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Background

- Painful musculoskeletal conditions such as osteoarthritis (OA) and low back pain (LBP) are common disorders that result in substantial adverse clinical and economic outcomes in the United States, including the potential for decreased mobility, lost time from work, and decreased productivity and functional capacity¹
- Initial drug treatment for these pain conditions includes acetaminophen (APAP) and non-steroidal anti-inflammatory drugs (NSAIDs)
- For OA and CLBP patients whose pain is not effectively managed by APAP or NSAIDs, opioids have been shown to be valuable treatment alternatives
- The efficacy of extended-release opioids in the management of chronic pain, such as in OA and LBP, have been demonstrated in a number of randomized controlled studies²⁻⁴
- Furthermore, extended-release opioids have demonstrated improvement in work productivity in these chronic pain conditions⁵
- However, limited information was found on the effect of immediate-released opioids on work productivity

Objective

- As extended-release opioids have demonstrated improvement in work productivity in previous chronic pain studies⁵, the purpose of this study was to determine if immediate-released opioids have similar effects on work productivity by estimating indirect costs associated with absenteeism in persons with chronic pain secondary to OA or LBP.

Methods

- A retrospective analysis was performed using the Human Capital Management Services Research Reference Database (HCMS RRDb) from January 2001 to March 2008
- Comparisons were made within the two immediate-released (IR) combination opioid cohorts (APAP/Hydrocodone (HC) and APAP/Oxycodone(Oxy)) comparing the pre-index period and the post-index period (both 24 weeks and 56 weeks)
- Outcomes for both cohorts included employee work absences and indirect costs associated with payments for absences, including sick leave (SL), short- and long-term disability (STD, LTD) and workers' compensation (WC)
- Two-part regression analysis modeled the cost differences between pre- and post-index time periods within each study cohort
- All data are expressed as average weekly data over the time period
- All costs were inflation-adjusted to June 2008 US dollars using the non-seasonally adjusted all goods and services component of the Consumer Price Index (CPI)

Methods

- Inclusion Criteria:**
- At least 2 ICD-9-CM diagnostic codes for OA (715.xx) or LBP
 - Prescription claim for either IR APAP/HC or IR APAP/Oxy after first OA or LBP diagnosis in study period (defined as index date)
 - At least 60 days' supply of prescription pain medications during the year following the index date
 - Continuous enrollment throughout study period with at least 12 weeks enrollment pre-index date and minimum 24 weeks enrollment post-index date.
- Exclusion Criteria:**
- Employees who did not have pre-specified continuous enrollment
 - Less than 60 days' supply of prescription pain medications during study period

Results

Table 1 Descriptive Statistics for the Study Groups

Study Group	Descriptive Statistics for Employees ^a with Osteoarthritis or Low Back Pain who Received	
	IR APAP/HC	IR APAP/Oxy
N	1,617	1,100
Variable	Mean (S.E.) or %	Mean (S.E.) or %
Age (at index date) ^b	44.77 (0.24)	44.52 (0.28)
Tenure (at index date) ^c	9.33 (0.20)	8.97 (0.24)
Female	47.1%	43.5%
Married ^d	51.6%	52.3%
White ^e	66.3%	71.7%
Black ^f	9.0%	7.8%
Hispanic ^g	6.7%	3.7%
Exempt	23.9%	24.0%
Full Time	95.4%	95.5%
Annual Salary ^h	\$48,529 (\$692)	\$47,854 (\$820)
Prior Cancer Diagnosis ⁱ	7.5%	9.9%
Prior HIV Diagnosis ^j	0.2%	0.3%
Charlson Index ^k	0.31 (0.02)	0.42 (0.04)
Had APAP/Oxycodone Prescription ^l	27.1%	
Had APAP/Hydrocodone Prescription ^m		73.4%

^a APAP/Hydrocodone (N=1,557), APAP/Oxycodone (N=1,055)
^b APAP/Hydrocodone (N=1,312), APAP/Oxycodone (N=805)
^c APAP/Hydrocodone (N=811), APAP/Oxycodone (N=589)
^d Employees were required to have at least 60 days' supply of prescription pain medications (gabapentin, tramadol, or analgesic antipyretic opiate agonist) during the year following the first Study Drug prescription.
^e The index date is the date of the first Study Drug prescription after the first osteoarthritis or low back pain diagnosis in the study period.
^f During the 12 weeks prior to the index date.
^g Between 12 weeks before and 24 weeks after the index date.

