

Potential Misuse and Inappropriate Prescription Practices Involving Opioid Analgesics

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Background: Opioid misuse and abuse are growing concerns among the medical and public health communities.

Objectives: To examine the prevalence of indicators for potential opioid misuse in a large, commercially insured adult population.

Methods: We adapted existing indicators developed by expert panels to include having overlapping opioid prescriptions, overlapping opioid and benzodiazepine prescriptions, long-acting/extended release (LA/ER) opioids for acute pain, and high daily doses of opioids (≥ 100 morphine milligram equivalents). These indicators were assessed among continuously enrolled individuals aged 18-64 years from the 2009 Truven Health MarketScan databases. Analyses were stratified by sex.

Results: We identified 3,391,599 eligible enrollees who received at least 1 opioid prescription. On average, enrollees obtained 3.3 opioid prescriptions, and the average annual days of supply was 47 days. Twice as many enrollees received opioid prescriptions for acute pain as for chronic pain. About a quarter of the enrollees had at least 1 indicator of either potential misuse by patients or inappropriate prescription practices by providers. About 15% of enrollees had high daily doses; 7.8% had opioid overlap; and 7.9% had opioid and benzodiazepine overlap. Among those prescribed LA/ER opioids, 24.3% were treated for acute pain. Overlap indicators were more common among women.

Conclusions: Our findings underscore the critical need to develop programs aimed at promoting appropriate use of opioids. Retrospective opioid utilization reviews similar to our analyses can potentially help managed care organizations and healthcare providers improve patient care and reduce the risk of adverse outcomes related to these medications.

Am J Manag Care. 2013;19(8):648-658

For author information and disclosures,
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The problem of abuse and overdose of prescription drugs has emerged as a major public health issue in the United States.¹ In 2010, drug overdoses killed 38,329 Americans, more than the number killed in motor vehicle traffic crashes.² Misuse or abuse of prescription drugs also led to 1.2 million emergency department (ED) visits, compared with 1.0 million ED visits related to illicit drugs such as heroin and cocaine.³ Opioid analgesics alone or in combination with benzodiazepines or other drugs accounted for nearly half of the drug overdose deaths and more than three-fourths of prescription drug-related ED visits in 2009.^{2,3}

The majority of prescription opioids used for nonmedical reasons are diverted from prescriptions originally written for therapeutic use.⁴ Yet many opioid abusers obtain them directly from a doctor and/or pharmacy, often by fabricating pain symptoms, forging prescriptions, and engaging in doctor and pharmacy shopping (ie, obtaining multiple prescriptions from multiple providers or pharmacies).^{4,5} Providers and payers may be in a position to help enhance the safety of prescribed opioids and protect susceptible patients from becoming addicted to or overdosing on opioids. Among patients who were prescribed opioids, those receiving multiple opioid prescriptions, overlapping opioids, overlapping opioids and benzodiazepines, and opioids at high dosage levels are at greater risk for abuse and overdose.⁶⁻⁸

Despite the well-documented associations between usage patterns and risk, relatively little is known about the current prescription practices for opioid analgesics and the extent to which they might be contributing to the rising prescription drug abuse problem. A small number of studies using administrative data from a limited number of health plans have described general opioid use (eg, number of opioid prescriptions received, average daily dose, total days of supply) and/or potential misuse (eg, high daily dosage, overlapping opioids, overlapping opioids and benzodiazepines).⁹⁻¹³ However, these studies have generally limited their analyses to long-term (≥ 90 days) opioid users^{9,10} and/or populations with specific types of noncancer pain (eg, back pain, headache).^{11,13}

This study examines indicators of potential misuse by patients or inappropriate prescription practices by providers using one of the largest fully integrated commercial claims databases in the United States. The

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population of interest includes all adults with at least 1 opioid prescription regardless of their length of opioid use or indication for use with the exception of pain associated with cancer. Additional analysis reports differences in these indicators between men and women. Our results could be used to inform the monitoring of opioid use and to promote efforts to improve appropriate prescription practices by providers.

Take-Away Points

Opioid misuse and abuse are growing concerns in the United States.

- Using a large, fully integrated commercial claims database, we found a substantial prevalence of indicators of potential misuse by patients or inappropriate prescription practice by providers.
- Our findings underscore the critical need to develop programs to promote appropriate use of opioids.
- Managed care organizations and other insurers might help monitor opioid use and reduce the risk of adverse outcomes through retrospective opioid utilization reviews similar to our analyses.

METHODS

Data Source

We conducted secondary data analyses of the 2009 Truven Health MarketScan Commercial Claims and Encounters databases, which consisted of data from approximately 100 payers and health plans for about 50 million individuals from all 50 states.¹⁴ MarketScan contains standardized, fully integrated, enrollee-level, de-identified claims across inpatient, outpatient, and prescription drug services. Our analysis drew data primarily from the pharmaceutical claims, which included outpatient drug name, class, dosage, and quantity for about 17.8 million (10.3 million females and 7.5 million males) enrollees aged 18 to 64 years. In addition, the outpatient service claims and inpatient admission records were used to identify the underlying pain diagnoses related to opioid use. Inpatient admission records were necessary because some opioid prescriptions were prescribed to enrollees at discharge.

Study Population

Overall Study Population. We identified 13,097,589 opioid prescriptions for enrollees who were aged 18 to 64 years, were continuously enrolled in 2009, and did not have a cancer diagnosis in their outpatient or inpatient service claims (Figure). Cancer diagnoses were based on *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes including 338.3, 140-172.9, 174-215.9, 217-229.10, and 235-239.9. A list of analyzed opioids is provided in Table 1. Buprenorphine was excluded due to its primary use for treatment of opioid dependence. We excluded 1,216,388 (9.3%) opioid prescriptions that lacked the enrollee identification (ID) or dispensing information necessary for the calculation of predetermined outcome indicators. An additional 770,446 (5.9%) refill prescriptions were excluded due to inability to identify their original diagnoses. This selection process resulted in 11,110,755 (84.8%) opioid prescriptions filled by 3,391,599 enrollees as our overall study population.

