

Clinical and Cost Outcomes of Buprenorphine Treatment in a Commercial Benefit Plan Population

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ABSTRACT

Objectives: Opioid dependency is a significant societal burden. Buprenorphine has improved access and safety for outpatient detoxification services. The objectives of this study were to determine, based on assessment of administrative medical and pharmacy claims, if use of buprenorphine induction (with or without naloxone) in an opioid-dependent population with commercial benefit coverage improved clinical and cost outcomes compared with buprenorphine without induction and with no use of buprenorphine.

Study Design: This is a retrospective observational claims review with a 4-month pre- and posttreatment study design and analysis of medical, behavioral health, and pharmacy utilization patterns for all levels of service.

Methods: We analyzed claims data from a sample of 648 Cigna customers using analyses of variance to assess differences before and after treatment among groups (buprenorphine with induction, buprenorphine without induction, and no buprenorphine) and general linear regression to compare adjusted cost ratios.

Results: Induction and noninduction buprenorphine treatment were associated with significantly reduced inpatient utilization (81.8% reduction in hospitalizations vs 43.1% reduction in the no-treatment group; $P < .05$) and lower total medical, behavioral health, outpatient, and pharmacy costs (cost ratio, 0.52:1; $P < .001$). There was a cost and utilization shift from inpatient toward outpatient, and we observed a shift in pharmacy claims from medical to behavioral health services; we observed a cost ratio of 1.58:1 for total pharmacy ($P < .05$) and 2.26:1 for nonpsychotropic pharmacy ($P < .0001$).

Conclusions: Our findings support the use of buprenorphine with and without induction to decrease inpatient utilization and substantially lower total medical, behavioral health, and pharmacy costs.

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According to the United States Substance Abuse and Mental Health Services Administration and recent research, more than 4.3 million Americans engaged in nonmedical use of prescription painkillers in 2014.^{1,2} Opioid dependence is a growing epidemic, impacting people of all socioeconomic backgrounds and age groups.³ Recidivism is high, and treatment programs, including pharmacotherapy options, have been limited.

The introduction of buprenorphine^{4,5} has offered a relatively rapid, safe, and effective means to detoxify opioid-dependent people in an office-based setting.⁴ Standard induction protocol generally spans 3 days and is described in detail in the Center for Substance Abuse Treatment Clinical Guidelines for Use of Buprenorphine in the Treatment of Opioid Addiction.⁶ Recent studies in low-income populations have demonstrated increased outpatient referrals and fewer hospitalizations/emergency department visits following buprenorphine induction,^{7,8} stabilization, and linkage to outpatient treatment in opioid-dependent inpatients (injection and noninjection drug users). There is great need for cost and utilization studies among commercial benefit plan populations.

Our objective was to determine, based on assessment of behavioral health and medical claims, if use of buprenorphine induction (with or without naloxone, heretofore referred to as buprenorphine, unless specifically stated otherwise) was associated with improved clinical and cost outcomes in opioid-dependent individuals with commercial coverage compared with buprenorphine without induction and compared with no use of buprenorphine.

METHODS

Data Source and Comparison Groups

Eligible claims for this retrospective observational study were drawn from health maintenance organization (HMO), point-of-service (POS), and preferred provider organization Cigna products. We analyzed 69,495 behavioral health administrative claims for 8503 opioid-dependent Cigna customers 18 years and older, with dual eligibility for

medical and behavioral health benefits. Individuals were included if they had a primary, secondary, or tertiary diagnosis of opioid dependence for a date of service between October 1, 2006, and December 31, 2007, that was documented on a behavioral health claim, including *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition*, diagnosis codes 304.0-304.03 and 304.7-304.73 (referring to all opioid dependence diagnoses).

