Estimating the Potential Cost-Effectiveness of Long-Acting Naltrexone versus Oral Naltrexone for Alcohol Use Disorder

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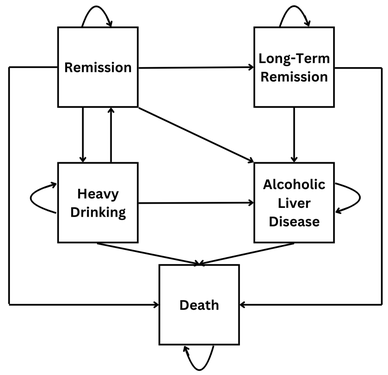
BACKGROUND

- Nearly 1 in 10 Americans have alcohol use disorder (AUD) – a debilitating disease with annually nearly 100,000 deaths and costs of roughly $249 billion[1-2]
- Despite the impact of the disease, less than 2% of AUD patients receive pharmacotherapy[3]
- Current FDA-approved medications for AUD are: acamprosate, disulfiram, oral naltrexone (PO-NTX) and long-acting naltrexone (LAI-NTX)[4]
- Naltrexone comes in the form of daily oral medication (PO-NTX) and in once monthly injectable form (LAI-NTX or Vivitrol®)
- LAI-NTX has the potential for improved adherence compared to PO-NTX given LAI-NTX's once monthly injection compared to PO-NTX's daily administration which could translate to better outcomes with LAI-NTX[5]
- There have been few recent randomized controlled trials (RCTs) for AUD medications, and the duration of these trials have been relatively short (12-24 weeks)[6]
- Cost-effectiveness analyses in this area has been sparse, and no published studies have yet compared the cost-effectiveness of LAI-NTX to PO-NTX in AUD
- This analysis estimates the potential cost-effectiveness of long-acting naltrexone (LAI-NTX) versus oral naltrexone (PO-NTX) for the treatment of AUD

Highlights of the Study

- **This is the first known analysis comparing the cost-effectiveness of long-acting naltrexone to oral naltrexone for individuals with alcohol use disorder**
- **Long-acting naltrexone was completely dominated by oral naltrexone treatment, because oral naltrexone is expected to cost less and to provide greater health benefits**
- **Data limitations are significant, and these results should be considered as preliminary**
- **Despite long-acting naltrexone being economically dominated, potential adherence benefits and broader impacts of long-acting naltrexone in the real-world setting should be explored**

Figure 1: Markov model linking AUD health states



METHODS

- A Markov model was developed to assess the potential cost-effectiveness of LAI-NTX compared to PO-NTX (Figure 1)
- A meta-analysis was used as the data source to compared the efficacy of different AUD medications, including LAI-NTX and PO-NTX[6]
- This analysis was conducted from a healthcare payer perspective in the US
- The model was for a typical patient who initiated treatment at age 21 and who was followed through the rest of their lifetime in monthly cycles
- Direct costs were calculated and inflated to the year 2024 for US$
- Outcomes were calculated as quality-adjusted life-years (QALYs) using health utility values captured by SF-6D and EQ-5D estimation methods
- All costs and outcomes were discounted by 3% annually
- An incremental cost-effectiveness ratio (ICER) was calculated for the base case using costs and QALYs
- A willingness-to-pay (WTP) threshold of $150,000/QALY was used for assessing the cost-effectiveness result
- Deterministic analysis was performed as one-way sensitivity analysis
- Probabilistic scenario analyses were performed and represented by an ICER scatterplot using 5,000 Monte Carlo simulations
- Threshold analysis were also performed assessing ICER values at varying patient time horizons from 5 years to 75 years (lifetime)

RESULTS

- Projected total discounted direct costs of LAI-NTX and PO-NTX were $256,368 and $7,684, respectively
- Projected total discounted QALYS for LAI-NTX and PO-NTX were 17.96 and 18.01, respectively
- The ICER for the base case resulted in LAI-NTX being completely dominated
- One-way sensitivity analysis elucidated the parameters that were most influential on the ICER (Figure 2)
- Probabilistic sensitivity analyses did not alter the result of LAI-NTX being dominated (Figure 3)
- Threshold analysis showed that the ICER increased over time across the different time horizons (Figure 4)

