Lifetime Survival, Societal Costs and Cost-Effectiveness of Nine Options to Treat Alcohol Use Disorder

Grishma KC, BS[1], Bradley C Martin, PharmD, PhD[1], Michael A Cucciare, PhD[2]
[1]Division of Pharmaceutical Evaluation and Policy, [2]Department of Psychiatry
University of Arkansas for Medical Sciences, Little Rock, AR

INTRODUCTION

- Alcohol use disorder (AUD) is a medical condition characterized by the lack of control over one's drinking with periods of heavy drinking with or without large daily consumption of alcohol.[1]
- In the United States, according to the 2022 National Survey on Drug Use and Health (NSDUH), there are about 29.5 million people, 12 years or older, who had AUD in the past year.[2]
- Out of which, only 7.6%(2.2 million adults) received treatment in the past year for AUD. [3] Thus, there is significant undertreatment for AUD.
- The COMBINE (Combined Pharmacotherapies and Behavioral Interventions) randomized controlled trial is one of the largest evaluations of AUD treatments with subsequent a short-term cost-effectiveness study however the long term cost effectiveness of AUD treatments are unknown.[4,5]
- **Study objectives:** This study estimated the life-time cost-effectiveness of nine AUD treatments.

METHODS

Treatments: Nine mutually exclusive combinations. All participants in eight groups received medical management(MM) and were randomized to receive matching placebo, acamprosate or naltrexone or both, with or without a combined behavioral intervention (CBI).The ninth group received CBI only without MM.

Participants: Patients with AUD that participated in the COMBINE trial where they received one of the 9 treatment options for a 16-week period. The mean starting age for the model was 44 years old with 10 years of standard deviation.

Primary outcomes: Costs in 2023 US dollars, Quality-adjusted life years (QALYs), Years in relapse (≥5 standard drinks per day for men and ≥4 drinks per day for women[4]), and Survival

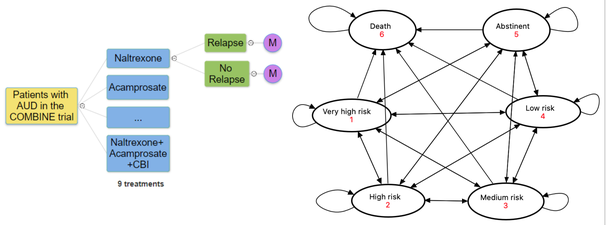
Model Structure:

- A decision tree combined with Markov model was developed using TreeAge 2023 software.
- An American societal perspective, yearly cycle length, and lifetime time horizon was used. Costs and QALYs were discounted by 3%.
- The decision tree captured probability of relapse one year post treatment as reported in the COMBINE trial.
- Patients then entered a Markov model with five AUD risk states and a death state that estimated lifetime probability of relapse and AUD related mortality.

Transition Probabilities and Model Inputs:

- Long-term drinking trajectories of alcohol-dependent treated population obtained from a study by Barbosa et al. were used as transition probabilities for the Markov model.[6] Additionally, utilities for each AUD risk states were acquired from Barbosa et al.[7]
- 3 sets of transition probabilities were used for the 5 AUD risk states: 0–3 years, 3–8 years and 8+ years.[6]
- Treatment cost that incorporated medication, space, labor, and laboratory costs were derived from a study by Zarkin et al.[6] Treatment costs also included patient time costs.[8]
- Societal costs due to crime and automobile accidents also were also included.[8]
- AUD risk state- and age-specific labor force participation probabilities were used to determine productivity costs. Age-specific consumption costs were incorporated.[8]
- Cost estimates were converted to 2023 US dollars by using the Consumer Price Index calculator.
- AUD risk state- and age-specific relative risk of mortality from a meta-analysis were applied to the Actuarial Life Tables.[9,10]

Figure 1: Decision Tree and Markov Model



AUD: Alcohol Use Disorder;
CBI: Combined Behavioral Intervention;
M:Markov Model

Markov State Transition Diagram

Analysis:

- Incremental cost-effective ratio (ICER) was used to evaluate cost-effectiveness of AUD treatments. A Willingness to Pay Threshold (WTP) of $100,000/QALY was used.
- Deterministic and probabilistic sensitivity analysis (PSA) were performed to assess parameter uncertainty.
- PSA was performed with 10,000 iterations. Gamma distribution was applied to all costs and beta distribution was applied to probabilities and utilities values.
- An additional sensitivity analysis was conducted using hazard ratios for AUD related mortality derived from a cohort study.[11]

RESULTS

Key Findings:

- MM+Acamprosate+Naltrexone dominated all other treatments in **base case analysis**.
- This treatment had a discounted cost of $713,247, discounted QALYs of 17.31, 7.01 relapse years and 37.76 survival years.