Three groups were identified for comparison: an induction treatment group, a noninduction treatment group, and a no-treatment group. The induction group was started on buprenorphine in the induction phase and continued to maintenance (or as long as treatment lasted). The noninduction group received buprenorphine, as seen in pharmacy claims, but not for induction; instead, this group received it as part of detoxification or while hospitalized (ie, no induction or implied maintenance). The no-treatment group was actually “no treatment with buprenorphine.” This group had treatment as usual (ie, inpatient or outpatient, detoxification, rehabilitation), but did not receive buprenorphine at any point. Inclusion criteria for the induction group consisted of diagnosis of opioid dependence, the Healthcare Common Procedure Coding System procedure code H0033 (defined as “oral medication administration, direct observation”), and a physician provider. Individuals were considered undergoing induction whether or not they used all 3 authorized induction sessions. Claims were then crossed with pharmacy claims to ensure that buprenorphine was employed as part of induction. The noninduction group was identified as those who received physician services and buprenorphine within the study interval but without an H0033 claim. The no-treatment group included customers with no treatment or pharmacy claims associated with opioid dependence diagnoses within the study interval.

The First DataBank generic formulation code numbers used to identify prescriptions analyzed in this study were 18973 and 18974 (buprenorphine HCl and naloxone HCl) and 64672 and 64673 (buprenorphine HCl). Ninety-three percent of prescriptions in the baseline period treatment groups contained buprenorphine plus naloxone, 7.15% contained buprenorphine alone, and 92.5% of prescriptions in the follow-up period treatment groups contained buprenorphine plus naloxone (Suboxone), compared with 7.5% containing buprenorphine alone (Subutex). The drug groups were not analyzed separately.

PRACTICAL IMPLICATIONS

We estimated the effects on utilization and costs of buprenorphine induction treatment in opioid-dependent Cigna Health and Life Insurance Company (Cigna) customers.

- Buprenorphine treatment with an induction protocol of 3 outpatient visits with the outpatient prescriber appears to substantially reduce inpatient costs associated with opioid dependency.
- Positive cost offset results from the shift from inpatient to outpatient treatment and pharmacy utilization.
- We recommend coverage of buprenorphine in benefit plan formularies to improve clinical outcomes and reduce net cost of treatment.

Eighty-eight customers were found to have the H0033 procedure on a claim. Twenty-three records were excluded because there were no corresponding pharmacy claims for buprenorphine; they were either ineligible for the benefit plan’s pharmacy (n = 8), their medical benefits enrollment was interrupted, or they resided in California, where providers submit encounter-only, rather than actual claims, data to Cigna (n = 9).

Service codes on the induction group’s outpatient claims indicated group, individual, and family therapy; nonspecific office visits (such as outpatient); and programmatic intensive outpatient level of care. Claims submitted were assigned to 1 of 3 benefit categories: detoxification, chemical dependence, and non-substance-related mental health. In order to match groups for claims submitted, only claims for these types of services were considered in the analysis for the noninduction group and the no-treatment group. This reduced the number of records included in the analytic sample by 61.7% in the noninduction group and by 94.9% in the no-treatment group.

Of the 8503 opioid-dependent individuals initially identified, 648 met the final criteria for study inclusion. The final study group consisted of 48 undergoing induction treatment, 241 undergoing noninduction, and 359 in the no-treatment group.

The 4-month baseline and follow-up periods were based on the date of the earliest H0033 procedure for the induction group (index date) and on the earliest opioid-related outpatient visit for the noninduction and no-treatment groups.

Outcomes

Mean age, gender, age, and number of unique baseline diagnoses were compared across groups. Baseline diagnoses were stratified into only nonpsychotropic (not including buprenorphine) prescriptions and psychotropic prescriptions.

Clinical outcomes included changes in the rates of medical and behavioral health hospitalizations and in

inpatient detoxification services from the baseline to the follow-up period. Four-month baseline and follow-up costs and services for medical and behavioral health outpatient, inpatient, nonpsychotropic, and psychotropic pharmacy were calculated and reported as per-customer/member per-month or utilization-per-1000 respectively. Claims with zero cost amounts were kept, but to mitigate the effects of outliers, total costs were capped at \$50,000 (corresponding with a “catastrophic spend”) based on the full 4 months of each period.

Statistical Analyses

Homogeneity tests between groups were conducted using χ^2 tests. Student's *t* tests, χ^2 distributions, and analyses of variance were used to compare demographics and clinical outcomes on the average number of diagnoses between and across groups.

