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## **Association of Opioid, Anti-depressant, and Benzodiazepines with Workers' Compensation Cost: A Cohort Study**

Dan L. Hunt, D.O.  
Medical Director,  
Corporate Administration office, AF Group,  
Lansing, Michigan  
Dan.Hunt@accidentfund.com

Ryan D. Artuso, Ph.D.  
Senior Data Scientist,  
Predictive Modeling, AF Group,  
Lansing, Michigan  
Ryan.Artuso@accidentfund.com

Nimisha Kalia, M.D., M.P.H., M.B.A.  
Assistant Professor of Medicine  
Division of Occupational and Environmental Medicine  
Department of Medicine, Johns Hopkins University School of Medicine  
nkalia2@jhmi.edu

Nina Leung, Ph.D., M.P.H.  
Assistant Professor of Population Health  
Dell Medical School, the University of Texas at Austin  
Assistant Professor of Medicine  
Department of Medicine, Johns Hopkins School of Medicine  
nina.Leung@austin.utexas.edu

Edward J. Bernacki, M.D., M.P.H.  
Professor of Population Health  
Dell Medical School, the University of Texas at Austin  
Professor Emeritus of Medicine  
Department of Medicine, Johns Hopkins University School of Medicine  
ed.bernacki@austin.utexas.edu

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Xuguang (Grant) Tao, M.D., Ph.D.  
Associate Professor and Research Director  
Division of Occupational and Environmental Medicine  
Department of Medicine, Johns Hopkins University School of Medicine  
[Xtao1@jhmi.edu](mailto:Xtao1@jhmi.edu)

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Correspondence: Xuguang (Grant) Tao, M.D., Ph.D., Associate Professor and Research Director, Division of Occupational and Environmental Medicine, Department of Medicine, Johns Hopkins University School of Medicine. 2024 E Monument St, Suite 1-300, Baltimore, MD 21205. Email: [Xtao1@jhmi.edu](mailto:Xtao1@jhmi.edu). Phone: 410-614-5242. Fax: 410-614-2995

Clinical Significance: This study found that antidepressant prescriptions are associated with increased total workers' compensation claim cost and delayed return to work. This information is important to clinicians when evaluating workers' who are prescribed such medications.

## Abstract

**Background:** Antidepressants, benzodiazepines and opioid medications are used to manage the pain, anxiety or depression associated with workplace injuries.

**Objective:** To evaluate the impact of these medications on workers' compensation costs and time lost from work.

**Methods:** A cohort of 22,383 indemnity claims from 2008-2013 were evaluated for the association of prescribed medications on claim cost and delayed claim closure controlling for confounders.

**Results:** Claims with anti-depressant, opioid or benzodiazepine prescriptions were 2.24 (95% CI: 2.00-2.51), 1.14 (95% CI: 1.02-1.27), and 1.38 (95% CI: 1.23-1.54) times more likely to remain open at the end of the study.

**Conclusion:** The concurrent treatment of pain, depression or anxiety and occupational injuries are associated with large increases in claim cost and delayed return to work.

**Keywords:** psychotropic medication, opioid, anti-depressant, benzodiazepines, occupational injury, workers' compensation

## Introduction

Historically, the simultaneous use of opioids and benzodiazepines has been associated with respiratory depression and increased risk of death.<sup>1, 2</sup> Recent studies have indicated that this combination of medications is commonly prescribed in the workers' compensation system.<sup>3, 4</sup> Multiple safety announcements from the FDA regarding the risks associated with the use of opioids and benzodiazepines in combination have been disseminated to the medical community.<sup>5-7</sup> When reviewing the history of 11,394 lost time claims from Louisiana Workers' Compensation Corporation from 1999 to 2002, Johns' Hopkins University (JHU) researchers uncovered a distinctive prescribing pattern. They found that the average benzodiazepine dosage increased up to 3 years post-injury then plateaued, however claim costs continued to increase. In addition, the average opioid dosage continued to increase year after year through claim closure. They concluded that the addition of benzodiazepines to an opioid treatment regimen was associated with increased workers' compensation costs.<sup>4</sup> The JHU team conducted another study on the relationship between the use of psychotropic and opioid medications with workers' compensation disability and costs on the same cohort. The multivariate logistic regression revealed that the odds of having final claim costs in excess of \$100,000 when antidepressants were prescribed was 2.93 (95% CI: 2.43-3.53) when controlling for age, sex, marital status, attorney involvement, spinal surgeries, and use of opioids/hypnotics/antipsychotics/anti-anxiety agents.<sup>3</sup>

