Healthcare Costs and Nonadherence Among Chronic Opioid Users

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Objectives: To assess the health economic burden of chronic opioid users and to determine whether opioid regimen nonadherence contributes to increased healthcare costs.

Study Design: Retrospective claims-based analysis of patients with long-term prescription opioid use (>120 days of supply over 6 months).

Methods: Twelve-month healthcare utilization and costs were compared for chronic opioid users (n = 49,425) and, among chronic opioid users with urine drug-monitoring results (n = 2100), between adherent patients versus patients with evidence of nonadherence to their opioid regimen. Likely nonadherence was based on urine test results indicating absence of the prescribed drug, higher or lower than expected drug levels based on a proprietary algorithm, or presence of unprescribed or illegal drugs. The influence of nonadherence on total healthcare costs was assessed using multivariate models.

Results: Prevalence of chronic opioid use was 1.3%. Chronic opioid users had significantly greater healthcare utilization and costs than matched nonusers ($23,049 vs $4975; P < .001). Adherent patients (n = 442) had lower total healthcare costs than likely nonadherent patients (n = 1658; $23,160 vs $26,433; P = .036). After adjustment for demographics, likely nonadherence was significantly associated with elevated total healthcare costs (cost ratio [CR] 1.136; 95% confidence interval [CI] 1.10, 1.29; P = .048). When adjusting for other types of nonadherence, the presence of higher than expected levels of the prescribed opioid was associated with significantly elevated costs (CR 1.121; 95% CI 1.01, 1.25; P = .039).

Conclusions: Chronic opioid users represent a substantial cost burden relative to similar patients without evidence of chronic pain. Among likely nonadherent chronic opioid users, those with evidence of opioid overuse had significantly elevated healthcare costs.

(Pain is a common reason to seek medical care. In contrast to acute pain, chronic pain ceases to serve a protective purpose, is persistent, and disrupts normal living.1 Chronic pain is highly prevalent by some estimates; in a US survey, 42% of participants aged ≥20 years and 57% of those aged ≥65 years reported pain lasting 1 year or more.2 Patients experiencing chronic pain have been found to use healthcare services more frequently than those without pain.3,4 Opioid analgesics have a recognized role in pain management.5-10 For chronic pain, opioids are often effective when prescribed and used appropriately as part of a structured pain management plan.7,8,10 Current pain management recommendations include periodic monitoring of pain control and functional goal achievement, as well as monitoring medication use and aberrant behaviors.7,10,11 The need for oversight of prescription opioid use is supported by multiple recent studies. One 2010 report indicated that nearly 10% of patients admitted for substance abuse treatment in 2008 reported prescription pain reliever abuse—an increase from 2% among admissions in 1998.12 The 2008 National Survey on Drug Use and Health reported that among Americans aged ≥12 years, the prevalence of nonmedical use of prescriptions (ie, pain relievers, tranquilizers, stimulants, sedatives) was second only to marijuana use among types of illicit drug use.13 Changes in the prevalence of prescription pain reliever abuse paralleled an increase in hospitalizations for poisoning by prescription opioids, sedatives, and tranquilizers: from 1999 to 2006, US hospitalizations for these medications increased by 65%.14 Monitoring adherence, or the accuracy and consistency with which a patient follows the pharmacological regimen, is an important aspect of a chronic pain management plan. Nonadherence could include taking too much of the prescribed medication, diverting medication to other individuals, self-medicating with unprescribed or illegal drugs, or taking medication inconsistently.15-17 Urine toxicology testing is one means of monitoring opioid adherence and assessing whether the prescribed regimen is being followed.7,10,17-19

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tive to similar patients without evidence of chronic pain. In a separate analysis of chronic opioid users with urine drug testing results, we explored whether opioid regimen nonadherence contributed to an increase in annual healthcare costs.

METHODS

Data Sources

Data were obtained from a managed care claims database including geographically diverse commercial, Medicare Advantage, and Medicaid health plan members in the United States. Approximately 18 million people were enrolled in the health plans during the study period from July 1, 2005, through September 30, 2008. Data for adherence classification were obtained from an independent database of urine drug testing results.

Identification of Chronic Opioid Users and Matched Controls

Patients with evidence of long-term prescription opioid use during January 1, 2006, through September 30, 2007 (identification period) were selected for the study. Chronic opioid use was defined as at least 120 days of a qualifying opioid (eAppendix A available at www.ajmc.com) over any consecutive 6 months during the identification period. The date of the first qualifying opioid fill was the index date.

