Implementation Related Outcomes in the NIDA CTN SWIFT trial

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Presented at the ASAM Conference on 4/25/2025

Disclosure Information

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April 25th 2025 3:00 PM – 4:15 PM

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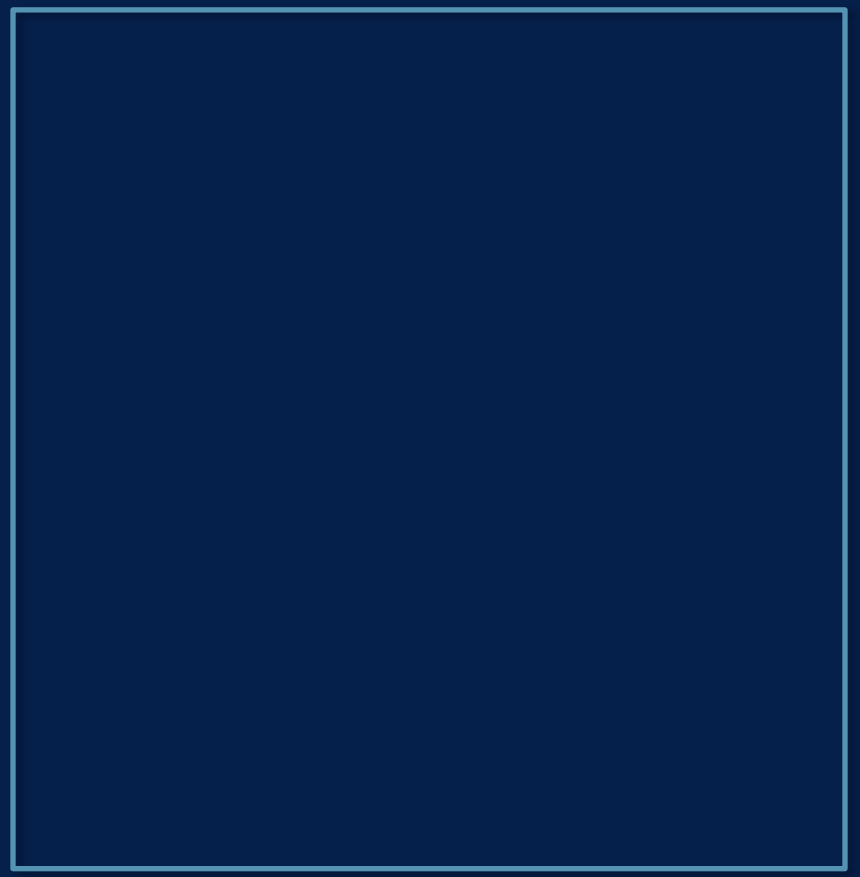
- No Disclosures



Learning Objectives

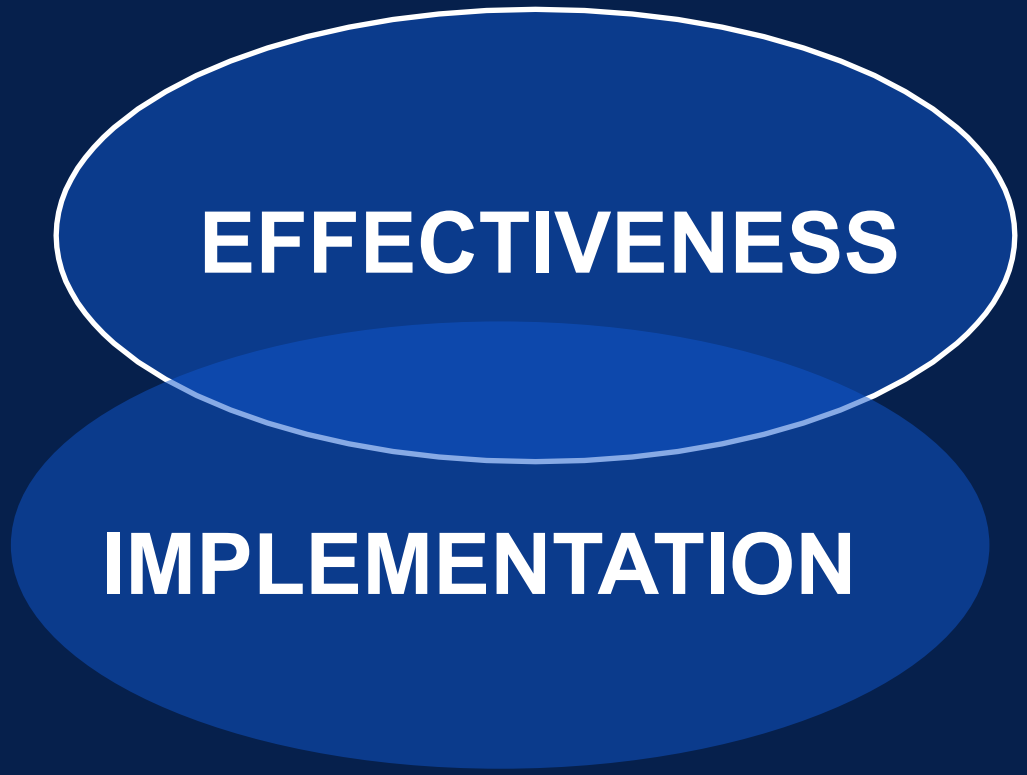
- Review the SWIFT trial design
- Describe the major findings
- Understand the implications of the hybrid design and review medication related implementation outcomes from the trial