The Accident Fund (AF) Group had previously identified the risk of high medical cost and claim duration when opioids were prescribed in 2012.<sup>8</sup> Subsequently, papers began to appear suggesting that anti-depressant medication in combination with opioids is a recommended approach to treating chronic pain. Cymbalta (a selective serotonin and norepinephrine reuptake inhibitor antidepressant) received FDA approval for treating musculoskeletal pain.<sup>7</sup>

AF Group, a workers' compensation insurance carrier, manages workers' compensation claims across the United States and contains a database of detailed medication data including opioid and psychoactive drugs such as benzodiazepines and anti-depressants. This database was used in this study. The objective of the study was to quantify the costs associated with treating workplace injuries while concurrently treating psychosocial and pain issues that arose out of the injury or predated it. We used combinations of anti-depressants and opioid prescriptions as proxies for comorbid psychosocial and pain diagnoses

## Methods

### Cohort selection

This analysis included 22,383 work-related, indemnity claims from AF Group, a workers' compensation insurance carrier operating as Accident Fund Insurance Company of America, United Heartland, Third Coast Underwriters, and CompWest Insurance Company. Claims (>3 days of missed work) reported between 2008 to 2013 that were followed until December 31, 2017 were included in the analysis with the following criteria: at least 3 years of development, at least 1 day of Temporary Total Disability (TTD) Benefits, and a non-catastrophic claim (e.g., less than \$1 million expected total incurred). All claims were evaluated 3 years after the date of the report of the claim. Because we included claims with injury dates between 2008-2013 with follow-up to Dec 31, 2017, the shortest claim development period in this cohort was 4 years.

### Data Collection

Workers' compensation claims data and prescription medication data from the AF Group database system was used in the study. The prescription of opioids, antidepressants, and benzodiazepines were evaluated for the first 3 years after the date of the injury being reported (Appendix A, <http://links.lww.com/JOM/A530>). Chronic pain was identified via International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) codes 338.2, 338.21, 338.22, 338.28, 338.29, 338.3, and 338.4.

### Medical complexity score

To control for known risk factors associated with high severity claims we utilized the medical complexity scoring system that was used in a previous study.<sup>9</sup> This metric, uses a mix of elastic net regression<sup>10</sup> and stochastic gradient boosting<sup>11</sup> The predictive model targets claim duration and incorporates the following independent variables: age at accident, nature of injury, primary body part injured, cause of injury, claimant's benefit state, claimant's class code, and claimant's ICD9 codes. On a randomly chosen, 30% validation set, the Spearman Correlation between predicted and actual values was 0.64. The final score is calculated by mapping each prediction to a 1-100 scale by way of one percentile groupings, whereby 1 represents the lowest medical complexity and 100 represents the highest.

## Statistical Analysis

Descriptive statistics were used to classify the medication groups by different combinations of opioid, benzodiazepines, and anti-depressant medications. A summary of the frequency of claims, closure rate, average medical cost, and average total claim costs by these drug combination groups are examined from the date of report to the end of the follow-up period (December 31, 2017).

We utilized a multivariable logistic regression model to evaluate the association of anti-depressant prescription with open claims at the end of follow-up, when controlling for opioid and benzodiazepine prescriptions, age at injury, medical complexity, and the number of years of claim development. A linear regression model was used to analyze the increase in medical and total claim costs associated with anti-depressant medications (controlling for the same set of confounders). SAS software was used for all analysis.<sup>12</sup>

## Result

Table 1 presents the number and average costs related to different combinations of the three medication groups. Out of 22,383 indemnity claims, 5,201 claims (23.2%) were never prescribed opioid, benzodiazepines, and anti-depressant medications during the first three years, while 13,564 claims (60.6%) were prescribed opioids only. All other prescriptions (one medication only and combinations) represented the remainder of the claim population. The proportions of patients prescribed anti-depressants and benzodiazepine, only was 0.1% and 0.5%, respectively. Claims with prescriptions for all drug classes represented 3.4% of claims. The slowest claim closure rate occurred among claimants with prescriptions for all three types of medications (58.3%), followed by claims with both opioid and anti-depressant (64.8%) prescriptions. The group without any drugs had the highest closure rate (91.8%) followed by the group with only opioid (89.1%) prescriptions.