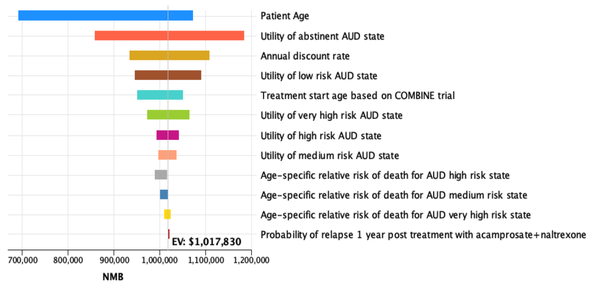
Table 1: Lifetime Cost and QALYs of Nine Mutually Exclusive AUD Treatment Strategies

Treatment Strategy	Costs ($)	Effectiveness (QALY)	ICER: Dominance	Number of relapses	Survival (years)
MM+Acamprosate+ Naltrexone	**$713,247**	**17.311**	**Undominated**	**7.008**	**37.765**
MM+Naltrexone	$713,736	17.309	Abs. Dominated	7.117	37.773
MM+CBI +Naltrexone	$714,045	17.309	Abs. Dominated	7.075	37.770
MM+CBI +Acamprosate	$714,477	17.308	Abs. Dominated	7.146	37.775
MM+Acamprosate	$714,552	17.306	Abs. Dominated	7.269	37.784
MM+CBI +Placebo	$714,974	17.305	Abs. Dominated	7.273	37.784
MM+Placebo	$715,238	17.302	Abs. Dominated	7.441	37.797
MM+CBI +Acamprosate+Naltrexone	$715,590	17.303	Abs. Dominated	7.386	37.793
CBI only	$716,181	17.299	Abs. Dominated	7.601	37.809

MM: Medical Management; QALY: Quality-adjusted life years; Abs.: Absolute

- **One way sensitivity analysis** identified age, utility of the abstinence and low risk states, and start age as some of the most influential parameters.

Figure 2: Tornado diagram-Top 12 influential model parameters



NMB: Net Monetary Benefit; EV: Expected Value; AUD: Alcohol Use Disorder; COMBINE: Combined Pharmacotherapies and Behavioral Interventions

Table 2: Monte Carlo(PSA) Acceptability for Each Strategy at $100,000 WTP

Strategy	Acceptability	Strategy	Acceptability
MM+Placebo	52.4%	MM+CBI +Naltrexone	1.6%
MM+Naltrexone	17.3%	MM+CBI +Placebo	1.4%
MM+Acamprosate +Naltrexone	8.9%	MM+CBI +Acamprosate	1.3%
MM+Acamprosate	8.7%	MM+CBI +Acamprosate+Naltrexone	1.1%
CBI only	7.2%		

WTP: Willingness to Pay; MM: Medical Management; CBI: Combined Behavioral Intervention

- The **additional sensitivity analysis** using hazard ratios for mortality with AUD also showed MM+acamprosate+naltrexone dominating all other treatments.

DISCUSSION

Conclusions:

- ❖ Medical management + acamprosate + naltrexone was determined to be the most cost-effective treatment.
- ❖ However, there is high uncertainty in this finding as nearly all the AUD treatments examined have similar survivals and quality adjusted survivals.
- ❖ Since the costs and QALYs of the nine treatments only vary slightly, receiving any treatment for AUD may be beneficial for patients.

Strengths:

- This study leverages long-term drinking trajectories to assess long-term cost effectiveness of AUD treatments which is difficult to capture through trial studies.
- Age-specific and AUD-specific productivity, consumption, crime and accident costs were incorporated to better reflect societal costs.

Limitations:

- As the COMBINE trial only provides information on one treatment session, it was assumed that patients would not seek future treatments during their lifetime.
- Patients in medium risk AUD state were exposed to probabilities of adverse events and labor force participation associated with those who had a relapse as data was only available for relapse or no relapse state.

