference vocabulary established by the Drug Alert and Warning Network.¹²

Among decedents with contributory prescription pharmaceuticals, CSMP and OCME sources were used to determine whether decedents had ever had a documented prescription. For Schedule II drugs, CSMP and OCME sources were also used to determine if decedents had a prescription dispensed within 30 days of death. In West Virginia, Schedule II drugs may only be dispensed up to a 30-day supply with no refills. Decedents enrolled in an OTP at the time of death were con-

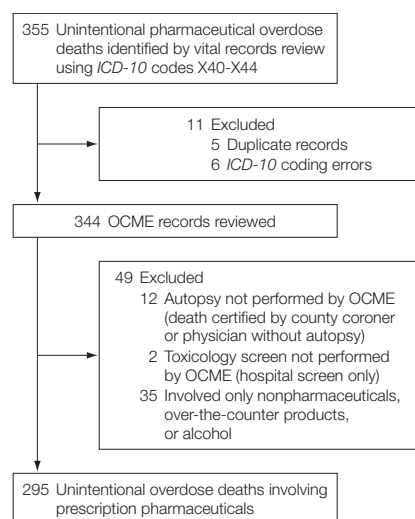
sidered to have current prescriptions for methadone. Records from the CSMP also provided the number of prescribing clinicians and dispensing pharmacies for controlled substances for each decedent during the 12 months prior to death. Records from the OCME were the sole source of information for non-controlled prescription drugs not included in the CSMP.

Statistical Analysis

Census estimates for 2006^{13,14} were used to calculate death rates per 100 000 population and rate ratios with corresponding 95% confidence intervals (CIs). Consistent with Census methodology, the analysis of highest level of education attained was limited to decedents 25 years or older, and marital status analysis included only decedents 15 years or older. As a proxy for socioeconomic status, the decedents' counties of residence were categorized into quartiles based on the percentage of families with income below the poverty line, on the basis of 2005 poverty estimates.¹⁵ The threshold used to determine poverty status depends on family size and composition, as defined by the US Census Bureau.¹⁶ To evaluate overdose death rates by rural residence, counties were also categorized into quartiles of population density on the basis of 2006 Census data and 2000 land-area estimates.¹⁷ Trends in rates were tested using the Mantel-Haenszel χ^2 test for trend.

We examined 2 mechanisms by which decedents had obtained their drugs: being given or purchasing diverted drugs on the street and doctor shopping. A death involving drug diversion was defined as one involving a prescription drug used without documented prescription records. Doctor shopping was defined as having received prescriptions for controlled substances from 5 or more clinicians during the year prior to death. Associations between both diversion and doctor shopping and demographic factors and other indicators of substance abuse were quantified by odds ratios (ORs) and corresponding 95% CIs. The specific sub-

Figure. Study Population and Sample Selection From All Unintentional Pharmaceutical Overdose Deaths Occurring Among West Virginia Residents, 2006



ICD-10 indicates *International Classification of Diseases, 10th Revision*; OCME, Office of the Chief Medical Examiner.

stance abuse indicators analyzed included nonmedical route of drug administration, history of substance abuse based on OCME and medical records, previous overdose, current OTP enrollment, presence of a contributory illicit drug, and presence of contributory alcohol.

We also classified decedents based on the specific pharmaceuticals that contributed to death. For each drug, we calculated the proportion of decedents with prescription documentation as well as the proportion with documentation within 30 days of death for Schedule II drugs. We calculated the proportion of decedents using each drug who also were using other contributory prescription drugs, illicit drugs, alcohol, or no other contributory substances. All analyses were performed using Epi Info version 3.4 (Centers for Disease Control and Prevention, Atlanta, Georgia), with significance set at 95% based on 2-sided testing.

RESULTS

Based on vital records, we identified 355 unintentional pharmaceutical over-

dose deaths with the appropriate ICD-10 codes. Cross-referencing with OCME records identified 5 duplicate records and 6 ICD-10 coding errors in the vital records database, leaving 344. Of these, we excluded 49, leaving a study population of 295 (FIGURE).

The overall unintentional pharmaceutical overdose death rate was 16.2 per 100 000 population (TABLE 1). Men accounted for 198 (67.1%) of fatalities and had a drug overdose death rate more than 2 times that of women. The age range was 18 to 70 years (mean, 39 years; median, 39 years). The majority (91.9%) of decedents were aged 18 to 54 years, and each age group within this range had a significantly greater death rate than that of persons 55 years

or older. Significantly greater death rates were also observed among divorced and never-married decedents compared with married decedents. Lower educational attainment and increased poverty in the decedent's county of residence were both associated with greater death rates in a dose-response fashion (χ^2 for trend, $P < .001$). No significant differences in rates were observed for county population density.

