Alcohol-related Liver Disease in the US: Projections of Future Burden and Economic Evaluation of Pricing Policies

by

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Dedication

To my lolo*,*
Rolando (1929-2020),
for inspiring me to write

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This dissertation was possible only with the support and encouragement of many folks and communities who relentlessly believed in me, so allow me to take the next few pages to express my gratitude.

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List of Acronyms and Abbreviations

AAPI	Asian American and Pacific Islander
AC	alcohol-related cirrhosis
AFLD	alcohol-related fatty liver disease
AH	alcohol-related hepatitis
AIAN	American Indian and Alaska Native
ALD	alcohol-related liver disease
ASH	alcoholic steatohepatitis
AUD	alcohol use disorder
CC	compensated cirrhosis
CDC	Centers for Disease Control and Prevention
CI	credible interval
CEA	cost-effectiveness analysis
CPI	Consumer Price Index
DC	decompensated cirrhosis
DCEA	distributional cost-effectiveness analysis
DSM	Diagnostic and Statistical Manual of Mental Disorders
EDEH	equally distributed equivalent of health
HCC	hepatocellular carcinoma
ICER	incremental cost-effectiveness ratio
MUP	minimum unit pricing
NESARC	National Epidemiologic Survey on Alcohol and Related Conditions
NHANES	National Health and Nutrition Examination Survey
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NIH	National Institutes of Health
NSDUH	National Survey on Drug Use and Health
OPTN	Organ Procurement and Transplantation Network
PSA	probabilistic sensitivity analysis
QALE	quality-adjusted life expectancy
QALY	quality-adjusted life year
SES	socioeconomic status
SSE	sum of squared errors
TTB	Alcohol and Tobacco Tax and Trade Bureau
UK	United Kingdom

US	United States
WHO	World Health Organization

Acronyms and abbreviations are reintroduced in each chapter for clarity.

Abstract

Alcohol-related liver disease (ALD) is a set of conditions caused by repeated liver injury that results from chronic and excessive alcohol consumption. ALD is a significant cause of morbidity and mortality in the US; it is currently the cause of half of all cirrhosis-related deaths and is the leading indication for liver transplantation. ALD-related mortality rates are increasing in the US, especially among women, certain racial/ethnic minority groups, and young adults, which raises health equity concerns. The burden of ALD is expected to rise as alcohol use and misuse continue to increase in these populations.

To advance our understanding of ALD and the potential impact of evidence-based policy interventions in the US, I conducted three studies. In the first study (Chapter 2), I developed a calibrated microsimulation model and projected the future burden of ALD across different subgroups. I estimated that ALD cases and deaths may increase in the US as rates of alcohol misuse rise. I found that average ALD incidence and mortality rates masked stark differences between sociodemographic groups. I also found that groups that have been disproportionately affected by ALD in the past are still likely to bear its health burden in the future.

In the second study (Chapter 3), I compared the long-term costs, health benefits, and cost-effectiveness of two pricing policies, namely increases to alcohol excise taxes and minimum unit pricing (MUP). I found that alcohol tax increases and MUP are cost-saving or cost-effective interventions when compared to the status quo. Among all interventions, an MUP that increased the price of the cheapest alcohol by 100% had the highest probability of providing the most value for money, though results were sensitive to parameter uncertainty.

In the third and final study (Chapter 4), I applied a distributional cost-effectiveness analysis framework to evaluate the cost-effectiveness and equity impacts of beer and liquor taxes. I leveraged previous estimates of the heterogeneous effects of pricing policies across racial/ethnic and gender groups. I found that a 30% liquor tax increase was the most economically efficient intervention compared to the status quo or to other liquor and beer taxes included in the analysis. However, the 30% liquor tax was associated with the highest health inequality, which is likely outweighed by the total health benefits produced.

The studies in dissertation found that that the burden of ALD is expected to increase in the US, and that pricing policies are effective interventions to reverse this trend. However, pricing policies may have heterogeneous effects across subgroups that require further evaluation. This dissertation emphasizes the need to explore the distributional effects of interventions to ensure that they are effective, efficient, and equitable.

Chapter 1: Background and Motivation

Alcohol-related liver disease (ALD) is a spectrum of conditions caused by repeated liver injury that results from chronic and excessive alcohol consumption (see Appendix 1 for more on ALD etiology and treatment).[1,2] The natural progression of ALD is well-understood (Figure 1) and spans alcohol-related fatty liver disease (AFLD) or steatosis, alcohol-related steatohepatitis, alcohol-related cirrhosis (AC), and liver cancer or hepatocellular cancer (HCC).[1,3] A separate but related acute clinical syndrome called alcohol-related hepatitis may occur in people with or without AC, which is characterized by rapid onset of jaundice after weeks to months of heavy drinking and subsequent liver failure and is associated with extremely high mortality rates of up to 60%.[4–6] While these stages have distinct characteristics, they can occur in the same person at the same time.[7] ALD risk is modified by various biological and social factors, such as genetics, sex, obesity and nutritional status, and smoking status.[1]

