

Drivers of Excess Costs of Opioid Abuse Among a Commercially Insured Population

Lauren M. Scarpati, PhD; Noam Y. Kirson, PhD; Miriam L. Zichlin, MPH; Zitong B. Jia, BA; Howard G. Birnbaum, PhD; and Jaren C. Howard, PharmD

Prescription opioid pain relievers can be highly effective in providing relief for patients suffering from chronic pain.¹ At the same time, prescription opioid abuse, dependence, overdose, and poisoning (hereinafter “abuse”) have collectively become a national public health concern. Policy interventions, such as states’ prescription drug monitoring programs and rescheduling certain opioids, as well as technological innovations, such as the introduction of abuse-deterrent formulations, have been implemented with the goal of curbing opioid misuse while trying to maintain appropriate access to care for patients.

Opioid abuse is also costly; societal costs of opioid abuse in 2007 were estimated at \$55.7 billion.² Payers face a large proportion of these costs; previous estimates of the annual per-patient economic burden to payers of opioid abuse range from \$10,000 to \$20,000.³⁻⁵ Despite growing concern, the current literature has only begun to address the drivers of these excess costs of opioid abuse in terms of place of service and comorbid conditions.

This paper first seeks to replicate the findings of a newly published study performed using a commercial claims database from OptumHealth Care Solutions, Inc (Optum). The original study presented recent refined estimates of the excess costs of opioid abuse from a payer perspective and investigated the trajectory and drivers of those excess costs. The goal of this study was to replicate the findings using a different, more expansive database: the Truven MarketScan Commercial Claims and Encounter database (Truven). In addition, we extend those findings by presenting updated rates of diagnosed prevalence and incidence of opioid abuse, as well as the incremental per-member-per-month (PMPM) cost of abuse to payers.

METHODS

Data

We analyzed de-identified administrative claims data from Truven, which cover more than one-third of the US population

ABSTRACT

OBJECTIVES: To replicate and extend a recently published analysis of the drivers of excess costs of opioid abuse.

STUDY DESIGN: Retrospective data analysis using de-identified claims data from the Truven MarketScan Commercial Claims and Encounter database.

METHODS: Medical and prescription drug claims from beneficiaries covered by large self-insured US companies were used to select patients with incident diagnoses of opioid abuse between 2012 and 2015. Two cohorts, abusers and nonabusers, were matched using propensity score methods. Excess healthcare costs were estimated over a 6-month baseline period and 12-month follow-up period. Cost drivers were assessed by diagnosis (3-digit *International Classification of Diseases, Ninth Revision, Clinical Modification* groupings) and place of service.

RESULTS: The analysis included 73,714 matched pairs of abusers and nonabusers. Relative to nonabusers, abusers had considerably higher annual healthcare costs of \$10,989 per patient, or \$1.98 per member per month. Excess costs were similar, yet lower, than the previous analysis using another commercial claims database. In both analyses, a ramp-up in excess costs was observed prior to the incident abuse diagnosis, followed by a decline post diagnosis, although not to baseline levels. Key drivers of excess costs in the 2 studies included opioid use disorders, nonopioid substance misuse, and painful and mental health conditions. From 2010 to 2014, the prevalence of diagnosed opioid abuse doubled, with incidence rates exhibiting an increasing, though flatter, trend than earlier in the period.

CONCLUSIONS: Opioid abuse imposes a considerable economic burden on payers. Many abusers have complex healthcare needs and may require care beyond that which is required to treat opioid abuse. These results are robust and consistent across different data sources.

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(ie, 117 million commercially insured beneficiaries, including employees, children spouses, and retirees) of large, self-insured companies located throughout the United States and in a broad array of industries and job types. The databases aggregate data from a large number of plan types (eg, fee-for-service and health maintenance organizations [HMOs]).⁶ The data include medical claims (service date, diagnoses received, procedures performed, place of service, and payment amounts), pharmacy claims (fill dates, national drug codes, and payment amounts), and eligibility information (patient demographic characteristics and enrollment history) for the period of January 2010 to September 2015. The Optum data used in the prior study contained a similar commercially insured population from different companies, industries, and regions.

Study Design and Statistical Analysis

To ensure replicability, the methodology applied for the replication analysis paralleled that in the original analysis to the extent possible. Full details of the sample selection procedure and baseline characteristics can be found in the original study.⁷

Incident abuse diagnoses between January 2012 and September 2015 were identified in the medical claims using the following *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes for opioid abuse, dependence, or overdose/poisoning: 304.0x, 304.7x, 305.5x, 965.00, 965.02, and 965.09.⁷ The index date for abusers was defined as the date of the first abuse, dependence, or overdose/poisoning diagnosis. For nonabusers, the index date was the date of a random medical claim during this same period.

The follow-up period over which each individual was observed was defined as the 6-month period prior to the index date and 0 to 6 months thereafter. Including the 6 months prior to the index date in the follow-up period was important because abuse may result in greater use of medical resources prior to a formal diagnosis. Claims and costs 7 to 12 months before the incident diagnosis (the baseline period) were used in propensity score matching. A graphical depiction of the study period can be found in the **eAppendix (available at www.ajmc.com)**.

Two nonoverlapping cohorts of incident opioid abusers and nonabusers were selected. A 10% random sample of nonabusers was used. Patients in both cohorts had to be aged 18 to 64 years throughout the study period. In addition, we required continuous eligibility in non-HMO plans throughout the baseline and preindex follow-up periods (ie, up to and including the index date). After that, we followed patients for an additional 6 months, regardless of eligibility, to avoid bias from dropping patients who either died or lost healthcare coverage due to their abuse.

TAKEAWAY POINTS

- ▶ Commercially insured patients who receive a diagnosis of prescription opioid abuse, dependence, or overdose/poisoning incur annual excess healthcare costs of \$10,989 (or \$1.98 per member per month) relative to matched nonabusers, confirming a large burden to commercial payers as shown by the results of a recently published study.
- ▶ An assessment of the key cost drivers associated with opioid abuse highlights that abusers often face multiple mental health, substance use, and/or other health issues beyond opioid abuse, suggesting a need for more comprehensive care.
- ▶ The prevalence of diagnosed opioid abuse doubled between 2010 and 2014, with incidence rates exhibiting a flatter, although also increasing, trend.

Propensity score matching of abusers and nonabusers was used to account for observable confounding factors associated with healthcare costs. A complete list of baseline characteristics, which were used as covariates in the propensity score model, and clinical codes can be found in the eAppendix. Abusers were matched 1:1 to nonabusers based on propensity scores \pm one-fourth of a standard deviation using a greedy-matching algorithm.⁸ Baseline period characteristics for the postmatch cohorts were then compared to assess the quality of the match.

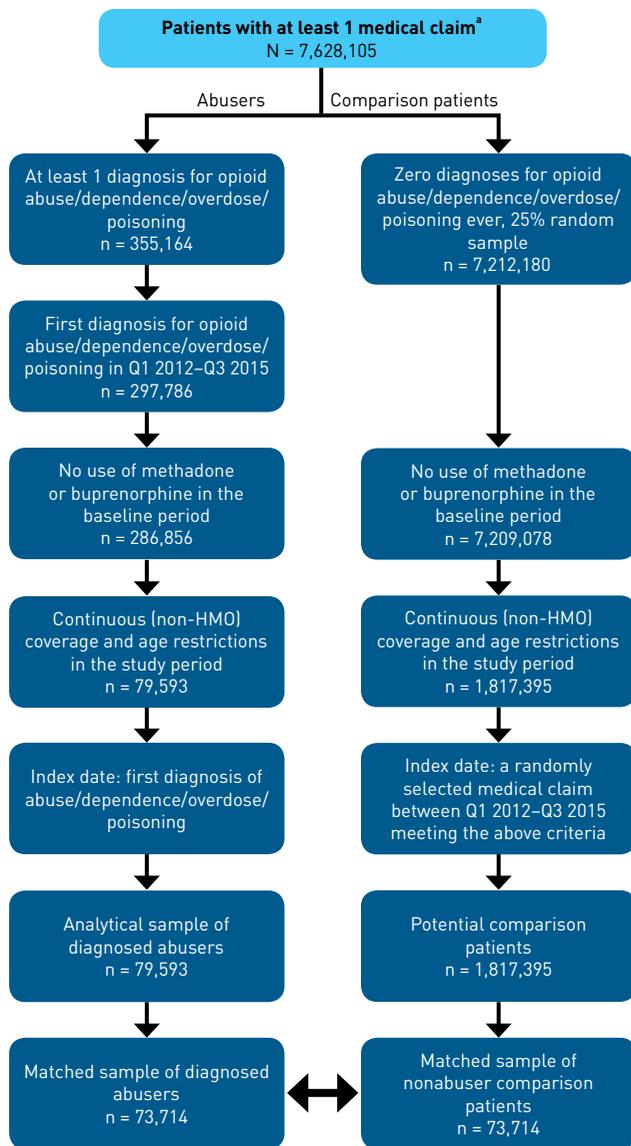
Outcomes

We compared abusers' and nonabusers' average healthcare costs to payers during 6-month increments of the study period: 1) the baseline period (7 to 12 months before the index event), the preindex period (1 to 6 months before the index event), and the postindex period (0 to 6 months following the index event). Medical costs were categorized by place of service: inpatient, emergency department (ED), outpatient/other (eg, skilled nursing facilities), and rehabilitation facilities (costs attributed to rehabilitation facilities include those for care received in inpatient and outpatient substance abuse facilities, including all treatment received for other, both abuse and non-substance abuse-related conditions). All costs were inflated to 2015 US dollars using the medical care component of the Consumer Price Index. To assess cost drivers, the top diagnoses contributing to excess medical costs were reported by 3-digit *ICD-9-CM* groupings.

