Participants' Preferences for BUP-NX or XR-NTX and Associations with Induction Success and Relapse Rates in the NIDA-CTN-0051, Extended-Release Naltrexone vs. Buprenorphine for Opioid Treatment (X:BOT)

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Abstract

Aim: Sublingual buprenorphine-naloxone (BUP-NX), a partial opioid agonist, and extended-release injection naltrexone (XR-NTX), an opioid antagonist, are very different opioid relapse-prevention pharmacotherapies. This analysis examined participants' preferences for BUP-NX and XR-NTX and whether these preferences, in combination with the medication to which they were randomized, were associated with induction success rates or relapse outcomes in the NIDA CTN-0051 Extended-Release Naltrexone vs. Buprenorphine for Opioid Treatment study.

Methods: An 11-item Motivation and Attitudes Regarding Study Medications survey was administered to participants at screening. Five-point Likert scale items assessed motivation for participating in the study and attitudes and expectations regarding study medications.

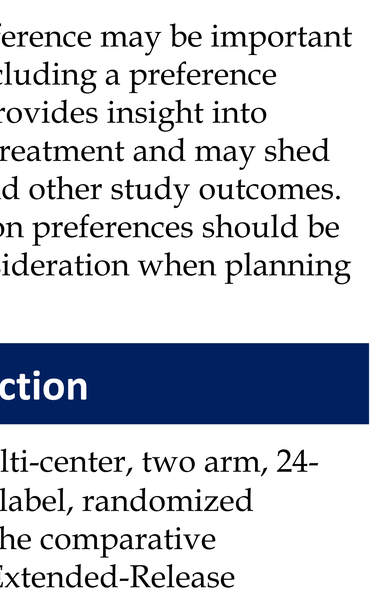
Results: 570 participants (100%) completed the survey. Willingness to accept either medication was a study inclusion criterion. However, 29% indicated preference for XR-NTX and 25% indicated preference for BUP-NX. Medication preference was significantly associated with induction success when participants were randomized to their preferred treatment. Specifically, participants preferring XR-NTX were more likely to fail induction if they were randomized to BUP-NX (18.7%), compared with those preferring BUP-NX (1.3%), p <0.001. There was no significant difference between participants preferring BUP-NX and those preferring XR-NTX in XR-NTX induction failures.

Medication preference may also be associated with relapse. Participants who preferred *and* were successfully inducted onto XR-NTX had lower relapse rates (47.1%) compared with those who preferred BUP-NX but were inducted onto XR-NTX (60.3%), although that difference was not significant (p = 0.16). For participants who were successfully inducted onto BUP-NX, there was no difference in relapse rates related to whether they were inducted onto their preferred medication (55.8%) or the alternative (55.7%).

Conclusion: Medication preference may be important clinically and in research. Including a preference measure in clinical studies provides insight into participants' perceptions of treatment and may shed light on induction success and other study outcomes. In clinical practice, medication preferences should be explored and taken into consideration when planning treatment.

Introduction

- NIDA-CTN-0051 was a multi-center, two arm, 24-week, parallel-group, open-label, randomized controlled trial to examine the comparative effectiveness and safety of Extended-Release Naltrexone (XR-NTX) versus Buprenorphine + Naloxone (BUP-NX).
- Primary endpoint of the study was time to relapse event across a 24-week treatment phase.
- Induction status was an important aspect of the analyses once the study was closed. Primary analyses were completed on the intent-to-treat (ITT) population and were also completed on the population of participants who inducted successfully onto treatment.
- In this population, it was more difficult to successfully induct onto XR-NTX than it was to induct onto BUP-NX. Preference for medication to which participants were assigned may be helpful for this induction process.
- Preference for the medication that was assigned is also potentially motivating for participants to stay with the treatment program and to not relapse back to opioids.



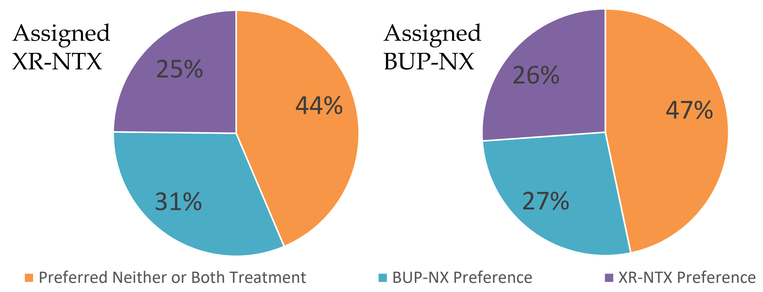
Methods

- The 11-item Motivation and Attitudes Regarding Study Medications survey was administered at screening. Participants responded using a 5-point Likert scale to statements assessing preference for either treatment.
- Participants who had no preference or showed preference for both treatments are not included in these analyses.
- Pearson's χ^2 test of association was used for comparisons of preference and induction status within each treatment assignment group, as well as preference and relapse status within each treatment assignment group.