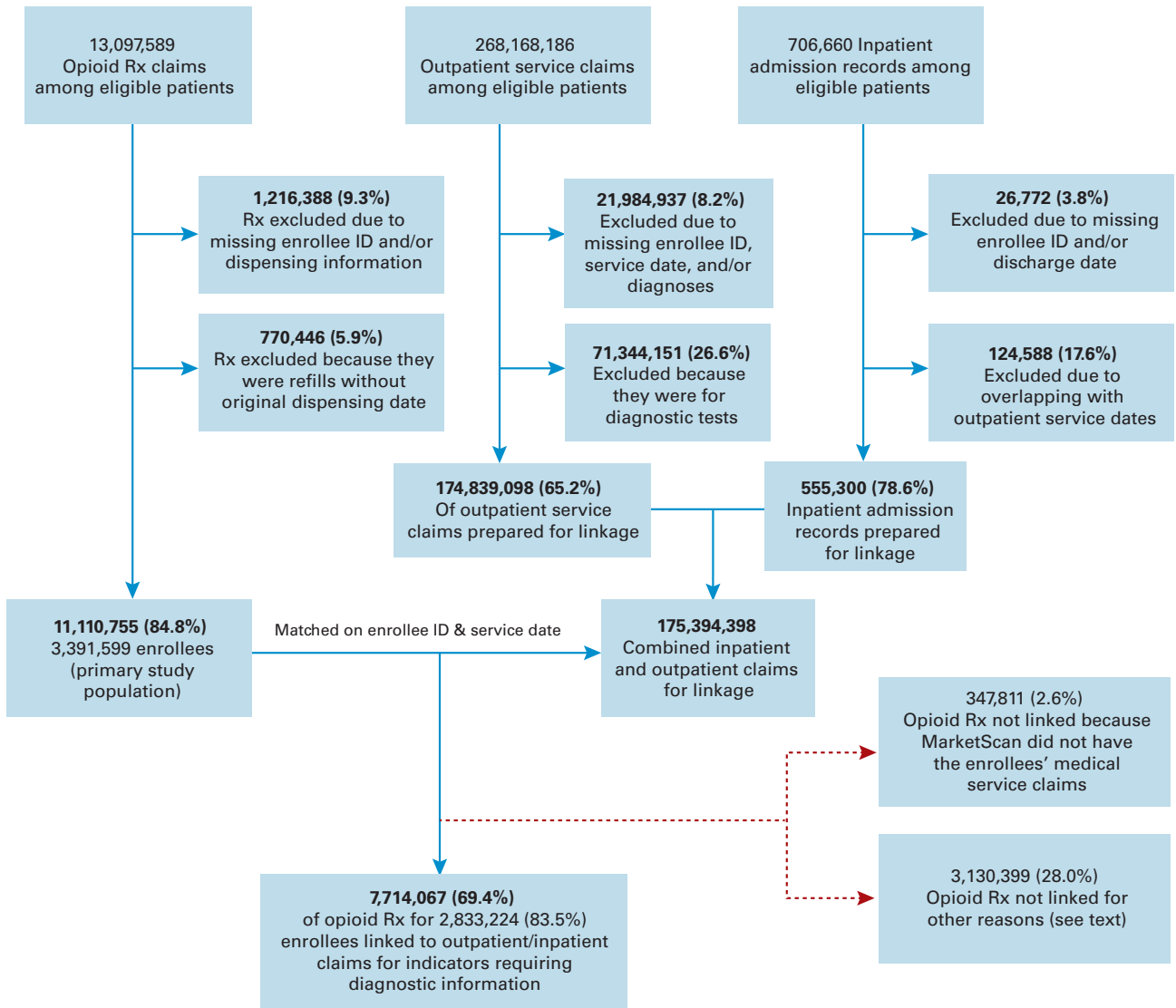
Subpopulation With Identified Diagnoses. To calculate a subset of outcome indicators that are specific to certain types of pain, we linked opioid prescription claims to the diagnoses on outpatient or inpatient service claims by matching enrollee ID and the date of service. Consistent with the existing literature,¹⁵ we linked opioid prescriptions to the outpatient services or inpatient discharges that occurred within 14 days of the prescription dispensing dates. If multiple outpatient or inpatient records existed within this interval, we linked to the ones that occurred on the day closest to the drug dispensing dates. When inpatient and outpatient dates of service overlapped, we used the outpatient claims for the linkage. Prescription refills were assigned the diagnoses on the original prescriptions. We successfully linked 7,714,067 (69.4%) of the 11,110,755 opioid prescriptions to diagnoses for 2,833,224 enrollees (85.3% of the overall study population). Of the remaining 30.6% of prescriptions, 28.0% could not be linked because the outpatient services or inpatient admissions had occurred more than 14 days prior to the prescription dispensing date or in 2008; 2.6% could not be linked because MarketScan did not have the enrollee's outpatient service claims.

Outcome Indicators

We adapted outcome indicators from clinical guidelines and those developed previously by expert panels.^{8,11,12,16-19} These indicators captured both general opioid use as well as potential misuse by patients or inappropriate prescription practices by providers.

At the enrollee level, indicators of opioid general use included the total number of opioid prescriptions obtained, total days of supply, and medical diagnoses (eg, acute pain, chronic pain, or both) associated with opioid prescriptions. Acute pain and chronic pain diagnoses were based on *ICD-9-CM* codes (Table 2, footnotes b and c). Benzodiazepine and muscle relaxant use in combination with opioids was also examined. Indicators of potential misuse or inappropriate prescription practices consisted of (1) opioid overlap, defined as opioid prescriptions that overlap by 7 or more days (including early refills);

■ **Figure.** Flow Chart Describing Study Population Selection



ID indicates identification; Rx, prescriptions.