Percent change from the index period to the postindex period for inpatient detoxification and medical or behavioral health hospitalization (inpatient levels of care for psychiatric illness or substance abuse, other than detoxification units) was compared using a test for difference in proportions, with $\alpha = 0.05$. Primary, secondary, or tertiary *International Classification of Diseases, Ninth Revision, Clinical Modification* codes included 337.0-337.9, 338.4, 339.00-339.89, 346.00-346.93, 350.1, 353, 354.1-354.9, 355.0-355.9, 356.0-356.9, 357.1-357.7, 531.3, 617.0-617.9, 625.5, 696, 710, 711.8, 714.0-714.33, 715.00-715.09, 715.3-715.9, 720.0-720.9, 721.0-721.90, 723.4, and 725-729.99.

Difference in differences analysis among groups was used to examine the change in total healthcare costs and utilization from baseline to the 4-month follow-up. General linear regression was used to compare adjusted cost ratios. Unadjusted ratios and actual costs were also reported. Although most outcomes were adjusted for age, gender, the interaction between age and gender, and type of benefit plan, inpatient cost and utilization outcomes were unadjusted due to scarce follow-up volume of service.

RESULTS

Sample Characteristics

The presentation rate for opioid dependence was 0.271% (8503/3,137,173); no significant gender differences existed between the groups, although there was a difference of 8 percentage points between females in the no-treatment group compared with the noninduction group (43.7% v. 35.3%; $P < .05$). The no-treatment group had a significantly higher proportion of people ≥ 50 years (16.7%; $P < .05$). The induction group had a significantly higher proportion (89.6%) of HMO and POS products ($P < .05$) compared

with the no-treatment group (73.3%; $P < .05$) and with the noninduction group (68.5%; $P < .01$). The number of baseline comorbid pain diagnoses was significantly different between the induction and noninduction groups (37.5% v. 32.0%; $P < .05$), but there was no significant difference between the induction group and the no-treatment group (37.5% vs 21.6%) (see **TABLE 1**).

More Cigna customers had medical diagnoses in the no-treatment group (5.37%) compared with the noninduction group (4.12%) taking psychotropic medications ($P < .01$), and there were 1.01 mental health diagnoses compared with 0.74 ($P < .05$). Customers in the no-treatment group had higher rates of both medical (5.31 vs 3.85; $P < .01$) and mental health diagnoses (0.96 vs 0.65; $P < .01$). The no-treatment group had more combined mental health and substance abuse diagnoses per person compared with the noninduction group (1.69 vs 1.35; $P < .05$).

Inpatient Utilization and Cost

We observed a 100% reduction in the use of detoxification services per person and in the number using detoxification services in the induction group in the 4 months following induction, compared with a reduction of 48.2% ($P < .05$; services) and 50.0% ($P < .05$; persons) in the use of detoxification services per person. Similar significant relationships existed for the same groups when comparing behavioral health hospitalizations. In the induction group, there were significant reductions of 81.8% in behavioral health hospitalizations and 90.0% of persons using those services compared with 43.1% and 41.9% reductions, respectively, in the no-treatment group ($P < .05$ and $P < .05$; **TABLE 2**). A significant reduction was also noted in those same indices between the induction group and the noninduction group ($P < .05$), but not compared with the no-treatment group.

There was an 81.8% reduction pre- to post treatment and an 80.8% reduction in the number using medical hospital services in the induction group. The noninduction group showed a 7.6% reduction in hospitalizations ($P < .001$) and a 33.3% reduction in those accessing those services ($P = .05$). In the no-treatment group, compared with the induction group, behavioral health hospital admissions dropped by 25.3% ($P < .001$) and the number using those services dropped by 36.6% ($P < .05$). There was greater reduction of medical hospitalizations (−7.6% vs −25.3%; $P < .05$) in the noninduction group compared with the no-treatment group, but there was no difference in the number using these hospital services. The findings suggest a correlation between the use of induction services and reduced hospital-level service utilization.