Figure 1. Spectrum of alcohol-related liver disease

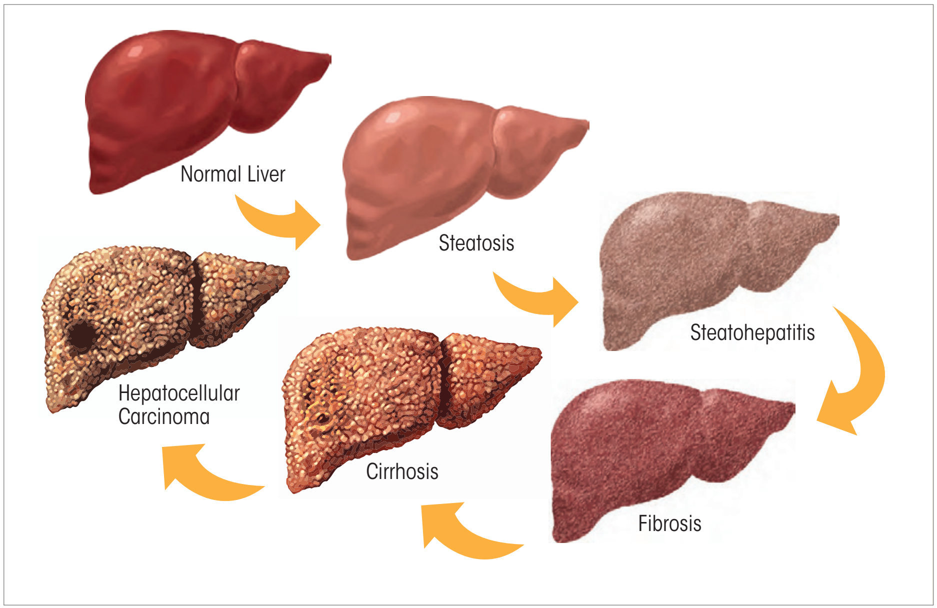


Image from Osna et al. (2017)[3]

EPIDEMIOLOGY OF ALD

The health burden of ALD in the US is significant. An estimated 4.7% of adults have AFLD, and the share of adults with more advanced stages (≥2 fibrosis stage) has risen from 0.6% in 2002 to 1.5% in 2016.[8] The prevalence of AC rose from 0.07 to 0.10% between 2009 and 2015[9], and AC is the underlying cause of roughly 44% of all liver disease-related deaths (29,505 of 65,807 in 2020).[10] Alarmingly, recent studies found that AC-related mortality among adults of all ages has increased between 1999 and 2017.[11,12] ALD is also the main diagnosis of patients on liver transplant waitlists.[13–15]

Several trends suggest that the burden of ALD is shifting in the population. ALD-related discharges are increasing more rapidly among women compared to men.[16] The gap in ALD mortality between men and women has also been decreasing, especially among those younger than 34 years.[17] While ALD mortality rates have been historically highest among middle-aged adults[17], adults less than 35 years old have faced the steepest increases in ALD deaths. For example, between 2009 and 2016, ALD mortality rose by 10% (95% CI: 8.9-12.2%) per year among 25-34-year-olds.[11]

Racial/ethnic groups have also experienced different changes in ALD mortality (Figure 2). One study estimated that annual changes in ALD mortality were 3.7%, 1.2%, 2.5%, and 2.1% for Whites, Blacks, Asian Americans, and Hispanics, respectively, between 2007-2016.[18] Another study that included Native Americans found that their age-adjusted mortality rate for ALD was 2.6 times higher than Whites in 2017.[12] However, when analyzed by race/ethnicity and gender, starker differences are revealed. In one study, Black men and women and Hispanic men saw decreases in ALD mortality rates, while White men and women and Hispanic men have seen 2-5% annual percent changes across all ages.[17,19]

Figure 2. Age-adjusted mortality rates from alcohol-related cirrhosis by sex, race, and Hispanic origin, 2000-2017