(2) opioid and benzodiazepine overlap, defined as opioid and benzodiazepine prescriptions that overlap by 7 or more days; (3) long acting/extended release (LA/ER) opioid prescriptions written for acute pain conditions; (4) high daily opioid dosage, defined as a prescribed daily dose of 100 morphine milligram equivalents (MMEs) or greater (MME conversion factors are provided in Table 1); and (5) opioid dose escalation, measured as having a 50% or greater increase in mean MMEs per month twice consecutively during the year.

At the prescription level, indicators of opioid general use included the number of days of supply and the prescribed daily doses for opioid prescriptions for acute, chronic, and back pain. Back pain included both acute and chronic back

pain and was based on ICD-9-CM codes recommended by the American College of Occupational and Environmental Medicine practice guidelines.²⁰ Indicators of potential misuse or inappropriate prescription practices included the proportion of opioid prescriptions involved in opioid overlap or opioid and benzodiazepine overlap, similar to the enrollee-level analysis, and 3 indicators specific to LA/ER prescriptions given their elevated risk for addiction and abuse: (1) overlapping LA/ER opioid prescriptions; (2) LA/ER prescriptions written for acute pain; and (3) LA/ER prescriptions obtained by an opioid-naïve person, defined as a person who had no use of an opioid for at least 60 days prior to LA/ER drug initiation.

Potential Misuse and Inappropriate Prescription Practices

Table 1. List of Opioid Analgesics Prescribed to the Study Population, Opioid Drug Classification, and Morphine Equivalent Conversion Factors per Milligram^a

| Opioids | Morphine Equivalent Conversion Factor (Milligrams of Opioid) |
|---|--|
| Short-acting | |
| Butorphanol | 7.00 |
| Codeine phosphate + acetaminophen or aspirin | 0.15 |
| Codeine sulfate | 0.15 |
| Dihydrocodeine + acetaminophen or aspirin | 0.25 |
| Fentanyl (citrate transmucosal) lozenge/tablet ^b | 0.13 |
| Fentanyl film/oral spray ^c | 0.18 |
| Hydrocodone + acetaminophen, ibuprofen or homatropine | 1.00 |
| Hydromorphone | 4.00 |
| Meperidine hydrochloride (with or without promethazine) | 0.10 |
| Morphine sulfate | 1.00 |
| Nalbuphine | 1.00 |
| Opium | 1.00 |
| Oxycodone (with or without aspirin, acetaminophen, ibuprofen) | 1.50 |
| Oxymorphone | 3.00 |
| Pentazocine (with or without acetaminophen or aspirin) | 0.37 |
| Propoxyphene (with or without acetaminophen or aspirin) | 0.23 |
| Tapentadol | 1.00 |
| Tramadol (with or without acetaminophen) | 0.10 |
| Levorphanol tartrate | 11.00 |
| Long-acting/extended-release | |
| Fentanyl (transdermal) patch, extended-released | 7.20 |
| Methadone | 3.00 |
| Morphine sulfate sustained-release/extended-release | 1.00 |
| Oxycodone hydrochloride controlled-release | 1.50 |
| Oxymorphone extended-release | 3.00 |
| Tramadol extended-release | 0.10 |

^aAdapted from reference 13 and other sources.

^bTransmucosal fentanyl conversion to morphine equivalents assumes a 50% bioavailability of transmucosal fentanyl and that 100 µg of transmucosal fentanyl is equivalent to 12.5 mg to 15 mg of oral morphine.

^cBased on roughly 40% greater exposure for film or oral spray compared with lozenge.

^dThe morphine equivalent conversion factor for fentanyl patches is 2.4, but each patch is usually worn for 3 days. Therefore, the conversion factor is given as 7.2. The conversion factor is multiplied by the dosage in micrograms per hour.

Statistical Analysis

We calculated the distributions of various levels of usage among all enrollees receiving an opioid prescription overall, by sex, and by pain type. The prevalences of indicators of potential misuse by patients or inappropriate prescription practices by providers were calculated as both percentages of enrollees and percentages of prescriptions. We used χ^2 tests for comparisons by sex. Because of the large sample sizes, differences by sex might have been statistically significant ($P < .05$) but not clinically meaningful. Therefore, we only provide test results for sex differences that were considered meaningful.

RESULTS

Enrollee-Level Indicators

Among the overall study population of opioid recipients, 59% were female (Table 2). The mean age of opioid recipients was 44.7 years among males and 43.2 years among females. Males and females received comparable amount of opioids, as measured by the number of prescriptions and total days of supply received per person in 2009. More than half of all recipients had only 1 opioid prescription; fewer than one-third of recipients (28.3%) had 3 or more opioid