Table 1. Demographic and Clinical Characteristics of Study Population (N = 648)

	Group A (n = 48) Buprenorphine Induction Treatment Group		Group B (n = 241) Buprenorphine Noninduction Treatment Group		Group C (n = 359) No-Buprenorphine Treatment Group		A vs B P	A vs C P	B vs C P
	Count	Percent	Count	Percent	Count	Percent			
Female	19	39.6%	85	35.3%	157	43.7%	.57	.59	.03
Age (years)									
18-24	11	22.9%	55	22.8%	71	19.8%	.82	.86	.03
25-34	11	22.9%	68	28.2%	70	19.5%			
35-49	19	39.6%	92	38.2%	158	44.0%			
50+	7	14.6%	26	10.8%	60	16.7%			
Plan type									
Health maintenance organization	14	29.2%	54	22.4%	74	20.6%	.01	.04	.29
Point-of-service	29	60.4%	111	46.1%	189	52.6%			
Preferred provider organization	5	10.4%	76	31.5%	96	26.7%			
	Mean	SD	Mean	SD	Mean	SD	P value	P value	P value
Age (continuous, in years)	37.4	12.4	34.8	10.8	37.9	11.9	.14	.80	.002
Number of unique diagnoses									
Beneficiaries with psychotropic prescriptions	4.94	4.31	4.12	4.35	5.37	5.55	.30	.66	.008
Medical	0.92	1.02	0.74	0.93	1.01	1.25	.31	.68	.01
Mental health	0.94	0.79	0.75	0.73	0.78	0.80	.15	.25	.69
Substance abuse and related	1.86	1.55	1.50	1.32	1.79	1.71	.14	.81	.04
Behavioral health									
Beneficiaries with nonpsychotropic prescriptions									
Medical	4.44	4.07	3.85	4.16	5.31	5.04	.37	.20	.001
Mental health	0.79	1.01	0.65	0.89	0.96	1.25	.33	.37	.001
Substance abuse and related	0.83	0.78	0.70	0.71	0.73	0.80	.26	.40	.73
Behavioral health	1.63	1.51	1.35	1.29	1.69	1.72	.20	.81	.01

P values are for χ^2 tests.

Table 2. Utilization Comparison Between Changes Over 4 Months in Buprenorphine Induction and No-Treatment Groups (N = 407)

	Buprenorphine Induction Treatment Group (n = 48)		No-Buprenorphine Treatment Group (n = 359)		P Service	P Beneficiary
	Service % change	Beneficiary % change	Service % change	Beneficiary % change		
Detoxification	100.0	100.0	48.2	50.0	.05	.05
Behavioral health hospitalizations	81.8	90.0	43.1	41.9	.05	.05
Medical hospitalizations	81.8	80.8	25.3	36.6	<.001	<.05

P values are for analysis of variance tests.

Outpatient Utilization and Cost Comparisons

Compared with the no-treatment group, the induction group had significantly fewer total inpatient and outpatient costs (cost ratio, 0.52:1; $P < .001$), as well as lower total behavioral health (mental health/substance abuse) costs (cost ratio, 0.48:1 ; $P < .05$).

There was a 19.3% reduction in total outpatient costs in the induction group compared with a 23.7% increase in the no-treatment group. A significant reduction in medical outpatient costs was demonstrated between the induction group (-59.4%) compared with the no-treatment group (+24.2%) (cost ratio, 0.54:1 ; $P < .05$). Behavioral health

outpatient costs were higher in the induction group, as expected, but not significantly higher.

The induction group attended significantly more outpatient behavioral health sessions compared with the noninduction group (rate ratio, 1.36:1; $P < .05$) or with the no-treatment group (rate ratio, 1.43:1; $P < .05$). Medical outpatient office visits decreased by 44.1% in the induction group compared with a 1.7% increase in the no-treatment group (rate ratio, 0.71:1; $P < .05$). Emergency department occurrences and related costs were not significantly affected by treatment type.

Pharmacy Utilization and Cost Comparisons

Total and medical (nonpsychotropic) prescriptions were significantly higher in the induction group compared with the no-treatment group (rate ratios of 1.43:1 and 1.68:1, respectively; $P < .001$). There was no difference in the number of prescriptions between the induction and noninduction groups. The change in total and nonpsychotropic pharmacy costs increased significantly in the posttreatment interval for the induction group (+97.2% for total and +102.4% for nonpsychotropic) compared with the no-treatment group (+1.1% and -17.7% for nonpsychotropic, respectively); the cost ratios were 1.58:1 for total pharmacy ($P < .05$) and 2.26:1 for nonpsychotropic pharmacy ($P < .0001$).