A control cohort of patients with no evidence of chronic pain or chronic opioid use was also identified (eAppendix B at www.ajmc.com). Patients in the control cohort could have no more than 1 claim for any opioid, no more than 2 claims for any other pain-related medications (nonsteroidal anti-inflammatory drugs including salicylates and COX-2 inhibitors, and migraine therapies), and no diagnosis for chronic pain (International Classification of Diseases, Ninth Revision, Clinical Modification codes 338.0, 338.2x-338.4, 780.96) during the study period. An index date was randomly assigned during the identification period. Both chronic opioid users and matched controls were required to have continuous medical and pharmacy benefits coverage for 6 months prior to (baseline period) through 1 year following (follow-up period) the index date (eAppendix B).

The chronic opioid and control cohorts were matched 1 to 1 based on age (±1 year), sex, geographic region, insurance type, mental health benefit, and preindex Charlson comorbidity score21 (±2). Patients who could not be matched were excluded. All data were de-identified and accessed with protocols compliant with the Health Insurance Portability and Accountability Act.22

Identification of Chronic Opioid Users With Urine Drug Testing and Adherence Classification

A subset of chronic opioid users with 4 or more claims with codes indicating urine drug testing for opiates, benzo­diazepines, barbiturates, and amphetamines on the same date of service was identified. These patients were matched with a database of urine drug test results based on patient date of birth, sex, 5-digit zip code, and testing date (±3 days). Privacy board approval was obtained for the use of protected health information for database matching purposes.

For patients with urine drug monitoring results, results from the first test following the index date were used to assign patients to adherent and likely nonadherent cohorts. Nonadherence was determined using urine testing data, which indicated whether individual assay results aligned with reported medication type (ie, presence of prescribed opioid, absence of unprescribed controlled or illegal drugs).23 Patients were also classified as likely nonadherent if their urine drug levels were not within the concentration ranges expected for their prescribed regimen (eg, total daily dose) after adjustment for physiologic factors as determined by applying a proprietary algorithm (Rx Guardian, Ameritox, Ltd, Baltimore, MD) to the urine assay.23,24 The likely nonadherent classification is not synonymous with substance abuse, although certain types of nonadherence could suggest abuse or misuse of controlled or illicit drugs.

For patients with urine drug monitoring results, the baseline period was the 6 months before the test, and the follow-up period was the year following the test.

Determination of Cohort Characteristics

Enrollment and claims information were used to determine baseline demographic information, comorbid conditions, and medication use for the cohorts of interest. The Charlson comorbidity score, an estimate of comorbidity burden, was calculated.21,27,28 General comorbid conditions in the baseline period were identified from claims using Healthcare Cost & Utilization Project Comorbidity Software, version 3.2 (Agency for Healthcare Research and Quality, Rockville, MD). Opioid (including heroin) abuse/dependence, opioid

Take-Away Points

Healthcare utilization and costs were compared between patients on chronic opioid therapy and matched controls, and between chronic opioid users who were likely nonadherent based on urine drug monitoring results versus adherent users.

- Over 1 year of follow-up, chronic opioid users had more ambulatory, emergency, and hospital visits than controls, and higher annual healthcare costs.
- Likely nonadherent chronic opioid users were predicted to be 14% more expensive than adherent patients, and had significantly more hospital days.
- Nonadherence to the opioid regimen, likely overuse of the prescribed drug, appears to contribute to elevated costs.
Determination of Healthcare Utilization and Costs

Healthcare resource utilization during the follow-up period was calculated for each patient as number of office visits, outpatient visits, emergency department visits, inpatient admissions, and hospital days.

Pharmacy costs and medical costs, including ambulatory, emergency service, inpatient, and other medical costs, were tabulated from claims in the follow-up period and adjusted to 2008 dollars.29 Healthcare costs included both health plan and patient-paid amounts. “Other” medical costs include costs associated with durable medical equipment, home care, and services such as laboratory testing (including urine drug testing).

Claims with codes for pain-related services and procedures (eAppendix D at www.ajmc.com) were used to determine pain-related costs.

Analyses

Baseline characteristics, healthcare utilization, and costs were analyzed descriptively, comparing the chronic opioid cohort with the matched control cohort, and the cohorts of adherent and likely nonadherent chronic opioid users. Significance was determined as \( P < .05 \).