■ **Table 2.** Demographic Characteristics and General Opioid Use Indicators Among Enrollees Prescribed Opioid Analgesics, 2009

| Indicators | Males | | Females | | Total | |
|---|------------------|------------|------------------|------------|------------------|------------|
| | No. | % | No. | % | No. | % |
| Age, y | | | | | | |
| 18-34 | 321,468 | 23.0 | 557,121 | 28.0 | 878,589 | 25.9 |
| 35-44 | 302,809 | 21.6 | 438,907 | 22.0 | 741,716 | 21.9 |
| 45-54 | 403,299 | 28.8 | 536,158 | 26.9 | 939,457 | 27.7 |
| 55-64 | 371,329 | 26.5 | 460,508 | 23.1 | 831,837 | 24.5 |
| Mean | 44.7 | | 43.2 | | 43.8 | |
| Median | 47.0 | | 45.0 | | 46.0 | |
| Medication use | | | | | | |
| Number of opioid Rx obtained | | | | | | |
| 1 | 746,795 | 53.4 | 1,053,221 | 52.9 | 1,800,016 | 53.1 |
| 2 | 256,972 | 18.4 | 373,118 | 18.7 | 630,090 | 18.6 |
| 3 or more | 395,138 | 28.2 | 566,355 | 28.4 | 961,493 | 28.3 |
| Mean | 3.3 | | 3.3 | | 3.3 | |
| Median | 1.0 | | 1.0 | | 1.0 | |
| Number of LA/ER opioid Rx obtained | | | | | | |
| None | 1,341,927 | 96.3 | 1,918,963 | 96.3 | 3,260,890 | 96.3 |
| 1 | 17,384 | 1.2 | 20,974 | 1.1 | 38,358 | 1.1 |
| 2 | 5,460 | 0.4 | 7,343 | 0.4 | 12,803 | 0.4 |
| 3 or more | 34,134 | 2.1 | 45,414 | 2.2 | 79,548 | 2.2 |
| Mean | 0.3 | | 0.3 | | 0.3 | |
| Median | 0.0 | | 0.0 | | 0.0 | |
| Total days of supply of opioids per enrollee | | | | | | |
| <30 | 1,098,880 | 78.6 | 1,564,345 | 78.5 | 2,663,225 | 78.5 |
| 30-59 | 94,933 | 6.8 | 133,612 | 6.7 | 228,545 | 6.7 |
| 60-89 | 37,521 | 2.7 | 53,978 | 2.7 | 91,499 | 2.7 |
| 90+ | 167,571 | 12.0 | 240,759 | 12.1 | 408,330 | 12.0 |
| Mean | 47.4 | | 46.8 | | 47.0 | |
| Median | 7.0 | | 7.0 | | 7.0 | |
| Number of benzodiazepine Rx obtained | | | | | | |
| None | 1,223,934 | 87.4 | 1,614,894 | 81.0 | 2,838,828 | 83.7 |
| 1 | 66,526 | 4.8 | 138,651 | 7.0 | 205,177 | 6.0 |
| 2 | 24,874 | 1.8 | 58,582 | 2.9 | 83,456 | 2.5 |
| 3 or more | 83,571 | 6.0 | 180,567 | 9.1 | 264,138 | 7.8 |
| Mean | 0.6 | | 0.8 | | 0.7 | |
| Median | 0.0 | | 0.0 | | 0.0 | |
| Types of Rx obtained in 2009^a | | | | | | |
| Opioid only | 942,946 | 67.4 | 1,137,166 | 57.1 | 2,080,112 | 61.3 |
| Opioid and benzodiazepine | 174,971 | 12.5 | 377,800 | 19.0 | 552,771 | 16.3 |
| Opioid and muscle relaxant | 239,561 | 17.1 | 375,335 | 18.8 | 614,896 | 18.1 |
| Opioid, benzodiazepine, and muscle relaxant | 41,427 | 3.0 | 102,393 | 5.1 | 143,820 | 4.2 |
| Reason for opioid use | | | | | | |
| Acute pain only ^b | 403,695 | 28.9 | 543,630 | 27.3 | 947,325 | 27.9 |
| Chronic pain only ^c | 190,520 | 13.6 | 272,958 | 13.7 | 463,478 | 13.7 |
| Both acute and chronic pain conditions ^d | 343,480 | 24.6 | 477,508 | 24.0 | 820,988 | 24.2 |
| Other diagnoses | 214,188 | 15.3 | 387,245 | 19.4 | 601,433 | 17.7 |
| Unknown ^e | 247,022 | 17.7 | 311,353 | 15.6 | 558,375 | 16.5 |
| Total | 1,398,905 | 100 | 1,992,694 | 100 | 3,391,599 | 100 |

^aICD-9-CM indicates *International Classification of Diseases, Ninth Revision, Clinical Modification*; LA/ER, long-acting/extended-release; Rx, prescriptions.

^bOpioids and benzodiazepine prescriptions could be obtained at any time during 2009 and did not need to be prescribed in the same office visit.

^cAcute pain was determined by whether the enrollee had a diagnosis of a disease or an injury or a surgical procedure that could cause acute pain. Diagnoses for acutely painful diseases and injuries and their ICD-9-CM codes were sickle cell with crisis (282.62); acute pain (338.11, 338.12, 338.18, 338.19); dental abscess with sinus (522.5); dental abscess without sinus (522.7); gallstone (574); acute pancreatitis (577); kidney stone (592); pathologic fracture (733.1); acute injury (800-904.9); other acute injury (910-959.9); and external cause of injury codes (E800-E849.9; E880-E909.9; E916-E928.9; E953-E968.9; E970-E976.9; E983-E999.9). After the exclusion of minor procedures, surgical procedures included excision of breast tissue; other major skin, breast, or musculoskeletal surgeries; other major respiratory, cardiovascular, hemic and lymphatic, digestive, eye/ocular, ear/auditory, or urinary procedures; repair of inguinal hernia procedures; major male genital procedures; dilation and curettage; major female genital procedures; decompression, carpal tunnel surgery; major endocrine system and nervous system procedures; cataract removal; other major surgery procedures; cesarean section deliveries; major maternity procedures and related care; and dental or major restorative surgery.

^dDiagnoses likely to be associated with chronic pain and their ICD-9-CM codes included chronic pain (338.21, 338.22, 338.28, 338.29, 338.4); migraine headache (346.0-346.9); tension headache (307.81); arthritis or joint pain (710.0-719.9); dorsopathies or back pain (720.0-724.9); and arthritis or joint pain (725.0-729.9).

