Published in final edited form as:

Addiction. 2010 September ; 105(9): 1616–1624. doi:10.1111/j.1360-0443.2010.03001.x.

Cost-effectiveness of Extended Buprenorphine-Naloxone Treatment for Opioid-Dependent Youth: Data from a Randomized Trial

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Abstract

Introduction—The objective is to estimate cost, net social cost, and cost-effectiveness in a clinical trial of extended buprenorphine-naloxone treatment versus brief detoxification treatment in opioid-dependent youth.

Methods—Economic evaluation of a clinical trial conducted at 6 community outpatient treatment programs from July 2003 to December 2006 including 152 patients aged 15 to 21 years who were randomized to 12 weeks of buprenorphine-naloxone (BUP) or a 14-day taper (DETOX). BUP patients were prescribed up to 24 mg per day for 9 weeks and then tapered to zero at the end of week 12. DETOX patients were prescribed up to 14 mg per day and then tapered to zero on day 14. All were offered twice weekly drug counseling. Data were collected prospectively during the 12-week treatment and at follow-up interviews at months 6, 9, and 12.

Dr Woody is a member of the RADARS postmarketing study external advisory group whose job is to assess abuse of prescription medications. Denver Health administers RADARS and Abbott, Cephalon, Endo, Pricara/Ortho-McNeil, Purdue Pharma, and Shire subscribe to its data. Ortho-McNeil and Purdue Pharma funded similar work by him prior to his joining RADARS and Schering-Plough, the European distributor for buprenorphine-naloxone, funded his travel costs to meetings in Sweden and Finland in June 2008 to present data from the study on whose outcomes this study is based. There are no other conflicts of interest to report. There are no contractual constraints on publishing imposed by the funder.

Clinical trial registration: Clinical trials.gov identification number for the trial upon which these data were obtained is: NCT00078130.

Results—The 12-week outpatient study treatment cost was \$1514 ($p<0.001$) higher for BUP relative to DETOX. One-year total direct medical cost was only \$83 higher for BUP ($p=0.97$). The cost-effectiveness ratio of BUP relative to DETOX was \$1,376 in terms of 1-year direct medical cost per quality-adjusted life year (QALY) and \$25,049 in terms of outpatient treatment program cost per QALY. The acceptability curve suggests that the cost-effectiveness ratio of BUP relative to DETOX has an 86% chance of being accepted as cost-effective for a threshold of \$100,000 per QALY.

Conclusions—Extended buprenorphine-naloxone treatment relative to brief detoxification is cost effective in the U.S. health care system for the outpatient treatment of opioid-dependent youth.

Keywords

Buprenorphine; cost-effectiveness; opioid-dependent youth

The standard of treatment for opioid dependent youth remains brief detoxification followed by counseling despite documented high relapse rates.¹ While methadone maintenance is accepted as one of the most effective treatments for opioid dependence, the use of opioid agonists in adolescents is limited. Reasons include availability of agonists to only those over 18 years of age; daily visits to specialized treatment programs; concerns raised by both providers and the community about starting a youth on treatment that is often long-term and with unknown long-term consequences; and reluctance to bring young patients into daily contact with older persons having extensive histories of addiction and antisocial behavior.

Sublingual buprenorphine, a schedule-III, mu-opioid receptor partial-agonist, may be an effective alternative for acute management and longer-term treatment of opioid-dependent youth.^{2,3} Buprenorphine may be particularly attractive to young adults because of the lower risk for death from overdose and the fact that it can be prescribed by licensed physicians including primary care providers in their medical offices. Yet buprenorphine-naloxone (sold as Suboxone® in the U.S.) is expensive, which can substantially limit access. Given the cost-constrained environment, gaps in private insurance coverage (generally and specifically for buprenorphine-naloxone), and the large role of public funding for this population, understanding the cost-effectiveness of buprenorphine for adolescents and young adults is critical for addressing treatment barriers.