The average medical costs for claims with opioids alone was \$28,563 whereas the combination of opioids and benzodiazepines was \$53,366; this combination resulted in a slower closure rate of 75.8% (compared to 89.1% for opioids alone). We observed unexpected results when examining anti-depressant use and opioid use. This combination resulted in higher average medical costs (\$64,507) and had the second slowest closure rate (64.8%) compared to all other medication combinations. When evaluating claims with opioids, benzodiazepines, and anti-depressants the average medical costs were the highest at

\$93,667 and had the lowest closure rate at 58.3%. Figure 1 shows the closure rate by the various medication combinations. Figures 2 and 3 shows the medical and total claim cost by medication combinations, respectively. The more drug types prescribed the lower the closure rate and the higher the cost.

Table 2 shows the association between prescribed medications and the probability of remaining open. The odds ratio for not closing at the end of study for anti-depressant was 2.24 (95% CI: 2.00-2.51), while for opioid 1.14 (95% CI: 1.02-1.27) and for benzodiazepines 1.38 (95% CI: 1.23-1.54), respectively. This suggests that anti-depressants had the highest independent impact on return to work, compared to opioid and benzodiazepines. Having anti-depressants prescribed was associated with an additional \$22,318 in medical cost and \$50,911 in total claim cost, respectively (Tables 3 and 4). In addition, anti-depressant prescriptions were associated with the greatest increase in overall claim costs.

### **Discussion**

Previous studies involving the workers' compensation system have demonstrated a relationship between opioid medication prescribing and escalating medical costs as well as increased claim duration.<sup>3, 4, 13-18</sup> This study was conducted to evaluate the impact of benzodiazepines and anti-depressants in combination with opioids on workers' compensation claim cost and closure rates. We found that prescriptions for more psychotropic drugs in multiple treatment classes resulted in overall higher claim costs and delayed claim closures. As expected, claims without any of the medication groups studied had the lowest cost (\$19,604 vs. \$93,667) and highest closure rate (91.8% vs. 58.3%). This information expands on the relationships reported by Tao et al. who found that claims without opioid prescriptions or psychotropic drugs had the lowest average paid costs with the shortest claim duration.<sup>3</sup>

The overall direction of our findings were expected. It is logical to assume that injured workers who are experiencing a significant amount of pain or suffering from depression or anxiety will require more medical services than injured workers not experiencing such symptoms or psychosocial disorders. Our findings are consistent with observations from studies in the general medical literature investigating the longitudinal cost of medical care for individuals with psychological disorders.<sup>19-24</sup> The prevalence of cardiovascular, respiratory, endocrine and many other disorders are higher in patients with mental disorders than those without. As such, the cost of simultaneously treating psychiatric conditions and physical illness is associated with comparatively higher medical care costs.<sup>23</sup>

While our findings were expected, the magnitude of the cost differences associated with anti-depressant medications did surprise us.

Perhaps the most interesting finding from this study is the relationship between anti-depressant prescriptions on claim closure and costs. Even when controlling for age, chronic pain, medical complexity, and claim development (years), anti-depressant claims to a greater degree, were more likely to remain open at the end of the study period. The effect on total paid costs associated with anti-depressant prescription were greater in magnitude compared to all other drug classes. This finding is similar to the study by Tao et al. who observed that anti-depressant prescriptions were nearly 3 times as likely to result in a claim in excess of \$100,000.<sup>18</sup>

While this analysis focuses on a large cohort of 22,383 claims (with at least 3 years of development), there are several limitations to this study. Information regarding comorbid conditions and medication use prior to injury (compensable by the workers' compensation system) was not available. Therefore, criteria for temporality cannot be satisfied. Prior opioid, anti-depressant, and benzodiazepine use for other pre-existing medical conditions may influence assessed claim outcomes, particularly among high-dose opioid claimants.<sup>12, 13</sup> These data were not available. In addition, claimants with newly developed or prior complex psychosocial issues tend to have delayed return-to-work. While prescriptions for the assessed medications may serve as a proxy for chronic pain and/or mental health diagnoses, prior diagnoses for mental illness was not available to study these associations directly. Additional studies will be necessary to better understand if specific classes of anti-depressants result in different clinical and cost trajectories.