^eEnrollees listed as having acute and chronic pain conditions associated with opioid drugs included those who had both types of pain diagnoses listed in a single opioid-related office visit as well as those who had separate opioid-related visits for each type of pain.

^fCauses for opioid use were unknown because these enrollees' opioid prescriptions could not be linked to any outpatient/inpatient service claims.

Potential Misuse and Inappropriate Prescription Practices

Table 3. Indicators of Potential Misuse or Inappropriate Prescription Practices Among Enrollees Prescribed Opioid Analgesics, 2009

| Indicator | Males | | Females | | Total | |
|--|------------------|------------|------------------|------------|------------------|------------|
| | No. | % | No. | % | No. | % |
| Opioid overlap^a | | | | | | |
| None | 1,290,003 | 92.2 | 1,836,336 | 92.2 | 3,126,339 | 92.2 |
| Once | 43,274 | 3.1 | 60,108 | 3.0 | 103,382 | 3.0 |
| Two or more incidents | 65,628 | 4.7 | 96,250 | 4.8 | 161,878 | 4.8 |
| Opioid/benzodiazepine overlap^b | | | | | | |
| None | 1,309,560 | 93.6 | 1,811,335 | 90.9 | 3,120,895 | 92.0 |
| One | 24,343 | 1.7 | 50,421 | 2.5 | 74,764 | 2.2 |
| Two or more incidents | 65,002 | 4.6 | 130,938 | 6.6 | 195,940 | 5.8 |
| LA/ER opioids for acute pain^c | | | | | | |
| None | 1,385,053 | 99.0 | 1,974,788 | 99.1 | 3,359,841 | 99.1 |
| One | 9260 | 0.7 | 11,919 | 0.6 | 21,179 | 0.6 |
| Two or more incidents | 4592 | 0.3 | 5987 | 0.3 | 10,579 | 0.3 |
| High daily opioid dose^d | | | | | | |
| None | 1,213,988 | 86.8 | 1,670,048 | 83.8 | 2,884,036 | 85.0 |
| One | 120,792 | 8.6 | 218,445 | 11.0 | 339,237 | 10.0 |
| Two or more incidents | 64,125 | 4.6 | 104,201 | 5.2 | 168,326 | 5.0 |
| Opioid dose escalation^e | | | | | | |
| None | 1,382,017 | 98.8 | 1,967,592 | 98.7 | 3,349,609 | 98.8 |
| One or more | 16,888 | 1.2 | 25,102 | 1.3 | 41,990 | 1.2 |
| Number of indicators | | | | | | |
| None | 1,086,084 | 77.6 | 1,459,692 | 73.3 | 2,545,776 | 75.1 |
| One | 240,429 | 17.2 | 409,787 | 20.6 | 650,216 | 19.2 |
| Two | 51,884 | 3.7 | 89,269 | 4.5 | 141,153 | 4.2 |
| Three or more | 20,508 | 1.5 | 33,946 | 1.7 | 54,454 | 1.6 |
| Total | 1,398,905 | 100 | 1,992,694 | 100 | 3,391,599 | 100 |

LA/ER indicates long-acting/extended-release; MME, morphine milligram equivalent.

^aDays of supply of 1 opioid prescription overlap with another opioid prescription for at least 7 days for a given enrollee.

^bDays of supply of 1 opioid prescription overlap with 1 or more benzodiazepine prescriptions for at least 7 days for a given enrollee.

^cA total of 51,117 males and 67,691 females received LA/ER opioids.

^d>100 MMEs.

^eHaving a 50% or greater increase in mean MMEs per month twice consecutively during the year.

prescriptions. Notably, 2.3% of enrollees had 20 or more opioid prescriptions during the data year—with nearly 0.1% of enrollees receiving 50 or more opioid prescriptions (data not shown).

More than three-fourths of the recipients (78.5%) received fewer than 30 days of supply of opioids; about 12% of recipients received more than 90 days of supply of opioids. Among all opioid recipients, 16.3% also filled a benzodiazepine prescription during the data year, and 10.3% filled 2 or more such prescriptions. A higher proportion of females than males received both an opioid and benzodiazepine (19.0% vs 12.5%; $P < .05$).

We were able to identify the underlying medical diagnoses for opioid prescriptions for 82.3% of the overall study

population. About 27.9% of the recipients obtained opioids for acute pain conditions only; 13.7% received opioids for chronic pain conditions only; and 24.2% obtained opioids for both acute and chronic pain conditions. Another 17.7% of the recipients received opioid prescriptions for diagnoses not included in the lists of acute or chronic pain conditions. Nearly a quarter of opioid recipients showed at least 1 indicator (Table 3). The most common indicator was having high daily doses; an estimated 15.0% of the study population had daily doses of 100 MMEs or higher. The prevalence of opioid overlap and opioid and benzodiazepine overlap was 7.8% and 8.0%, respectively. About 0.9% of enrollees received LA/ER opioids for acute pain, and 1.2% had opioid dose escalation. A higher percentage of females versus males