We also calculated annual prevalence and incidence rates of opioid abuse for 2010 to 2014. Prevalence and incidence rates for 2015 were not available due to the incomplete year of data available at the time of the study. Prevalence rates reflect all patients with at least 1 claim for opioid abuse within a given year, whereas incidence rates reflect patients with incident diagnoses within a given year. The denominator for both incidence and prevalence comprises patients with at least 1 month of coverage within a year.

Incidence rates for those aged 18 to 64 years (ie, a rate of episodes per member) for 2012 to 2014 were averaged and combined with the estimate of annual, incremental excess costs due to opioid abuse to arrive at a PMPM estimate. Because annual excess costs of abuse were calculated for patients experiencing incident abuse

FIGURE 1. Sample Selection



*The number of patients with at least 1 medical claim (N = 7,628,105) includes all abusers and 10% of nonabusers in the Truven data between 2010 and 2015.

episodes, incidence rates were considered more appropriate than prevalence for calculating a PMPM estimate of the burden of opioid abuse to payers.

RESULTS

Prematch Cohort Characteristics

Figure 1 describes the sample selection criteria that resulted in an analytic sample of 79,593 abusers and 1,817,395 nonabusers,

for which prematch baseline characteristics were computed. The eAppendix Table (section i) compares baseline characteristics between the abusers and nonabusers prior to matching. Abusers were statistically different from controls on key demographic measures, with abusers more likely to be male (53.9% vs 45.5%; $P < .0001$) and younger (39.0 vs 43.0; $P < .0001$). There were also significant differences in the prematch comorbidity profile and healthcare resource utilization. During the baseline period, abusers were substantially more likely to have been diagnosed with abuse of nonopioid substances (15.3% vs 2.0%; $P < .0001$), major depressive disorder (8.5% vs 1.8%; $P < .0001$), other psychoses (7.9% vs 1.1%; $P < .0001$), and other mental health disorders (30.2% vs 9.1%; $P < .0001$). A complete list of the clinical codes and diagnoses used to construct these categories can be found in the eAppendix.

Overall, abusers used significantly more healthcare resources during the baseline period. For example, abusers spent more days in an inpatient hospital (0.8 vs 0.1 days; $P < .0001$) and more time in the ED (0.6 vs 0.1 visits; $P < .0001$) than nonabusers. These differences resulted in average baseline healthcare costs among abusers being nearly 4 times that of nonabusers (\$8563 vs \$2371; $P < .0001$).

Postmatch Cohort Characteristics

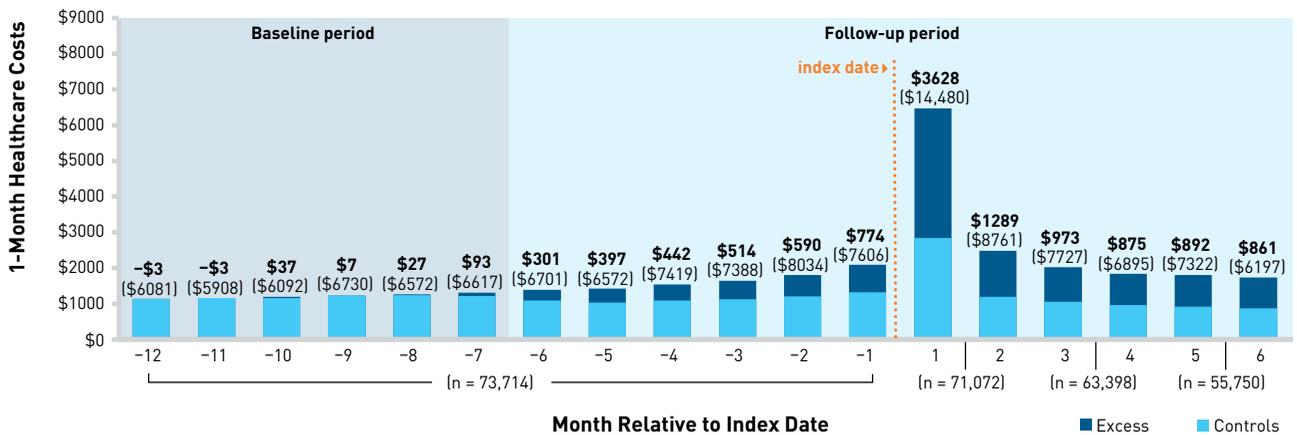
The propensity score procedure successfully matched 73,714 abusers 1:1 with nonabusers for a 93% match rate. These matched samples were well balanced with respect to the baseline characteristics (eAppendix Table [section ii]). There were 3 notable differences between the 2 cohorts, although the magnitude of these differences was small: 1) abusers were less likely to be the child of a primary beneficiary than nonabusers (27.3% vs 30.2%; $P < .0001$), 2) a larger proportion of abusers had extended-release opioid use during the baseline period (9.6% vs 7.9%; $P < .0001$), and 3) abusers had 2% higher costs than nonabusers during the baseline period (\$7306 vs \$7149; $P = .0209$).

Costs of Abuse

Figure 2 displays the average monthly excess costs during the study period. As observed in the original analysis, monthly excess costs increased during the 9 months leading up to the index date, from \$7 eight months before to \$774 in the month prior to the index date. Excess costs reached their maximum, \$3628, in the index month, and although they dropped subsequently, remained well above baseline levels (between \$1289 and \$861) thereafter.

Tables 1 and 2 present the costs of abusers and controls during the two 6-month segments of the follow-up period (preindex, and postindex) by place of service, as well as the leading conditions driving excess medical costs. The average per-patient healthcare costs of abusers were \$3018 more than nonabusers in the 6 months before the abuse episode and \$7971 more than nonabusers in the 6 months after the abuse episode. Stated differently, abusers' annual costs were estimated to be \$25,069 compared with \$14,080 for

FIGURE 2. Mean per-Patient-per-Month Excess Healthcare Costs During the 18-Month Study Period^{a,b,c}



^aMean monthly costs post index exclude patients in months for which they no longer have continuous eligibility.

^bStandard deviations are shown in parentheses.

^cCounts reflect abusers with eligibility in a given month.

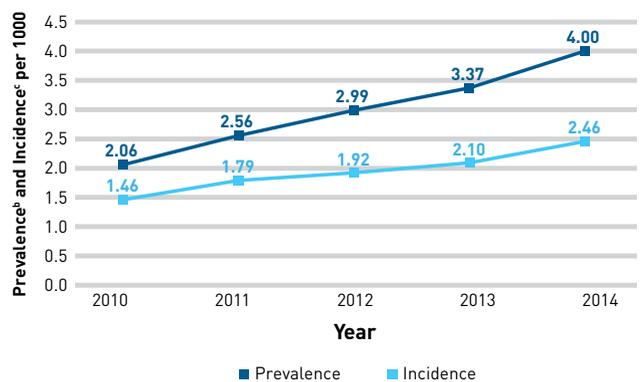
Source: Truven MarketScan Commercial Claims and Encounters data.

matched controls, resulting in an extra \$10,989. In the 6-month preindex period, most excess healthcare costs were incurred in an inpatient setting (49%; \$1471), followed by ED (18%; \$531), rehabilitation facilities (17%; \$503), outpatient (12%; \$371), and prescription drugs (5%; \$143). During the preindex period, the most costly conditions associated with opioid abuse included those related to nonopioid drug/alcohol abuse and dependence (19% of preindex excess costs), back pain (11%), and mental health-related disorders (6%).

In the 6 months after the index date, 53% (\$4215) of excess healthcare costs could be attributed to care in a rehabilitation facility setting, 31% (\$2429) in an inpatient setting, 8% (\$610) in an ED setting, 5% (\$432) on prescription drugs, and 4% (\$284) on outpatient care. Similarly, opioid dependence, abuse, and poisoning (30%) and nonopioid drug/alcohol abuse/dependence (28%) were prominent excess cost drivers following the formal abuse diagnosis. As in the pre-index period, we also observed mental health-related (7%) and back pain-related (2%) conditions associated with the excess costs of abuse.