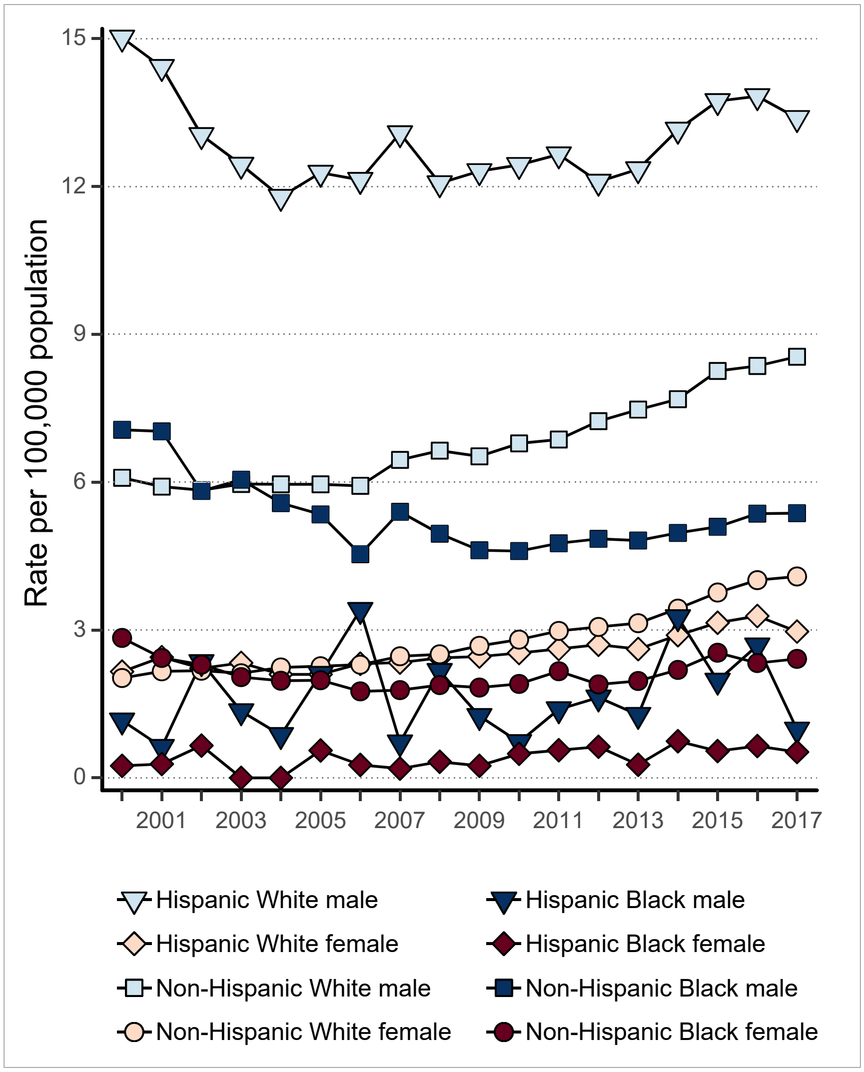


Figure from Yoon and Chen (2019)[20]

TRENDS IN ALCOHOL CONSUMPTION

The burden of ALD in the US is expected to further increase due to alarming trends in alcohol consumption. Data from the two most-recent waves of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) found that 12-month alcohol use, high-risk drinking, and alcohol use disorder (AUD) as defined in the 5th edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; see Box 1) has increased by 11.2%, 29.9%, and 49.4%, respectively between 2001-2002 and 2011-12.[21] Among the sociodemographic groups assessed, women, older adults, racial/ethnic minorities, and individuals with low socioeconomic status (SES) experienced the largest increases in all three measures of drinking (Figure 3),[21] and several studies have confirmed these trends using other nationally representative surveys (Figure 4).[22–27] These shifts occurred while per-capita consumption of alcohol in the US increased by 5% during the same period from 2.18 gallons to 2.29 gallons.[28] However, alcohol use among youth (ages 12-17) and some young adults (ages ≤25 years) across all racial groups have been steadily declining in the US, implying that some interventions currently in place (e.g., public health education and messaging, school-based education, enforcement of existing laws) are working in this population and should be scaled, while targeted approaches that address alcohol consumption behaviors among adults are critically needed.[22,29,30]

Box 1. Measures of alcohol consumption and unhealthy use

Alcohol use: refers to consumption of any alcoholic beverage (i.e., containing ethanol). Usually measured in surveys as any use in a person's lifetime or in the past 12 months; quantity and frequency of use are also typically measured to estimate high-risk drinking as well as abstentions.

Alcohol use disorder (AUD): diagnosis used in DSM-5 that refers to a "problematic pattern of alcohol use leading to clinically significant impairment or distress"[31] which may be classified as mild, moderate, or severe depending on the number of behavioral and physical symptoms exhibited by a person (2-3 for mild, 4-5 for moderate, and 6 or more for severe) in the last 12 months, which may include withdrawal, tolerance, and/or craving. Combines two conditions called alcohol abuse and alcohol dependence in DSM-IV.[32]

Binge drinking: also called "heavy episodic drinking" and refers to drinking more than five drinks for men and four drinks for women in a single occasion, usually over two hours, on at least one day in the past month.[33] These amounts bring a person's blood alcohol concentration levels to 0.08 g/dL.

Heavy drinking: drinking more than two drinks for men and one drink for women on average per day (or 15 drinks or more for men and 8 drinks or more for women per week).[34]