■ **Table 4.** Characteristics of Opioid Prescriptions Linked to Diagnoses by Type of Pain, 2009

| Indicator | Prescriptions for Males | | Prescriptions for Females | | Total Prescriptions | |
|---|-------------------------|------------|---------------------------|------------|---------------------|------------|
| | No. | % | No. | % | No. | % |
| Diagnoses associated with opioid prescriptions | | | | | | |
| Acute pain ^a | 831,513 | 26.7 | 1,126,364 | 24.5 | 1,957,877 | 25.4 |
| Chronic pain ^b | 919,131 | 29.5 | 1,306,083 | 28.4 | 2,225,214 | 28.8 |
| Acute and chronic pain ^c | 518,646 | 16.6 | 683,438 | 14.9 | 1,202,084 | 15.6 |
| Other | 845,768 | 27.2 | 1,483,124 | 32.2 | 2,328,892 | 30.2 |
| Back pain ^d | 180,065 | 5.8 | 356,067 | 7.7 | 536,132 | 6.9 |
| Total^e | 3,115,058 | 100 | 4,599,009 | 100 | 7,714,067 | 100 |
| Days of supply per prescription | | | | | | |
| For acute pain ^a | | | | | | |
| ≤9 | 637,528 | 76.7 | 874,456 | 77.6 | 1,511,984 | 77.2 |
| 10-29 | 114,532 | 13.8 | 144,744 | 12.9 | 259,276 | 13.2 |
| 30-49 | 74,736 | 9.0 | 99,643 | 8.8 | 174,379 | 8.9 |
| 50-69 | 756 | 0.1 | 1166 | 0.1 | 1922 | 0.1 |
| 70-89 | 97 | 0.0 | 204 | 0.0 | 301 | 0.0 |
| ≥90 | 3864 | 0.5 | 6151 | 0.5 | 10,015 | 0.5 |
| Mean | 8.3 | | 8.2 | | 8.2 | |
| Median | 5.0 | | 5.0 | | 5.0 | |
| For chronic pain ^b | | | | | | |
| ≤9 | 307,103 | 33.4 | 460,253 | 35.2 | 767,356 | 34.5 |
| 10-29 | 250,537 | 27.3 | 346,563 | 26.5 | 597,100 | 26.8 |
| 30-49 | 352,906 | 38.4 | 482,385 | 36.9 | 835,291 | 37.5 |
| 50-69 | 1649 | 0.2 | 2836 | 0.2 | 4485 | 0.2 |
| 70-89 | 225 | 0.0 | 491 | 0.0 | 716 | 0.0 |
| ≥90 | 6711 | 0.7 | 13,555 | 1.0 | 20,266 | 0.9 |
| Mean | 18.4 | | 18.2 | | 18.3 | |
| Median | 15.0 | | 15.0 | | 15.0 | |
| For back pain ^d | | | | | | |
| ≤9 | 54,625 | 30.3 | 113,414 | 31.9 | 168,039 | 31.3 |
| 10-29 | 48,386 | 26.9 | 92,967 | 26.1 | 141,353 | 26.4 |
| 30-49 | 75,556 | 42.0 | 146,414 | 41.1 | 221,970 | 41.4 |
| 50-69 | 284 | 0.2 | 534 | 0.1 | 818 | 0.2 |
| 70-89 | 61 | 0.0 | 100 | 0.0 | 161 | 0.0 |
| ≥90 | 1153 | 0.6 | 2638 | 0.7 | 3791 | 0.7 |
| Mean | 19.2 | | 18.9 | | 19.0 | |
| Median | 20.0 | | 20.0 | | 20.0 | |

(Continued)

(9.1% vs 6.3%; $P < .01$) had 1 or more incidents of opioid and benzodiazepine overlap. A higher percentage of females versus males also had 1 or more incidents of high daily dose of opioids (16.2% vs 13.2%; $P < .01$). Overall, females were more likely than males to have any type of indicator (26.7% vs 22.4%; $P < .05$).

Prescription-Level Indicators

Among the 7,714,067 prescriptions that were linked to diagnoses, about a quarter of them were written for acute pain conditions. A slightly higher proportion (28.8%) were for chronic pain, and 15.6% were associated with both acute and chronic pain (Table 4). The remaining 30.2% of the pre-

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■ **Table 4.** Characteristics of Opioid Prescriptions Linked to Diagnoses by Type of Pain, 2009 (Continued)

| Indicator | Prescriptions for Males | | Prescriptions for Females | | Total Prescriptions | |
|---|-------------------------|------|---------------------------|------|---------------------|------|
| | No. | % | No. | % | No. | % |
| Daily dose per prescription, MME | | | | | | |
| For acute pain ^a | | | | | | |
| <40 | 402,840 | 48.5 | 545,283 | 48.4 | 948,123 | 48.4 |
| 40-59 | 183,435 | 22.1 | 234,228 | 20.8 | 417,663 | 21.3 |
| 60-79 | 115,688 | 13.9 | 147,062 | 13.1 | 262,750 | 13.4 |
| 80-99 | 40,704 | 4.9 | 55,307 | 4.9 | 96,011 | 4.9 |
| 100-119 | 32,714 | 3.9 | 48,424 | 4.3 | 81,138 | 4.1 |
| 120-199 | 41,745 | 5.0 | 71,691 | 6.4 | 113,436 | 5.8 |
| ≥200 | 13,885 | 1.7 | 23,412 | 2.1 | 37,297 | 1.9 |
| Unknown | 502 | 0.1 | 957 | 0.1 | 1459 | 0.1 |
| Mean | 53.5 | | 55.7 | | 54.8 | |
| Median | 40.0 | | 40.0 | | 40.0 | |
| For chronic pain ^b | | | | | | |
| <40 | 451,065 | 49.1 | 685,891 | 52.5 | 1,136,956 | 51.1 |
| 40-59 | 161,370 | 17.6 | 211,749 | 16.2 | 373,119 | 16.8 |
| 60-79 | 114,231 | 12.4 | 148,379 | 11.4 | 262,610 | 11.8 |
| 80-99 | 57,998 | 6.3 | 82,516 | 6.3 | 140,514 | 6.3 |
| 100-119 | 13,357 | 1.5 | 18,968 | 1.5 | 32,325 | 1.5 |
| 120-199 | 74,132 | 8.1 | 104,627 | 8.0 | 178,759 | 8.0 |
| ≥200 | 46,425 | 5.1 | 53,124 | 4.1 | 99,543 | 4.5 |
| Unknown | 553 | 0.1 | 829 | 0.1 | 1382 | 0.1 |
| Mean | 64.9 | | 59.6 | | 61.8 | |
| Median | 40 | | 37.5 | | 37.5 | |
| For back pain ^d | | | | | | |
| <40 | 88,971 | 49.4 | 187,994 | 52.8 | 276,965 | 51.7 |
| 40-59 | 31,415 | 17.5 | 57,522 | 16.2 | 88,937 | 16.6 |
| 60-79 | 22,014 | 12.2 | 40,043 | 11.3 | 62,057 | 11.6 |
| 80-99 | 11,099 | 6.2 | 21,619 | 6.1 | 32,718 | 6.1 |
| 100-119 | 2028 | 1.1 | 4339 | 1.2 | 6367 | 1.2 |
| 120-199 | 14,997 | 8.3 | 28,925 | 8.1 | 43,922 | 8.2 |
| ≥200 | 9462 | 5.3 | 15,428 | 4.3 | 24,887 | 4.6 |
| Unknown | 79 | 0.04 | 197 | 0.1 | 276 | 0.05 |
| Mean | 65.9 | | 60.0 | | 62.0 | |
| Median | 40 | | 37.5 | | 37.5 | |