In what follows, we present data on the costs and effects that were observed in a trial that compared a more extended course of counseling and buprenorphine-naloxone treatment to counseling and short-term detoxification. We use a common clinical effectiveness measure, opioid-free urine, but also broaden the definition of effectiveness to include the patient's quality of life and social consequences related to addiction and its treatment.^{4–6} We evaluated costs and effects from the perspective of the payer of health care services (i.e. the insurer), the substance abuse outpatient treatment program (i.e., the provider), and society. The multiple perspectives provide insight into not only the economic impact on different stakeholders resulting from more extended use of buprenorphine-naloxone, but also its social benefits.

METHODS

The Trial

This clinical trial, conducted by the U.S. National Institute of Drug Abuse Clinical Trials Network, recruited youth ages 15–21 who met DSM-IV criteria for opioid dependence with physiologic features in 6 community outpatient treatment programs in New Mexico, North Carolina, Maryland, Maine, and Pennsylvania.⁷ 152 participants were randomized between July 2003 and December 2005 to either a 2-week buprenorphine-naloxone detoxification (DETOX) or a 12-week course of buprenorphine-naloxone (BUP). Patients in the DETOX

group were prescribed up to 14 mg per day and then tapered to 0 mg on day 14. Patients in the BUP group were prescribed up to 24 mg per day for 9 weeks. Tapering began at 9 weeks and ended with 0 mg at the end of week 12. Participants were observed 1.5 to 2 hours during the induction phase and only as needed during the maintenance phase. All participants were offered individual and group counseling for 12 weeks using standard manualized techniques.⁸ Participants' clinical status was assessed weekly during the 12 weeks of study treatment and at months 6, 9, and 12.

The study found that participants in the BUP group had lower proportions of opioid-positive urine test results at weeks 4 and 8 but not at week 12 ($p = 0.09$). During weeks 1 through 12, participants in the BUP group reported less opioid use ($p = 0.001$), less injecting ($p = 0.01$), and less nonstudy addiction treatment ($p = 0.001$). The design and clinical results of the study have been reported previously.³ Participants on average were 19 years of age, had used opioids for 2.5 years, and had preference-weighted health status scores that averaged 0.50. Heroin was the main substance used for 41% of participants, opiate analgesics for 26%, and poly-drug for 8%. There were no significant differences between the groups for any of the baseline characteristics.

Cost measurement

Study outpatient treatment program costs were derived from the therapy and medications delivered in the participating outpatient programs. Buprenorphine and naloxone were valued based on wholesale acquisition cost; prices for other pharmaceuticals that patients received were based on adjusted average wholesale price.⁹ Drug administration and counseling were valued by use of average unit costs derived from surveys that used the methods of the substance abuse services cost analysis program (SASCAP)¹⁰ which we administered to the study outpatient treatment programs in early 2006. Resulting cost estimates were \$27, \$9, and \$30 per individual, group, and family therapy session and \$74, and \$22 for BUP administration during the induction and maintenance phases.

Medical service use incurred outside the study treatment programs was derived from self-report. Non-medical services were derived from self-reported travel time to therapy sessions, school attendance, workforce participation, and criminal behavior. These measures were collected at baseline, weeks 4, 8, and 12, and months 6, 9, and 12. We valued the medical service use based on the mean of reimbursements and out-of-pocket expenditures for beneficiaries aged 12–25 years with addictive disorders derived from the 2003 MEDSTAT MarketScan database

Per-person costs are then computed by summing across the multiplication of the units of service times their unit prices. All costs were based on U.S. prices and health care expenses and adjusted by the consumer price index to reflect 2006 U.S. dollars. [Price weights are available upon request]

Measures of effectiveness

The primary clinical effectiveness endpoint is a measure of the time free of opioids, which we refer to as opioid-free years. This measure is based on the urine test results during weeks 1 through 12 and months 6, 9 and 12. The primary economic effectiveness endpoint is a measure that captures both the duration of life and the quality of life, the quality-adjusted life year (QALY). Given that there was only one death in the study, this measure primarily reflects the preference-weighted results of the EQ-5D, 11¹² a generic instrument for measuring health-related quality of life, that was administered at weeks 4, 8, and 12, and months 6, 9, and 12. The preference-weighted EQ-5D produces a score between −0.594 and 1 that reflects a preference for the respondent's current health state. −0.594 is the preference for the fully

dysfunctional health state (worse than death) and 1 is the preference for the fully functional health state.

