Cost-effectiveness of alcohol use treatments in patients with alcohol-related cirrhosis

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Table S1. Impact Inventory.

Sector	Type of Impact	Healthcare perspective	Societal perspective	Notes on sources of evidence
Formal healthcare sector				
Health	Longevity	X	X	
	Health-related quality-of-life effects	X	X	
	Other health effects (e.g., caregiver health-related quality of life)			Excluded due to lack of data
	Medical costs paid for by third-party payers	X	X	See Table 2
	Medical costs paid for by patients out-of-pocket			Excluded; assumed to be included in medical costs
	Future related medical costs	X	X	See Table 2
	Future unrelated medical costs	X	X	See Table 2
Informal healthcare sector				

Health	Patient costs		X	See Supporting Information
	Unpaid caregiver time costs		X	See Supporting Information
	Transportation costs			Excluded due to lack of data
Non-healthcare sectors				
Productivity	Formal labor market earnings lost		X	See Table 2
	Cost of unpaid lost productivity due to illness		X	See Supporting Information
	Cost of uncompensated household production		X	See Supporting Information
Consumption	Future consumption unrelated to health		X	See Table 2
Social services	None			
Legal/criminal justice	Costs associated with the justice system, police protection, judicial			Excluded due to lack of data

	and legal costs, and corrections			
Education	Impact of intervention on educational achievement of population			Excluded due to lack of data
Housing	None			
Environment	None			

The Impact Inventory allows analysts to consider all the consequences of a health intervention from various perspectives. Marks (X) indicate the whether a particular impact was included in the perspective listed at the top of the column.

Transition probabilities

Estimating the probability of transplantation among decompensated patients

We based the probability of transplantation among patients with decompensated cirrhosis and hepatocellular cancer on data from the Organ Procurement and Transplantation Network (OPTN) annual reports. However, since only waitlisted alcohol-related cirrhosis (AC) patients are included in OPTN reports, we had to estimate the total number of AC patients that includes both waitlisted and non-waitlisted patients.

To do this, we used data from a single transplant center to estimate the total number of non-waitlisted AC patients. Based on the work by McElroy et al. (2020), the sex-weighted proportion of waitlisted patients among all decompensated AC patients is 16% (range: 11-19%).[5] Based on data from UNOS, the total waitlisted population was 3,712 in 2016 (the most recent year available).[17] Thus, the estimated total number of waitlisted and non-waitlisted AC patients is 22,664 (range: 19,537-33,745). With 1,764 total liver transplantations among AC patients in 2016, the estimated probability of transplantation among decompensated AC liver patients is 0.0778 (range: 0.0523-0.0903).[17]

Estimating the probability of transplantation among hepatocellular cancer patients

We followed a similar process to estimate the probability of transplantation among hepatocellular cancer (HCC). We used the liver transplant waitlist rate reported by Goldberg

et al. (2016).[6] We took the average transplantation rate between males and females and used that as the base estimate; the higher, male-specific rate was used as an upper limit, while the lower, female-specific rate was used as a lower limit. We multiplied the base estimate and lower and upper limits by the liver transplantation rate for HCC waitlisted patients reported in the 2018 OPTN annual report to get the transplantation rate among HCC patients.[7]

Converting rates to probabilities

Annual transition probabilities (Table 1 in main manuscript) were estimated based on peer-reviewed articles and gray literature that were found through several literature searches conducted by the authors between July-November 2019 using MEDLINE (via PubMed), as well as through citation tracking and expert recommendations. We used Eq. 1. below to transform annual rates intro annual probabilities:

$$p = 1 - e^{-rt} \quad \text{(Eq. 1)}$$

where *p* is probability, *r* is rate, *e* is the base of the natural logarithm, and *t* is the time period (in years).