Among all decedents, 186 (63.1%) had used contributory pharmaceuticals without documented prescriptions (ie, diversion), and 63 (21.4%) had 5 or more clinicians prescribe them controlled substances in the year prior to death (ie, doctor shopping) (TABLE 2). Women were significantly

more likely to have evidence of doctor shopping than men (30.9% vs 16.7%; OR, 2.2; 95% CI, 1.2-4.1), although no differences in prevalence of diversion were noted by sex. Prevalence of diversion was greatest among the group aged 18 through 24 years; in this group, 41 (91.1%) of the decedents lacked prescription documentation for 1 or more contributory pharmaceutical. Furthermore, diversion rates consistently decreased among each successive age group (χ^2 for trend, $P < .001$). In contrast, relative to all other age groups, the group aged 35 through 44 years was associated with a significantly greater rate of doctor shopping (30.7% vs 18.2%; OR, 2.0; 95% CI, 1.1-3.8). Decedents who had never been married were more likely to have evidence of diversion than those who were married at the time of death (76.3% vs 53.4%; OR, 2.8; 95% CI, 1.5-5.4). No significant differences in rates of diversion or doctor shopping were noted by education or poverty level.

Of all 295 decedents, 279 (94.6%) had at least 1 indicator of substance abuse (TABLE 3). Indicators associated with pharmaceutical diversion were not the same as those associated with doctor shopping. Compared with deaths involving prescribed pharmaceuticals, deaths involving diversion were associated with history of substance abuse (82.3% vs 71.6%; OR, 1.8; 95% CI, 1.0-3.4), nonmedical route of pharmaceutical administration (26.3% vs 15.6%; OR, 1.9; 95% CI, 1.0-3.8), and a contributory illicit drug (19.4% vs 10.1%; OR, 2.1; 95% CI, 1.0-4.9). In contrast, decedents with evidence of doctor shopping were significantly more likely to have had a previous overdose (30.2% vs 13.4%; OR, 2.8; 95% CI, 1.4-5.6) and significantly less likely to have used contributory alcohol (7.9% vs 19.8%; OR, 0.3; 95% CI, 0.1-0.9), compared with decedents who had fewer than 5 clinicians prescribe them controlled substances in the year prior to death. A significant negative association was observed between drug diversion and doctor shopping (OR, 0.3; 95% CI, 0.1-0.5), with only 24 dece-

Table 1. Sociodemographic Characteristics of Unintentional Pharmaceutical Overdose Deaths, West Virginia, 2006 (N = 295)

Characteristic	Total Deaths, No. (%)	Death Rate per 100 000 Population ^a	Rate Ratio (95% CI)
Sex			
Women	97 (32.9)	10.5	1 [Reference]
Men	198 (67.1)	22.2	2.1 (1.7-2.7)
Age, y			
<18	0	0	
18-24	45 (15.3)	27.5	5.8 (3.5-9.9)
25-34	69 (23.4)	29.6	6.3 (3.9-10.3)
35-44	75 (25.4)	30.6	6.5 (4.0-10.3)
45-54	82 (27.7)	29.4	6.2 (3.9-10.1)
≥55	24 (8.1)	4.7	1 [Reference]
Marital status ^b			
Married	103 (34.9)	12.3	1 [Reference]
Never married	97 (32.9)	26.3	2.3 (1.8-3.0)
Divorced	86 (29.2)	49.7	4.5 (3.5-5.9)
Widowed	9 (3.1)	7.5	0.6 (0.3-1.2)
Highest education ^c			
<12th grade	77 (26.1)	37.9	3.6 (2.5-5.3)
High school diploma	128 (43.4)	23.7	2.7 (1.9-3.8)
Any college	43 (14.6)	8.9	1 [Reference]
Below poverty line in county of residence, % ^d			
Quartile 1 (range, 9.4-15.8)	72 (24.4)	11.7	1 [Reference]
Quartile 2 (range, 16.1-18.3)	65 (22.0)	15.1	1.3 (0.9-1.8)
Quartile 3 (range, 18.6-21.9)	62 (21.0)	16.1	1.4 (1.0-2.0)
Quartile 4 (range, 22.1-38.9)	96 (32.5)	24.7	2.1 (1.5-2.9)
Total		16.2	

Abbreviation: CI, confidence interval.