Figure 3 shows the diagnosed prevalence and incidence for opioid abuse, dependence, and overdose/poisoning combined. Prevalence rates between 2010 and 2014 nearly doubled (2.06 per 1000 in 2010 to 4.00 per 1000 in 2014), whereas incidence rates exhibited a flatter trend (1.46 per 1000 in 2010, to 2.46 per 1000 in 2014). As described in the Outcomes subsection of the Methods section above, combining incidence rates (the average incidence rate per 1000 for 2012 to 2014 is 2.16) and average annual excess costs (\$10,989), we arrived at an estimate of \$1.98 PMPM in costs to payers of opioid abuse.

FIGURE 3. Prevalence and Incidence Rates of Opioid Abuse, 2010-2014^a



^aOpioid abuse, dependence, and poisoning/overdose were identified using the following *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes: 305.5x (abuse); 304.0x and 304.7x (dependence); and 965.00, 965.02, and 965.09 (poisoning/overdose).

^bPrevalence of diagnosed opioid abuse, dependence, and poisoning/overdose was measured in the claims data as the proportion of covered lives (aged 18 to 64 years) with at least 1 month of eligibility in the calendar year that had at least 1 diagnosis for opioid abuse, dependence, or poisoning/overdose in that year. Each patient contributed a maximum of 1 episode in each calendar year.

^cIncidence of diagnosed opioid abuse, dependence, or poisoning/overdose was measured in the claims data as the proportion of covered lives (aged 18 to 64 years) with at least 1 month of eligibility in the calendar year that had a first diagnosis for opioid abuse, dependence, or poisoning/overdose in that year. First diagnoses were defined as diagnoses among patients with no prior diagnoses of opioid abuse, dependence, or poisoning/overdose in their prior medical claims history.

Source: Truven MarketScan Commercial Claims and Encounters data.

TABLE 1. Excess Healthcare Costs During the Preindex Period^{a,b,c}

Preindex (-6 to 0 months relative to the index date)	Abusers [A] Mean (SD)	Controls [B] Mean (SD)	Excess [A] - [B] Mean (SD)
Healthcare cost drivers by places of service ^d			
Total healthcare costs ^e	\$9903 (\$29,390)	\$6885 (\$23,972)	\$3018**
Prescription drug costs	\$1554 (\$5996)	\$1412 (\$5280)	\$143**
Total medical costs	\$8349 (\$28,173)	\$5474 (\$22,584)	\$2875**
Inpatient	\$3491 (\$22,083)	\$2020 (\$17,115)	\$1471**
Emergency department	\$1007 (\$5822)	\$477 (\$3098)	\$531**
Rehabilitation facility	\$579 (\$5132)	\$77 (\$1799)	\$503**
Outpatient/other	\$3271 (\$10,503)	\$2900 (\$10,577)	\$371**
Overall medical cost drivers by ICD-9-CM diagnosis grouping			
304.xx ^f Drug dependence (excluding opioids)	\$258 (\$3149)	\$19 (\$638)	\$239
303.xx Alcohol dependence syndrome	\$229 (\$2739)	\$42 (\$1099)	\$187
722.xx Intervertebral disc disorders	\$288 (\$3675)	\$162 (\$2524)	\$126
724.xx Other and unspecified disorders of back	\$290 (\$2392)	\$170 (\$1668)	\$120
305.xx ^f Nondependent abuse of drugs (excluding opioids)	\$185 (\$1204)	\$68 (\$1024)	\$117
296.xx Episodic mood disorders	\$193 (\$1531)	\$89 (\$939)	\$104
789.xx Other symptoms involving abdomen and pelvis	\$155 (\$1303)	\$82 (\$823)	\$73
721.xx Spondylosis and allied disorders	\$137 (\$1616)	\$65 (\$912)	\$72
276.xx Disorders of fluid electrolyte and acid-base balance	\$140 (\$1981)	\$68 (\$1288)	\$72
300.xx Anxiety, dissociative and somatoform disorders	\$150 (\$1054)	\$85 (\$788)	\$64

ICD-9-CM indicates *International Classification of Diseases, Ninth Revision, Clinical Modification*; SD, standard deviation.

** indicates $P < .05$; *** indicates $< .01$.

^aThe 12-month follow-up period was defined as the 6 months prior to and 6 months following the index date.

^bThe index date for abusers was defined as the date of first diagnosis of abuse, dependence, or poisoning/overdose in quarter (Q) 1 2012 to Q3 2015. The index date for controls was defined as a random medical claim in Q1 2012 to Q3 2015.

^cAbusers were matched to potential controls based on propensity score (within a quarter of a standard deviation).

^dP values were calculated using Wilcoxon signed rank tests.

^eHealthcare costs were inflated to 2015 values using the medical care component of the Consumer Price Index.

^fExcluding codes used to identify opioid abuse.

Source: Truven MarketScan Commercial Claims and Encounters data.

DISCUSSION

To replicate the original analysis, the analyses above first examined the excess costs of opioid abuse and highlighted the substantial burden imposed on commercial payers: on average, a diagnosed opioid abuser had excess annual healthcare costs of \$10,989. This figure is within the range of estimates from the existing literature³⁻⁵ and translates into \$1.98 PMPM. This is comparable to the \$14,810 in excess costs associated with opioid abuse in the original analysis.⁷ The difference between \$10,989 and \$14,810 may be explained by the unmatched patients in the Truven analysis. The match rate in Truven was 93% compared with 99% in Optum. The 7% of unmatched patients in Truven tended to be considerably more costly than those who matched; the much higher Optum match rate translated into including many of these costlier patients in that sample, resulting in higher excess cost estimates. Should the costlier Truven patients have matched, we may have observed very similar excess costs as those from Optum.

Next, the trajectory of excess costs by month was compared with that in the original analysis and confirmed the following: abusers' mean healthcare costs began to build up prior to the formal diagnosis, spiked during the diagnosis month, and then flattened out. Notably, excess costs did not return to baseline levels. This pattern is similar to one recently observed among patients with cardiovascular disease⁹: for both low- and high-risk cohorts, incremental costs were observed accumulating in the year prior to a new cardiovascular event (2012: €148-€589; for comparison to our estimates, 2015: US\$197-US\$784 [2012 currency conversion rate: 1 US dollar = 0.81 euros¹⁰]; the Bureau of Labor Statistics medical care component of the Consumer Price index was used to adjust to 2015 US\$¹¹), peaked in the year of the new event (2012: €8346-€8663; 2015: US\$11,108-\$11,530), and persisted above pre-event levels for 2 years thereafter (2012: €1228-€1732 in the second year after the new cardiovascular event; 2015: US\$1634-US\$2305). As noted within the literature, such prolonged costs post index may be associated with consid-

erable long-term costs. The assessment of longer-term incremental costs of opioid abuse may be a fruitful area of future research from which payers could benefit.

The final piece of the replication was to assess the drivers of excess costs. We found that a large proportion of excess costs was associated with opioid and nonopioid substance abuse (including alcohol), painful conditions (eg, intervertebral disc disorders, spondylosis, allied disorders), and mental health disorders (eg, episodic mood disorders, depression, anxiety). The associations between opioid and nonopioid substance abuse and between mental health disorders and substance abuse^{12,13} are consistent with the existing literature.

Other identified cost drivers were associated with vague diagnoses, including observation and evaluation for suspected conditions not found, general symptoms, and encounter for other and unspecified procedures and aftercare. One area for further research may be an evaluation of the extent to which such ambiguous diagnoses are associated with drug-seeking behavior. These predictors may help to identify improved treatment strategies for these complex patients by providing a rationale for an assessment for opioid use disorder.

Although it is well documented in the literature that the excess costs of opioid abuse impose a substantial burden on payers, this analysis contributes by highlighting the drivers of those costs. As evidenced in this analysis, patients given an opioid abuse diagnosis often present with numerous other complex and often costly conditions. This multifaceted clinical paradigm, along with recent increases in both the prevalence and incidence of opioid abuse, underscore the importance to public health and the healthcare system of diagnosing and treating opioid abuse and the multiple comorbidities that may accompany it. A more thorough understanding of the drivers of these costs may enable payers and policy makers to implement policies and patient care guidelines to more rapidly identify abuse and associated comorbidities, which may, in turn, help to lower costs.