Figure 2: One-way sensitivity analyses reveal uncertainty around utility values has the greatest impact on the ICER

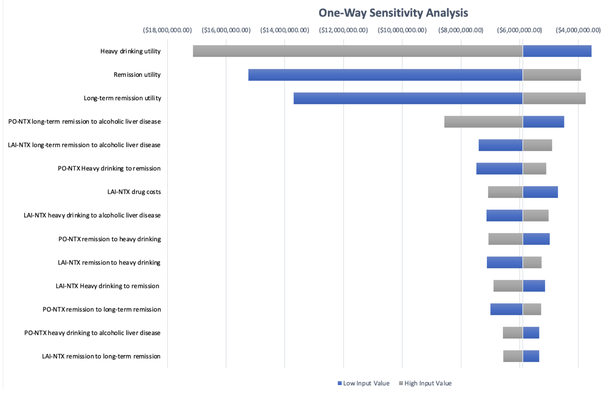


Figure 3: Monte Carlo simulations show LAI-NTX is dominated in each simulation

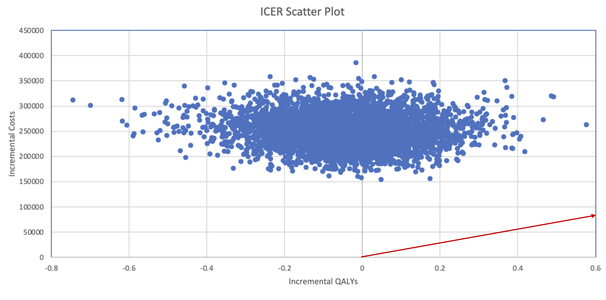
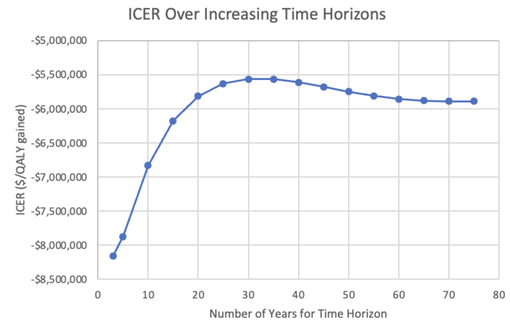


Figure 4: Threshold analysis shows LAI-NTX is dominated at all time horizons



DISCUSSION

- Findings showed that LAI-NTX is not projected to be cost-effective compared to oral naltrexone
- Similar to an Institute for Clinical and Economic Review (ICER) 2018 report comparing LAI-NTX to PO-NTX in opioid use disorder, LAI-NTX is project to cost much more and, on average, have no positive net health benefit over PO-NTX[7]
- Additionally, real-world studies comparing outcomes between the two agents in AUD have had mixed results[8-9]
- One study found longer time to relapse in LAI-NTX compared to PO-NTX while another found lower healthcare resource utilization in the PO-NTX individuals
- Clinical trials in AUD have had short trial durations, and current estimates of long-term efficacy are lacking[6]
- Data limitations are substantial with short clinical trial durations, lack of long-term efficacy data, and little evidence on the real-world utilization and outcomes of these medications
- However, the continued use of LAI-NTX with substantial sales (>$400 million), poor uptake of naltrexone, and possible heterogeneity of treatment effect suggests the need for further long-term real-world studies
- Specifically, assessing the impact of adherence for LAI-NTX formulations and expanding to broader societal impacts on productivity losses and family spillovers is warranted
- Further research should be conducted to address these shortcomings before recommending against all access to this higher cost treatment for AUD given current treatment underutilization and substantial unmet need

References

Full citation list found here:
https://docs.google.com/document/d/1aTzRFfJg2fGBbQOjkv4o13ywFxo_YIh288XyD1D5xgE/edit?usp=sharing