Cost-effectiveness

Our primary outcomes are from the perspective of the payer: the 1-year direct medical cost per QALY and the 1-year direct medical costs per opioid-free year. Direct medical costs include the costs of the study outpatient treatment program-provided therapy and buprenorphine-naloxone, as well as all medical costs incurred outside the treatment program. The incremental cost per QALY ratio allows for broader economic interpretation because the effectiveness measure is a final outcome and permits comparisons across diseases and interventions. The incremental cost per opioid-free year ratio allows for more specific interpretation within the substance abuse treatment field.

Our secondary cost-effectiveness outcomes take the narrower perspective of the outpatient treatment program. The difference between the secondary and primary cost-effectiveness outcomes is the substitution of outpatient treatment costs for the sum of all direct medical costs. For all of our endpoints we also report results for a 12-week time horizon.

Net social cost

We also take a broader social perspective by estimating net social cost which includes, in addition to direct medical costs, crime costs, travel costs, and benefit offsets associated with school attendance and workforce participation. We valued absence from school during the trial based on lost earnings resulting from less education. We valued a full year of lost education at \$80,000 in lost lifetime earnings based on econometric estimates in the U.S. of the returns to a year of schooling¹³ and of lifetime earnings for persons aged 20 to 24.¹⁴ We valued the benefits of total time in workforce participation by the reported wage. Finally, we valued crime based on the recent work of McCollister and colleagues¹⁵ where they estimate the sum of a valuation of victim costs and the risk of a homicide, and the value of charges and convictions for crimes based on criminal justice system costs. These per crime estimates were used to value self-reports of assault, robbery, auto theft, shoplifting, drug offenses, and other non-victim crimes.

Net social costs are calculated as the sum of all costs and negative benefits. We estimate net social costs over the 1-year time horizon and also make estimates over the 12-week time horizon. The social valuation of education, work, and crime is more conceptual than concrete, therefore, we treat it as a secondary outcome measure.

Analysis

We compared participant characteristics by use of Fisher's exact tests for categorical variables and Student's t-tests for continuous variables.

We used separate multivariable models to predict the cost of 1) study-provided therapy, 2) study-provided buprenorphine-naloxone, 3) nonstudy-provided therapy, 4) nonstudy-provided buprenorphine-naloxone, buprenorphine, and methadone, 5) detoxification, rehabilitation, and hospitalization, 6) other medical services, 7) other pharmaceuticals, 8) criminal activity, 9) travel, 10) school attendance, and 11) workforce participation. Separate models were necessary because of the differences in the data generating mechanism and amount of missing data across cost elements. Predicted study outpatient treatment costs were the sum of the predictions from models 1 and 2; predicted total direct medical costs were the sum of the predictions from models 1–7; and predicted net social costs were the sum of all 11 models. The 12-week estimates were based on summing over the weekly or monthly predictions for the first 12 weeks, and the 1-

year estimates were based on summing over the predictions for the first 12 weeks plus months 6, 9, and 12.

We also used multivariable models to predict preference-weighted quality of life and the probability of opioid-positive urine. Predicted QALYs and opioid-free years were calculated by taking the area under the curve of the predicted results plotted over the first 12-weeks for the 12-week estimates, and over the year for the 1-year estimates. We used the method of recycled predictions¹⁶ to estimate predicted costs, QALYs, and opioid-free years.

