Cost-Effectiveness of Extended-Release Naltrexone versus Buprenorphine-Naloxone to Prevent Opioid Relapse

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Introduction

- Evidence-based pharmacotherapy is recommended as the first line of treatment for OUD.[1]
- Buprenorphine, a partial opioid agonist, is typically combined with naloxone (BUP-NX) to address risks of misuse and diversion.
- Naltrexone, a full opioid antagonist, is frequently administered as a monthly extended-release injection (XR-NTX) to improve adherence.
- Evidence regarding the economic value of BUP-NX and, to a larger extent, XR-NTX is limited, particularly evidence from clinical trials.[2,3]
- **The objective of this NIDA CTN study was to evaluate the cost-effectiveness of XR-NTX versus BUP-NX in the US randomized clinical trial testing their effectiveness in the prevention of opioid relapse among individuals initiating these pharmacotherapies in an inpatient detoxification setting.**

Methods

- Costs were evaluated from the healthcare sector and societal perspectives over the 24-week intervention and through the 36-week observation period.
- Our primary measure of effectiveness was the Quality-Adjusted Life-Year (QALY).
- We calculated incremental cost-effectiveness ratios (ICERs) to compare incremental costs to incremental effectiveness.
- Acceptability curves were constructed to estimate the uncertainty around the ICER point estimates. Acceptability curves display the probability that an ICER would fall below a given willingness-to-pay for a unit of the desired outcome, and thus be considered a good value (i.e., cost-effective).
- Sensitivity analyses included assuming a higher cost of XR-NTX (the Federal Supply Schedule price of $704/injection vs the wholesale acquisition cost of $1,309/injection), substituting BUP-NX film for the generic tablets, and excluding participants who were not successfully initiated on their randomized treatment (i.e. per-protocol).

Predicted Mean Costs and Outcomes

Healthcare Sector Perspective

	24-Weeks				36-Weeks			
Outcomes	**XR-NTX**	**BUP-NX**	**Diff (SE)**	**P-value**	**XR-NTX**	**BUP-NX**	**Diff (SE)**	**P-value**
Costs								
Study-provided detoxification	$3,114	$2,687	$427 (39)	<0.001	$3,114	$2,687	$427 (39)	<0.001
Study-provided treatment	$2,167	$917	$1,250 (113)	<0.001	$2,167	$917	$1,250 (113)	<0.001
Non-study treatment	$2,475	$1,862	$613 (566)	0.28	$3,650	$3,189	$462 (757)	0.54
Other non-study medical cost	$11,168	$8,140	$3,027 (2,065)	0.14	$18,065	$15,692	$2,374 (40,095)	0.56
Total Costs	**$18,923**	**$13,606**	**$5,317 (2,120)**	**0.01**	**$26,997**	**$22,484**	**$4,512 (4,152)**	**0.28**
Effectiveness								
QALYs*	0.790	0.797	-0.007 (0.011)	0.66	0.850	0.856	-0.006 (0.012)	0.77
Abstinent Years*	0.476	0.533	-0.057 (0.032)	0.08	0.545	0.596	-0.051 (0.029)	0.08

Societal Perspective

	24-Weeks				36-Weeks			
Outcomes	**XR-NTX**	**BUP-NX**	**Diff (SE)**	**P-value**	**XR-NTX**	**BUP-NX**	**Diff (SE)**	**P-value**
Costs								
Study-provided detoxification	$3,114	$2,687	$427 (39)	<0.001	$3,114	$2,687	$427 (39)	<0.001
Study-provided treatment	$2,167	$917	$1,250 (113)	<0.001	$2,167	$917	$1,250 (113)	<0.001
Non-study treatment	$2,475	$1,862	$613 (566)	0.28	$3,650	$3,189	$462 (757)	0.54
Other non-study medical cost	$11,168	$8,140	$3,027 (2,065)	0.14	$18,065	$15,692	$2,374 (4,095)	0.56
Criminal activity	$2,801	$5,630	-$2,829 (2,082)	0.17	$4,371	$8,550	-$4,180 (4,420)	0.34
Workplace productivity (offset)^	-$10,243	-$11,511	$1,268 (966)	0.19	-$15,293	-$16,667	$1,374 (1,170)	0.24
Patient costs	$78	$295	-$217 (13)	<0.001	$78	$295	-$217 (13)	<0.001
Total Costs	**$11,559**	**$8,020**	**$3,540 (3,215)**	**0.27**	**$16,153**	**$14,663**	**$1,490 (6,268)**	**0.81**
Effectiveness								
QALYs*	0.790	0.797	-0.007 (0.011)	0.66	0.850	0.856	-0.006 (0.012)	0.77
Abstinent Years*	0.476	0.533	-0.057 (0.032)	0.08	0.545	0.596	-0.051 (0.029)	0.08