The CDC opioid guidelines for chronic pain published in 2017 recommended the reduction of the number and strength of opioid prescriptions.<sup>20</sup> This effort has highlighted the need for alternative, non-opioid treatments for chronic pain. Anti-depressants have been considered an efficacious medication in combination with opioids to improve clinical outcomes. Our results show that the addition of anti-depressants to opioids, magnifies the association between delayed claim closure and higher overall cost of This research will assist nurse claim managers in recognizing the impact of behavioral issues and psychotropic medications on workers' compensation claim outcomes. It will also allow adjusters to recognize that significantly more resources are required to address the treatment needs of patients with co-morbid behavioral conditions. It will also alert claims administrators that the



presence of anti-depressant medications on a claim is an indicator of potentially costly claim development. In addition, careful consideration should be given when providers are utilizing opioids, benzodiazepines, and anti-depressants in combination.

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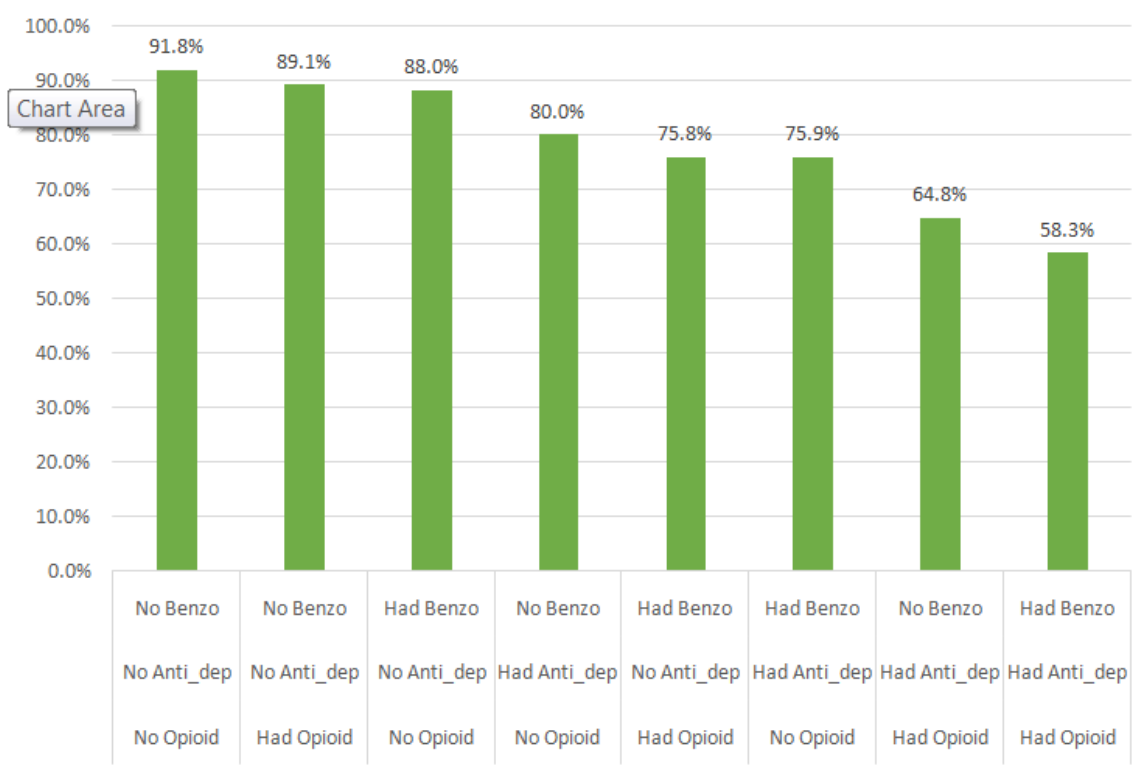
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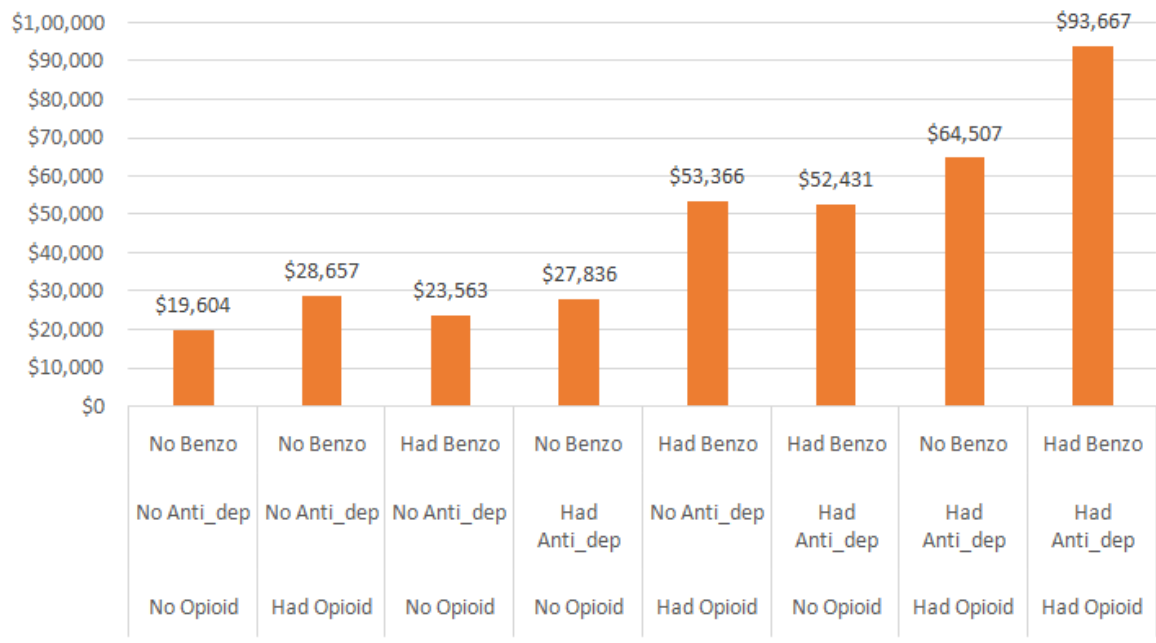
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Figure 1. Closed Claim Percentage by Medication Combinations