^aBased on 2006 Census estimates and American Community Survey, US Census Bureau.^{14,15}

^bIndividuals 15 years or older (n = 295).

^cIndividuals 25 years or older with known education level (n = 248).

^dBased on 2005 income.¹⁶ Quartile 1 comprises Jefferson, Putnam, Berkeley, Morgan, Hancock, Brooke, Pendleton, Hardy, Pleasants, Mineral, Marshall, Kanawha, Ohio, and Monroe counties; quartile 2 comprises Hampshire, Jackson, Grant, Ritchie, Tyler, Randolph, Pocahontas, Greenbrier, Preston, Marion, Tucker, Wood, Wetzel, and Raleigh counties; quartile 3 comprises Nicholas, Harrison, Taylor, Doddridge, Boone, Mason, Cabell, Lewis, Wayne, Wirt, Upshur, Roane, and Barbour counties; and quartile 4 comprises Fayette, Mercer, Monongalia, Calhoun, Braxton, Logan, Gilmer, Lincoln, Wyoming, Mingo, Clay, Summers, Webster, and McDowell counties. Counties in each quartile are listed in ascending order of percentage below the poverty line.

dents (8.1%) meeting the definition of both.

Based on OCME conclusions, 234 decedents (79.3%) had used multiple substances contributing to their fatal overdoses. The mean number of contributory prescription drugs was 2.0, with a range of 1 to 5 drugs. The specific drug combinations and prescription documentation for each drug are described in TABLE 4. Opioid analgesics were the most prevalent class of drugs, contributing to 275 deaths (93.2%); of these, only 122 (44.4%) included evidence of prescription documentation for all of the contributory opioids. Furthermore, among the 227 decedents for whom Schedule II opioid analgesics contributed to death, 66 (29.1%) had prescriptions dispensed within 30 days prior to death, as would be required in West Virginia. Among all decedents using contributory opioid analgesics, 59 (21.5%) were using no other contributory substances, such as alcohol, illicit drugs, or other prescription pharmaceuticals. The most common drug identified was methadone, which was involved in 112 (40.0%) of all deaths. The percentage of decedents with valid prescriptions for methadone (32.1%) was lower than the percentage of those with valid prescriptions for hydrocodone (85.1%) or oxycodone (60.7%).

Psychotherapeutic drugs contributed to 144 deaths (48.8%), though all but 1 of these deaths (attributed to amitriptyline) involved other contributory substances, primarily opioid analgesics. Benzodiazepines were involved in 113 (78.5%) of the deaths involving psychotherapeutic drugs. Decedents who overdosed on psychotherapeutic drugs had a lower prevalence of contributory illicit drugs (8.3%) and a higher prevalence of contributory alcohol (20.8%) than decedents who used opioid analgesics (16.0% and 13.5%, respectively).

COMMENT

In recent years, West Virginia has had one of the highest unintentional drug overdose mortality rates in the United

States. This study of such deaths in 2006 revealed that almost all the unintentional drug overdose deaths in West Virginia involved prescription drugs. Moreover, almost all the prescription drug-related deaths showed signs of drug abuse. Risk factors for prescription drug deaths included being male, having less education, and living in the most impoverished counties of the state. Prescription opioid analgesics played a dominant role in the deaths, with a secondary contribution from psychotherapeutic drugs. Relatively few deaths (<25%) involved alcohol, illicit drugs,

or nonmedical routes of administration such as injection.

A number of factors may have contributed to West Virginia's steep increase in overdose rates and high rank among states. Rapid rate increases between 1999 and 2004 have been correlated with the percentage of the population living in rural areas,⁹ and West Virginia was the third most rural state in 2000.¹⁴ Previous work has associated higher rates of unintentional drug overdose mortality with high levels of use of opioids per capita,¹⁸ and Drug Enforcement Administration data indi-

Table 2. Rates of Pharmaceutical Diversion and Doctor Shopping Among Unintentional Pharmaceutical Overdose Deaths by Sociodemographic Characteristics, West Virginia, 2006