TABLE 2. Excess Healthcare Costs During the Postindex Period^{a,b,c}

Postindex (0 to 6 Months Relative to the Index Date)	Abusers [A] Mean (SD)	Controls [B] Mean (SD)	Excess [A] - [B] Mean
Healthcare cost drivers by places of service ^d			
Total healthcare costs ^e	\$15,165 (\$36,658)	\$7194 (\$26,171)	\$7971**
Prescription drug costs	\$1679 (\$5269)	\$1247 (\$4518)	\$432**
Total medical costs	\$13,486 (\$35,909)	\$5947 (\$25,241)	\$7539**
Inpatient	\$4877 (\$29,216)	\$2448 (\$21,069)	\$2429**
Emergency department	\$1149 (\$4048)	\$539 (\$2657)	\$610**
Rehabilitation facility	\$4281 (\$14,808)	\$66 (\$1566)	\$4215**
Outpatient/other	\$3180 (\$9637)	\$2895 (\$9768)	\$284**
Overall medical cost drivers by ICD-9-CM diagnosis grouping			
304.xx ^f Drug dependence (opioids)	\$2132 (\$7196)	\$0 (\$0)	\$2132
304.xx ^g Drug dependence (excluding opioids)	\$1109 (\$7394)	\$21 (\$807)	\$1088
303.xx Alcohol-dependence syndrome	\$619 (\$4417)	\$34 (\$901)	\$584
296.xx Episodic mood disorders	\$430 (\$2340)	\$81 (\$899)	\$348
305.xx ^g Nondependent abuse of drugs (excluding opioids)	\$356 (\$1705)	\$80 (\$874)	\$276
292.xx Drug-induced mental disorders	\$192 (\$1172)	\$3 (\$204)	\$188
300.xx Anxiety, dissociative, and somatoform disorders	\$260 (\$1456)	\$80 (\$687)	\$180
965.xx ^f Poisoning by analgesics, antipyretics, and antirheumatics (opioids)	\$145 (\$1827)	\$0 (\$0)	\$145
724.xx Other and unspecified disorders of back	\$286 (\$2487)	\$148 (\$1405)	\$139
V58.xx Encounter for other and unspecified procedures and aftercare	\$252 (\$1820)	\$115 (\$1451)	\$137

ICD-9-CM indicates *International Classification of Diseases, Ninth Revision, Clinical Modification*; SD, standard deviation.

** indicates $P < .05$; *** indicates $P < .01$.

^aThe 12-month follow-up period was defined as the 6 months prior to and 6 months following the index date.

^bThe index date for abusers was defined as the date of first diagnosis of abuse, dependence, or poisoning/overdose in quarter (Q) 1 2012 to Q3 2015. The index date for controls was defined as a random medical claim in Q1 2012 to Q3 2015.

^cAbusers were matched to potential controls based on propensity score (within a quarter of a standard deviation).

^dP values were calculated using Wilcoxon signed rank tests.

^eHealthcare costs were inflated to 2015 values using the medical care component of the Consumer Price Index.

^fLimited to codes used to identify opioid abuse.

^gExcluding codes used to identify opioid abuse.

Source: Truven MarketScan Commercial Claims and Encounters data.

Limitations

First, the results rely on the accuracy of the administrative data. Therefore, any miscoding could affect our results, although we have no reason to suspect that any inaccuracies in the data affected the abusers or nonabuser control patients differently. Second, by definition, undiagnosed opioid abusers do not receive any of the ICD-9-CM diagnosis codes for abuse, and it is not out of the question that undiagnosed abusers may be included in the nonabuser cohort. Although the extent to which this applies to this particular sample is unknown, if undiagnosed abusers are more costly than a true nonabuser population, this would suggest that the estimated excess costs of diagnosed abuse understate the true excess cost differential between abusers and true nonabusers. Third, while our definition of abusers includes patients with overdose/poisoning diagnoses, the administrative data do not differentiate between patients who intentionally versus unintentionally overdose. Some unintentional overdoses may not reflect an abuse or misuse issue. Lastly, our findings may not generalize to noncommercially insured populations, although existing studies evaluating the excess costs of opioid abuse on other populations have generated similar estimates.¹⁴

CONCLUSIONS

This study confirms the findings contained in a recent publication: opioid abuse is costly to payers. Within a commercially insured population, opioid abuse, dependence, and overdose/poisoning were associated with \$1.98 PMPM, or \$10,989, in excess costs in the year centered around the initial diagnosis. The trajectory of opioid abuse–related costs is also robust across analyses: excess costs begin increasing 9 months prior to the index date, driven by nonopioid drug and alcohol abuse. Following diagnosis, costs were largely driven by the treatment of opioid abuse and nonopioid drug and alcohol abuse, as well as back pain and mental health-related conditions. Opioid abuse often occurs amidst a background of multiple comorbidities, including polysubstance abuse and other psychiatric disorders. Understanding the context in which opioid abuse occurs may promote a more comprehensive treatment approach among payers and providers. ■

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Author Affiliations: Analysis Group, Inc (LMS, NYK, MLZ, ZBJ, HGB) Boston, MA; Purdue Pharma, L.P. (JCH) Stamford, CT.

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Authorship Information: Concept and design (LMS, NYK, ZBJ, HGB, JCH, MLZ); acquisition of data (NYK); analysis and interpretation of data (LMS, NYK, ZBJ, HGB, JCH, MLZ); drafting of the manuscript (LMS, NYK, JCH); critical revision of the manuscript for important intellectual content (LMS, NYK, HGB, JCH); statistical analysis (ZBJ, MLZ); and supervision (NYK, HGB).

Address Correspondence to: Lauren M. Scarpati, PhD, Analysis Group, Inc, 111 Huntington Ave, 14th Floor, Boston, MA 02199. E-mail: lauren.scarpati@analysisgroup.com.

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eAppendix

Table. Demographics, Comorbidities, and Medical Resource Use in the Baseline Period^{a,b}

	Unmatched Sample (i)		Matched Sample (ii)	
	Abusers	Controls	Abusers	Controls
	N (%)	N (%)	N (%)	N (%)
Total patients	79,593 (100%)	1,817,395 (100%)	73,714 (100%)	73,714,342 (100%)
Patient characteristics ^c				
Age, years: mean (SD)	39.0 (14.0)**	43.0 (13.0)	38.9 (14.0)**	38.1 (14.2)
Male	42,913 (53.9%)**	826,652 (45.5%)	39,955 (54.2%)**	40,672 (55.2%)
Employee status of primary beneficiary				
Active	49,139 (61.7%)**	1,035,360 (57.0%)	45,537 (61.8%)**	44,766 (60.7%)
Retirement/early retirement	6570 (8.3%)**	103,876 (5.7%)	5892 (8.0%)	5954 (8.1%)
Short-term disability/long-term disability	430 (0.5%)**	2211 (0.1%)	340 (0.5%)	329 (0.4%)
Other ^d	23,454 (29.5%)**	675,948 (37.2%)	21,945 (29.8%)**	22,665 (30.7%)
Relationship to primary beneficiary				
Self	35,730 (44.9%)**	1,136,320 (62.5%)	33,721 (45.7%)**	32,656 (44.3%)
Child	21,460 (27.0%)**	207,636 (11.4%)	20,115 (27.3%)**	22,280 (30.2%)
Spouse	22,403 (28.1%)**	473,439 (26.1%)	19,878 (27.0%)**	18,778 (25.5%)
Selected comorbidities ^e				
Nonopioid substance abuse	12,165 (15.3%)**	35,887 (2.0%)	9494 (12.9%)**	9132 (12.4%)
Major depressive disorder	6738 (8.5%)**	32,767 (1.8%)	5437 (7.4%)	5373 (7.3%)
Other psychoses	6324 (7.9%)**	20,669 (1.1%)	4929 (6.7%)	4873 (6.6%)
Other mental disorder	24,071 (30.2%)**	165,626 (9.1%)	20,423 (27.7%)	20,633 (28%)
Headache	8540 (10.7%)**	69,882 (3.8%)	7159 (9.7%)	6985 (9.5%)
Neuropathic pain	8279	56,852	6830	6656

	(10.4%)**	(3.1%)	(9.3%)	(9.0%)
Arthropathies and related disorders (excluding osteoarthritis and rheumatoid arthritis)	17,035 (21.4%)**	155,232 (8.5%)	14,586 (19.8%)	14,409 (19.5%)
Rheumatoid arthritis	345 (0.4%)**	2684 (0.1%)	298 (0.4%)	275 (0.4%)
Osteoarthritis	6468 (8.1%)**	54,508 (3%)	5501 (7.5%)	5427 (7.4%)
Back/neck pain	31,707 (39.8%)**	223,875 (12.3%)	27,101 (36.8%)*	26,742 (36.3%)
Rheumatism, excluding the back (excludes fibromyalgia, neuralgia)	16,026 (20.1%)**	167,964 (9.2%)	13,660 (18.5%)	13,394 (18.2%)
Abdominal pain	10,711 (13.5%)**	92,304 (5.1%)	8968 (12.2%)	8930 (12.1%)
Chronic pain	5427 (6.8%)**	6484 (0.4%)	3732 (5.1%)**	3119 (4.2%)
Other pain	4914 (6.2%)**	6429 (0.4%)	3323 (4.5%)**	2830 (3.8%)
Baseline healthcare resource use				
Inpatient days, mean (SD)	0.8 (4.3)**	0.1 (1.5)	0.6 (3.8)	0.6 (3.6)
ED visits, mean (SD)	0.6 (1.8)**	0.1 (0.5)	0.5 (1.3)**	0.5 (1.3)
Rehabilitation facility days, mean (SD)	0.5 (3.9)**	0.0 (0.6)	0.3 (2.5)**	0.2 (2.5)
Outpatient/other visits, mean (SD)	8.5 (10.6)**	4.0 (6.4)	7.9 (10.1)*	7.7 (9.8)
Selected musculoskeletal surgeries ^f				
Hip	113 (0.1%)**	841 (0.0%)	104 (0.1%)	95 (0.1%)
Knee	265 (0.3%)**	1704 (0.1%)	226 (0.3%)	250 (0.3%)
Shoulder	102 (0.1%)**	590 (0.0%)	78 (0.1%)	90 (0.1%)
Spine	927 (1.2%)**	2667 (0.1%)	749 (1%)	774 (1.1%)
Number of prescriptions filled, mean (SD)	17.2 (18.5)**	6.3 (9.1)	15.4 (16.8)**	15 (17.5)
Number of unique NDCs filled, ^g mean (SD)	8.0 (7.8)**	3.2 (4)	7.2 (7.1)**	7.1 (7.1)
Any use of selected classes of pain relievers ^h				