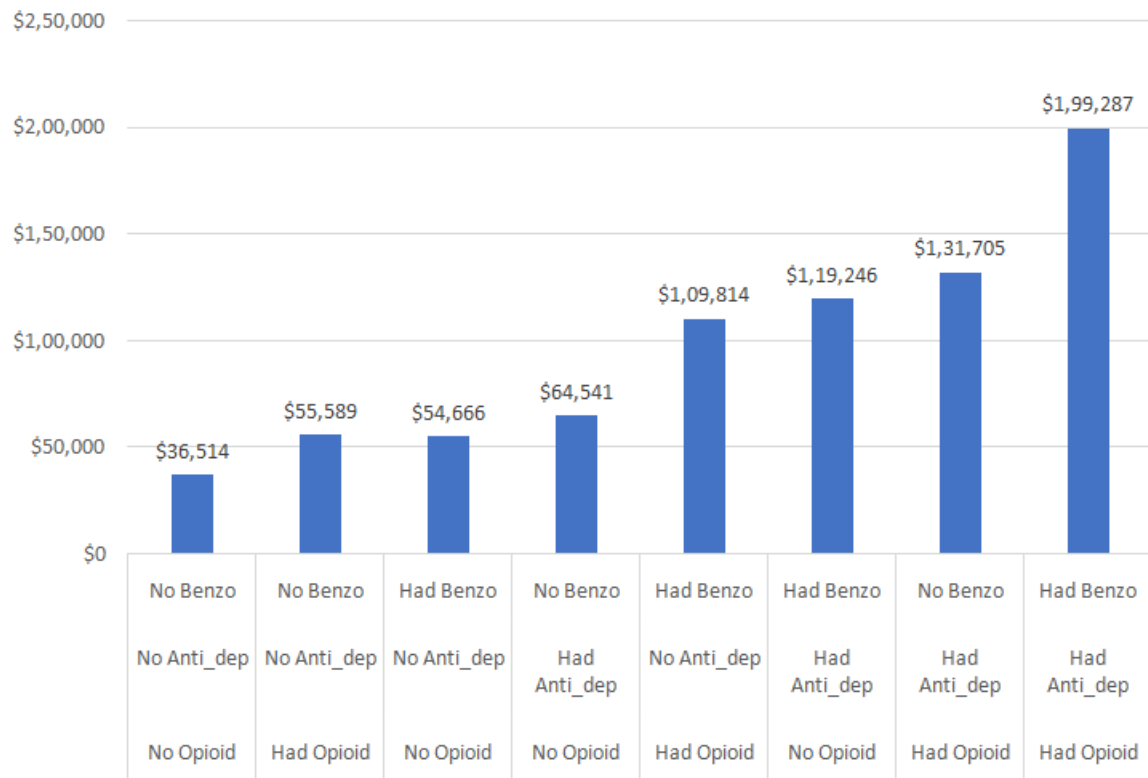
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Figure 2. Medical Cost by Medication Combinations