Background

- XR-naltrexone is the only FDA approved antagonist treatment for opioid use disorder
- 10-14 day initiation procedure recommended in Prescribing Information is a barrier
- Shorter approaches have shown promise to be more effective

Study Objectives

Type 1 Hybrid Effectiveness-Implementation Trial



- To determine whether the Rapid Procedure (RP) is **non-inferior** to a Standard Procedure (SP) on the successful initiation of XR-naltrexone.
- To study barriers and facilitators to RP implementation and to develop an Implementation Strategy for dissemination of RP.

Study Design

- Open-label, multisite, optimized stepped-wedge, randomized trial
- Five 14-week steps
- Six community-based inpatient sites (N=450)

KEY Features of the Rapid Protocol	
Day 2	Minimum necessary buprenorphine dose
Day 3	24 hour “opioid washout” period
Days 4-7	Low-dose naltrexone titration (0.5, 3mg, 6 mg)
Day 7	XR-naltrexone injection
Days 1-7	standing adjunctive medications


Western States Node
Ohio Valley Node
Texas Node
New York Node
Mid-Atlantic Node
Florida Node Alliance

Interest in XR-naltrexone

Summary of Pre-screening	
Number pre-screened	**3993**
No current and active OUD	**91 (2.6%)**
Not eligible for XR-NTX	**426 (12.0%)**
Not attempting XR-NTX induction	**2443 (69.0%)**
Not satisfying basic eligibility to move forward in the study	582 (16.4%)
Consented	415 (10.4%)

Results: Primary Outcome: Received 1st XR-NTX injection

Induction Procedure	Number Enrolled	First Injection Administered While on the Unit
Rapid	225	141 **(62.7%)**
Standard	190	68 **(35.8%)**
Total	**415**	**209 (50.4%)**

- **Both noninferiority and superiority were demonstrated**
- Non-inferiority of RP to SP was demonstrated with OR of 3.60 with a 95% CI of 2.12–6.10
  - lower bound exceeded the non-inferiority margin of 0.67
- With non-inferiority established, superiority of RP was tested and demonstrated
  - 95% CI for the odds ratio was above 0.67 and also above 1; $p<0.0001$

Medication Related Implementation Findings

Adjunctive Medications:
To be Used Throughout the Detoxification Procedures

- ☐ clonidine 0.2 mg **standing** every 4 hours
  - hold or lower dose if sBP<90 or HR<50 or if patient sedated
- ☐ clonazepam 1mg **standing** every 6 hours, hold for sedation
- ☐ prochlorperazine 10 mg every 8 hours as needed for nausea
- ☐ trazodone 100mg at night as needed for insomnia
- ☐ zolpidem 10mg at night as needed for insomnia
- ☐ ibuprofen 600 mg every 8 hours as needed for myalgias
- ☐ nicotine replacement therapy as indicated

Clonidine Side Effects (From Study Trainings)

The most important thing to look out for is low blood pressure or orthostatic hypotension.