Table 1. Baseline Characteristics of Chronic Opioid Users Versus Matched Nonusers and Adherent Versus Likely Nonadherent Chronic Opioid Users

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Chronic Opioid Users (n = 49,425)</th>
<th>Nonusers (n = 49,425)</th>
<th>( P^a )</th>
<th>Adherent (n = 442)</th>
<th>Likely Nonadherent (n = 1658)</th>
<th>( P^a )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-17</td>
<td>74 (0.2)</td>
<td>74 (0.2)</td>
<td>&gt; .99</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>.651</td>
</tr>
<tr>
<td>18-44</td>
<td>14,856 (30.1)</td>
<td>14,852 (30.1)</td>
<td>1.74</td>
<td>39.4</td>
<td>685 (41.3)</td>
<td></td>
</tr>
<tr>
<td>45-64</td>
<td>24,889 (50.4)</td>
<td>24,898 (50.4)</td>
<td>261</td>
<td>59.1</td>
<td>953 (57.5)</td>
<td></td>
</tr>
<tr>
<td>≥65</td>
<td>9606 (19.4)</td>
<td>9601 (19.4)</td>
<td>7</td>
<td>1.6</td>
<td>20 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>27,835 (56.3)</td>
<td>27,835 (56.3)</td>
<td>1.00b</td>
<td>254</td>
<td>57 (55.2)</td>
<td>.518</td>
</tr>
</tbody>
</table>

Insurance type

<table>
<thead>
<tr>
<th></th>
<th>Commercial (90.6)</th>
<th>Medicare Advantage (7.1)</th>
<th>Medicaid (2.3)</th>
<th>1.00b</th>
<th>Commercial (90.6)</th>
<th>Medicare Advantage (7.1)</th>
<th>Medicaid (2.3)</th>
<th>.044</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>44,760 (90.6)</td>
<td>3530 (7.1)</td>
<td>1135 (2.3)</td>
<td>1.00b</td>
<td>44,760 (90.6)</td>
<td>3530 (7.1)</td>
<td>1135 (2.3)</td>
<td>.044</td>
</tr>
</tbody>
</table>

Region

|                      | Northeast (9.8)                | Midwest (28.5)          | South (44.6)  | 1.00b  | West (17.2)       | Northeast (9.8)         | Midwest (28.5) | South (44.6)  | 1.00b  | West (17.2)       | Northeast (9.8)         | Midwest (28.5) | South (44.6)  | 1.00b  | West (17.2)       | Northeast (9.8)         | Midwest (28.5) | South (44.6)  | 1.00b  | West (17.2)       | Northeast (9.8)         | Midwest (28.5) | South (44.6)  | 1.00b  | West (17.2)       |

Mental health benefit

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>( P^c )</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>( P^c )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbidity score</td>
<td>0.81 (1.29)</td>
<td>0.76 (1.23)</td>
<td>&lt; .001d</td>
<td>0.49 (0.92)</td>
<td>0.61 (1.08)</td>
<td>.016</td>
</tr>
<tr>
<td>Unique medications</td>
<td>8.3 (5.7)</td>
<td>3.2 (3.4)</td>
<td>&lt; .001</td>
<td>9.4 (5.9)</td>
<td>10.9 (6.4)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Total medication dispensings</td>
<td>22.2 (18.3)</td>
<td>8.1 (10.4)</td>
<td>&lt; .001</td>
<td>28.1 (18.1)</td>
<td>33.7 (20.8)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Unique opioids</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.85 (0.97)</td>
<td>2.08 (1.06)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Opioid dispensings</td>
<td>4.1 (4.7)</td>
<td>0.1 (0.2)</td>
<td>&lt; .001</td>
<td>8.8 (5.4)</td>
<td>10.4 (5.9)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Days of supply of opioids</td>
<td>69.3 (79.6)</td>
<td>0.3 (1.7)</td>
<td>&lt; .001</td>
<td>171.3 (77.6)</td>
<td>194.8 (89.4)</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

\( a \) \( P < 1.000 \) resulted from exact-matching patients on these factors; the cohorts were not randomly selected.

\( b \) \( P < .05 \) attributable to match process allowing scores ±2.

\( c \) Any medication, not exclusively opioids.

overdose/poisoning, alcoholism or drug abuse, depression, and anxiety during the baseline period were detected using the codes listed in eAppendix C at www.ajmc.com.