Characteristic	All Deaths, No.	Any Diverted Pharmaceuticals ^a		≥5 Clinicians ^b	
		No. (%) ^c	OR (95% CI)	No. (%) ^c	OR (95% CI)
Sex					
Women	97	60 (61.9)	0.9 (0.5-1.6)	30 (30.9)	2.2 (1.2-4.1)
Men	198	126 (63.6)	1 [Reference]	33 (16.7)	1 [Reference]
Age, y					
<18	0				
18-24	45	41 (91.1)	12.1 (2.9-58.8)	5 (11.1)	0.6 (0.1-3.5)
25-34	69	51 (73.9)	3.4 (1.2-9.9)	13 (18.8)	1.2 (0.3-5.5)
35-44	75	45 (60.0)	1.8 (0.6-5.0)	23 (30.7)	2.2 (0.6-9.8)
45-54	82	38 (46.3)	1.0 (0.4-2.8)	18 (22.0)	1.4 (0.4-6.4)
≥55	24	11 (45.8)	1 [Reference]	4 (16.7)	1 [Reference]
Marital status ^d					
Married	103	55 (53.4)	1 [Reference]	25 (24.3)	1 [Reference]
Never married	97	74 (76.3)	2.8 (1.5-5.4)	13 (13.4)	0.5 (0.2-1.1)
Divorced	86	51 (59.3)	1.3 (0.7-2.4)	22 (25.6)	1.1 (0.5-2.2)
Widowed	9	6 (66.7)	1.8 (0.4-11.3)	3 (33.3)	1.6 (0.2-7.9)
Highest education ^e					
<12th grade	77	47 (61.0)	1.4 (0.6-3.1)	18 (23.4)	1.2 (0.4-3.1)
High school diploma	128	73 (57.0)	1.2 (0.5-2.4)	31 (24.2)	1.2 (0.5-3.1)
Any college	43	23 (53.5)	1 [Reference]	9 (20.9)	1 [Reference]
Below poverty line in county of residence, % ^f					
Quartile 1 (range, 9.4-15.8)	72	43 (59.7)	1 [Reference]	19 (26.4)	1 [Reference]
Quartile 2 (range, 16.1-18.3)	65	41 (63.1)	1.2 (0.6-2.4)	18 (27.7)	1.1 (0.5-2.4)
Quartile 3 (range, 18.6-21.9)	62	46 (74.2)	1.9 (0.9-4.3)	8 (12.9)	0.4 (0.2-1.1)
Quartile 4 (range, 22.1-38.9)	96	56 (58.3)	0.9 (0.5-1.8)	18 (18.8)	0.6 (0.3-1.4)
Total	295	186 (63.1)		63 (21.4)	

Abbreviations: CI, confidence interval; OR, odds ratio.
^a Diverted pharmaceuticals include those that contributed to death but that were not prescribed to the decedent.
^b Includes clinicians who prescribed controlled substances to the decedent during the year prior to death, based on Controlled Substances Monitoring Program records.
^c Percentages among given sociodemographic group (row percentages) are reported.
^d Individuals 15 years or older (n = 295).
^e Individuals 25 years or older with known education level (n = 248).
^f Based on 2005 income.¹⁶ Quartile 1 comprises Jefferson, Putnam, Berkeley, Morgan, Hancock, Brooke, Pendleton, Hardy, Pleasants, Mineral, Marshall, Kanawha, Ohio, and Monroe counties; quartile 2 comprises Hampshire, Jackson, Grant, Ritchie, Tyler, Randolph, Pocahontas, Greenbrier, Preston, Marion, Tucker, Wood, Wetzel, and Raleigh counties; quartile 3 comprises Nicholas, Harrison, Taylor, Doddridge, Boone, Mason, Cabell, Lewis, Wayne, Wirt, Upshur, Roane, and Barbour counties; and quartile 4 comprises Fayette, Mercer, Monongalia, Calhoun, Braxton, Logan, Gilmer, Lincoln, Wyoming, Mingo, Clay, Summers, Webster, and McDowell counties. Counties in each quartile are listed in ascending order of percentage below the poverty line.

cate that West Virginia had one of the highest rates of opioid use per capita in the United States in 2006.⁶ This may be in part because higher prevalences

of prescription opioid use are associated with eligibility for Medicaid and with lower family income,¹⁹ and West Virginia is the third poorest state.¹⁵ The

increase in the overdose rate is not likely owing to a change in the classification of suicidal overdoses to unintentional overdoses, because the rate of drug-related suicide in West Virginia did not decline between 1999 and 2004.²⁰