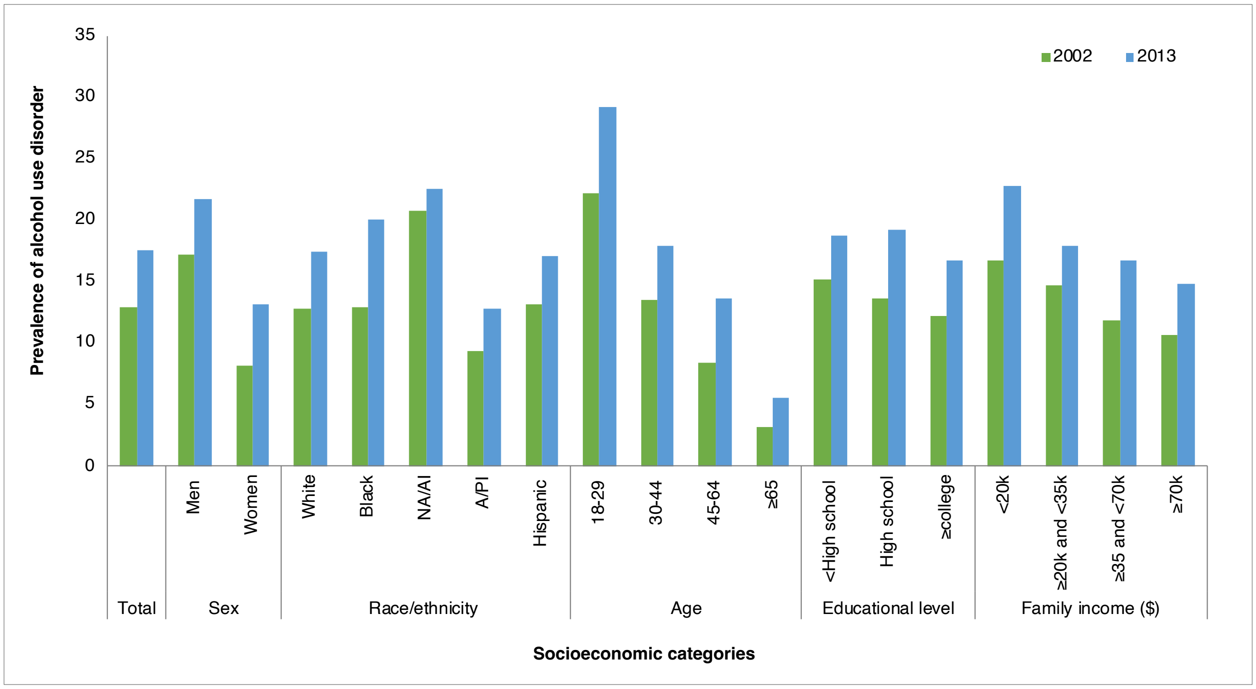
Moderate drinking: up to 1 drink per day for women and up to 2 drinks per day for men (defined by the US Department of Health and Human Services and US Department of Agriculture).[33]

Standard drink: refers to 14 grams or about 0.6 fl oz of pure ethanol and used to measure levels of alcohol consumption. Since the amount of ethanol in alcoholic beverages vary by volume, one standard drink (or alcoholic drink equivalent) in the US are 12 fl oz of beer, 89 fl oz of malt liquor, 5 fl oz of wine, and 1.5 fl oz of distilled spirits[a] (e.g., gin, rum, tequila, whiskey).[35]

[a] Distilled spirits and liquor are used interchangeably in this document.

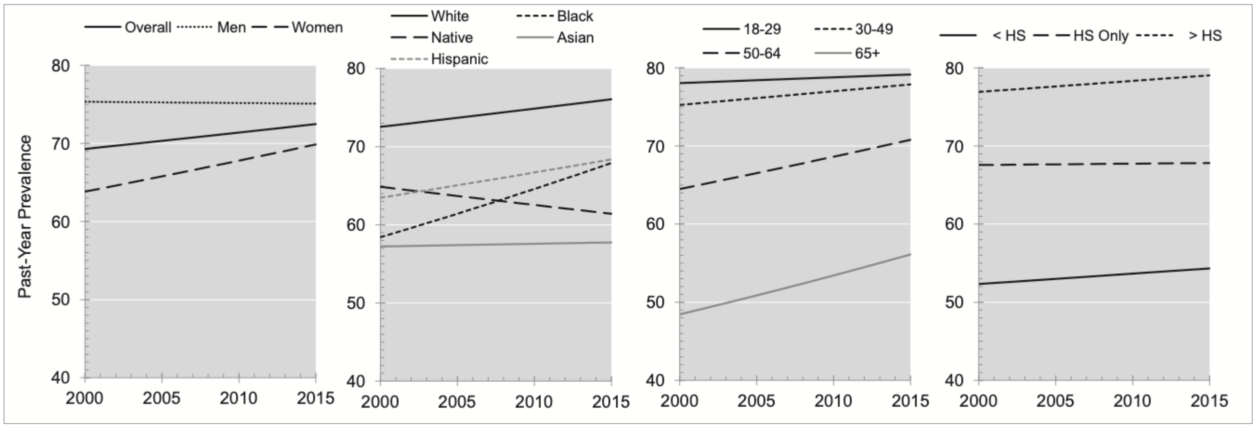
DSM, Diagnostic and Statistical Manual of Mental Disorders.

Figure 3. Prevalence and change in 12-month alcohol use, high-risk alcohol consumption, and DSM-5 alcohol use disorder in the US



This graph uses data on the prevalence of DSM-5 alcohol use disorder from Grant et al. (2017)[21]. All prevalence changes between 2002 and 2013 are statistically significant ($p < 0.05$).
DSM, Diagnostic and Statistical Manual of Mental Disorders.

