

Cost-Effectiveness of ALPHA-2 Adrenergic Agonist (Lofexidine) and Long-Acting Injectables for Treatment of Opioid Use Disorder (OUD)

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Opioid Crisis Facts :

- **Opioid-related mortality:**
47,590 overdose deaths in the U.S. (2019)¹
6,946 in Canada (April 2020 to March 2021)²
9,200 in Europe-27 EU member states, UK, Norway, Turkey (2018)³
- **Economic burden:**
US\$1,021 bn in the U.S (2017)⁴
US\$6 bn in Canada (2017)⁵

OUD Pharmacotherapies:

- Pharmaco-therapy coupled with psychotherapy can reduce burden.⁶
- Conventional pharmacotherapies: Buprenorphine (BUP); buprenorphine-naloxone (BUP-NX), methadone (MET)
- Long-acting formulations: Extended-release naltrexone (XR-NTX), extended-release buprenorphine (XR-BUP) depot injection, buprenorphine implants
- Lofexidine (LFX) approved by the U. S FDA in 2018 for opioid withdrawal
- LFX cost: 12 times of BUP-NX; > 300 times of methadone (MET)
- XR-BUP cost: 1.34 times of XR-NTX; > 700 times of BUP-NX

Research Objective:

To evaluate the cost-effectiveness of LFX, XR-NTX and XR-BUP relative to usual treatment (BUP-NX) and no treatment from the U.S healthcare perspective

Methods:

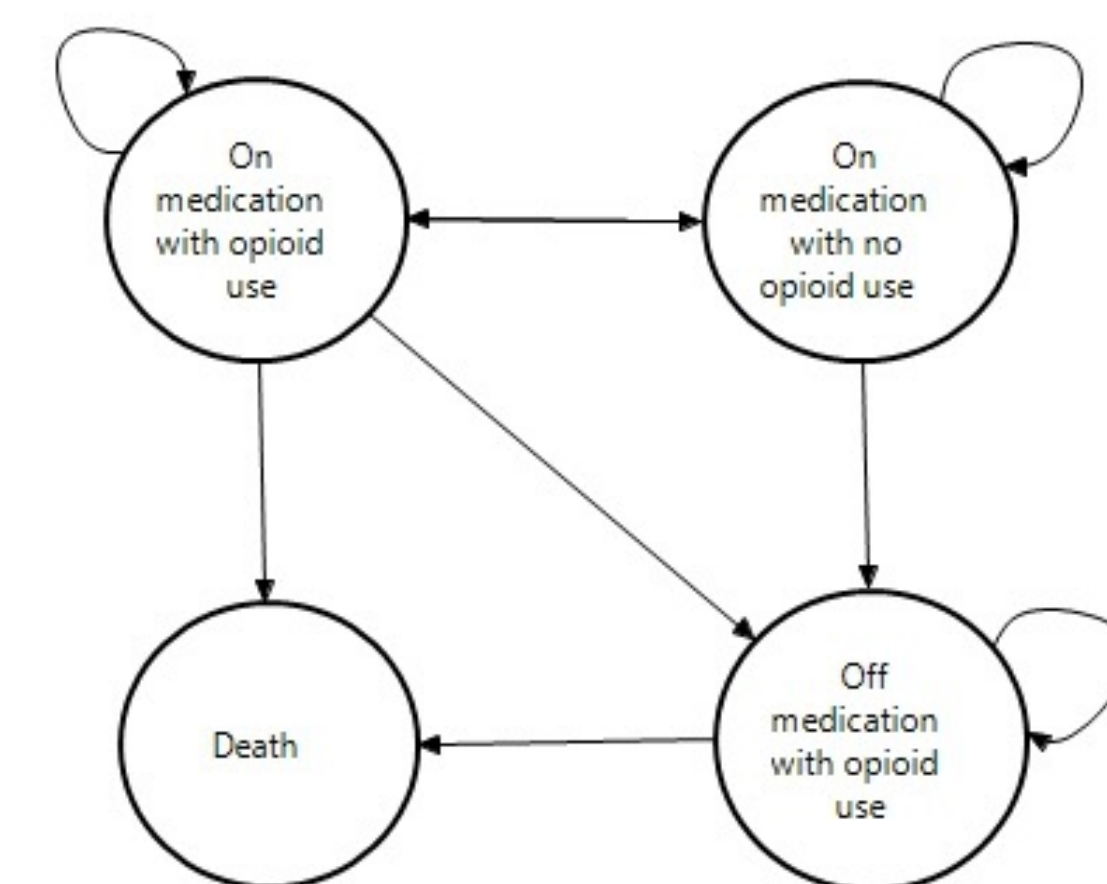


Fig: State Transition Diagram

Study design: Hybrid Decision Tree-Markov model

Population: Injection and non-injection drug users

Study period: One year with monthly cycle

Costs are in 2020 US\$

Effectiveness measures: Quality-adjusted life years (QALY), treatment retention and opioid free days gained.

Willingness-to-pay (WTP) threshold: US\$100,000/QALY

No WTP threshold for retention and opioid-free days

Sensitivity analysis: Deterministic and probabilistic analyses (1000 iterations)

Explorative analysis: Costs of loss of productivity associated with OUD

Methods (cont.):

Table 1. Detoxification and maintenance stages of the treatment strategies

Strategy	Detoxification regimen	Maintenance regimen
A	Oral MET (taper)-LFX	Sublingual BUP-NX
B	Oral MET (taper)-LFX	Intramuscular XR-NTX
C	Sublingual BUP-NX	Subcutaneous XR-BUP
D (usual treatment)	Sublingual BUP-NX	Sublingual BUP-NX
No treatment	None	None

$$ICER = \frac{\text{Cost of treatment 1} - \text{Cost of treatment 2}}{\text{Effectiveness of treatment 1} - \text{Effectiveness of treatment 2}}$$

Strategy that yields maximum effectiveness (within the cost threshold for QALY only) will be considered, cost-effective.

Results:

Table 2: ICER with outcome as QALY gained

Strategy	Cost (US\$)	Effectiveness (QALY)	ICER (US\$/QALY)
Panel A: All strategies			
No treatment	24,464	0.670	-
Strategy D	26,460	0.691	95,760
Strategy A	28,914	0.693	1,247,528
Panel B: Strategy C and B versus no treatment			
No treatment	24,464	0.670	-
Strategy C	30,802	0.689	330,265
Strategy B	44,088	0.691	5,860,107

Table 3: ICER with outcome as number of days of treatment retention and opioid-free gained

Strategy	Cost (US\$)	Effectiveness (Day)	ICER (US\$/day)
Panel A: Cost per day of retention gained			
Strategy D	26,460	146	-
Strategy A	28,914	160	175
Panel B: Cost per day of opioid-free gained			
Strategy D	26,460	27	-
Strategy A	28,914	29	1,227

In both Table 2 (panel A) and Table 3, strategies C and B cost more but provide lower effectiveness than A (i.e., dominated)

Key findings:

- **All strategies:**
 1. B and C are dominated by A
 2. Strategy A vs D: A, higher effectiveness but not cost-effective
 - 3.Strategy A: Cost-effective relative to D if lofexidine cost is reduced by 99%.
- **Strategy B and C vs no treatment:** B, highest effectiveness but not cost-effective
- **Probabilistic sensitivity analysis:** A is cost-effective in 9%; D in 47% of 1000 iterations.
- Similar results in the explorative analysis; strategy A providing maximum reduction on costs of productivity loss from OUD.

Treatment and Policy Implications:

- Usual treatment with BUP-NX (strategy D) is the optimal treatment option in the defined WTP for QALY.
- With treatment goals of increased treatment retention and opioid-free days, MET-LFX detoxification and BUP-NX maintenance (strategy A) is predicted to be beneficial
- Patients who seek opioid-free or once-a-month treatment may benefit more from MET-LFX detoxification and XR-NTX maintenance but at a higher cost than the WTP threshold.

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