The prescription histories of the decedents revealed that drug diversion and doctor shopping involved different subpopulations of persons abusing prescription drugs. Those in the group using diverted drugs resemble those traditionally associated with the abuse of street drugs in that more than two-thirds were men, half were younger than 35 years, and most were unmarried or divorced.²¹ Consistent with this profile, individuals who had used diverted drugs were more likely to have used a nonmedical route of exposure and to have combined prescription with illicit drugs in their fatal overdose and were more likely to have a recognized history of substance abuse. Those with a history of abusing prescription drugs report beginning use of psychothera-

Table 3. Substance Abuse Indicators Among Unintentional Pharmaceutical Overdose Deaths Involving Pharmaceutical Diversion and Doctor Shopping, West Virginia, 2006

Substance Abuse Indicator	All Deaths, No. (%)	Any Diverted Pharmaceuticals ^a		≥5 Clinicians ^b	
		No. (%) ^c	OR (95% CI) ^d	No. (%) ^c	OR (95% CI) ^d
History of substance abuse	231 (78.3)	153 (82.3)	1.8 (1.0-3.4)	49 (77.8)	1.0 (0.5-2.0)
Any diverted pharmaceuticals ^a	186 (63.1)	NA	NA	24 (38.1)	0.3 (0.1-0.5)
Nonmedical route of administration	66 (22.4)	49 (26.3)	1.9 (1.0-3.8)	9 (14.3)	0.5 (0.2-1.1)
≥5 Clinicians prescribed controlled substances ^b	63 (21.4)	24 (12.9)	0.3 (0.1-0.5)	NA	NA
Contributory alcohol	51 (17.3)	34 (18.3)	1.2 (0.6-2.4)	5 (7.9)	0.3 (0.1-0.9)
Previous overdose	50 (16.9)	29 (15.6)	0.8 (0.4-1.5)	19 (30.2)	2.8 (1.4-5.6)
Contributory illicit drug ^e	47 (15.9)	36 (19.4)	2.1 (1.0-4.9)	9 (14.3)	0.9 (0.3-1.9)
Current OTP enrollment	12 (4.1)	4 (2.2)	0.3 (0.1-1.1)	2 (3.2)	0.7 (0.1-3.5)
Any indicator ^f	279 (94.6)	167 (89.8)	1.5 (0.7-3.3)	55 (87.3)	0.5 (0.2-1.5)
Total	295 (100)	186 (100)		63 (100)	

Abbreviations: CI, confidence interval; NA, not applicable; OR, odds ratio; OTP, opiate treatment program.
^aDiverted pharmaceuticals include those that contributed to death but that were not prescribed to the decedent.
^bIncludes clinicians who prescribed controlled substances to the decedent during the year prior to death, based on Controlled Substances Monitoring Program records.
^cPercentages among those with any diverted pharmaceuticals or ≥5 clinicians (column percentages) are reported.
^dOdds ratio compares those with given substance abuse indicator vs those without as the reference group.
^eIncludes cocaine, heroin, and methamphetamines.
^fExcludes not applicable indicators, as noted.

Table 4. Contributory Drugs Involved in Unintentional Pharmaceutical Overdose Fatalities, West Virginia, 2006

Contributory Prescription Drug	Deaths, Total (%)	Prescribed, % ^a	Dispensed Within 30 d of Death, % ^b	Taken With Other Contributory Substances, %			
				Other Prescription Drugs	Illicit Drugs ^c	Alcohol	None
Opioid analgesic	275 (93.2)	44.4	29.1	63.3	16.0	13.5	21.5
Methadone	112 (40.0)	32.1	26.8	62.5	13.4	9.8	25.9
Hydrocodone	67 (22.7)	85.1	NA	83.6	9.0	11.9	7.5
Oxycodone	61 (20.7)	60.7	39.3	70.5	14.8	9.8	18.0
Morphine	46 (15.6)	21.7	15.2	54.3	28.3	28.3	21.7
Fentanyl	31 (10.5)	41.9	32.3	77.4	19.4	9.7	12.9
Other Schedule II opioid analgesic ^d	4 (1.4)	25.0	25.0	100	25.0	0	0
Other Schedule III opioid analgesic ^e	24 (8.1)	50.0	NA	91.7	8.3	8.3	0
Psychotherapeutic	144 (48.8)	54.9	NA	93.8	8.3	20.8	0.7
Diazepam	66 (22.4)	45.5	NA	92.4	7.6	19.7	0
Alprazolam	54 (18.3)	64.8	NA	100	5.6	11.1	0
Other benzodiazepine ^f	5 (1.7)	80.0	NA	100	0	20.0	0
Antidepressant ^g	49 (16.6)	71.4	NA	93.9	10.2	20.4	2.0
Other psychotherapeutic ^h	16 (5.4)	68.8	NA	93.8	0	37.5	0
Other prescription drug ⁱ	33 (11.2)	60.1	NA	97.0	9.1	12.1	3.0
All decedents	295 (100)	36.9	NA	62.4	15.9	17.3	20.7