Missing data—Because they were recorded when provided to participants, there were no missing data for study-provided medication or therapy sessions. A total of 24.7% of nonstudy medical service use data were missing, as were 40.4% of data on criminal activity, 39.1% of data on preference-weighted quality of life, and 47.6% of data on opioid-positive urine. Because the clinical paper reported no significant evidence of departures from ignorable missingness³, we addressed missing data by use of inverse probability weighting (IPW).^{17,18}

Statistical Models—Continuous variables were fit by use of weighted generalized linear models (GLM) with the selection of link functions and families guided by the fit of the data.¹⁶ Categorical variables -- including the missing weights -- were fit by use of logistic regression models.

Sampling Uncertainty—P-values and standard errors were estimated by use of a nonparametric bootstrap within the multivariate framework. Acceptability curves -- which report the likelihood that the therapy is good value for different thresholds for defining value -- were estimated by use of parametric methods based on the parameters estimated via the non-parametric bootstrap.¹⁶

Sensitivity Analysis

We test the sensitivity of our estimates to model specification by re-estimating regressions using ordinary least squares (OLS) rather than GLM models. We also tested the influence of site-specific cost estimates, an allocation of fixed-costs of 36% (based on DATCAP survey) to outpatient treatment program activities, and the influence on our estimates of generic pricing of BUP at 30% of wholesale acquisition cost.¹⁹

RESULTS

Costs

Table 1 shows the predicted costs experienced by the treatment groups. Results for the first 12 weeks are on the left and results for the entire year are on the right. Costs of the 12-week outpatient treatment program were \$1514 (SE, 117; $p < 0.001$) higher for BUP relative to DETOX. The sum of all therapy and treatment drug costs related to substance abuse treatment, regardless of whether they were incurred as part of the study outpatient treatment program, was \$983 (SE, 195; $p \leq .001$) higher for BUP at 12 weeks and \$1316 (SE, 462; $p = 0.005$) higher for BUP at 1 year.

The point estimate for the incremental direct medical costs during the year of follow-up was \$83 (SE, 2415) higher for the BUP group, which indicates that medical savings elsewhere in the healthcare system offset the increased cost associated with longer-term therapy and treatment drugs. As would be expected when there is no apparent difference in cost, the \$83 difference was not significant ($p = 0.97$). Similar patterns were observed at 12 weeks, but the cost-offsets were smaller resulting in a larger cost differences.

As shown when comparing the first two sets of bars in Figure 1, costs were not very sensitive to model specification. When costs are modeled with more transparent, but less robust and less efficient ordinary least squares regressions, the 12-week results are nearly identical and the 1-year results are even more favorable toward BUP. The difference in cost was not sensitive to variations in treatment center-specific cost nor to the consideration of fixed costs at these centers. The one area where the costs of BUP relative to DETOX could change considerably is if a generic alternative to Suboxone becomes available. Given that the U.S. patent is set to expire soon, this may be important.

Net Social Costs

Table 1 also shows nonmedical social costs by type of cost. Among the categories of nonmedical social costs, the difference in crime costs was the largest, $-\$26,224$ (SE, 23,967; $p=0.28$) at one year. This difference dwarfed all other categories of costs, but the high variance of crime costs - driven by infrequent high cost crimes - kept it from being statistically significant. (We summarize the elements of crime costs in the Appendix table.) Only travel time for study-provided treatment was statistically significant (1-year incremental cost, $\$183$ higher for BUP; SE, 50; $p < 0.001$). Total net social costs, which include total direct medical costs, were substantially less for BUP over the entire year ($-\$31,264$; SE=24,375; $p=0.20$), but this result was also not statistically significant.

QALYs and Opioid-Free Years

Finally, table 1 shows the average QALYs and opioid-free years experienced by the treatment groups. During the first 12 weeks, BUP patients experienced an average of 0.183 (out of a possible 0.25) QALYs; DETOX patients experienced an average of 0.165 QALYs; for a significant increase of 0.018 QALYs (SE, 0.009; $p = 0.04$). During the same period the average increase in opioid-free years was 0.064 (SE, 0.017; $p < 0.001$). During the full 1 year, the point estimate for the difference in QALYs was 0.060 (SE, 0.034; $p = 0.08$), while the difference in incremental opioid-free years was 0.270 years (SE, 0.068; $p < 0.001$).