Results

Table 2 Adjusted Absence Costs for Employees^a with Osteoarthritis or Low Back Pain

Index Treatment	Health Benefit Cost Category	Adjusted ^b Costs per Employee per Week 12 Weeks Prior to Index Date vs. 24 Weeks After Index Date					Adjusted ^b Costs per Employee per Week 12 Weeks Prior to Index Date vs. 56 Weeks After Index Date ^c				
		N	Pre-Index Period	Post-Index Period	Δ	P-Value	N	Pre-Index Period	Post-Index Period	Δ	P-Value
Immediate-released APAP/HC	Sick Leave	709	\$19	\$18	\$0	0.787	462	\$20	\$15	-\$5	0.011
	Short-term Disability	894	\$35	\$89	\$54	<0.0001	602	\$30	\$49	\$19	<0.0001
	Long-term Disability	1277	\$1	\$3	\$2	0.0007	850	\$1	\$3	\$2	0.0003
	Workers' Compensation	1451	\$37	\$48	\$11	0.178	952	\$25	\$39	\$14	0.068
	Indirect Costs		\$92	\$158	\$66			\$75	\$106	\$30	
Immediate-released APAP/Oxy	Sick Leave	504	\$15	\$13	-\$2	0.181	309	\$10	\$8	-\$3	0.102
	Short-term Disability	671	\$38	\$119	\$81	<0.0001	422	\$29	\$74	\$45	<0.0001
	Long-term Disability	888	\$1	\$5	\$3	0.0002	540	\$2	\$9	\$7	<0.0001
	Workers' Compensation	987	\$23	\$32	\$9	0.184	593	\$14	\$32	\$17	0.007
	Indirect Costs		\$77	\$169	\$92			\$55	\$122	\$67	

^a Employees were required to have over 60 days' supply of prescription pain medications (gabapentin, tramadol, or analgesic antipyretic opiate agonist) during the year following the index date. The index date is the date of the first index date prescription after the first osteoarthritis or low back pain diagnosis in the study period. All employees were required to have enrollment in a health plan (and possibly other benefit enrollment) from 12 weeks before the index date to 24 weeks after the index date.
^b Costs were adjusted using regression modeling to control for age, gender, marital status, race, salary, exempt status, full-time/part-time status, region, cancer, HIV, the Charlson Comorbidity Index, and the use of APAP/Hydrocodone or APAP/Oxycodone (other than the index treatment medication type) if sample size allowed and after examining collinearity. Costs were also adjusted for inflation to 2008 dollars. Only employees eligible for each specific benefit were included in the regression models for that benefit. Sick leave costs include all costs from leave accrued in the pre-index period in the study timeframe. Short-term disability, long-term disability, and workers' compensation costs include all costs accrued during the in-the-specific study timeframe. Differences in adjusted absence days between pre- and post-index time periods are statistically significant if P<0.05.
^c If by 6 weeks of health plan and benefit enrollment after the index date were required for these employees.

Table 3 Adjusted Absence Days for Employees^a with Osteoarthritis or Low Back Pain

Index Treatment	Absence Category	Adjusted ^b Absence Days per Employee per Week 12 Weeks Prior to Index Date vs. 24 Weeks After Index Date					Adjusted ^b Absence Days per Employee per Week 12 Weeks Prior to Index Date vs. 56 Weeks After Index Date ^c				
		N	Pre-Index Period	Post-Index Period	Δ	P-Value	N	Pre-Index Period	Post-Index Period	Δ	P-Value
Immediate-released APAP/HC	Sick Leave	709	0.109	0.124	0.015	0.126	462	0.107	0.098	-0.009	0.393
	Short-term Disability	894	0.273	0.736	0.463	<0.0001	602	0.240	0.389	0.149	<0.0001
	Long-term Disability	1277	0.025	0.064	0.038	0.007	850	0.016	0.056	0.039	0.005
	Workers' Compensation	1451	0.033	0.049	0.016	0.164	952	0.031	0.044	0.014	0.273
	Totals		0.441	0.973	0.533			0.394	0.587	0.194	
Immediate-released APAP/Oxy	Sick Leave	504	0.091	0.092	0.000	0.965	309	0.057	0.050	-0.007	0.409
	Short-term Disability	671	0.324	0.962	0.638	<0.0001	422	0.251	0.562	0.311	<0.0001
	Long-term Disability	888	0.043	0.092	0.048	0.021	540	0.063	0.175	0.112	0.002
	Workers' Compensation	987	0.028	0.042	0.014	0.271	593	0.021	0.045	0.023	0.108
	Totals		0.486	1.187	0.701			0.392	0.832	0.440	