Opioid analgesics				
Immediate release	41,688 (52.4%)**	223,086 (12.3%)	36,300 (49.2%)**	36,961 (50.1%)
Extended release	10,284 (12.9%)**	8657 (0.5%)	7079 (9.6%)**	5793 (7.9%)
Antianxiety medications	25,359 (31.9%)**	137,035 (7.5%)	21,192 (28.7%)	21,106 (28.6%)
Antidepressants	29,639 (37.2%)**	242,034 (13.3%)	25,364 (34.4%)	25,367 (34.4%)
Antiepileptics	15,458 (19.4%)**	66,342 (3.7%)	12,443 (16.9%)*	12,117 (16.4%)
Muscle relaxants	18,617 (23.4%)**	86,773 (4.8%)	15,472 (21%)	15,270 (20.7%)
Other pain relievers ⁱ	9002 (11.3%)**	46,601 (2.6%)	7638 (10.4%)	7,810 (10.6%)
Baseline healthcare costs, ^j mean (SD)	\$8563 (\$26,570)**	\$2371 (\$11,527)	\$7306 (\$24,413)*	\$7149 (\$21,935)

ED indicates emergency department; SD, standard deviation.

“**” indicates $P < .05$; “***” indicates $P < .01$.

^aThe index date for abusers was defined as the date of first diagnosis of abuse, dependence, or poisoning/overdose in quarter (Q) 1 2012 to Q3 2015. The index date for controls was defined as a random medical claim in Q1 2012 to Q3 2015.

^b P values were calculated using Wilcoxon signed rank tests.

^cPatient characteristics were evaluated on the index date.

^dOther statuses include COBRA (Consolidated Omnibus Budget Reconciliation Act), surviving spouse or dependent, and unknown.

^eSee eAppendix Table A.2 for a list of *International Classification of Diseases, Ninth Revision, Clinical Modification* codes used to identify other selected comorbidities.

^fSee eAppendix Table A.2 for a list of *Current Procedural Terminology, 4th Edition*, codes used to identify musculoskeletal surgeries.

^gIdentified using 9-digit National Drug Codes codes.

^hSee eAppendix Table A.2 for a list of Generic Product Identifiers used to identify pain relievers.

ⁱOther pain relievers include tramadol, butorphanol, pentazocine, nalbuphine, and dihydrocodeine.

^jHealthcare costs were inflated to 2015 values using the medical care component of the Consumer Price Index.

Source: Truven MarketScan Commercial Claims and Encounters data.

Figure A-1. Study Period

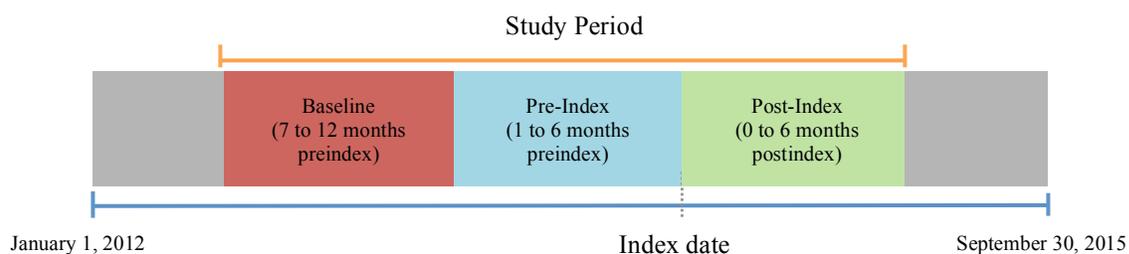


Table A-1. Baseline Characteristics^{a,b}

Patient characteristics ^c	Unmatched				Matched			
	Abusers		Controls		Abusers		Controls	
	(N = 79,593)		(N = 1,817,395)		(N = 73,714)		(N = 73,714)	
Age, mean (SD)	39.0**	(14.0)	43.0	(13.0)	38.9**	(14.0)	38.1	(14.2)
Male, n (%)	42,913**	(53.9%)	826,652	(45.5%)	39,955**	(54.2%)	40,672	(55.2%)
US Census Division,^d n (%)								
Northeast	17,514**	(22.0%)	303,633	(16.7%)	16,276**	(22.1%)	16,837	(22.8%)
Midwest	15,427**	(19.4%)	450,560	(24.8%)	14,440	(19.6%)	14,573	(19.8%)
South	33,036	(41.5%)	756,875	(41.6%)	30,495*	(41.4%)	30,101	(40.8%)
West	12,770**	(16.0%)	282,439	(15.5%)	11,708**	(15.9%)	11,366	(15.4%)
Unknown	846**	(1.1%)	23,888	(1.3%)	795	(1.1%)	837	(1.1%)
Employee status of primary beneficiary, n (%)								
Active	49,139**	(61.7%)	1,035,360	(57.0%)	45,537**	(61.8%)	44,766	(60.7%)
Retirement/early retirement	6,570**	(8.3%)	103,876	(5.7%)	5,892	(8.0%)	5,954	(8.1%)
Short-term disability/long-term disability	430**	(0.5%)	2,211	(0.1%)	340	(0.5%)	329	(0.4%)
Other ^e	23,454**	(29.5%)	675,948	(37.2%)	21,945**	(29.8%)	22,665	(30.7%)
Relationship to primary beneficiary, n (%)								
Self	35,730**	(44.9%)	1,136,320	(62.5%)	33,721**	(45.7%)	32,656	(44.3%)
Child	21,460**	(27.0%)	207,636	(11.4%)	20,115**	(27.3%)	22,280	(30.2%)

Spouse	22,403**	(28.1%)	473,439	(26.1%)	19,878**	(27.0%)	18,778	(25.5%)
Year of index date, n (%)								
2012	23,513**	(29.5%)	776,628	(42.7%)	22,275**	(30.2%)	22,798	(30.9%)
2013	21,364**	(26.8%)	398,160	(21.9%)	19,640	(26.6%)	19,457	(26.4%)
2014	23,430**	(29.4%)	378,499	(20.8%)	21,306	(28.9%)	21,023	(28.5%)
2015	11,286**	(14.2%)	264,108	(14.5%)	10,493	(14.2%)	10,436	(14.2%)
Duration of continuous insurance coverage following the index date, n (%)								
0-1 months	2,752**	(3.5%)	105,844	(5.8%)	2,642	(3.6%)	2,735	(3.7%)
1-2 months	3,892**	(4.9%)	113,789	(6.3%)	3,668	(5.0%)	3,760	(5.1%)
2-3 months	4,282**	(5.4%)	115,732	(6.4%)	4,006*	(5.4%)	4,214	(5.7%)
3-4 months	4,167**	(5.2%)	101,628	(5.6%)	3,895	(5.3%)	3,956	(5.4%)
4-5 months	4,030**	(5.1%)	97,462	(5.4%)	3,753	(5.1%)	3,838	(5.2%)
5-6 months	3,731**	(4.7%)	90,373	(5.0%)	3,470	(4.7%)	3,497	(4.7%)
≥6 months	56,739**	(71.3%)	1,192,567	(65.6%)	52,280**	(70.9%)	51,714	(70.2%)