Figure 4. Past-year binge drinking prevalence in the US, 2000-2015



This figure from Gurcza et al. (2018) shows simulated trend lines of past-year binge drinking prevalence based on a meta-analysis of six national surveys on alcohol use. Estimates are shown by gender, race/ethnicity, age, and education level.
HS, high school.

Increasing rates of alcohol misuse may lead to ALD in populations that are at higher risk of morbidity and mortality.[36] For example, due to physiological differences, women[*] suffer from the hepatotoxic effects of alcohol at lower levels of consumption than men.[38,40] Women develop advanced ALD more quickly than men at lower levels of alcohol use[41], and women with AC have increased liver-related mortality when drinking at similar levels to men.[42] Thus, if the gender gap in heavy drinking continues to narrow, a disproportionate increase in ALD and ALD-related harms may occur in this population.[27,43] Similarly, older adults absorb alcohol faster than younger people; thus, alcohol can increase their risk of ALD, interact with existing conditions and medications, and impact their balance, gait, cognition, and ability to drive.[44]

Rising alcohol misuse may also exacerbate existing socioeconomic and health disadvantages. Though many racial and ethnic minorities and people with low SES report lower or similar levels alcohol use[21,45], they experience higher rates of death from ALD, greater alcohol-related harms, and more severe social consequences of alcohol use compared their counterparts with similar sociodemographic characteristics—a phenomenon referred to as alcohol harm paradox.[46–52] Racial and ethnic minorities are also less likely to seek any care for AUD primarily due to stigma associated with AUD and barriers to accessing behavioral healthcare.[53]

Greater attention and action on rising alcohol consumption can prevent additional harms other than ALD. Alcohol is a leading risk factor for preventable diseases and deaths—the 6th in the US and the 7th globally.[54] Systematic reviews have reported that alcohol use is causally linked to at least 40 diseases and conditions and associated with another 200[42,55,56]; for example, alcohol consumption is estimated to directly cause 4.1% of all new cancers around the globe.[57] Studies have shown that alcohol use is

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[*] "Women" here technically refers to females at birth, which is a category of physiological sex. Females have lower levels of gastric alcohol dehydrogenase, higher inflammatory activation in response to alcohol, and have different fat and muscle composition compared to males that all contribute to a higher risk of liver disease progression.[37,38] Though sex and gender are distinct constructs[39], the term "women", which is a gender identity category, is used interchangeably with "female" throughout the document, as is common practice in the ALD literature. In reality, the gender category women may include males at birth who identify as female (e.g., gender queers, transwomen) whose risk for ALD is understudied.[39]

associated with cardiovascular diseases[58–61], disputing previous epidemiological research that suggested an association between low and moderate alcohol use with a lower risk of high-blood pressure.[62] The research to date suggests that there may be no safe level of alcohol consumption (especially for men)[63,64], and that reducing alcohol consumption through a harm-reduction approach leads to improved cardiovascular outcomes.[65,66] Alcohol use can also exacerbate other liver conditions such as viral hepatitis infections and non-alcohol-related fatty liver disease.[7,67] Aside from these health consequences, alcohol consumption is associated with myriad negative externalities such as property and violent crimes, motor vehicle accidents, injuries, and productivity losses.

EXISTING RESEARCH ON PRICING POLICIES

Several policy interventions (Figure 5) have been proposed to reduce unhealthy alcohol consumption and rising ALD rates.[68–70] These interventions address at least one of three drivers of alcohol use—affordability, availability, and acceptability. In this section, I only focus on fiscal measures or pricing policies, which have the strongest evidence base to date. (I evaluate the potential impact of these policies in Chapters 3 and 4 of this dissertation.)

Taxation

Among the most well-studied interventions is taxation, which reduces alcohol consumption by raising its price.[68] Raising taxes on potentially unhealthy products[†] has been the mainstay of tobacco and alcohol control (Box 2) and is increasingly being adopted by localities in the US and elsewhere to reduce consumption of sugar-sweetened beverages.[73–76]

[†] Consumption taxes on products and activities that generate negative externalities are also referred to as “sin” or “Pigouvian” taxes in the literature.[71] These taxes aim to “align private consumption levels with the socially optimal level of consumption.”[72]

Box 2. Alcohol tax policy in the US

In the US, both federal and state governments are constitutionally permitted to regulate alcohol, leading to a two-tier tax system in the country.[77] The federal government, through its Alcohol and Tobacco Tax and Trade Bureau (TTB) of Department of the Treasury which licenses alcohol producers and importers, imposes excise taxes on beer, wine, ciders, and distilled spirits.[77,78] TTB's excise tax on wines are volume-based or volumetric, which means that the tax rate depends in part on the amount of alcohol by volume contained by the product.

State alcohol taxes vary widely and include a combination of volumetric and ad valorem[‡] taxes, as well as other per-unit fees and taxes that depend on different characteristics such as container size, place of purchase, place of production, and alcohol content, among others.[79] All 50 states and the District of Columbia impose excise taxes on beers, while only selected states levy duties on wine and liquor producers. The variation is due, in part, to whether states are license or control states[§]. States apply taxes at the production, wholesale, or retail levels.