Cost-effectiveness

Table 2 shows the cost-effectiveness ratios from the perspective of the payer and the outpatient treatment program (no cost-effectiveness ratios are calculated from the societal perspective, only net social costs). For the 1-year time horizon, the direct medical cost per QALY was $\$1,376$ (incremental costs of $\$83$ divided by incremental QALYs of .060), while the study outpatient treatment program cost per QALY was higher at $\$25,049$. The incremental direct medical cost per opioid-free year of BUP was $\$308$, while the study outpatient treatment program cost per opioid-free year was $\$5,610$. Comparisons of costs and effects over the shorter 12 weeks of follow-up are similar, but not as favorable as the 1-year results.

We display statistical uncertainty for the 1-year cost per QALY by use of an acceptability curve (Figure 2). This curve illustrates that high levels of confidence are achieved at relatively low levels of willingness to pay per QALY (i.e., over 60% confidence at $\$40,000$ per QALY), but the curve flattens out before it reaches 95% confidence. For example, for a willingness to pay of $\$100,000$ per QALY, we can be 86% confident that BUP was good value. At any level of willingness to pay, the cost per QALY from the perspective of the study outpatient treatment program always has a lower probability of being acceptable. The 95% confidence intervals for the cost-effectiveness ratios of cost per opioid-free year are (Dominates to $\$21,096$) for direct medical costs and ($\$3,784$ to $\$10,642$) for study outpatient treatment costs.

DISCUSSION

From the perspective of the payer of direct medical costs, the cost-effectiveness ratio over the 1-year horizon was \$1,376 per QALY and \$308 per opioid-free year. While the point estimates of cost-effectiveness are well within the range of what would be considered cost effective, there is a considerable range of sampling uncertainty, particularly with respect to the results based on QALYs. For example, the acceptability curve shows that the cost-effectiveness ratio of BUP relative to DETOX has an 86% chance of being accepted as cost-effective for a threshold of \$100,000 per QALY.²⁰ This finding means that at this threshold we cannot reject the null hypothesis of no difference with 95% confidence. However, the 95% confidence interval for the cost per opioid-free year suggests that for this endpoint the study result was positive so long as we are willing to pay \$21,100 per opioid-free year. Putting these two results together, we conclude that the trial provides good, but not definitive, evidence that extended buprenorphine-naloxone treatment versus brief detoxification represents good value for this population of opioid-dependent youth.

A definitive declaration of cost-effectiveness would require that the cost-effectiveness ratio be below society's willingness to pay for the unit of effectiveness 95% of the time. One problem with such a declaration is that the willingness to pay for a unit of effectiveness is unknown and can vary by setting. For example, in the U.S. the cited range is typically from \$50,000 to \$200,000 per QALY.²⁰ For effectiveness measures that are clinical in nature, such as an opioid-free year, even rules of thumb are unavailable. A second problem, specific to our study, is that the differences in QALYs are only marginally significant and lead to a cost-effectiveness ratio that is not statistically cost-effective. The clinical outcome is highly statistically significant, but there is no threshold from which to test the statistical significance of the cost-effectiveness ratio base on the clinical outcome. Thus, we are left with good, but not definitive evidence.

From the perspective of the outpatient treatment program initiating the intervention, the cost-effectiveness ratio over the 1-year horizon was \$25,049 per QALY and \$5,610 per opioid-free year. The lower ratio faced by payers of direct medical costs may suggest that they have a greater incentive for adoption of the intervention than do the treatment programs and that insurers would benefit from covering extended buprenorphine treatment.