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Figure 3. Total Paid by Medication Combinations



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Table 1. Indemnity Claim (2008-2013) Closure and Medical and Total Paid by Medication Combinations during First 3 Years

Opioid	Anti-depressant	Benzo	# Closed	Closed %	Total Claims	% of Claims	Average Medical Paid	Average Total Paid
No	No	No	4,774	91.8%	5,201	23.2%	\$19,604	\$36,514
<b>Yes</b>	No	No	12,084	89.1%	13,564	60.6%	\$28,657	\$55,589
No	No	<b>Yes</b>	81	88.0%	92	0.4%	\$23,563	\$54,666
No	<b>Yes</b>	No	96	80.0%	120	0.5%	\$27,836	\$64,541
<b>Yes</b>	No	<b>Yes</b>	1,144	75.8%	1,509	6.7%	\$53,366	\$109,814
No	<b>Yes</b>	<b>Yes</b>	22	75.9%	29	0.1%	\$52,431	\$119,246
<b>Yes</b>	<b>Yes</b>	No	724	64.8%	1,118	5.0%	\$64,507	\$131,705
<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	437	58.3%	750	3.4%	\$93,667	\$199,287
Total			19,362	86.5%	22,383	100.0%	\$32,194	\$63,556



Table 2. Odds Ratio of "Still Open" Associated with Medications among Indemnity Claims

Variables	OR*	95% CI		P values
Had Opioid vs No	1.14	1.02	1.27	0.0202
Had Anti-depressant vs No	2.24	2.00	2.51	<.0001
Had Benzo vs No	1.38	1.23	1.54	<.0001
Age at Accident 30-39 y vs <30 y	1.21	1.04	1.41	0.0151
Age at Accident 40-49 y vs <30 y	1.41	1.22	1.63	<.0001
Age at Accident 50-59 y vs <30 y	1.37	1.18	1.59	<.0001
Age at Accident 60+ vs <30 y	1.44	1.20	1.72	<.0001
Has Chronic Pain vs No	2.78	2.44	3.16	<.0001
Medical Complexity Group 2 vs 1	1.65	1.40	1.95	<.0001
Medical Complexity Group 3 vs 1	2.65	2.27	3.10	<.0001
Medical Complexity Group 4 vs 1	7.73	6.67	8.95	<.0001
Years Developed (increase 1 year)	1.03	1.01	1.05	0.0192
ORs are multiplicative				

Table 3. Multivariate Analysis on Medical Paid Associated with Medications among Indemnity Claims

Variables	Association*	SE	t	P
Had Opioid vs No	\$6,305	\$659	9.57	<.0001
Had Anti-depressant vs No	\$22,318	\$1,028	21.72	<.0001
Had Benzo vs No	\$13,984	\$949	14.73	<.0001
Age at Accident (year)	\$122	\$23	5.4	<.0001
Had Chronic Pain vs No	\$30,707	\$1,226	25.04	<.0001
Medical Complexity Group (increase 1 unit)	\$14,744	\$257	57.3	<.0001
Years Developed (increase 1 year)	\$757	\$156	4.85	<.0001
*Dollar amounts are additive				

Table 4. Multivariate Analysis on Total Paid Associated with Medications among Indemnity Claims

Variables	Association*	SE	t	P
Had Opioid vs No	\$14,303	\$1,195	11.97	<.0001
Had Anti-depressant vs No	\$50,991	\$1,863	27.37	<.0001
Had Benzo vs No	\$34,211	\$1,721	19.87	<.0001
Age at Accident (year)	\$370	\$41	9.01	<.0001
Had Chronic Pain vs No	\$60,878	\$2,223	27.39	<.0001
Medical Complexity Group (increase 1 unit)	\$28,729	\$467	61.58	<.0001
Years Developed (increase 1 year)	\$3,020	\$283	10.67	<.0001
*Dollar amounts are additive				

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