**Determinations of Healthcare Utilization and Costs**

Healthcare resource utilization during the follow-up period was calculated for each patient as number of office visits, outpatient visits, emergency department visits, inpatient admissions, and hospital days.

Pharmacy costs and medical costs, including ambulatory, emergency service, inpatient, and other medical costs, were tabulated from claims in the follow-up period and adjusted to 2008 dollars.29 Healthcare costs included both health plan and patient-paid amounts. “Other” medical costs include costs associated with durable medical equipment, home care, and services such as laboratory testing (including urine drug testing).

Claims with codes for pain-related services and procedures (eAppendix D at www.ajmc.com) were used to determine pain-related costs.

**Analyses**

Baseline characteristics, healthcare utilization, and costs were analyzed descriptively, comparing the chronic opioid cohort with the matched control cohort, and the cohorts of adherent and likely nonadherent chronic opioid users. Significance was determined as \( P < .05 \).
The relationship between 12-month follow-up total healthcare costs and likely nonadherence to the prescribed opioid treatment regimen was modeled using a generalized linear model with gamma distribution and log link,\textsuperscript{30} controlling for demographics, mental health benefit, insurance type, and index month. A similar model was developed to assess the relationship between individual categories of nonadherence and total healthcare costs while controlling for each type of nonadherence.

RESULTS

Chronic Opioid Users Versus Matched Controls

The prevalence of chronic opioid use was 1.3% among enrollees meeting the 18-month continuous enrollment requirement. Characteristics of chronic opioid and matched control cohorts are shown in Table 1. Most patients were commercially insured and, consistent with the health plan distribution, the South was the most heavily represented geographic region.

The number of unique medications and total medication dispensings in the baseline period was greater among chronic opioid users than matched control patients (Table 1). Eighteen of the 20 most common comorbidities identified in the cohorts occurred more frequently among chronic opioid users and are often associated with pain, including disorders such as spondylosis, intervertebral disc disorders, and other back problems; nontraumatic joint disorders; and mood disorders (\textsuperscript{eAppendix E} at \texttt{www.ajmc.com}). Chronic opioid users had a greater frequency of alcoholism or other drug abuse than matched control patients, and although the proportion of patients with evidence of opioid abuse/dependence or overdose/poisoning was low overall, it was significantly greater for chronic opioid users compared with matched control patients (\textsuperscript{eAppendix E}).

Chronic opioid users had more ambulatory and emergency visits, and more hospital admissions than nonusers (Table 2). Total healthcare costs were more than 4 times higher for the chronic opioid cohort compared with matched nonusers ($23,049 ± $42,798 vs $4975 ± $13,185; \textit{P} < .001), with medical costs approximately 5 times greater and pharmacy costs 3.5 times greater for chronic opioid users (Table 3).

Adherent Versus Likely Nonadherent Chronic Opioid Users

Cohort Characteristics. The selection of the patient population with urine testing results is shown in \textsuperscript{eAppendix B}. Baseline characteristics of this subsample (\textit{n} = 2100) according to adherent/likely nonadherent classification are shown in Table 1. The adherent cohort comprised 21.1% of tested patients, but most patients were likely nonadherent (Figure). Nonadherence due to a higher than expected level of the prescribed opioid was the type observed most frequently (Figure).

During the baseline period, likely nonadherent patients filled a significantly higher number of unique prescriptions and had a greater total number of medication dispensings than adherent patients (Table 1). They also filled significantly more unique opioid types, had a greater number of opioid dispensings, and had more days of supply of opioids (Table 1). Hydrocodone and oxycodone were the most commonly filled opioids (\textsuperscript{eAppendix F} at \texttt{www.ajmc.com}).

Comorbidity scores were higher for likely nonadherent patients (Table 1). These patients had a greater prevalence of mood-related disorders and alcoholism/other drug abuse, whereas prevalences of both opioid abuse/dependence and opioid overdose/poisoning were low and did not differ significantly between the cohorts (\textsuperscript{eAppendix E}).