- **Blood pressure should be checked before each dose**
- Hold the dose and notify prescriber if systolic blood pressure is less than 90 or if the heart rate is below 50
- Strongly encourage patient to drink powerade/gatorade/pedialyte or the equivalent to support BP
- If hypotension occurs, prescribers should consider lowering the dose

Clonazepam Side Effects (From Study Trainings)

- The most likely side effects is sedation/poor coordination leading to dizziness and falls
- Observe the patient for signs of excessive sedation and hold the dose if the case (some level of sedation is desired- “sleeping through detox”)
- Patients may also seem to be seeking clonazepam (it is a controlled substance)
- Generally, it is better to give the prescribed medication even if there is a concern that the patient is medication seeking because the risks of untreated withdrawal (i.e., premature discharge) if higher than risk of clonazepam overuse

Medication Received in Rapid Phase

		Clonidine	Clonazepam
Pre-Buprenorphine Day 1 (N=147)	Number of participants	80 (54.4%)	23 (15.6%)
	Average TDD (mg)	0.2	1.3
Pre-Buprenorphine Day 2 (N=30)	Number of participants	23 (76.7%)	8 (26.7%)
	Average TDD (mg)	0.3	1.6
Buprenorphine Day 1 (N=159)[1]	Number of participants	142 (89.3%)	98 (61.6%)
	Average TDD (mg)	0.4	2.2
Buprenorphine Day 2 (N=73)	Number of participants	68 (93.2%)	50 (68.5%)
	Average TDD (mg)	0.4	2.0
Buprenorphine Day 3 (N=18)	Number of participants	17 (94.4%)	15 (83.3%)
	Average TDD (mg)	0.4	1.7
Buprenorphine Washout Day 1 (N=128)	Number of participants	127 (99.2%)	128 (100%)
	Average TDD (mg)	0.5	3.2

Medication Received in Rapid Phase

		Oral Naltrexone	Clonidine	Clonazepam
Naltrexone Day 1 (N=133)	Number of participants	133 (100%)	130 (97.7%)	129 (97.0%)
	Average TDD (mg)	1.7	0.5	3.4
Naltrexone Day 2 (N=107)	Number of participants	104 (97.2%)	102 (95.3%)	105 (98.1%)
	Average TDD (mg)	3.3	0.5	3.3
Naltrexone Day 3 (N=56)	Number of participants	54 (96.4%)	54 (96.4%)	54 (96.4%)
	Average TDD (mg)	5.6	0.5	3.3
Day of XR-NTX Injection Success (N=141)	Number of participants	135 (95.7%)	108 (76.6%)	123 (87.2%)
	Average TDD (mg)	6.1	0.3	2.1

Is it more effective to administer adjunctive medications proactively?

Preliminary analysis: Dr. Kara Rudolph

- We harnessed the natural variations in clinical management
- We compared outcomes for three approaches to administering clonidine/clonazepam:
  - In response to mild/moderate withdrawal severity (COWS≥5)
  - In response to mild withdrawal severity (COWS≥3)
  - Medications were given regardless of withdrawal symptoms (COWS 0-2)
- Administering adjunctive medications clonidine and clonazepam daily (as compared to waiting until w/d is present) increased the likelihood of XR-naltrexone initiation

Safety and Adverse Events: Induction Phase

Serious Adverse Events (SAE)	Standard (N=190)	Rapid (N=225)	Fisher's P
# of participants with at least one SAE	2 (1.1%)	3 (1.3%)	1.00
Overdose	0	1	
Suicidal Ideation/ Attempt	0	1	
Medical complications (decreased level of consciousness, infectious ileitis, seizures)	2	1	

Targeted Safety Events (TSE)			
# of participants with a TSE	4 (2.1%)	12 (5.3%)	0.124
Fall event	0	4	
Acute change in mental status	1	0	
Acute medical complication likely exacerbated by the stress of w/d	3 seizures during withdrawal (1) precipitated withdrawal (2)	8 vomiting (5) precipitated withdrawal (2) wheezing/SOB* (1)	
Acute psychiatric symptoms	0	0	

Final Takeaways/Summary

- A more rapid approach to induction for XR-naltrexone is superior to a traditional buprenorphine taper
- About 10% of patients with OUD entering withdrawal management treatment programs were interested and eligible for XR-naltrexone
- Prescribers used lower than recommended doses of comfort medications in the trial
- To increase the likelihood of XR-naltrexone initiating providers may consider giving clonidine and clonazepam preemptively to manage even mild withdrawal symptoms

SWIFT
CTN-0097

TEAM

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Funded by: UG1DA013035, NIH HEAL Initiative study

ASAM

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