Costs

Various cost categories were considered depending on the perspective of the analysis (see Impact Inventory in Table A1). The healthcare perspective included various treatment/medical costs, including future related and unrelated medical costs. The societal perspective included all costs in the healthcare perspective, as well as patient time costs, future consumption, and future productivity. All costs were inflated to 2017 U.S. dollars (US$) using general consumer price index data with 2010 as the reference year.[18] All future costs were discounted at 3% in the base case, then varied to 2 and 5% in the one-way sensitivity analysis.

Future medical costs

Future related medical costs were assumed to be included in treatment/medical costs which vary depending on the health state a patient is in. We assumed that all future unrelated medical costs were additive and are included in future consumption costs (Table A4).

Patient time costs

Alcohol-related liver disease patients spend significant amounts of time for routine care and hospitalizations, and participation in alcohol cessation interventions only adds to this lost time for work or leisure. Time costs or forgone productivity were calculated by multiplying the median daily earnings of full-time working adults (disaggregated by age) reported by the U.S. Bureau of Labor Statistics [19] by the annual average length of disease and/or length of hospitalization reported in the literature (in days) for various health states included in the

model (Table A2). We also calculated the time costs of receiving alcohol use treatments. We excluded any caregiver time costs.

Table S2. Lost days from care-seeking for various health states

Type of care	**Base estimate of time lost**	**References**
Medical care	(in days)	
Compensated cirrhosis	4	[20]
Decompensated cirrhosis	4	[20]
Hepatocellular carcinoma	5.6	[21]
Transplantation <12 months	17.6	[22]
Transplantation ≥12 months	21	[23]
Alcohol use treatment	(in hours)	
MAT	31.3	[24]
Counseling	34.9	[24]

MAT, medication-assisted therapy.

Future productivity

We relied on productivity estimates by Grosse et al. (2019) which used gross human capital approach to estimate market (i.e., earnings) and non-market (i.e., household) productivity (Table A3).[25]

Table S3. Productivity by age group (in 2017 US$)

Age	Annual average*
45-54	85,129.53
55-64	69,438.26
65-74	39,324.18
75+	16,358.18

*Detailed explanation for calculating average annual productivity is found in Grosse et al. (2019).[25]

Consumption costs

Future consumption was based on expenditure data from the U.S. Bureau of Labor Statistics 2018 Expenditure Survey (Table A4).[26] The expenditure data includes healthcare spending, so we did not value those separately. We assumed that future related medical costs are included in the treatment/medical costs above.

Table S4. Consumption by age group (in 2017 US$)

Age	Annual average*
45-54	13,341.32
55-64	14,707.31
65-74	27,307.13
75+	33,012.35

*The average consumption for each age group is based on the age of a reference person.

Additional Results

Table S5. Cost-effectiveness results with varying assumptions about frequency of intervention costs (healthcare perspective only)

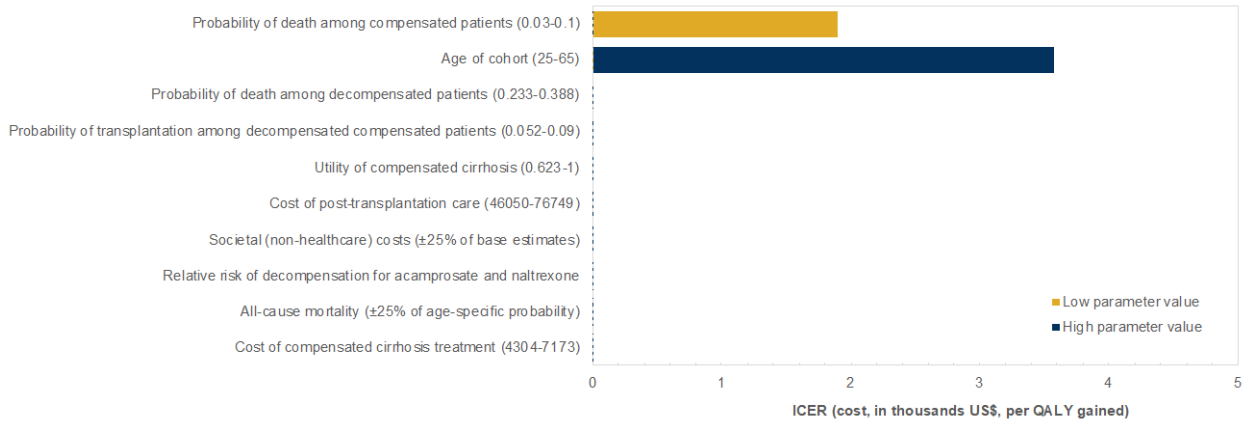
	One-time intervention costs*			Annual intervention costs over 5 years			Annual intervention costs over 10 years		
	Cost	QALYs gained†	ICER	Cost	QALYs gained†	ICER	Cost	QALYs gained†	ICER
Do-nothing	259,101	5.79	NA	259,101	5.79	NA	259,101	5.79	NA
Baclofen, gabapentin, and topiramate	250,712	6.05	Cost-saving	252,098	6.05	Cost-saving	252,376	6.05	Cost-saving
Acamprosate and naltrexone	249,055	6.12	Cost-saving	252,147	6.12	Cost-saving	252,809	6.12	Cost-saving
Counseling	255,044	5.94	Cost-saving	257,341	5.94	Cost-saving	257,748	5.94	Cost-saving