Federal alcohol taxes have not increased since 1991. In 2017, federal alcohol tax rates were temporarily reduced as part of the 2017 Tax Cuts and Jobs Act of 2017.[82] Federal and state taxes levied on alcohol products have not kept up with inflation or rising incomes; therefore, the impact of taxes on consumption and drinking has severely waned.[71,77,83,84] A drink per day of the cheapest spirit is only 0.29% of disposable income in 2011 compared to 4.46% in 1950.[85] Across US states, the average alcohol excise tax per drink in 2015 was \$0.03 for beer, \$0.05 for spirits, and \$0.03 for wine, and these rates are 30%, 32%, and 27% lower for beer, spirits, and wine, respectively, than the average state alcohol excise tax rates in 1991.[86]

Higher alcohol prices and taxes have been associated with various public health endpoints; for example, a meta-analysis in 2010 estimated that a doubling of alcohol taxes is associated with 35% reduction in alcohol-related mortality.[87,88] Other studies have found an association between higher alcohol taxes and lower youth motor vehicle fatalities, liver cirrhosis rates, workplace injuries, suicide rates, sexually transmitted infections, other drug use and property and violent crimes.[77,79,83,87,89] Conversely, there have been documented increases in alcohol consumption, alcohol-related

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[‡] Ad valorem (Latin for "according to value") taxes are based on the value of a transaction, property, or good. Most common ad valorem taxes are sales taxes and value-added taxes.

[§] Control states are jurisdictions where state governments have monopoly control over the wholesale, retail ("off-premise") sale, and/or distribution of alcoholic beverages. There are 17 control states in the US, and several areas within Alaska, Maryland, Minnesota, and South Dakota have adopted policies similar to control states.[80] Limited research suggests that liquor prices in control states are higher than in license states.[81]

hospitalizations, and alcohol-related sudden deaths in settings where alcohol taxes were reduced.[90–93]

Figure 5. Alcohol policy options to reduce alcohol-related liver diseases

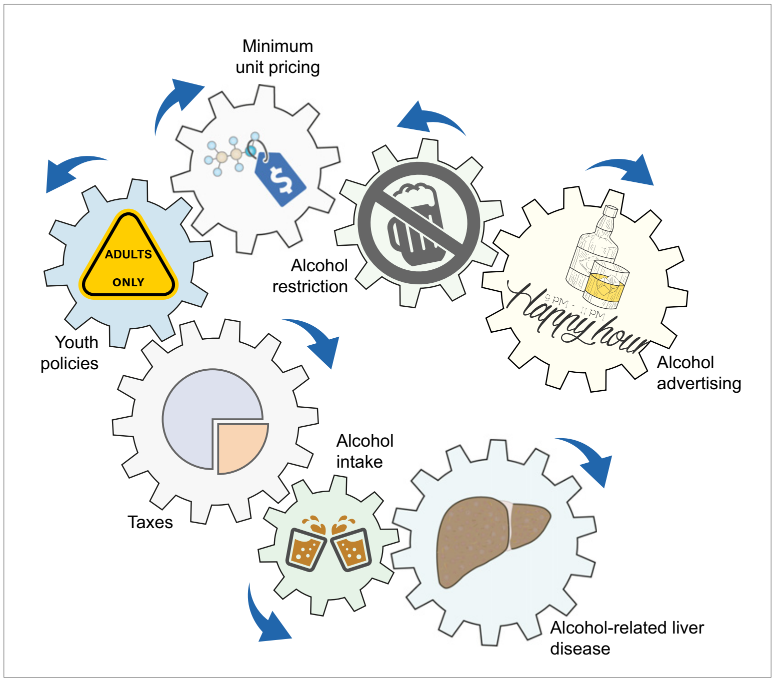

Image from Ventura-Cots et al. (2019).[94]

Demand for alcohol has been shown to be inelastic[**] or only fairly sensitive to changes in price.[95] Systematic reviews suggest that a 10% increase in the price of alcohol reduces overall consumption by about 5% and per-capita consumption by 4.4%, though more conservative estimates have also been reported (Table 2).[68,88,96] This elasticity is comparable to that of tobacco which is around -0.40.[73] The US Department of Agriculture, on the other hand, has estimated the price elasticity of alcohol products to be -0.71 when conditional on expenditures of other goods in the same category and -1.15 when conditional to total expenditures on food and beverage.[97] The price elasticity of demand[††] of alcohol also varies by type of beverage, with beer being the most

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[**] Price elasticity of demand is expressed as the percentage change in consumption resulting from a one-percent increase in price. Economists consider goods with absolute values of price elasticities less than 1 to be inelastic since the percentage change in demand is less than the change in price (i.e., a one percentage change in price is associated with less than one percentage change in consumption or demand).