Abbreviation: NA, not applicable.
^aFor decedents with multiple contributory drugs from a given category, percentage includes only those who had all drugs prescribed to them.
^bApplicable to 227 decedents with Schedule II drugs, which can be dispensed as no more than a 30-day supply with no refills in West Virginia. For decedents with multiple contributory drugs from a given category, percentage includes only those who had all drugs dispensed to them within 30 days of death.
^cIncludes cocaine, heroin, and methamphetamine.
^dIncludes hydromorphone and meperidine.
^eIncludes codeine, dihydrocodeine, and propoxyphene.
^fIncludes chlordiazepoxide, clonazepam, and temazepam.
^gIncludes amitriptyline, bupropion, citalopram, desipramine, doxepin, fluoxetine, imipramine, mirtazapine, nortriptyline, paroxetine, sertraline, trazodone, and venlafaxine.
^hIncludes carbamazepine, hydroxyzine, phenobarbital, quetiapine, topiramate, and zolpidem.
ⁱIncludes butalbital, carisoprodol, cyclobenzaprine, diltiazem, phenytoin, promethazine, and tramadol.

peutic drugs as a way to moderate the effects of street drugs and beginning use of prescription opioids as a substitute when street drugs are not available.²¹

The Drug Enforcement Administration confirms that drug diversion was widespread in West Virginia²² and the Appalachian region²³ during this period. The primary methods of diversion were illegal sale and distribution by health care professionals, employee theft, forged prescriptions, and the Internet.²³ Persons arrested for drug-related crime in West Virginia during 2003-2004 resembled the young men using diverted drugs in this study.²⁴

A much smaller subset of decedents, roughly 1 in 5, met our definition of doctor shopping. In contrast to the group defined by their use of diverted drugs, doctor shoppers were 48% women, and only 29% were younger than 35 years. The doctor shoppers resemble patients typically receiving opioid analgesics in their greater average age²⁵ and more equal proportions of men and women.²⁶ Doctor shoppers tended to come from higher-income counties, to be less likely to have been drinking when they overdosed, and to take their drugs orally. Doctor shoppers may represent that part of the drug-abusing population that is less willing to engage in illegal or deviant activities.

Among all deaths, opioid analgesics were involved in 93% and psychotherapeutic drugs in 49%. Among the 61 single-drug deaths, however, only 1 was due to a psychotherapeutic drug, suggesting that fatal overdose is less likely with a single psychotherapeutic drug than with a single opioid analgesic. Methadone was responsible for more single-drug deaths and was involved in far more deaths than any other drug. The Drug Enforcement Administration has listed methadone along with hydrocodone, diazepam, and alprazolam as drugs commonly diverted and abused in West Virginia²² but has not published any comparisons of the rates at which different opioids are being diverted.

Methadone was prescribed in much smaller volumes than other opioids in

West Virginia in 2006. Not including methadone from OTPs, methadone was distributed at a rate of 2375 g/100 000 population in West Virginia, whereas the rate for oxycodone was 17 385 g/100 000 population and that for hydrocodone was 20 390 g/100 000 population.⁶ Even accounting for methadone's greater potency,²⁷ there is no indication that it is being used more often than these other opioids. Given the small number of methadone decedents enrolled in the OTP, it is also unlikely that OTP-provided methadone contributed much to the total methadone deaths. This suggests either that methadone is for unknown reasons favored by drug diverters or that methadone is more risky to users than other opioids.

This study did not examine the sources of the involved opioids. However, the majority of persons using prescription pain relievers for nonmedical indications report receiving their drugs for free from a friend or relative; among these, the majority report that the friend or relative received the drug from a single clinician.¹⁹ National data from 2003-2004 indicate that 40% of opioids were prescribed by primary care clinicians, and 39% were prescribed by physicians in emergency departments.²⁵

Strengths of this study include the consistency provided by having a single medical examiner's office and toxicology laboratory as the source for most information, completeness of toxicology testing in West Virginia, and availability of historical prescription and narcotics treatment program records. To our knowledge, no previous studies have made use of the prescription monitoring program records of all decedents.