This table shows the costs and health benefits of each intervention when the duration in which alcohol cessation costs incurred by compensated alcohol-related cirrhosis patients are varied deterministically. ICERs are calculated by comparing each alcohol cessation intervention's cost and QALYs to the do-nothing scenario from a healthcare perspective. "Cost-saving" (or "dominant") refers to an intervention that incurs less costs and produces more QALYs compared to its comparator; cost-saving interventions are preferred because they outperform their comparator in both costs and benefits. ICER, incremental cost-effectiveness ratio; NA, not applicable; QALY, quality-adjusted life year.

*Same results as in base-case analysis found in Table 2 of the main paper

†Refers to lifetime QALYs and are discounted at 3% to present value.

Fig. S1. Tornado diagram for acamprosate and naltrexone compared to a do-nothing scenario from a societal perspective



A tornado diagram shows the full ICER range when a parameter in the model is varied from its lowest to highest estimated value while keeping the other parameters constant. Only the top 10 most influential parameters are included in this figure. Only two parameters—the probability of death among compensated patients and age of cohort—at their extreme values make acamprosate and naltrexone no longer cost-saving but still cost-effective given a cost-effectiveness threshold of <$4,000 per QALY gained. All other parameters at their extreme values make acamprosate and naltrexone cost-saving from a societal perspective.

AC, alcohol-related cirrhosis (i.e., compensated cirrhosis); ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; US$, US dollar.

Table S6. Average results from the probabilistic sensitivity analyses

Intervention	**Societal perspective**				**Intervention**	**Healthcare perspective**			
	QALYs gained*	Cost	ICER compared to do-nothing	ICER compared to the next most expensive, undominated option		QALYs gained*	Cost	ICER compared to do-nothing	ICER compared to the next most expensive, undominated option
Acamprosate and naltrexone	5.90	262,819	Cost-saving	NA	Acamprosate and naltrexone	5.88	236,013	Cost-saving	NA
Baclofen, gabapentin, and topiramate	5.83	265,876	Cost-saving	Dominated†	Baclofen, gabapentin, and topiramate	5.81	237,614	Cost-saving	Dominated†
Do-nothing	5.60	267,616	NA	Dominated†	Counseling	5.71	241,759	Cost-saving	Dominated†
Counseling	5.73	268,780	9,213	Dominated†	Do-nothing	5.59	245,098	NA	Dominated†

This table shows the results for the probabilistic sensitivity analysis for a patient cohort aged 54 years. Interventions are arranged by increasing costs. ICERs are calculated by dividing incremental costs by incremental QALYs between two interventions. “Cost-saving” (or “dominant”) refers to an intervention that incurs less costs and produces more QALYs compared to its comparator; cost-saving interventions are preferred because they outperform their comparator in both costs and benefits. “Dominated” refers to an intervention that incurs more costs and produces less QALYs compared to its comparator; dominated interventions are rejected because their cost-effectiveness is inferior to their comparator. All costs are in 2017 US$, rounded to the nearest dollar, and have been discounted at 3% to the present.