[††] Price elasticity of demand, also referred to as own-price elasticity, is influenced by (1) the type of good (e.g., necessity vs. luxury item); (2) a consumer's share of income spent on that good; and (3) the availability of substitutes

inelastic among the most commonly studied products.[89,95,98–102] Research has particularly found that young people are especially sensitive to alcohol price changes. Interventions effective among youth are of particular interest to public health because drinking patterns at young ages is associated with drinking patterns later in life.[78,83]

Research suggests that price elasticity of demand[‡‡] also differs across drinking patterns or types of drinkers.[104] Seminal work by Manning et al. (1995) using National Health Interview Survey data found that light and heavy drinkers (defined as people in the lowest and highest drinking quantiles) were much less sensitive to price than moderate or median drinkers.[105] Recent research by Pryce et al., (2019) in the UK found similar results, reporting -0.71 and -0.35 price elasticities of demand for the lightest and heaviest drinkers (based on quartiles of drinking), respectively.[104] Similar findings have been reported in Australia, where moderate drinkers had lower (i.e., less negative) price elasticities than hazardous and harmful drinkers for all types of beverages and places of purchase.[103] In a meta-analysis, Wagenaar et al. (2009) reported lower price elasticities for heavy drinking, with a mean of -0.28 across 10 studies and a meta-estimate of -0.01 when limited to individual-level studies.[98] In other US-based studies, however, the price elasticities of demand among heavy and binge drinkers were found to be much higher (up to -1.325 in one study[106]), indicating that pricing policies may also play a role in deterring high-risk drinking.[89,106]

Two factors may influence the effectiveness of taxation on alcohol consumption. The first is the degree of substitution. Studies have shown that when alcohol prices increase, consumers move to cheaper beverages; for example, heavy drinkers buy cheaper products in the same category of their preferred beverage.[98,104,105,107] This substitution effect is reflected in cross-price or cross elasticity of demand, which estimates the change in consumption or demand of a good when the price of another good changes.

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or complementary goods.[73] Price elasticity of demand is different from other elasticities of demand, such as income elasticity (change in consumption following a change in income) and cross-price elasticity (change in consumption of one good following a change in price of another good).

[‡‡] Price elasticity of demand for alcohol can also vary by length of time (short- and long-run elasticities) and place of purchase (on- and off-premises). However, very few studies have explored these specific elasticities.[102,103]

While cross-price elasticities of demand have been widely studied among European countries[108–110], there are no comparable estimates in the US.

The second factor is the pass-through rates of taxes, which is the extent to which tax increases are passed on to consumers. In theory, an increase in alcohol excise taxes should lead to an equivalent or proportional increase in retail price; however, the extent to which this occurs is a function of the price elasticities of buyers and sellers, as well as other factors (e.g., presence of competitors/availability of substitutes, timing of the tax).[111] For example, at one extreme, a good with a perfectly elastic supply will lead to a fully-shifted tax where the price will increase by the amount of the tax imposed.[112] In reality, buyers and sellers share tax incidence, and pass-through rates ideally lie between 0 and 1.[112]

Several economic evaluations have been performed on alcohol pricing policies, though only one from 2000 has been specific to the US context, which found that a 20% alcohol tax added to the pretax retail price of alcohol is cost-saving.[113] Volumetric taxation in Australia has been found to be a cost-saving option compared to a do-nothing scenario.[114,115] Research by the World Health Organization suggests that policy interventions are cost-effective on a national or regional level.[69,116,117]

Minimum unit pricing

Because of the challenges with alcohol taxes, minimum unit pricing (MUP)[§§] has been promoted as an alternative intervention to increase the price of alcohol. MUP involves a mandatory, government-enforced floor price below which alcohol and alcoholic beverages cannot be sold.[119] MUP was first implemented in Canada (where it is more commonly referred to as social reference pricing) starting in the late 1980s[120]; today, most Canadian provinces, Russia, Scotland, Australia’s Northern Territory, and, most recently, Wales have MUP policies in place.[121–124] Some control states in the US (e.g.,

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[§§] Minimum prices can be established through indirect means, such as by banning the sale of large-volume alcohol containers and price promotions such as “two-for-one deals” or “happy hours.”[118]

Kansas, Ohio) have imposed minimum markups on alcohol products and have effectively set minimum prices.[121] In July 2021, Oregon, another control state, imposed a minimum price on distilled spirits ($8.95 per 750 ml bottle), which raised prices of 1-2% of products by an average of 16%.[125]

Table 1. Price elasticity of demand of alcoholic products from selected systematic reviews and meta-analyses

	Nelson (2013)[95]		Elder et al. (2010)[89]	Fogarty (2010, 2008)[99,100]			Wagenaar et al. (2009)[98]			Gallet (2007)[102]		Fogarty (2006)[101]
All alcohol	-0.54[a]	-0.49 (0.05)[b]	-0.77 (-2.00, -0.50)[c]	NA	NA	NA	-0.51[a]	-0.44[e]	-0.03[f]	-0.50[c]	NA	NA
Beer	-0.32[a]	-0.30 (0.02)[b]	-0.50 (-0.91, -0.36)[c]	-0.44 (0.46)[a]	-0.52 (0.49)[d]	-0.33[b]	-0.46[a]	-0.17[e]	-0.12[f]	-0.36[c]	-0.83[g]	-0.38[a]
Wine	-0.57[a]	-0.45 (0.04)[b]	-0.64 (-1.03, -0.38)[c]	-0.65 (0.51)[a]	-0.55 (0.45)[d]	-0.55[b]	-0.69[a]	-0.30[e]	-0.14[f]	-0.70[c]	-1.11[g]	-0.77[a]
Spirits	-0.67[a]	-0.55 (0.04)[b]	-0.79 (-0.90, -0.24)[c]	-0.73 (0.56)[a]	-0.60 (0.51)[d]	-0.76[b]	-0.80[a]	-0.29[e]	-0.10[f]	-0.68[c]	-1.09[g]	-0.70[a]

Studies included in these systematic reviews and meta-analyses include non-US studies, unless otherwise specified.