ICD-9-CM indicates *International Classification of Diseases, Ninth Revision, Clinical Modification*; MME, morphine milligram equivalent.

^aSee Table 2, footnote b for diagnosis codes for acute pain conditions.

^bSee Table 2, footnote c for diagnosis codes for chronic pain conditions.

^cBoth acute and chronic pain diagnoses were present for the same linked prescription.

^dBack pain could be either acute or chronic. ICD-9-CM diagnostic codes included 307.89, 721.2, 721.3, 724.2, 724.4, 724.5, 724.6, 724.7, 724.8, 846, 846.0, 846.1, 846.2, 846.3, 846.8, 846.9, 847, 847.2, 847.4, and 847.9.

^eTotal excluded back pain because it overlaps with both acute pain and chronic pain.

■ **Table 5.** Indicators of Potential Misuse or Inappropriate Prescription Practices Among Opioid Analgesic Prescriptions by Type of Opioid, 2009

| Prescription-Level Indicator | Prescriptions for Males | | Prescriptions for Females | | Total Prescriptions | |
|--|-------------------------|------|---------------------------|------|---------------------|------|
| | No. | % | No. | % | No. | % |
| Opioid prescriptions | 4,564,846 | 100 | 6,545,909 | 100 | 11,110,755 | 100 |
| Opioids overlap ^a | 926,826 | 20.3 | 1,312,681 | 20.1 | 2,239,507 | 20.2 |
| Opioids and benzodiazepines overlap ^b | 565,304 | 12.4 | 1,117,866 | 17.1 | 1,683,170 | 15.1 |
| LA/ER opioid prescriptions | 382,575 | 100 | 489,057 | 100 | 871,632 | 100 |
| LA/ER opioids overlap ^c | 92,156 | 24.1 | 116,177 | 23.8 | 208,333 | 23.9 |
| LA/ER opioids for opioid-naïve persons ^d | 9921 | 2.6 | 12,406 | 2.5 | 22,327 | 2.6 |
| LA/ER opioids prescribed for acute pain ^e | 23,804 | 6.2 | 30,100 | 6.2 | 53,904 | 6.2 |

LA/ER indicates long-acting/extended-release.

^aSee Table 3, footnote a for the definition of opioid overlap.

^bSee Table 3, footnote b for the definition of opioid and benzodiazepine overlap.

^cSee Table 3, footnote c for the definition of LA/ER opioids overlap.

^dOpioid-naïve persons were defined as those who did not have any opioid prescription in the 60 days prior to the first LA/ER prescription date.

^eSee Table 2, footnote b for diagnosis codes for acute pain conditions.

scriptions were linked to diagnoses not included in the lists of acute or chronic pain conditions. In addition, about 6.9% of the opioid prescriptions were written for either acute or chronic back pain conditions.

The median days of supply for acute pain, chronic pain, and back pain were 5, 15, and 20 days, respectively. For acute pain, 22.8% of prescriptions were written for 10 or more days, and 9.5% were written for 30 or more days. For chronic pain, more than one-third of the prescriptions were for 30 or more days. The duration distribution for back pain, whether acute or chronic, was similar to that for chronic pain. The distributions for the days of supply for acute pain, chronic pain, and back pain were similar for males and females.

The median daily opioid dose for prescriptions for acute pain was similar for both sexes at 40 MME. The median daily dose for opioid prescriptions for chronic pain was higher for males (40.0 MME) than for females (37.5 MME). Among both acute pain and chronic pain prescriptions, 11.8% to 14.0% had a daily dose of 100 MME or greater; 1.9% to 4.5% of prescriptions were for 200 MME or greater.

Roughly one-fifth of opioid prescriptions overlapped with other opioid prescriptions, and 15.1% overlapped with a benzodiazepine prescription (Table 5). Opioid prescriptions written for female versus male recipients were significantly more likely to overlap with 1 or more benzodiazepine prescriptions (17.1% vs 12.4%; $P < .05$). Among LA/ER opioid prescriptions, nearly a quarter overlapped with other LA/ER opioid prescriptions; more than 6% of LA/ER prescriptions were written for acute pain conditions; and 2.6% were obtained by opioid-naïve patients.

DISCUSSION

In 2009, more than 11 million opioid prescriptions were written for 3.4 million (or 19.1%) of the 17.8 million adults without cancer diagnoses, with continuous enrollment, and with at least 1 outpatient drug claim in the MarketScan Commercial Claims and Encounters databases. Most patients obtained single-opioid prescriptions without also getting prescriptions for benzodiazepines. Although more patients were treated for acute pain, more prescriptions were written for chronic pain. The majority of prescriptions were written for fewer than 30 days, and the average prescription provided roughly 60 MMEs per day. There were signs of potential opioid misuse by patients or providers among the study population: nearly a quarter of patients had at least 1 indicator of potential misuse of opioids and more than 5% had 2 or more indicators of potential misuse.