DISCUSSION

Of the 47,055 US drug overdose deaths in 2014, 28,647 (60.9%) involved an opioid.⁹ The 2016 Comprehensive Addiction and Recovery Act¹⁰ was signed into law to address the opioid epidemic in part through a medication-assisted treatment and intervention demonstration program.¹¹ Our findings of utilization shift from inpatient to outpatient and reductions in cost add to evidence for clinical utility of buprenorphine compared with methadone, including reduced mortality, crime, and personal costs.¹²⁻¹⁶ and focused on short-term (up to 1-year follow-up).

We observed significant reductions in utilization and cost, as well as in medical and behavioral health morbidity, in favor of buprenorphine induction. A lesser but still significant benefit was also found for buprenorphine without induction. Use of induction services was associated with reduced cost and utilization of inpatient detoxification and of medical and behavioral health services. While the reduction of inpatient detoxification for those using buprenorphine services was expected,⁵ the significantly reduced use of both medical and behavioral health hospital services, and lower overall costs, was not expected within the brief time interval for this study, given the higher degree of medical and behavioral health morbidity in the

no-treatment group. The impact of induction may be due to the higher degree of patient-centered and supportive services that accompany the use of the drug, facilitating a more individualized treatment plan, a closer doctor-patient relationship, and a system of support.

One strength of this study was that we compared utilization and included total costs across the inpatient, outpatient, pharmacy, behavioral health, and medical care areas. This enabled us to observe the effects of buprenorphine on total costs across all levels of service, and show an even greater impact than have other studies that were limited to specific levels. For example, Kaur et al evaluated the impact of buprenorphine use on pharmacy utilization and cost outcomes in a group dependent on prescription opioids. The reduced opioid prescription cost they found in the first 6 months was neutralized by the increased cost of buprenorphine, and the reduction was lost altogether at 1 year.¹¹

Our findings are noteworthy in that they evaluate the effectiveness of buprenorphine in reducing use and costs for behavioral health or for medical inpatient services. Barnett found a similar cost benefit loss at 6 months when comparing buprenorphine with methadone in a Veterans Administration population.¹³ In line with Kaur and colleagues, we observed escalated pharmacy costs; like Barnett, however, we found that any upward cost shift was significantly offset by reduced overall services, including use of inpatient services, which were not evaluated by Barnett. In the context of other recent study findings confirming the utility of buprenorphine in improving costs and outcomes, including findings from the SUMMIT trial and by Ruger et al and Schackman et al,^{5,19-22} our findings strongly support formulary inclusion of buprenorphine coverage by benefit plans.

Limitations

Our data did not include reasons why prescribers chose to place a given customer in an induction versus a non-induction group. Claims information for methadone prescriptions was not available because methadone is administered by state-run clinics and is typically not covered under commercial benefit plans. No review was done to determine if any customer had been prescribed other medications, such as naloxone. Our study was limited by the constraints of eligibility and claims-paid data elements, the retrospective and observational design, reporting limitations, and relatively short-term outcomes. Generalizability was reduced by the fact that we considered service use a proxy for clinical effectiveness, since abstinence could not be directly assessed. The fact that our no-treatment

group had significantly higher comorbidities and greater use of prescriptions further limits those conclusions. Future studies should examine the sustainability of these outcomes over longer time periods. Although our study data are from 2007, our analyses address the persistence and urgency of a worsening epidemic that has only become exacerbated in recent years,¹ and they provide evidence for an important step that health plans can take to reduce costs and improve health and safety.

CONCLUSIONS

We observed significantly reduced costs and utilization of inpatient and outpatient medical services in those who received buprenorphine induction or noninduction compared with the no-treatment group. The effect was most pronounced in the induction group. The benefit appears to be driven largely by reductions in the use of higher levels of care detoxification, behavioral health and medical admissions, and combined outpatient services. [ajpb](#)

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