Results

- 570 participants completed the survey at screening.
  - 167 (29%) indicated preference for XR-NTX
  - 145 (25%) indicated preference for BUP-NX
  - 258 (45%) indicated preference for neither or both.

Figure 1. Preference for BUP-NX and XR-NTX by Assigned Treatment Arm



- Of participants randomized to XR-NTX
  - 70 showed preference for XR-NTX, of which 19 (27.1%) were considered induction failures
  - 89 showed preference for BUP-NX, of which 31 (34.8%) were considered induction failures
  - Pearson's χ^2 test comparing these groups showed no significant difference (p=0.3)
- Of participants successfully inducted onto XR-NTX
  - 51 showed preference for XR-NTX, of which 24 (47.1%) relapsed by week 24
  - 58 showed preference for BUP-NX, of which 35 (60.3%) relapsed by week 24
  - Pearson's χ^2 test comparing these groups showed no significant difference (p=0.16)

Table 1. Induction and Relapse Status by Preference in the XR-NTX Arm

	Preference BUP-NX	Preference XR-NTX
Number of Participants Randomized	89	70
Induction Status N (%)		
Induction Success	58 (65.1%)	51 (72.9%)
Induction Failure	31 (34.8%)	19 (27.1%)
Number of Participants Successfully Inducted	58	51
Relapse Status N (%)		
Did Not Relapse	23 (40.0%)	27 (52.9%)
Relapsed	35 (60.3%)	24 (47.1%)

- Of participants randomized to BUP-NX
  - 75 showed preference for XR-NTX, of which 14 (18.7%) were considered induction failures
  - 78 showed preference for BUP-NX, of which 1 (1.3%) was considered an induction failure
  - Pearson's χ^2 test comparing these groups showed a statistically significant difference (p=<0.001)
- Of participants successfully inducted onto BUP-NX
  - 61 showed preference for XR-NTX, of which 34 (55.7%) relapsed by week 24
  - 77 showed preference for BUP-NX, of which 43 (55.8%) relapsed by week 24
  - Pearson's χ^2 test comparing these groups showed no significant difference (p=0.99)

Table 2. Induction and Relapse Status by Preference in the BUP-NX Arm

	Preference BUP-NX	Preference XR-NTX
Number of Participants Randomized	78	75
Induction Status N (%)		
Induction Success	**77 (98.7%)**	**61 (81.3%)**
Induction Failure	**1 (1.3%)**	**14 (18.7%)**
Number of Participants Successfully Inducted	77	61
Relapse Status N (%)		
Did Not Relapse	34 (44.2%)	27 (44.3%)
Relapsed	43 (55.8%)	34 (55.7%)

Significant associations found by Pearson's χ^2 test are in bold.

Discussion

- **Medication preference was significantly associated with induction success.** Participants preferring XR-NTX were significantly more likely to fail induction if they were randomized to BUP-NX (18.7%), compared with those preferring BUP-NX (1.3%). There was no significant difference between participants preferring BUP-NX and those preferring XR-NTX in XR-NTX inductions.
- **Preference was not found to be significantly associated with relapse.** Participants who preferred *and* received XR-NTX had lower relapse rates (47.1%) compared with those who preferred BUP-NX but received XR-NTX (60.3%), although that difference was not significant. For those who received BUP-NX, there was no difference in relapse rates related to whether they received their preferred medication (55.8%) or the alternative (55.7%).
- These results may support the important role of patient participation in treatment choice. This is consistent with studies in the area of substance use indicating that treatment preferences were related to reduction in substance use, although a recent meta-analysis demonstrated no effects in the majority of studies investigated ("Patient Preferences and Shared Decision Making," 2016).
- Overall, the idea of shared decision making between patients and providers seems important and useful for consideration in treatment decisions
- Future exploratory analyses:
  - Is there a difference in time to relapse between the different baseline preference groups?
  - Is there an association of baseline preference with relapse status in the ITT group?
- Limitations:
  - The survey used to assess preference asked one question about BUP-NX preference and a separate question about XR-NTX
    - Allows for participants to indicate they prefer both medications
    - Could instead ask (from another CTN study): "What best describes your preference for medication-based treatment?" with a 10-scaled continuum response ranging from (1) *Strongly prefer buprenorphine or methadone (agonist treatment)* to (10) *Strongly prefer extended release naltrexone (antagonist treatment).*
  - Only 55% of participants showed preference for only one treatment arm – XR-NTX or BUP-NX and therefore limited our sample size in each arm

Conclusions

- Baseline medication preference was significantly associated with inducting onto BUP-NX, although not with XR-NTX induction.
- Of participants randomized onto BUP-NX, participants who showed preference for XR-NTX at baseline were more likely to be induction failures than participants who showed preference for BUP-NX.
- Overall, there was no statistically significant association between baseline medication preference and relapse status at week 24.

References

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The authors of this poster have no conflicts of interest to declare.

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