Providing 12 weeks of buprenorphine-naloxone treatment compared to brief detoxification with buprenorphine-naloxone increased the outpatient program treatment cost by \$1514 ($P < .001$). When all direct medical costs are considered, rather than only study-provided drug treatment, the 1-year incremental direct medical costs were only \$83 ($p = 0.97$). From a societal perspective, in which nonmedical costs are also included, there was a net social savings of \$31,264 ($p = 0.20$). These differing cost estimates reinforce the finding that the economic impact of BUP depends on the perspective from which it is evaluated. While the outpatient treatment program initiating the intervention would incur additional expenses, these expenses appear to be offset elsewhere in the healthcare system with additional savings generated in society largely from crime reduction. These offsets were considerable even in a population of youth with shorter addiction histories than are typical in outpatient treatment programs that serve older patients. They result largely because opioid dependent youth present to treatment with multiple co-existing conditions such as poor school attendance, criminal behaviors and juvenile justice system involvement and psychiatric disorders.²¹ The favorable, though not statistically significant, net social costs of the intervention suggest that social benefits may result if treatment programs implement buprenorphine treatment for youth.

This is the first cost-effectiveness study of extended buprenorphine-naloxone treatment in opioid-dependent youth relative to detoxification. While in adults the comparison has usually been relative to methadone treatment^{22–24}, the limited use of agonist maintenance for youth

makes comparison with detoxification the more relevant comparator. Methadone use for adolescents has been limited by stigma and regulations that require those under 18 to have two documented, unsuccessful drug-free treatments within a 12-month period, and that a legal guardian provide consent in writing before starting methadone maintenance.

The low follow-up rate is a limitation of this study. Because we did not find evidence of non-ignorable missingness, we addressed this issue with missing data methods that assume the data are missing at random. Lack of difference between our results and results observed when we employ an assumption of missing completely random means it is unlikely that the low follow-up rates negate our main findings. The low follow-up rate, however, does reduce the power of the 1-year result.

This study is also limited in its ability to inform policy related to the ideal duration of treatment. The economic impact of long-term maintenance with buprenorphine-naloxone may be very different than the 12-week extended-treatment protocol studied here, but this alternative would require further study. Substantial use of the treatment drug within the BUP group after the 12 week course of treatment was evident in our data, but those extending treatment did so beyond the treatment protocol and can not be reliably evaluated outside of the intent-to-treat approach taken in this analysis. Finally, the use of opioid-free urines for the calculation of cost-effectiveness ignores decreases in use of opioids which may have additional cost-benefits.

In conclusion, extended Buprenorphine-naloxone treatment for youth relative to detoxification may have social benefits and be cost-effective. It is of greater value to the insurer than to the outpatient treatment program because the effectiveness of treatment results in medical cost offsets that are not captured by the treatment program. This suggests that there is an incentive within health insurance plans to cover the provision of these services. Similarly, the apparent reduction in crime-related costs in the BUP group is a benefit to society that is not captured by the health care system. This finding suggests a role for public funding of effective treatment programs such as extended buprenorphine-naloxone treatment for opioid-dependent youth.

Acknowledgments

NIDA grant: R01 DA017221 (Dr. Polsky) and NIDA grants #U10-DA 13043 and K05-DA 17009 (Dr. Woody); NIDA-AACAP-K12 DA00357 (Subramaniam, P.I.).

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Appendix Table

Crimes committed and charged

Crime	Crimes Committed		Crimes Committed	
	events	% of total	Cost	% of total
assault	16	8%	\$ 2,499,952	92.5%
robbery	2	1%	\$ 63,116	2.3%

Crime	Crimes Committed		Crimes Committed		
	events	% of total		Cost	% of total
auto theft	4	2%	\$	26,536	1.0%
shoplifting	17	8%	\$	9,673	0.4%
drug offense	150	73%	\$	93,487	3.5%
other	17	8%	\$	10,387	0.4%
Total	206	100%	\$	2,703,151	100%

Crime	Charges/Convictions		Charges/Convictions		
	events	% of total		Cost	% of total
assault	10	14%	\$	106,060	19.2%
robbery	1	1%	\$	15,612	2.8%
auto theft	2	3%	\$	8,420	1.5%
shoplifting	8	11%	\$	27,184	4.9%
drug offense	52	71%	\$	395,148	71.5%
other	3	4%	\$	19,757	3.6%
Total	73	100%	\$	552,424	100%