The majority of limitations of this study are related to missing or possibly erroneous information concerning decedents' histories and circumstances of their drug use and the potential for reporting bias when information is provided by friends or family members. Therefore, the reported prevalences of histories of substance abuse and previous drug overdoses and other measures likely are underestimates. In addition,

prescription information does not include prescriptions filled outside West Virginia or those filled at the limited number of nonparticipating pharmacies in West Virginia; therefore, the reported prescription histories (eg, number of prescription-dispensing occurrences) are likely underestimates. Finally, findings from rural states such as West Virginia might not apply to other states.

Clinicians have a critical role to play in preventing the diversion of prescription drugs. Clinicians and pharmacists need to counsel patients who are prescribed opioids not only about the risk of overdose to themselves but also about the risk to others with whom they might share their medication. In addition, clinicians should follow recent published guidelines for the management of chronic pain^{28,29} and refer patients as needed to pain management specialists. Clinicians should also make use of state prescription drug monitoring programs to determine whether their patients are getting scheduled drugs from other clinicians. Clinicians can now obtain such information about their patients from prescription drug monitoring programs in most states.³⁰

Future studies should focus on exploring in greater detail the interactions between persons dying from overdoses of prescription drugs and the clinicians who wrote their prescriptions. Such studies could determine the reasons for the drug use, the extent to which the clinicians and pharmacists were aware of additional sources of drugs used by their patients, and the measures clinicians had taken to handle problems in patient adherence that had occurred in the course of care. Such studies might be accomplished using the records of prescription drug monitoring programs.

Author Contributions: Dr Hall had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Hall, Logan, Kaplan, Bixler, Crosby, Paulozzi.

Acquisition of data: Hall, Logan, Toblin, Kaplan, Kraner. *Analysis and interpretation of data:* Hall, Logan, Toblin, Kaplan.

Drafting of the manuscript: Hall, Logan, Bixler, Paulozzi. *Critical revision of the manuscript for important intellectual content:* Hall, Logan, Toblin, Kaplan, Kraner, Bixler, Crosby, Paulozzi.

Statistical analysis: Hall, Logan, Toblin.
Administrative, technical, or material support: Kraner, Bixler, Crosby, Paulozzi.

Study supervision: Hall, Bixler, Crosby, Paulozzi.

Financial Disclosures: None reported.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Additional Contributions: Edna McKinstry, MD (Centers for Disease Control and Prevention), provided assistance with data abstraction. David Potters, JD (West Virginia Board of Pharmacy), Tom Light (West Virginia Health Statistics Center), and Jeanette Capocefalo (West Virginia Office of the Chief Medical Examiner) provided access to data. Rebecca Hall, PharmD, BCPS (Charleston Area Medical Center), provided expert consultation on psychiatric and general pharmacy practice. None of these individuals received compensation for their contributions.

REFERENCES

1. American Society of Anesthesiologists. Practice guidelines for chronic pain management: a report of the American Society of Anesthesiologists Task Force on Pain Management, Chronic Pain Section. *Anesthesiology*. 1997;86(4):995-1004.
2. American Academy of Pain Medicine and American Pain Society. The use of opioids for the treatment of chronic pain: a consensus statement from the American Academy of Pain Medicine and the American Pain Society. *Clin J Pain*. 1997;13(1):6-8.
3. Foley K. Dismantling the barriers: providing palliative and pain care. *JAMA*. 2000;283(1):115.
4. Model policy for the use of controlled substances for the treatment of pain. Federation of State Medical Boards of the United States Inc Web site. http://www.fsmb.org/pdf/2004_grpol_Controlled_Substances.pdf. Accessed June 21, 2007.
5. Gilson AM, Joranson DE, Maurer MA. Improving state pain policies: recent progress and continuing opportunities. *CA Cancer J Clin*. 2007;57(6):341-353.
6. ARCOS: Automation of Reports and Consolidated Orders System. US Department of Justice Drug Enforcement Administration Web site. <http://www.deadiversion.usdoj.gov/arcos/index.html>. Accessed March 27, 2005.