Baseline comorbidities ^f	Unmatched				Matched			
	Abusers		Controls		Abusers		Controls	
	(N = 79,593)		(N = 1,817,395)		(N = 73,714)		(N = 73,714)	
CCI components, n (%)								
Myocardial infarction	464**	(0.6%)	4,032	(0.2%)	384	(0.5%)	386	(0.5%)
Congestive heart failure	1,002**	(1.3%)	8,998	(0.5%)	829	(1.1%)	821	(1.1%)
Peripheral vascular disease	1,179**	(1.5%)	10,282	(0.6%)	990	(1.3%)	1,014	(1.4%)
Cerebrovascular disease	1,355**	(1.7%)	12,528	(0.7%)	1,101	(1.5%)	1,095	(1.5%)
Dementia	48**	(0.1%)	337	(0.0%)	39	(0.1%)	31	(0.0%)
Chronic pulmonary disease	7,279**	(9.1%)	71,784	(3.9%)	6,206	(8.4%)	6,258	(8.5%)
Rheumatologic disease	1,660**	(2.1%)	15,056	(0.8%)	1,398	(1.9%)	1,367	(1.9%)
Peptic ulcer disease	518**	(0.7%)	2,762	(0.2%)	387	(0.5%)	394	(0.5%)
Mild liver disease	2,066**	(2.6%)	17,456	(1.0%)	1,724	(2.3%)	1,758	(2.4%)
Mild to moderate diabetes	5,165**	(6.5%)	94,278	(5.2%)	4,584	(6.2%)	4,569	(6.2%)
Diabetes with chronic complications	1,155**	(1.5%)	13,928	(0.8%)	993	(1.3%)	990	(1.3%)
Hemiplegia or paraplegia	325**	(0.4%)	1,990	(0.1%)	258	(0.4%)	275	(0.4%)
Renal disease	996**	(1.3%)	10,867	(0.6%)	849	(1.2%)	863	(1.2%)
Any malignancy including lymphoma and leukemia	1,514**	(1.9%)	30,463	(1.7%)	1,360	(1.8%)	1,403	(1.9%)
Moderate or severe liver disease	198**	(0.2%)	864	(0.0%)	153	(0.2%)	163	(0.2%)
Metastatic solid tumor	336**	(0.4%)	3,999	(0.2%)	305*	(0.4%)	368	(0.5%)
HIV/AIDS	235**	(0.3%)	2,854	(0.2%)	209	(0.3%)	219	(0.3%)
Other selected comorbidities, n (%)								
Non-opioid substance abuse	12,165**	(15.3%)	35,887	(2.0%)	9,494* *	(12.9%))	9,132	(12.4%))

Major depressive disorder	6,738**	(8.5%)	32,767	(1.8%)	5,437	(7.4%)	5,373	(7.3%)
Other psychoses	6,324**	(7.9%)	20,669	(1.1%)	4,929	(6.7%)	4,873	(6.6%)
Other mental disorder	24,071**	(30.2%)	165,626	(9.1%)	20,423	(27.7%)	20,633	(28.0%)
Headache	8,540**	(10.7%)	69,882	(3.8%)	7,159	(9.7%)	6,985	(9.5%)
Neuropathic pain	8,279**	(10.4%)	56,852	(3.1%)	6,830	(9.3%)	6,656	(9.0%)
Hernia	1,398**	(1.8%)	14,356	(0.8%)	1,189	(1.6%)	1,206	(1.6%)
Arthropathies and related disorders (excluding osteoarthritis and rheumatoid arthritis)	17,035**	(21.4%)	155,232	(8.5%)	14,586	(19.8%)	14,409	(19.5%)
Rheumatoid arthritis	345**	(0.4%)	2,684	(0.1%)	298	(0.4%)	275	(0.4%)
Osteoarthritis	6,468**	(8.1%)	54,508	(3.0%)	5,501	(7.5%)	5,427	(7.4%)
Back/neck pain	31,707**	(39.8%)	223,875	(12.3%)	27,101*	(36.8%)	26,742	(36.3%)
Rheumatism, excluding the back (excludes fibromyalgia, neuralgia)	16,026**	(20.1%)	167,964	(9.2%)	13,660	(18.5%)	13,394	(18.2%)
Fibromyalgia	6,099**	(7.7%)	34,132	(1.9%)	4,889*	(6.6%)	4,667	(6.3%)
Osteopathies, chondropathies, and acquired musculoskeletal deformities	4,466**	(5.6%)	62,972	(3.5%)	3,837	(5.2%)	3,785	(5.1%)
Abdominal pain	10,711**	(13.5%)	92,304	(5.1%)	8,968	(12.2%)	8,930	(12.1%)
Fractures, dislocations, & sprains/strains	11,044**	(13.9%)	108,468	(6.0%)	9,541	(12.9%)	9,538	(12.9%)
Other injuries	9,593**	(12.1%)	74,249	(4.1%)	8,079	(11.0%)	8,043	(10.9%)
Hereditary hemolytic anemias	113**	(0.1%)	1,066	(0.1%)	91	(0.1%)	102	(0.1%)
Pain and other symptoms associated with female genital organs	2,738**	(3.4%)	33,655	(1.9%)	2,339	(3.2%)	2,288	(3.1%)

Acute pain	2,292**	(2.9%)	9,245	(0.5%)	1,729	(2.3%)	1,690	(2.3%)
Chronic pain	5,427**	(6.8%)	6,484	(0.4%)	3,732* *	(5.1%)	3,119	(4.2%)
Dental pain	1,974**	(2.5%)	16,939	(0.9%)	1,719	(2.3%)	1,768	(2.4%)
Other pain	4,914**	(6.2%)	6,429	(0.4%)	3,323* *	(4.5%)	2,830	(3.8%)

Baseline healthcare resource use and costs	Unmatched				Matched			
	Abusers		Controls		Abusers		Controls	
	(N = 79,593)		(N = 1,817,395)		(N = 73,714)		(N = 73,714)	
Baseline healthcare resource use								
Inpatient days, mean (SD)	0.8**	(4.3)	0.1	(1.5)	0.6	(3.8)	0.6	(3.6)
Emergency department visits, mean (SD)	0.6**	(1.8)	0.1	(0.5)	0.5**	(1.3)	0.5	(1.3)
Rehabilitation facility days, mean (SD)	0.5**	(3.9)	0.0	(0.6)	0.3**	(2.5)	0.2	(2.5)
Outpatient/other visits, mean (SD)	8.5**	(10.6)	4.0	(6.4)	7.9*	(10.1)	7.7	(9.8)
Selected musculoskeletal surgeries, n (%)								
Hip	113**	(0.1%)	841	(0.0%)	104	(0.1%)	95	(0.1%)
Knee	265**	(0.3%)	1,704	(0.1%)	226	(0.3%)	250	(0.3%)
Shoulder	102**	(0.1%)	590	(0.0%)	78	(0.1%)	90	(0.1%)
Spine	927**	(1.2%)	2,667	(0.1%)	749	(1.0%)	774	(1.1%)
Number of prescriptions filled, mean (SD)	17.2**	(18.5)	6.3	(9.1)	15.4**	(16.8)	15.0	(17.5)
Number of unique NDCs filled,^g mean (SD)	8.0**	(7.8)	3.2	(4.0)	7.2**	(7.1)	7.1	(7.1)
Any use of selected classes of pain relievers, n (%)								
Opioid analgesics								
Immediate release	41,688**	(52.4%)	223,086	(12.3%)	36,300**	(49.2%)	36,961	(50.1%)
Extended release	10,284**	(12.9%)	8,657	(0.5%)	7,079**	(9.6%)	5,793	(7.9%)
Non-steroidal anti-inflammatory drugs (NSAIDs)	17,378**	(21.8%)	178,516	(9.8%)	15,325	(20.8%)	15,521	(21.1%)
Non-narcotic analgesics	2,064**	(2.6%)	13,837	(0.8%)	1,694	(2.3%)	1,698	(2.3%)
Antianxiety medications	25,359**	(31.9%)	137,035	(7.5%)	21,192	(28.7%)	21,106	(28.6%)
Antidepressants	29,639**	(37.2%)	242,034	(13.3%)	25,364	(34.4%)	25,367	(34.4%)
Antiepileptics	15,458**	(19.4%)	66,342	(3.7%)	12,443*	(16.9%)	12,117	(16.4%)
Muscle relaxants	18,617**	(23.4%)	86,773	(4.8%)	15,472	(21.0%)	15,270	(20.7%)
Other pain relievers ^h	9,002**	(11.3%)	46,601	(2.6%)	7,638	(10.4%)	7,810	(10.6%)
Baseline healthcare costs,ⁱ mean (SD)	\$8,563**	(\$26,570)	\$2,371	(\$11,527)	\$7,306*	(\$24,413)	\$7,149	(\$21,935)

Notes:

- a. The index date for abusers was defined as the date of first diagnosis of abuse, dependence, or poisoning/overdose in Q1 2012 - Q3 2015. The index date for controls was defined as a random medical claim in Q1 2012 - Q3 2015. This analysis was performed on the cohort of patients with ≥ 12 months of continuous coverage prior to the index date
- b. P-values were calculated using Wilcoxon signed rank tests. P-values < 0.05 are indicated with one asterisk (“*”); p-values < 0.01 are indicated with two asterisks (“**”).
- c. Patient characteristics were evaluated on the index date.
- d. Northeast: CT, MA, ME, NH, NJ, NY, PA, RI, VT; Midwest: IA, IL, IN, KS, MI, MN, MO, ND, NE, OH, SD, WI; South: AL, AR, DC, DE, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA, WV; West: AK, AZ, CA, CO, HI, ID, MT, NM, NV, OR, UT, WA, WY.
- e. Other statuses include COBRA, surviving spouse or dependent, and unknown.
- f. The baseline period was defined as the period between 12 months and 6 months prior to the index date.
- g. Identified using 9-digit NDC codes.
- h. Other pain relievers include tramadol, butorphanol, pentazocine, nalbuphine, and dihydrocodeine.
- i. Healthcare costs were inflated to 2015 values using the medical care component of the Consumer Price Index.