REFERENCES

1. Verbelen M, Weale ME, Lewis CM. Cost-effectiveness of pharmacogenetic-guided treatment: Are we there yet? Pharmacogenomics J. 2017;17(5):395-402. doi: 10.1038/tpj.2017.21.
2. Substance Abuse and Mental Health Services Administration, (SAMHSA2022 National Survey on Drug Use and Health. Table 5.9A—Alcohol use disorder in past year: among people aged 12 or older; by age group and demographic characteristics, numbers in thousands, 2021 and 2022. [cited 2023 Dec 8]. https://www.samhsa.gov/data/sites/default/files/reports/rpt42728/NSDUHDetailedTabs2022/NSDUHDetailedTabs2022/NSDUHDetTabsSect5pe2022.htm#tab5.9a
3. SAMHSA, Center for Behavioral Health Statistics and Quality. 2022 National Survey on Drug Use and Health. Table 5.32A – Received substance use treatment in past year: among people aged 12 and older; by age group and past year drug use disorder, past year alcohol use disorder, past year drug and alcohol use disorder, and past year substance use disorder, numbers in thousands, 2021 and 2022. https://samhsa.gov/data/sites/default/files/reports/rpt42728/NSDUHDetailedTabs2022/NSDUHDetailedTabs2022/NSDUHDetTabsSect5pe2022.htm?s=5.32&#tab5.32a
4. Anton RF, O'Malley SS, Ciraulo DA, Cisler RA, Couper D, Donovan DM, Gastfriend DR, Hosking JD, Johnson BA, LoCastro JS, Longabaugh R, Mason BJ, Mattson ME, Miller WR, Pettinati HM, Randall CL, Swift R, Weiss RD, Williams LD, Zweben A; COMBINE Study Research Group. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. JAMA. 2006 May 3;295(17):2003-17. doi: 10.1001/jama.295.17.2003. PMID: 16670409.
5. Zarkin GA, Bray JW, Aldridge A, et al. Cost and Cost-effectiveness of the COMBINE Study in Alcohol-Dependent Patients. Arch Gen Psychiatry. 2008;65(10):1214–1221. doi:10.1001/archpsyc.65.10.1214
6. Barbosa C, Dowd WN, Aldridge AP, Timko C, Zarkin GA. Estimating Long-Term Drinking Patterns for People with Lifetime Alcohol Use Disorder. Med Decis Making. 2019 Oct;39(7):765-780. doi: 10.1177/0272989X19873627. Epub 2019 Oct 3. PMID: 31580211; PMCID: PMC6842126.
7. Barbosa C, Bray JW, Dowd WN, Barnosky A, Wittenberg E. SF-6D utility scores for alcohol use disorder status and alcohol consumption risk levels in the US population. Addiction. 2021 May;116(5):1034-1042. doi: 10.1111/add.15224. Epub 2020 Aug 27. PMID: 33448504; PMCID: PMC7882636.
8. Kim, D. D., Basu, A., Duffy, S. Q., & Zarkin, G. The cost-effectiveness of treatments for individuals with alcohol use disorders: A reference case analysis. Oxford University Press. 2017(n P. J. Neumann, G. D. Sanders, L. B. Russell, J. E. Siegel, & T. G. Ganiats (Eds.), Cost-Effectiveness in Health and Medicine (2nd ed., pp. 385-430).).
9. Zhao J, Stockwell T, Naimi T, Churchill S, Clay J, Sherk A. Association Between Daily Alcohol Intake and Risk of All-Cause Mortality: A Systematic Review and Meta-analyses. JAMA Netw Open. 2023;6(3):e236185. doi:10.1001/jamanetworkopen.2023.6185
10. Social Security Administration. Actuarial life table. https://www.ssa.gov/oact/STATS/table4c6.html. Updated 2023.
11. Di Castelnuovo A, Costanzo S, Bonaccio M, McElduff P, Linneberg A, Salomaa V, Männistö S, Moitry M, Ferrières J, Dallongeville J, Thorand B, Brenner H, Ferrario M, Veronesi G, Pettenuzzo E, Tamosiunas A, Njølstad I, Drygas W, Nikitin Y, Söderberg S, Kee F, Grassi G, Westermann D, Schrage B, Dabboura S, Zeller T, Kuulasmaa K, Blankenberg S, Donati MB, de Gaetano G, Iacoviello L. Alcohol intake and total mortality in 142 960 individuals from the MORGAM Project: a population-based study. Addiction. 2022 Feb;117(2):312-325. doi: 10.1111/add.15593. Epub 2021 Jul 8. PMID: 34105209.