^a Employees were required to have over 60 days' supply of prescription pain medications (gabapentin, tramadol, or analgesic antipyretic opiate agonist) during the year following the index date. The index date is the date of the first index date prescription after the first osteoarthritis or low back pain diagnosis in the study period. All employees were required to have enrollment in a health plan (and possibly other benefit enrollment) from 12 weeks before the index date to 24 weeks after the index date.
^b Days were adjusted using regression modeling to control for age, gender, marital status, race, salary, exempt status, full-time/part-time status, region, cancer, HIV, the Charlson Comorbidity Index, and the use of APAP/Hydrocodone or APAP/Oxycodone (other than the index treatment medication type) if sample size allowed and after examining collinearity. Only employees eligible for each specific benefit were included in the regression models for that benefit. Sick leave days include all days from leave accrued in the pre-index period in the study timeframe. Short-term disability, long-term disability, and workers' compensation days include all days incurred during days in the specific study timeframe. Differences in adjusted absence days between pre- and post-index time periods are statistically significant if P<0.05.
^c If by 6 weeks of health plan and benefit enrollment after the index date were required for these employees.

- Disability costs and absences were all significantly greater for employees using the study drugs after therapy initiation compared with before therapy.
- As depicted in Table 2, total indirect costs (SL, STD, LTD and WC) for the immediate-released APAP/HC users increased 72% (86%) in the 24-week cohort and 41% (\$30) in the 56-week cohort, while the increases for the immediate-released APAP/Oxy were even greater, 119% (\$92) and 122% (\$67) in the 24-week and 56-week cohorts, respectively.
- Similarly, depicted in Table 3, total absence days for the immediate-released APAP/HC users increased 121% in the 24 week cohort and 49% in the 56 week cohort, while the increases for the immediate-released APAP/Oxy were even greater, 144% and 112% in the 24 week and 56 week cohorts, respectively.

Conclusions

- Based on study results, use of immediate-released opioids in chronic pain does not appear to improve work productivity as demonstrated by extended-release opioids in previous chronic pain studies.⁹
- When indicated, treatment with extended-release opioids may result in longer lasting pain control and may be related to enhanced patient compliance¹⁰ improved work productivity⁹, and improved perceived quality of life.¹¹
- This study adds to the limited literature of the effect of immediate-released opioid use among employees with OA or LBP.

References

1. US National Center for Chronic Disease Prevention and Health. Arthritis Types Overview. Available at: <http://www.cdc.gov/arthritis/aboutdisorders.htm>. Accessed 10/23/2008.
2. Nicholson B, Ross E, Swank J, Wald A. Randomized trial comparing proloperidine-controlled extended-release morphine sulfate to controlled-release oxycodone HCl in moderate to severe noncancer pain. *Curr Med Res Clin*. 2006;25(10):1503-1514.
3. Kalso E, Allen S, Anttila J, Falck U, Kalso E, Anttila J, et al. Recommendations for using opioids in chronic non-cancer pain. *Acta Anaesth Scand*. 2004;48(1):1-10.
4. Allen J, Hays R, Jensen NH, de Witmore LL, Ball M, Donald E, Kalso E. Randomized crossover trial of transdermal fentanyl and sustained-release morphine for chronic non-cancer pain. *BMJ*. 2001;323(7205):1154-8.
5. Compton M. *BMJ*. 2001;323(7205):1154-8.
6. Nicholson B, Ross E, Swank J, Wald A. Prolonged treatment with transdermal fentanyl in noncancer pain. *J Pain Symptom Manage*. 1998;10(1):64-73.
7. Miller R, Kallen-Makris M, Ruckert K, Holmes H, Donald R, Weiss H, et al. Evaluation of long-term efficacy and safety of transdermal fentanyl in the treatment of chronic noncancer pain. *J Pain*. 2001;2(4):197-204.
8. Marder R, Allen S, Anttila J, Falck U, Kalso E, Anttila J, et al. Efficacy of 12-hour extended-release hydrocodone/nalbuphine on pain-related work productivity: a subgroup analysis from a 56-week, open-label study. *Presented at American Academy of Pain Medicine meeting, February 12-16, 2007, Orlando, FL.*
9. Nicholson B et al. Management of chronic noncancer pain in the primary care setting. *South Med J*. 2007;100(10):1028-36.
10. McGarvey JL, Baskin LL. Long-acting agents for chronic pain: pharmacodynamic opportunities to enhance compliance, quality of life, and analgesia. *Ann N Y Acad Sci*. 2001;949:183-191.