Crime	Total		Total		
	events	% of total		Cost	% of total
assault	26	9%	\$	2,606,012	80.0%
robbery	3	1%	\$	78,728	2.4%
auto theft	6	2%	\$	34,956	1.1%
shoplifting	25	9%	\$	36,857	1.1%
drug offense	202	73%	\$	488,635	15.0%
other	19	7%	\$	30,145	0.9%
Total	279	100%	\$	3,255,575	100%

Figure 1.
Sensitivity Analysis of Costs*

*Baseline: Results from Table 1 which use GLM models. OLS: Results from Table 1 reproduced using ordinary least squares models. Site-specific: Costs of therapy and administration re-estimated with site-specific unit costs, rather than averages, estimated with OLS. 3mo fixed: Costs of therapy and administration re-estimated with study outpatient treatment program costs that include an allocation for fixed costs estimated with OLS. Generic: Study drug costs re-estimated at 30% of WAP price with OLS.

Figure 2.

Acceptability Curves*

*Acceptability curves for the cost per QALY calculated for 1 year of follow-up from the perspective of the substance abuse treatment program (dashed line) and the payer of health care services (solid line).

Table 1
Adjusted Mean Costs and Outcomes, Stratified by Time and Treatment Group

Cost category	12-Weeks				1-Year			
	BUP	DETOX	Diff	P-value	BUP	DETOX	Diff	P-value
Direct Medical costs								
Outpatient Substance abuse treatment								
Therapy								
Study-provided	383	148	234	<0.001	383	148	234	<0.001
Nonstudy	138	261	-123	0.07	879	870	9	0.97
Treatment Drugs								
Study-provided	1561	282	1279	<0.001	1561	282	1279	<0.001
Nonstudy	15	422	-407	0.002	1017	1223	-206	0.55
Nonstudy detoxification, rehabilitation, and hospitalization	584	775	-191	0.61	4289	5648	-1358	0.55
Other nonstudy medical services	92	121	-28	0.28	342	434	-92	0.28
Other nonstudy pharmaceuticals	220	160	60	0.33	822	605	217	0.34
Total study-provided outpatient substance abuse treatment cost	1944	430	1514	<0.001	1944	430	1514	<0.001
Total outpatient substance abuse treatment cost (study and nonstudy)	2097	1114	983	<0.001	3839	2523	1316	0.005
Total direct medical costs	2993	2169	824	0.07	9293	9210	83	0.97
Nonmedical social costs								
Crime cost	7810	19,181	-11,371	0.32	19,999	46,223	-26,224	0.28
Travel cost for drug treatment								
Study-provided treatment	342	159	183	<0.001	342	159	183	<0.001
Nonstudy treatment	103	143	-40	0.23	424	564	-140	0.23
Education (offset)	-5574	4524	-1050	0.45	-19,908	-15,975	-3933	0.46
Work (offset)	-2689	2379	-310	0.38	-11,301	-10,069	-1232	0.38
Total nonmedical social costs	-9	12,580	-12,588	0.28	-10,444	20,902	-31,347	0.20
Net social costs (nonmedical social costs + total direct medical costs)	2984	14749	-11,765	0.31	-1151	30,112	-31,264	0.20
Outcomes								
Quality-adjusted life years	0.183	0.165	0.018	0.04	0.779	0.718	0.060	0.08
Opioid-free years	0.178	0.114	0.064	<0.001	0.589	0.319	0.270	<0.001

In 2006 Dollars. Diff=BUP-DETOX.

Table 2

Incremental Cost-Effectiveness Ratios of BUP relative to DETOX

	12 weeks	1 year
Direct Medical Cost / QALY	44,672	1376
Study Cost / QALY	82,069	25,049
Study Cost / Opioid-Free year	23,602	5610
Direct Medical Cost / Opioid-Free year	12,847	308