Cost-Effectiveness Implications of Increasing the Efficiency of the Detoxification Process Prior to Extended-Release Naltrexone Initiation for Opioid Use Disorder Treatment

Sean M. Murphy[1], Philip J. Jeng[1], Kathryn E. McCollister[2], Jared A. Leff[1], Joshua D. Lee[3], Edward V. Nunes[4], Patricia Novo[5], John Rotrosen[5], Bruce R. Schackman[1]

[1]Department of Healthcare Policy & Research, Weill Cornell Medical College, New York, NY, USA; [2]Department of Public Health Sciences, University of Miami Miller School of Medicine, Miami, FL USA; [3]New York University School of Medicine, New York, NY USA; [4]New York State Psychiatric Institute, [5]Columbia University Medical Center, New York, NY USA

Background

A randomized comparative effectiveness trial, NIDA CTN-0051: Extended-Release Naltrexone vs. Buprenorphine for Opioid Treatment, **compared the two medications head-to-head among persons seeking treatment at an inpatient detoxification facility**. Treatment protocols require participants initiating extended-release naltrexone (XR-NTX), but not buprenorphine-naloxone (BUP-NX), to be fully detoxified from opioids, which resulted in fewer persons initiating XR-NTX, higher detoxification costs, and a higher relapse rate. Opioid relapse rates did not differ among participants who successfully initiated pharmacotherapy

Objective

To estimate the extent to which a more efficient model of XR-NTX initiation, characterized as increased probability of initiation and a shorter detoxification duration, would improve the economic value of XR-NTX relative to BUP-NX.

Methods

- **Sample:** all participants (n = 283) randomized to XR-NTX
- **Design:** secondary analysis of CTN-0051 participant data
- **Analysis**: latent class analysis to identify and assign detoxification pharmacotherapy use patterns including: clonidine, buprenorphine, methadone, benzodiazepines, GABA agents/muscle relaxants, and sleep/anxiety/antihistamine agents
- A two-stage, multivariable, generalized structural equation model (GSEM) was estimated to explore determinants of XR-NTX initiation and detoxification duration, while controlling for endogeneity/ simultaneity
- We combined results with information from our prior cost-effectiveness analysis, to recalculate expected costs and QALYs from the healthcare-sector perspective
- We tested for differences among alternative expected values of the XR-NTX arm and the existing mean values for the BUP-NX arm

Generalized Structural Equation Modeling Results

Characteristic	Stage 2: Initiated XR-NTX	Stage 1: Detoxification Duration (days)
Age	0.009	-0.003
Female	-0.001	0.109
White/Caucasian	0.592	0.027
High school	-0.352	0.109
Complications		
Medical	-1.600*	-0.246*
Alcohol	0.351	0.202
Drug	1.200	-0.385
Legal	0.253	0.274*
Family/Social	0.363	-0.036
Psychiatric	1.200	0.207
Class of pharmacotherapy combination		
1	Reference	Reference
2	0.365	0.038
3	-0.103	0.061
4	0.088	0.214
5	-1.000	0.412**
Site		
Site A	0.725	-0.709***
Site B	Reference	Reference
Site C	2.7*	-0.906***
Site D	4.4**	-1.100***
Site E	2.2	-0.748***
Site F	2.8**	-0.840***
Site G	0.523	-0.247
Site H	2.900	-1.900***
Detox days	0.059	Excluded
Constant	-2.1	2.700***
Public Insurance	Excluded	0.022
Private Insurance	Excluded	-0.326**
Employed	Excluded	-0.164**

P < 0.05 *, P < 0.01 **, P < 0.001 ***

Extended-release naltrexone & buprenorphine-naloxone could be of comparable economic value for treating opioid use disorder, if the initiation process is improved

Results

- We identified 5 detoxification pharmacotherapy combinations: 1) methadone, clonidine, muscle relaxants, anxiety medications (38%); 2) buprenorphine, clonidine, muscle relaxants (23%); 3) methadone (19%); 4) buprenorphine, anxiety agents (5%); and 5) muscle relaxants (15%)
- We identified 4 sites with better rates of XR-NTX initiation, shorter detoxification durations, and lower detoxification costs

Input/ Outcome	Original analysis	Revised Analysis			
		Site C	Site F	Site D	Site E
Inputs					
XR-NTX initiation probability	0.72	0.84	0.87	0.95	0.83
Detoxification daily cost	$424	$115	$177	$274	$348
detoxification days	8.00	5.47	6.92	6.50	6.47
Outcomes					
Average total cost to the healthcare sector for XR-NTX arm					
24 weeks	$18,923	$15,804	$15,923	$15,655	$17,218
36 weeks	$26,997	$22,377	$22,119	$20,852	$23,916
Average total cost to the healthcare sector for BUP-NX arm					
24 weeks	$13,606	$13,606	$13,606	$13,606	$13,606
36 weeks	$22,484	$22,484	$22,484	$22,484	$22,484
Average cost differential (XR-NTX vs. BUP-NX)					
24 weeks	$5,317*	$2,198	$2,317	$2,049	$3,612
36 weeks	$4,512	-$107	-$365	-$1,632	$1,432
Annualized QALY differential (XR-NTX vs. BUP-NX)					
24 weeks	−0.007	−0.007	−0.007	−0.007	−0.007
36 weeks	−0.006	-0.005	-0.005	-0.004	-0.005

P < 0.05 *

Discussion

- Treatment site was the only modifiable factor to simultaneously increase the likelihood of XR-NTX initiation and decrease detoxification duration
- The greater efficiencies associated with the 4 sites would reduce the average total 24-week cost of XR-NTX treatment to the healthcare sector, to the point where it does not differ significantly from BUP-NX treatment.
- QALYs did not differ between groups under any of the scenarios

Conclusion

Adopting an efficient model of XR-NTX initiation could result in XR-NTX and BUP-NX being of comparable economic value from the healthcare sector perspective for patients seeking treatment for opioid use disorder at an inpatient detoxification facility

Declaration of Interests

Dr. Murphy reports grants from NIH during the conduct of the study, and having consulted for Sandoz Inc. outside the submitted work. Ms. Novo reports grants from NIDA during the conduct of the study and outside the submitted work. Dr. Rotrosen reports grants from NIDA/NIH, medication for the present study from Indivior, and medication and/or funds for other studies (as principle investigator or investigator) from Indivior and Alkermes. Authors not named here have disclosed no conflicts of interest.

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