Source: Truven MarketScan Commercial Claims and Encounters data.

Table A-2. Excess Healthcare Costs During the Baseline Period^{a-c}

Baseline Costs (–12 to –6 Months Relative to the Index Date)		Abusers [A] Mean (SD)	Controls [B] Mean (SD)	Excess [A] – [B] Mean
Healthcare cost drivers by places of service ^d				
Total healthcare costs ^e		\$7306 (\$24,413)	\$7149 (\$21,935)	\$157*
Prescription drug costs		\$1393 (\$5431)	\$1330 (\$5180)	\$63**
Total medical costs		\$5914 (\$23,257)	\$5819 (\$20,711)	\$94
Inpatient		\$2376 (\$18,572)	\$2305 (\$15,661)	\$71
Emergency department		\$626 (\$2972)	\$583 (\$2737)	\$43*
Rehabilitation facility		\$132 (\$2097)	\$94 (\$1705)	\$38**
Outpatient/other		\$2780 (\$9655)	\$2838 (\$9197)	–\$57
Overall medical cost drivers by ICD-9-CM diagnosis grouping				
724.xx	Other and unspecified disorders of back	\$239 (\$2468)	\$181 (\$1767)	\$58
721.xx	Spondylosis and allied disorders	\$122 (\$1738)	\$83 (\$1324)	\$39
304.xx ^f	Drug dependence (excluding opioids)	\$56 (\$1226)	\$21 (\$798)	\$35
722.xx	Intervertebral disc disorders	\$238 (\$2940)	\$208 (\$2629)	\$30
276.xx	Disorders of fluid electrolyte and acid-base balance	\$97 (\$1702)	\$71 (\$1216)	\$26
577.xx	Diseases of pancreas	\$42 (\$1830)	\$20 (\$571)	\$21
789.xx	Other symptoms involving abdomen and pelvis	\$115 (\$879)	\$96 (\$804)	\$19
996.xx	Complications peculiar to certain specified procedures	\$64 (\$1410)	\$49 (\$1121)	\$15
303.xx	Alcohol dependence syndrome	\$65 (\$1270)	\$49 (\$893)	\$15
V58.xx	Encounter for other and unspecified procedures and aftercare	\$121 (\$1608)	\$106 (\$1623)	\$15

Q indicates quarter; SD, standard deviation.

^aThe 12-month follow-up period was defined as the 6 months prior to and 6 months following the index date.

^bThe index date for abusers was defined as the date of first diagnosis of abuse, dependence, or poisoning/overdose in quarter (Q) 1 2012 to Q3 2015. The index date for controls was defined as a random medical claim in Q1 2012 to Q3 2015.

^cAbusers were matched to potential controls based on propensity score (within a quarter of a standard deviation).

^d*P* values were calculated using Wilcoxon signed rank tests.

^eHealthcare costs were inflated to 2015 values using the medical care component of the Consumer Price Index.

^fExcluding codes used to identify opioid abuse.

“*” indicates $P < .05$; “***” indicates $< .01$.

Source: Truven MarketScan Commercial Claims and Encounters data.

Table A-3. *ICD-9-CM* codes used to identify component comorbidities of the Charlson Comorbidity Index^a

Condition	<i>ICD-9-CM</i> code(s)
Myocardial infarction	410.xx, 412.xx
Congestive heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4x-425.9x, 428.xx
Peripheral vascular disease	093.0x, 437.3x, 440.xx, 441.xx, 443.1x-443.9x, 447.1x, 557.1x, 557.9x, V43.4x
Cerebrovascular disease	362.34, 430.xx-438.xx
Dementia	290.xx, 294.1x, 331.2x
Chronic pulmonary disease	416.8x, 416.9x, 490.xx-505.xx, 506.4x, 508.1x, 508.8x
Rheumatologic disease	446.5x, 710.0x-710.4x, 714.0x-714.2x, 714.8x, 725.xx
Peptic ulcer disease	531.xx-534.xx
Mild liver disease	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6x, 070.9x, 570.xx, 571.xx, 573.3x, 573.4x, 573.8x, 573.9x, V42.7x
Mild to moderate diabetes	250.0x-250.3x, 250.8x, 250.9x
Diabetes with chronic complications	250.4x-250.7x
Hemiplegia or paraplegia	334.1x, 342.xx, 343.xx, 344.0x-344.6x, 344.9x
Renal disease	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582.xx, 583.0x-583.7x, 585.xx, 586.xx, 588.0x, V42.0x, V45.1x, V56.xx
Any malignancy including lymphoma or leukemia	140.xx-172.xx, 174.xx-194.xx, 195.0x-195.8x, 200.xx-208.xx, 238.6x
Moderate or severe liver disease	456.0x-456.2x, 572.2x-572.8x
Metastatic solid tumor	196.xx-199.xx
HIV/AIDS	042.xx-044.xx

Note:

a. Specific codes are either excluded or broken out to prevent redundancy in cases where there is overlap between codes listed in both Tables A-3 and A-4.

Table A-4. ICD-9-CM codes used to identify other selected comorbidities^a

Condition	ICD-9-CM code
Non-opioid substance abuse	
Alcohol dependence syndrome	303.xx
Sedative, hypnotic, or anxiolytic dependence	304.1x
Cocaine dependence	304.2x
Cannabis dependence	304.3x
Amphetamine and other psychostimulant dependence	304.4x
Hallucinogen dependence	304.5x
Other specified drug dependence	304.6x
Combinations of drug dependence excluding opioid type drug	304.8x
Unspecified drug dependence	304.9x
Alcohol abuse	305.0x
Tobacco use disorder	305.1x
Cannabis abuse	305.2x
Hallucinogen abuse	305.3x
Sedative, hypnotic, or anxiolytic abuse	305.4x
Cocaine abuse	305.6x
Amphetamine or related acting sympathomimetic abuse	305.7x
Antidepressant type abuse	305.8x
Other, mixed, or unspecified drug abuse	305.9x
Personal history of alcoholism	V11.3x
Major depressive disorder	
Major depressive disorder, single episode	296.2x
Major depressive disorder, recurrent episode	296.3x
Other psychoses	
Alcohol-induced mental disorders	291.xx
Drug-induced mental disorders	292.xx
Transient mental disorders due to conditions classified elsewhere	293.xx
Persistent mental disorders due to conditions classified elsewhere ^j	294.0x, 294.8x, 294.9x
Schizophrenic disorders	295.xx
Bipolar I disorder, single manic episode	296.0x
Manic disorder, recurrent episode	296.1x
Bipolar I disorder, most recent episode (or current) manic	296.4x
Bipolar I disorder, most recent episode (or current) depressed	296.5x
Bipolar I disorder, most recent episode (or current) mixed	296.6x
Bipolar I disorder, most recent episode (or current) unspecified	296.7x
Other and unspecified bipolar disorders	296.8x
Other and unspecified episodic mood disorder	296.9x
Delusional disorders	297.xx

Other nonorganic psychoses	298.xx
Pervasive developmental disorders	299.xx
Personal history of schizophrenia	V11.0x
Personal history of affective disorder	V11.1x

Table A-4. ICD-9-CM codes used to identify other selected comorbidities (cont.)^a

Condition	ICD-9-CM code
Other mental disorder	
Anxiety, dissociative, and somatoform disorders	300.xx
Personality disorders	301.xx
Sexual and gender identity disorders	302.xx
Physiological malfunction arising from mental factors	306.xx
Special symptoms or syndromes, not elsewhere classified	307.xx
Acute reaction to stress	308.xx
Adjustment reaction	309.xx
Specific nonpsychotic mental disorders due to brain damage	310.xx
Depressive disorder, not elsewhere classified	311.xx
Disturbance of conduct, not elsewhere classified	312.xx
Disturbance of emotions specific to childhood and adolescence	313.xx
Hyperkinetic syndrome of childhood	314.xx
Specific delays in development	315.xx
Psychic factors associated with diseases classified elsewhere	316.xx
Mild mental retardation	317.xx
Other specified mental retardation	318.xx
Unspecified mental retardation	319.xx
Personal history of neurosis	V11.2x
Personal history of other mental disorder	V11.8x
Personal history of unspecified mental disorder	V11.9x
Headache	
Other headache syndromes	339.xx
Migraine	346.xx
Headache	784.0x
Neuropathic pain¹	
Herpes zoster	053.xx
Disorders of the autonomic nervous system	337.xx
Trigeminal nerve disorders	350.xx
Facial nerve disorders	351.xx
Disorders of other cranial nerves	352.xx
Nerve root and plexus disorders	353.xx
Mononeuritis of upper limb and mononeuritis multiplex	354.xx
Mononeuritis of lower limb	355.xx
Hereditary and idiopathic peripheral neuropathy	356.xx
Inflammatory and toxic neuropathy	357.xx