Healthcare Utilization in the Follow-up Period. The mean number of ambulatory and emergency department visits per patient did not differ significantly between adherent and likely nonadherent cohorts (Table 2); nor did the mean number of hospital admissions. However, the number of hospital days was significantly greater for likely nonadherent patients (2370 days per 1000 patients) compared with adherent patients (1753 days per 1000 patients; \textit{P} < .001) because a greater percentage of patients in the likely nonadherent cohort had a hospital admission (24.3% vs. 19.5%; \textit{P} = 0.032) with longer average length of stay per admission (6.2 ± 5.1 days vs. 5.7±
6.1 days; \( P = 0.049 \)). Likely nonadherent patients continued to have significantly more opioid dispensings (20.7 ± 11.1 vs 18.2 ± 8.6; \( P < .001 \)) and more days of supply of opioids (414.9 ± 169.0 vs 391.8 ± 146.3; \( P = .004 \)) than adherent patients in the follow-up period.

**Healthcare Costs.** Among chronic opioid users with urine testing results, total healthcare costs per patient during the follow-up period were approximately 14% higher for likely nonadherent patients, a statistically significant difference from the adherent cohort (Table 3).

No statistically significant cost differences were observed for pain-related services between the adherent and likely nonadherent cohorts, although the relative magnitude of spending was notable: costs for surgery of the spine among patients with at least 1 relevant service date were $33,290 for adherent patients (\( n = 28 \)) and 23% higher for likely nonadherent patients, a statistically significant difference from the adherent cohort (Table 3).

**Table 3. Healthcare Costs (per Patient) in the 1-Year Follow-Up Period: Chronic Opioid Users Versus Matched Nonusers and Adherent Versus Likely Nonadherent Chronic Opioid Users**

<table>
<thead>
<tr>
<th>Type of Cost</th>
<th>Chronic Opioid Users, Mean (SD), $ (n = 49,425)</th>
<th>Nonusers, Mean (SD), $ (n = 49,425)</th>
<th>Adherent, Mean (SD), $ (n = 442)</th>
<th>Likely Nonadherent, Mean (SD), $ (n = 1658)</th>
<th>( P^a )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambulatory</td>
<td>9358 (21,436)</td>
<td>2223 (6981)</td>
<td>9237 (12,473)</td>
<td>9734 (14,334)</td>
<td>.472</td>
</tr>
<tr>
<td>Emergency</td>
<td>339 (1185)</td>
<td>87 (409)</td>
<td>331 (976)</td>
<td>421 (1170)</td>
<td>.967</td>
</tr>
<tr>
<td>Inpatient</td>
<td>7231 (27,350)</td>
<td>980 (8776)</td>
<td>4855 (16,937)</td>
<td>6361 (20,831)</td>
<td>.115</td>
</tr>
<tr>
<td>Other medical</td>
<td>1165 (7777)</td>
<td>275 (1832)</td>
<td>1573 (2879)</td>
<td>1957 (4326)</td>
<td>.027</td>
</tr>
<tr>
<td>Total medical</td>
<td>18,092 (40,961)</td>
<td>3565 (12,406)</td>
<td>15,995 (25,680)</td>
<td>18,473 (29,226)</td>
<td>.081</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>4956 (7175)</td>
<td>1410 (3145)</td>
<td>7165 (9673)</td>
<td>7960 (10,244)</td>
<td>.143</td>
</tr>
<tr>
<td>Total healthcare</td>
<td>23,049 (42,798)</td>
<td>4975 (13,185)</td>
<td>23,160 (28,251)</td>
<td>26,433 (32,077)</td>
<td>.036</td>
</tr>
</tbody>
</table>

\( ^a \) t test.  
\( ^b \) Total medical plus pharmacy costs.

**Figure. Distribution of Urine Test Results**

![Distribution of Urine Test Results](image)

The percentages of patients who were adherent or had evidence of any type of nonadherence are shown on the left. The distribution of the different types of nonadherence within the likely nonadherent cohort is shown on the right. Patients could be nonadherent in multiple categories.
Costs Among Chronic Opioid Users