7. The NSDUH report: patterns and trends in nonmedical prescription pain reliever use: 2002 to 2005. Substance Abuse and Mental Health Services Administration Web site. <http://www.oas.samhsa.gov/2k7/pain/pain.pdf>. Accessed February 27, 2008.
8. Drug Abuse Warning Network, 2005: national estimates of drug-related emergency department visits. Substance Abuse and Mental Health Services Administration Web site. <http://dawninfo.samhsa.gov/files/DAWN-ED-2005-Web.pdf>. Accessed February 20, 2008.
9. Centers for Disease Control and Prevention. Unintentional poisoning deaths—United States, 1999-2004. *MMWR Morb Mortal Wkly Rep*. 2007; 56(5):93-96.
10. Paulozzi LJ, Budnitz DS, Xi Y. Increasing deaths from opioid analgesics in the United States. *Pharmacoepidemiol Drug Saf*. 2006;15(9):618-627.
11. The Controlled Substances Act: Title 21—Food and Drugs: Chapter 13—Drug Abuse Prevention and Control. US Drug Enforcement Administration Web site. <http://www.usdoj.gov/dea/pubs/csa.html>. Accessed October 2, 2008.
12. Drug Abuse Warning Network (DAWN) vocabulary list. Substance Abuse and Mental Health Services Administration Web site. http://dawninfo.samhsa.gov/drug_vocab/default.asp. Accessed September 2, 2007.
13. 2006 annual state population estimates by demographic characteristics with 6 race groups. US Census Bureau Web site. <http://www.census.gov/popest/>. Accessed February 14, 2008.
14. 2006 American Community Survey. US Census Bureau Web site. <http://factfinder.census.gov>. Accessed February 13, 2008.
15. Small area income & poverty estimates, 2005. US Census Bureau Web site. <http://www.census.gov/hhes/www/saie/saie.html>. Accessed February 12, 2008.
16. Bishaw A, Stern S. Evaluation of poverty estimates: a comparison of the American Community Survey and the Current Population Survey. US Census Bureau Web site. http://www.census.gov/hhes/www/poverty/acs_cpspovcompreport.pdf. Accessed January 12, 2008.
17. Population, area, housing units, and density: 2000. US Census Bureau Web site. <http://factfinder.census.gov>. Accessed February 1, 2008.
18. Paulozzi LJ, Ryan GW. Opioid analgesics and rates

- of fatal drug poisoning in the United States. *Am J Prev Med*. 2006;31(6):506-511.
19. Results from the 2005 National Survey on Drug Use and Health: national findings. Substance Abuse and Mental Health Services Administration Web site. <http://www.oas.samhsa.gov/nsduh/2k5nsduh/2k5results.htm>. Accessibility verified November 6, 2008.
20. CDC WONDER. Centers for Disease Control and Prevention Web site. <http://wonder.cdc.gov>. 2007. Accessed October 5, 2007.
21. Inciardi JA, Surratt HL, Kurtz SP, Cicero TJ. Mechanisms of prescription drug diversion among drug-involved club- and street-based populations. *Pain Med*. 2007;8(2):171-183.
22. Drug Enforcement Administration. *DEA Appalachian Report: West Virginia 2007*. Washington, DC: US Dept of Justice; 2007.
23. National Drug Intelligence Center. *Drug Market Analysis 2008: Appalachia High Intensity Drug Trafficking Area*. Washington, DC: US Dept of Justice; 2008. Report 2008-R0813-001.
24. Turley E, Haas SM. Drug and violent crime control task force report, 2003-2004. Criminal Justice Statistical Analysis Center Web site. <http://www.wvdcs.com/publications/DVCTF0304.pdf>. 2005. Accessed October 24, 2008.
25. Health, United States, 2006: with chartbook on trends in the health of Americans. Centers for Disease Control and Prevention Web site. <http://www.cdc.gov/nchs/data/hs/hs06.pdf>. Accessed March 12, 2007.
26. Sullivan MD, Edlung MJ, Zhang L, Unutzer J, Wells KB. Association between mental health disorders, problem drug use, and regular prescription opioid use. *Arch Intern Med*. 2006;166(19):2087-2093.
27. Toombs JD, Kral LA. Methadone treatment for pain states. *Am Fam Physician*. 2005;71(7):1353-1358.
28. Trescot AM, Boswell MV, Atluri SL, et al. Opioid guidelines in the management of chronic non-cancer pain. *Pain Physician*. 2006;9(1):1-39.
29. Interagency guideline on opioid dosing for chronic non-cancer pain. Washington State Agency Medical Directors' Group Web site. <http://www.agencymed-directors.wa.gov>. Accessed March 31, 2008.
30. State prescription drug monitoring programs. Drug Enforcement Administration Web site. http://www.deadiversion.usdoj.gov/faq/rx_monitor.htm. Accessed October 12, 2008.