Costs are in 2016 US dollars

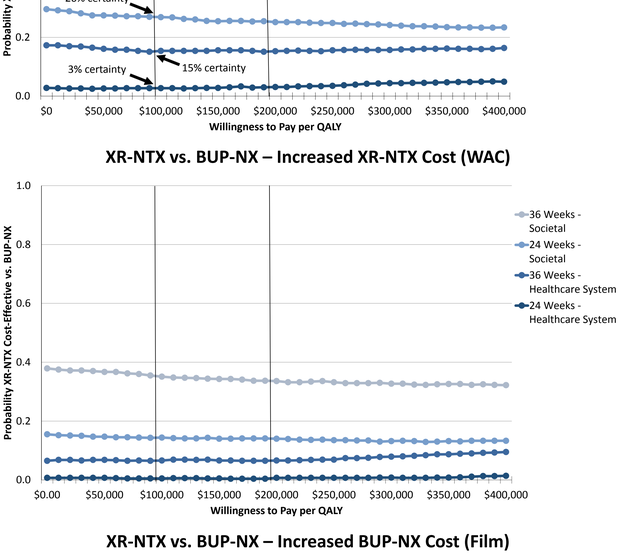
* Annualized

^ Offset indicates that a higher value is a benefit to society

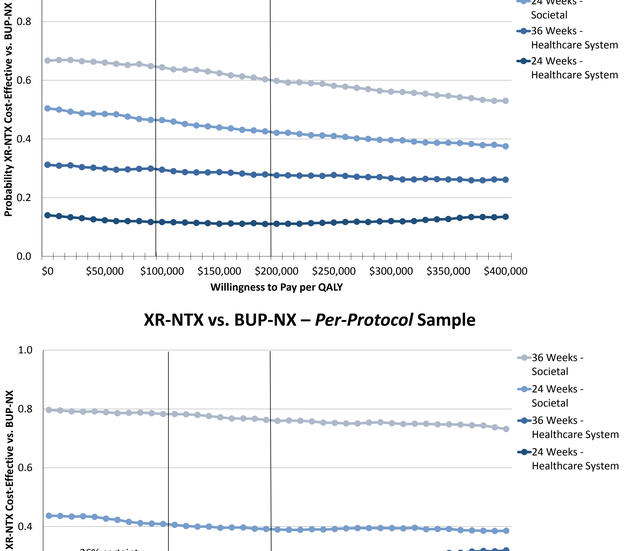
XR-NTX = extended-release naltrexone; BUP-NX = buprenorphine-naloxone; SE = standard error; QALY = quality-adjusted life-year

Cost-Effectiveness Acceptability Curves

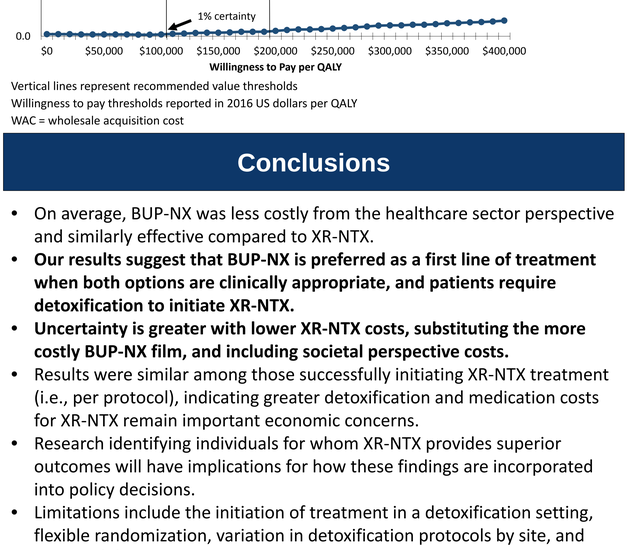
XR-NTX vs. BUP-NX



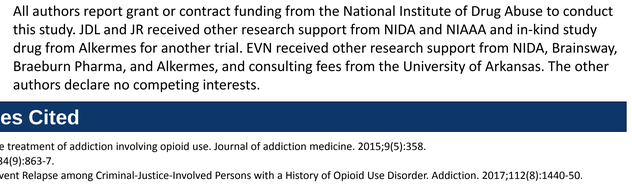
XR-NTX vs. BUP-NX – Increased XR-NTX Cost (WAC)



XR-NTX vs. BUP-NX – Increased BUP-NX Cost (Film)



XR-NTX vs. BUP-NX – *Per-Protocol* Sample



Vertical lines represent recommended value thresholds

Willingness to pay thresholds reported in 2016 US dollars per QALY

WAC = wholesale acquisition cost

Results

- The mean cost, per participant, of XR-NTX exceeded that of BUP-NX, including $427 greater study-provided detoxification cost and $1,250 greater study-provided medication/therapy cost.
- Although the average total costs for XR-NTX exceeded those for BUP-NX at each time point from both perspectives, only the 24-week average total healthcare sector cost difference was statistically significant.
- Differences in effectiveness were not statistically significant.
- **At $100,000/QALY, XR-NTX was preferred to BUP-NX from a healthcare-sector perspective with only 3% and 15% certainty at 24 and 36 weeks, respectively, and from a societal perspective with 26% and 48% certainty, respectively.**
- **Certainty rose assuming the higher cost of XR-NTX and fell substituting BUP-NX film.**
- **Among the per-protocol sample, XR-NTX remained the less preferred option from a healthcare sector perspective with 1% and 26% certainty at 24 and 36 weeks, respectively.**

Conclusions

- On average, BUP-NX was less costly from the healthcare sector perspective and similarly effective compared to XR-NTX.
- **Our results suggest that BUP-NX is preferred as a first line of treatment when both options are clinically appropriate, and patients require detoxification to initiate XR-NTX.**
- **Uncertainty is greater with lower XR-NTX costs, substituting the more costly BUP-NX film, and including societal perspective costs.**
- Results were similar among those successfully initiating XR-NTX treatment (i.e., per protocol), indicating greater detoxification and medication costs for XR-NTX remain important economic concerns.
- Research identifying individuals for whom XR-NTX provides superior outcomes will have implications for how these findings are incorporated into policy decisions.
- Limitations include the initiation of treatment in a detoxification setting, flexible randomization, variation in detoxification protocols by site, and censored data.

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Declaration of Interests

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