## Table 4. Multivariate Analyses of Total Follow-up Cost Adjusted for Likely Nonadherence

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1</th>
<th></th>
<th>P</th>
<th>Model 2</th>
<th></th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cost Ratio</td>
<td>95% CI</td>
<td></td>
<td>Cost Ratio</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>Likely nonadherent</td>
<td>1.136</td>
<td>1.00, 1.29</td>
<td>.048</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Higher than expected</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.121</td>
<td>1.01, 1.25</td>
<td>.039</td>
</tr>
<tr>
<td>Lower than expected</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.090</td>
<td>0.93, 1.28</td>
<td>.283</td>
</tr>
<tr>
<td>No prescribed medication</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.992</td>
<td>0.89, 1.11</td>
<td>.888</td>
</tr>
<tr>
<td>Unprescribed medication present</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.063</td>
<td>0.95, 1.19</td>
<td>.276</td>
</tr>
<tr>
<td>Illegal drug present</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.704</td>
<td>0.59, 0.84</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age</td>
<td>1.004</td>
<td>1.00, 1.01</td>
<td>.155</td>
<td>1.003</td>
<td>1.00, 1.01</td>
<td>.335</td>
</tr>
<tr>
<td>Male</td>
<td>0.800</td>
<td>0.72, 0.89</td>
<td>&lt;.001</td>
<td>0.815</td>
<td>0.73, 0.91</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>West region</td>
<td>1.155</td>
<td>0.87, 1.54</td>
<td>.328</td>
<td>1.100</td>
<td>0.83, 1.47</td>
<td>.515</td>
</tr>
<tr>
<td>Midwest region</td>
<td>0.807</td>
<td>0.61, 1.07</td>
<td>.141</td>
<td>0.793</td>
<td>0.60, 1.05</td>
<td>.107</td>
</tr>
<tr>
<td>South region</td>
<td>0.839</td>
<td>0.65, 1.08</td>
<td>.179</td>
<td>0.821</td>
<td>0.64, 1.06</td>
<td>.129</td>
</tr>
<tr>
<td>Mental health benefit</td>
<td>1.138</td>
<td>0.86, 1.50</td>
<td>.366</td>
<td>1.118</td>
<td>0.85, 1.48</td>
<td>.433</td>
</tr>
<tr>
<td>Medicare</td>
<td>0.691</td>
<td>0.50, 0.96</td>
<td>.025</td>
<td>0.718</td>
<td>0.52, 0.99</td>
<td>.044</td>
</tr>
<tr>
<td>Medicaid</td>
<td>0.797</td>
<td>0.51, 1.25</td>
<td>.320</td>
<td>0.807</td>
<td>0.52, 1.26</td>
<td>.344</td>
</tr>
<tr>
<td>Index month, by year</td>
<td>1.003</td>
<td>0.99, 1.01</td>
<td>.457</td>
<td>1.003</td>
<td>0.99, 1.01</td>
<td>.493</td>
</tr>
</tbody>
</table>

CI indicates confidence interval.  
*There were 2100 observations in each model. Model 1 estimated total costs while adjusting for the composite definition of nonadherence and indicated covariates. Model 2 adjusted for each type of nonadherence and indicated covariates.

Herent patients (n = 83) ($40,893; P = .468); mean cost for intrathecal or epidural drug infusion pump implantation and maintenance among patients with at least 1 relevant claim was $10,896 for adherent patients (n = 6) and 64% higher for likely nonadherent patients (n = 41) ($17,959; P = .370).

The relationship between adherence and total follow-up costs was further assessed using multivariate models (Table 4). Consistent with the unadjusted mean costs, costs predicted based on the adjusted model were also approximately 14% higher for the likely nonadherent cohort ($26,419) than for the adherent cohort ($23,263); this difference was significant (Table 4, Model 1).

Of the possible test results, patients with lower-than-expected urine drug levels and those with higher than expected levels had the highest predicted costs ($27,752 and $27,631, respectively), but only having higher than expected levels of the prescribed opioid was associated with statistically significantly greater predicted total healthcare expense in the adjusted model (Table 4, Model 2). Based on Model 2, patients with higher than expected opioid levels were predicted to have follow-up healthcare costs that were 12% higher than those of other patients. Predicted total healthcare costs for patients with evidence of an illegal drug ($18,606) were significantly lower than costs predicted for other patients.

**DISCUSSION**

Although the prevalence of chronic opioid therapy is not high, total medical spending on chronic opioid users is likely to be substantial in most managed care plans. Chronic opioid users had elevated healthcare resource use and incurred substantially greater healthcare costs than nonusers. Furthermore, some chronic opioid users generated higher costs than others and these excess costs were associated with indicators of nonadherence determined by urine drug monitoring. This was particularly evident in the cohort of patients with higher than expected drug levels.

Our results are consistent with previous studies suggesting that patients who use opioids for long-term pain incur greater healthcare costs than patients who are not on opioid therapy. Higher costs in the chronic opioid population are likely related to moderate to severe chronic pain as well as pain-related comorbidities such as arthritis or diabetic neuropathy. Other possible explanations for the reported cost differences include disproportionate use of expensive services or increased risk of unintentional effects of opioid use, such as overdose.