ICER, incremental cost-effectiveness ratio; NA, not applicable; QALY, quality-adjusted life year.

*Refers to lifetime QALYs and are discounted at 3% to present value.

†Compared to acamprosate and naltrexone

Table S7. Average results from the probabilistic sensitivity analyses across different cohort ages (societal perspective)

	Age 25			**Age 35**			**Age 45**			**Age 65**		
Intervention	QALYs gained*	Cost	ICER	QALYs gained*	Cost	ICER	QALYs gained*	Cost	ICER†	QALYs gained*	Cost	ICER
Do-nothing	6.76	271,638	NA	6.46	226,376	NA	6.04	257,751	NA	4.88	325,896	NA
Acamprosate and naltrexone	7.05	260,412	Cost-saving	6.76	214,730	Cost-saving	6.34	249,070	Cost-saving	5.16	327,405	5,490
Baclofen, gabapentin, and topiramate	6.99	265,181	Cost-saving	6.69	219,763	Cost-saving	6.28	253,191	Cost-saving	5.10	328,699	13,101
Counseling	6.88	270,484	Cost-saving	6.58	225,187	Cost-saving	6.17	257,528	Cost-saving	5.00	329,402	29,863

This table shows the results for the probabilistic sensitivity analysis for patient cohorts ages 25, 35, 45, and 65 years from a societal perspective. ICERs are calculated by comparing each alcohol cessation intervention's cost and QALYs to the do-nothing scenario from a healthcare perspective. "Cost-saving" (or "dominant") refers to an intervention that incurs less costs and produces more QALYs compared to its comparator; cost-saving interventions are preferred because they outperform

their comparator in both costs and benefits. All costs are in 2017 US$, rounded to the nearest dollar, and have been discounted at 3% to the present.

ICER, incremental cost-effectiveness ratio; NA, not applicable; QALY, quality-adjusted life year.

*Refers to lifetime QALYs and are discounted at 3% to present value.

Table S8. Average results from the probabilistic sensitivity analyses across different cohort ages (healthcare perspective)

	Age 25			**Age 35**			**Age 45**			**Age 65**		
Intervention	QALYs gained*	Cost	ICER	QALYs gained*	Cost	ICER	QALYs gained*	Cost	ICER	QALYs gained*	Cost	ICER
Do-nothing	6.75	332547	NA	6.46	310268	NA	6.05	278736	NA	4.89	195805	NA
Acamprosate and naltrexone	7.05	321641	Cost-saving	6.76	299833	Cost-saving	6.35	269001	Cost-saving	5.16	187821	Cost-saving
Baclofen, gabapentin, and topiramate	6.98	323696	Cost-saving	6.70	301735	Cost-saving	6.28	270723	Cost-saving	5.10	189138	Cost-saving
Counseling	6.88	328486	Cost-saving	6.59	306372	Cost-saving	6.18	275125	Cost-saving	5.01	192897	Cost-saving

This table shows the results for the probabilistic sensitivity analysis for patient cohorts ages 25, 35, 45, and 65 years from a healthcare perspective. ICERs are calculated by comparing each alcohol cessation intervention's cost and QALYs to the do-nothing scenario from a healthcare perspective. "Cost-saving" (or "dominant") refers to an intervention that incurs less costs and produces more QALYs compared to its comparator; cost-saving interventions are preferred because they outperform

their comparator in both costs and benefits. All costs are in 2017 US$, rounded to the nearest dollar, and have been discounted at 3% to the present. ICER, incremental cost-effectiveness ratio; NA, not applicable; QALY, quality-adjusted life year.

*Refers to lifetime QALYs and are discounted at 3% to present value.

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