Neuralgia, neuritis, and radiculitis, unspecified	729.2x
Disturbance of skin sensation	782.0x
Hernia	
Inguinal hernia	550.xx
Other hernia of abdominal cavity, with gangrene	551.xx
Other hernia of abdominal cavity, with obstruction, but without mention of gangrene	552.xx
Other hernia of abdominal cavity without mention of obstruction or gangrene	553.xx

Table A-4. ICD-9-CM codes used to identify other selected comorbidities (cont.)^a

Condition	ICD-9-CM code
Arthropathies and related disorders (excluding osteoarthritis and rheumatoid arthritis)	
Eosinophilia myalgia syndrome ^l	710.5x
Other specified diffuse diseases of connective tissue ^l	710.8x
Unspecified diffuse connective tissue disease ^l	710.9x
Arthropathy associated with infections	711.xx
Crystal arthropathies	712.xx
Arthropathy associated with other disorders classified elsewhere	713.xx
Other and unspecified arthropathies	716.xx
Internal derangement of knee	717.xx
Other derangement of joint	718.xx
Other and unspecified disorders of joint	719.xx
Rheumatoid arthritis^l	
Juvenile chronic polyarthritis	714.3x
Chronic postrheumatic arthropathy	714.4x
Unspecified inflammatory polyarthropathy	714.9x
Osteoarthritis	715.xx
Back/neck pain	
Ankylosing spondylitis and other inflammatory spondylopathies	720.xx
Spondylosis and allied disorders	721.xx
Intervertebral disc disorders	722.xx
Other disorders of cervical region	723.xx
Other and unspecified disorders of back	724.xx
Curvature of spine	737.xx
Acquired spondylolisthesis	738.4x
Other acquired deformity of back or spine	738.5x
Nonallopathic lesions, not elsewhere classified - Cervical region	739.1x
Nonallopathic lesions, not elsewhere classified - Thoracic region	739.2x
Nonallopathic lesions, not elsewhere classified - Lumbar region	739.3x
Nonallopathic lesions, not elsewhere classified - Sacral region	739.4x
Spina bifida	741.xx
Other specified anomalies of spinal cord	742.5x
Anomalies of spine	756.1x
Rheumatism, excluding the back (excluding fibromyalgia and neuralgia)^l	
Peripheral enthesopathies and allied syndromes	726.xx
Other disorders of synovium, tendon, and bursa	727.xx
Disorders of muscle, ligament, and fascia	728.xx
Rheumatism, unspecified and fibrositis	729.0x
Panniculitis, unspecified	729.3x
Fasciitis, unspecified	729.4x
Pain in limb	729.5x

Residual foreign body in soft tissue	729.6x
Nontraumatic compartment syndrome	729.7x
Other musculoskeletal symptoms referable to limbs	729.8x
Other and unspecified disorders of soft tissue	729.9x

Table A-4. ICD-9-CM codes used to identify other selected comorbidities (cont.)^a

Condition	ICD-9-CM code
Fibromyalgia	729.1x
Osteopathies, chondropathies, and acquired musculoskeletal deformities	
Osteomyelitis, periostitis, and other infections involving bone	730.xx
Osteitis deformans and osteopathies associated with other disorders classified elsewhere	731.xx
Osteochondropathies	732.xx
Other disorders of bone and cartilage	733.xx
Flat foot	734.xx
Acquired deformities of toe	735.xx
Other acquired deformities of limbs	736.xx
Acquired deformity of nose	738.0x
Other acquired deformity of head	738.1x
Acquired deformity of neck	738.2x
Acquired deformity of chest and rib	738.3x
Acquired deformity of pelvis	738.6x
Cauliflower ear	738.7x
Acquired deformity of other specified site	738.8x
Acquired deformity of unspecified site	738.9x
Nonallopathic lesions, not elsewhere classified - Head region	739.0x
Nonallopathic lesions, not elsewhere classified - Pelvic region	739.5x
Nonallopathic lesions, not elsewhere classified - Lower extremities	739.6x
Nonallopathic lesions, not elsewhere classified - Upper extremities	739.7x
Nonallopathic lesions, not elsewhere classified - Rib cage	739.8x
Nonallopathic lesions, not elsewhere classified - Abdomen and other	739.9x
Abdominal pain	789.xx
Fractures, dislocations, and sprains/strains	800.xx-848.xx
Other injuries	850.xx-904.xx, 910.xx-959.xx
Hereditary hemolytic anemias	282.xx
Pain and other symptoms associated with female genital organs	625.xx
Acute pain	338.1x
Chronic pain	338.2x
Dental pain	
Disorders of tooth development and eruption	520.xx
Diseases of hard tissues of teeth	521.xx

Diseases of pulp and periapical tissues	522.xx
Gingival and periodontal diseases	523.xx
Dentofacial anomalies, including malocclusion	524.xx
Other diseases and conditions of the teeth and supporting structures	525.xx
Diseases of the jaws	526.xx
Diseases of the salivary glands	527.xx
Diseases of the oral soft tissues, excluding lesions specific for gingiva and tongue	528.xx
Diseases and other conditions of the tongue	529.xx
Other pain	
Generalized pain	780.96
Central pain syndrome	338.0x
Neoplasm related pain (acute) (chronic)	338.3x
Chronic pain syndrome	338.4x

Note:

- a. Specific codes are either excluded or broken out to prevent redundancy in cases where there is overlap between codes listed in both Tables A-3 and A-4.

Table A-5. CPT-4 codes used to identify selected musculoskeletal surgeries

Surgery	Procedure code(s)
Hip	
Repair, revision, and/or reconstruction	27097, 27098, 27100, 27105, 27110, 27111, 27120, 27122, 27125, 27130, 27132, 27134, 27137, 27138, 27140, 27146, 27147, 27151, 27156, 27158, 27161, 27165, 27170, 27175, 27176, 27177, 27178, 27179, 27181, 27185, 27187
Arthrodesis	27279, 27280, 27282, 27284, 27286
Knee	
Repair, revision, and/or reconstruction	27380, 27381, 27385, 27386, 27390, 27391, 27392, 27393, 27394, 27395, 27396, 27397, 27400, 27403, 27405, 27407, 27409, 27415, 27416, 27418, 27420, 27422, 27424, 27425, 27427, 27428, 27429, 27430, 27435, 27437, 27438, 27440, 27441, 27442, 27443, 27445, 27446, 27447, 27448, 27450, 27454, 27455, 27457, 27465, 27466, 27468, 27470, 27472, 27475, 27477, 27479, 27485, 27486, 27487, 27488, 27495, 27496, 27497, 27498, 27499
Arthrodesis	27580
Shoulder	
Repair, revision, and/or reconstruction	23395, 23397, 23400, 23405, 23406, 23410, 23412, 23415, 23420, 23430, 23440, 23450, 23455, 23460, 23462, 23465, 23466, 23470, 23472, 23473, 23474, 23480, 23485, 23490, 23491
Arthrodesis	23800, 23802
Spine	
Arthrodesis	22532, 22533, 22534, 22548, 22551, 22552, 22554, 22556, 22558, 22585, 22586, 22590, 22595, 22600, 22610, 22612, 22614, 22630, 22632, 22633, 22634, 22800, 22802, 22804, 22808, 22810, 22812, 22818, 22819
Osteotomy	22206, 22207, 22208, 22210, 22212, 22214, 22216, 22220, 22222, 22224, 22226
Posterior extradural laminotomy or laminectomy for exploration/ decompression of neural elements or excision of herniated intervertebral disks	63001, 63003, 63005, 63011, 63012, 63015, 63016, 63017, 63020, 63030, 63035, 63040, 63042, 63043, 63044, 63045, 63046, 63047, 63048, 63050, 63051

Table A-6. Generic Product Identifiers (GPIs) used to identify pain relievers

Pain reliever class	GPI
Opioid analgesics	65xxxxxxxxxxxxx
NSAIDs	6610xxxxxxxxxxxx
Non-narcotic analgesics	64xxxxxxxxxxxxx
Antianxiety medications	57xxxxxxxxxxxxx
Antidepressants	58xxxxxxxxxxxxx
Antiepileptics	72xxxxxxxxxxxxx
Muscle relaxants	7510xxxxxxxxxxxx