Patients with misuse indicators probably account for a disproportionate share of adverse outcomes associated with opioid use. Increased numbers of opioid prescriptions, overlapping or early refill prescriptions, dose escalation, and more days of supply of opioids have all been associated with increased risk of clinically recognized abuse.^{7,8} Higher daily dose has been associated with misuse and overdoses.^{6,7,21} Opioid dependence has been associated with concurrent opioid and psychotropic drug use.²² Simultaneous prescribing of opioids and benzodiazepines, although it might be appropriate in some cases, has been associated with multiple-provider episodes, also known as doctor shopping.²³ Acute pain is not an indication for an LA/ER opioid, and such use is considered inappropriate by clinical guidelines.^{19,24} Many LA/

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ER opioids carry warnings against initiation among opioid-naïve patients.²⁵

Other patterns in prescribing for specific types of pain have not been previously flagged as indicators of possible misuse but run counter to the recommendations of some advisory groups. For example, the New York City Department of Health has recommended no more than a 7-day supply for acute pain.²⁴ However, in this study 22.8% of opioid prescriptions for acute pain were for 10 or more days, and 9.5% were for 30 or more days. The American College of Occupational and Environmental Medicine practice guidelines only recommend opioids on a limited basis for treatment of severe, acute low back pain, with treatment to last no more than 2 weeks.²⁰ In this study, 42.3% of opioid prescriptions for back pain were for 30 days or more, clearly much more than recommended.

Comparisons of our findings with the published literature were difficult because of use of different indicators or different study populations. In 1 managed care population with chronic noncancer pain during 1999 through 2005, 3.5% of person-years of opioid use were at dosages of 100 MME or more,⁷ and in a population of veterans with chronic pain during 2008, 3.4% of those treated with opioids were at dosages of 180 MME or more.²⁶ This compares with 14.0% of prescriptions for chronic pain over 100 MME and 4.5% over 200 MME in this study. In Massachusetts in 2006, 6.9% of patients treated with Schedule II drugs had early refills,²⁷ compared with 7.8% for any opioid overlap in this study.

Our study is consistent with previous literature in finding that women constitute the majority of users of opioids both alone and in combination with benzodiazepines.^{15,28} However, the number of opioid prescriptions and days of supply received per person per year were comparable between female and male opioid recipients. Despite the fact that men are more likely to use prescription painkillers nonmedically and to abuse opioids,^{4,8} indicators of possible misuse were not more prevalent among male opioid recipients in our study population. This might indicate that men misusing opioid analgesics are less likely to be commercially insured, or it might reflect changes in the demographics of the problem. Alternatively, the measures used here might reflect prescribing practices more than underlying patterns of patient misuse.

Limitations

Our study has several limitations. The potential misuse indicators were based on expert panels and validated by their association with misuse or abuse in other studies. In some cases, of course, such behaviors represent appropriate care for patients (eg, overlapping prescriptions resulting from changes in dosage or in drug type as a result of some adverse effect, legitimate early refills due to schedules, high daily dosages

in palliative care situations). Claims data were designed to support financial transactions rather than to capture clinical information. Pharmacy claims represent filled prescriptions reimbursed by health insurance rather than actual drug consumption. Due to large numbers of missing values for pharmacy ID and physician ID variables, we were not able to calculate doctor-shopping or pharmacy-shopping indicators, which are often considered strong indicators of opioid misuse.^{11,12} Lastly, reliance on ICD-9-CM codes to determine the reason for a prescription is subject to error. Many conditions are painful but are not usually counted among common causes of pain. Type of pain might also have been misclassified. Despite these limitations, our analysis represents a first comprehensive look at opioid use and potential misuse in the largest fully integrated commercial claims database in the United States.

CONCLUSIONS

While the majority of opioid prescriptions among this large commercially insured population might have been appropriate, a substantial number were prescribed in a manner that suggests potential patient misuse or inappropriate prescription practice by providers. Robust prescription opioid utilization review programs using integrated claims data, similar to our analyses, might help managed care organizations, third-party payers, professional societies, and governmental organizations (through guidelines) improve quality of care and reduce unnecessary healthcare costs.^{11,12} Managed care organizations and third-party payers can also use similar indicators to flag patients who might benefit from improved, coordinated pain management.

In addition, evidence-based clinical guidelines have suggested a number of tools and approaches clinicians should use to safely prescribe opioids. These include checking prescription drug monitoring programs, which track information on controlled substance prescriptions filled in a state,²⁹ taking a careful history of substance abuse and other mental health problems, conducting routine urine drug screens in concert with pain management agreements, and making use of pain medicine consultants when problems arise.¹⁶⁻²⁰ Such safeguards might help providers avoid improper opioid use and thereby reduce the risk of adverse outcomes related to opioid medications.

Author Affiliations: From the Centers for Disease Control and Prevention (YL, JEL, LJP, KZ, CMJ), National Center for Injury Prevention and Control, Division of Unintentional Injury Prevention, Atlanta, GA.

Funding Source: All work for this study was funded by the Centers for Disease Control and Prevention, and none of the authors had conflicts of interest.

Author Disclosures: The authors (YL, JEL, LJP, KZ, CMJ) report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

Authorship Information: Concept and design (YL, JEL, LJP, CMJ); analysis and interpretation of data (YL, JEL, LJP, KZ); drafting of the manuscript (YL, JEL, LJP, CMJ); critical revision of the manuscript for important intellectual content (YL, JEL, LJP, KZ, CMJ); statistical analysis (YL, JEL, KZ); administrative, technical, or logistic support (YL); and supervision (LJP).

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