The overall prevalence of nonadherence, while consistent with the finding of a previous study using the same urine drug testing database, is higher than nonadherence rates typically
found in studies of drug treatment for other disease states. For example, nonadherence with treatment for chronic conditions such as diabetes, hypertension, and hyperlipidemia has been reported to range from approximately 22% to 50%. Multiple reasons are likely to contribute to the higher proportion of likely nonadherent patients that we observed. First, nonadherence with therapy in most disease states refers exclusively to underuse or discontinuation of a drug. With respect to chronic opioid therapy, nonadherence includes underuse as well as drug abuse, supplementation with additional opioids, potential diversion, illicit drug use, and the concomitant use of other controlled drugs unbeknownst to the provider ordering the opioid. Criteria to detect abnormal results based on an expected range have not been applied in all studies of opioid nonadherence, and these additional criteria may also account for differences in the reported prevalence of nonadherence.

Second, although opioid urine drug monitoring is an integral part of current pain management recommendations, patients with urine toxicology results in this study might have been selected for testing because they were perceived to be at high risk for misuse. The data in eAppendix E suggest that mood disorders and substance abuse were more prevalent among patients with urine testing than among the population of chronic opioid users as a whole. Since patients with these comorbidities are more likely to be nonadherent, testing bias could also contribute to the high overall rate of nonadherence among tested patients.

Finally, clinicians who ordered urine drug testing were asked to indicate on the lab requisition form whether patients were taking a controlled drug on an “as needed” basis. It is possible that this was not consistently documented, which could increase the rate of nonadherence in the categories of “no prescribed opioid” or “lower than expected” drug level.

Detection of higher than expected drug levels appears to be a useful addition to criteria for defining abnormal results, as likely overuse was found to be associated with increased costs. Higher than expected levels of the prescribed opioid could indicate inadequate pain control (requiring additional use of opioid medication) or potential abuse. This behavior could put patients at risk for side effects or overdose, further increasing their need for healthcare services and leading to higher costs. Overuse constituting abuse has been associated with increased costs, but due to limitations of healthcare claims research, abuse was not specifically investigated here.

In contrast to the increased costs associated with overuse, use of illegal drugs was associated with lower healthcare costs. Possible explanations for this finding are that individuals who use illicit drugs might be less likely to seek healthcare, they might be less likely to have commercial insurance (which could in turn affect costs associated with their care), or they might require fewer healthcare services because their pain is fictitious. It is also possible that clinician mistrust of patients with evidence of illicit drug use influences treatment plans. Further investigation is needed to confirm and explore reasons for this finding.

Our findings suggest that appropriate use of an opioid regimen moderates excess costs. Identifying nonadherent patients, particularly those with high urine drug levels, for treatment plan adjustments and care management interventions could help to improve pain control, reduce drug misuse, and reduce excess costs associated with nonadherence. Other strategies to monitor opioid use (eg, use of screening instruments to identify aberrant behaviors, other risk assessment tools, online prescription databases) complement urine testing, and determining concordance between these measures could be of value to physicians. Additional research is needed to determine whether feedback to clinicians provided by drug monitoring directly reduces costs or guides care practices.

Limitations

All claims-based analyses are subject to certain limitations, such as possible coding errors, undercoding, and lack of generalizability. In this study, the classification of adherence was limited by possible misinformation provided to the testing facility regarding the prescribed opioid regimen. Determination of adherence based on expected urine drug levels was dependent on receipt of accurate information concerning the patient’s opioid regimen prescriptions as well as clinical information such as sex, height, and weight. If incomplete or inaccurate information was provided, some patients identified as nonadherent could have in fact been following their prescribed regimen. In addition, although the study samples comprised all available patients who fulfilled the inclusion criteria, the comparisons may not have been powered to detect moderate differences.

CONCLUSIONS

A high level of healthcare resource use and costs was generated by patients on chronic opioid regimens in comparison with patients who did not use opioid medications or have evidence of chronic pain. Urine drug testing can identify patients who are likely to be nonadherent and have significantly higher healthcare costs. In particular, patients with urine drug levels that were higher than expected using a proprietary algorithm were predicted to have significantly
higher costs than patients whose test results were within an expected range. Improving adherence could reduce costs incurred by patients with chronic pain.

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