[a] Unweighted mean (standard deviation)

[b] Estimated using cumulative meta-analysis correction method

[c] Median (interquartile range)

[d] US-specific elasticities

[e] Meta-estimate using aggregate-level studies

[f] Meta-estimate using individual-level studies

[g] Estimated using an ordinary least squares model

MUP may be appealing for several reasons. MUP is a more targeted approach since it increases the price of the cheapest alcohol available, which are preferred by the heaviest drinkers.[121,126] (In the US, the top decile of drinkers consume more than half of all alcohol consumed in the country.[77]) Research in the US and elsewhere has consistently shown that the heaviest drinkers consume considerably cheaper and stronger alcohol than more moderate drinkers.[110,127–129] By contrast, low and moderate drinkers are believed to be less adversely affected by MUP since their preferred beverages may cost about the same under such policy. Various modeling studies[119,130–135] as well as early evidence from Scotland's MUP appear to support this claim.[136]

Several studies have evaluated the effects of MUP on a range of population-level outcomes. MUP in Canada and Russia have been associated with reductions in alcohol consumption, alcohol-related crime, alcohol-attributable hospital admissions, and mortality even after just a few years after the policy increased alcohol prices.[137–142] A systematic review by Boniface et al. (2017) concluded that the evidence so far supports the causal link between MUP and reduced consumption and alcohol-related mortality.[143] Recent evidence from Scotland, where MUP was implemented in 2018 after a long legal battle in the European Union and Scottish courts, found that MUP led to a 7.6% reduction in weekly alcohol purchases, which is equal to 9.5 g of alcohol per adult per household.[136] Recent analyses revealed that price increases and purchase decreases were sustained in the second year of implementation.[136,144–147] One hospital in Glasgow found a statistically significant decrease in the number of ALD-related discharges and active drinkers among ALD patients after the implementation of MUP, though there was no difference in the share of severe disease among those with ALD.[148]

MOTIVATION AND GAPS IN RESEARCH

Several reasons make ALD and alcohol price policies suitable for in-depth study and evaluation. First, alcohol use and misuse are on the rise (Figure 3 and Figure 4), which highlights the need for policy interventions to reverse these trends. Recent epidemiological evidence also suggests that alcohol misuse and ALD are increasingly affecting populations that are at higher risk of mortality and other alcohol-related harms, including women, select racial/ethnic minorities, and older people.

Second, hepatology and public health researchers have historically paid less attention to alcohol and ALD compared to other causes of liver disease such as viral hepatitis, in part because of the high burden of viral hepatitis globally.[149] However, as hepatitis B vaccination have been scaled up and hepatitis C treatments become cheaper and more widely available, alcohol-related and non-alcohol-related fatty liver diseases have overtaken viral hepatitis as the leading causes of liver disease in the US and other high-income settings.[13]

Finally, existing research have little relevance to the US or its rapidly shifting alcohol and ALD landscape. The simulation-based studies that have focused on the US[150–152] have not examined the distribution of ALD or the heterogeneous effects of alcohol pricing policies on subgroups other than low- and high-risk drinkers.[153] Additionally, not one study, to my knowledge, has compared the potential impact of alcohol taxes and MUP in the US, though multiple studies in other countries have done so over the last decade.[119,121]This has been due, in part, to limited data, but recent studies have documented differences in responses to alcohol price changes across racial, ethnic, and gender groups.[154,155]

EQUITY-INFORMATIVE ECONOMIC EVALUATION

This dissertation will employ a novel type of economic evaluation called distributional cost-effectiveness analysis (DCEA). While conventional CEA is widely used to determine the most efficient intervention among competing alternatives, it is less suited to quantify the health equity effects of interventions, as well as potential tradeoffs between efficiency and equity that decision-makers often have to make.[156] (Health equity here is defined as the absence of unjust differences in health, which requires treating populations differently based on need or disadvantage and often implies prioritization. Equity is thus distinct from equality, which requires treating populations the same way.) These efficiency-equity tradeoffs are especially relevant in alcohol pricing policies because of their potential to impact population subgroups in different ways.

In recent years, several equity-informative economic evaluation methods have been developed to incorporate equity concerns in economic evaluation.[157] These innovations to traditional CEAs quantify the distributional effects of health interventions based on different equity criteria such as socioeconomic status, race/ethnicity, geography, and disease burden. Previous reviews[158,159] provide excellent introduction to these methods, including extended CEA, equity weighting, equity constraint analysis, and DCEA. Among the growing number of equity-informative economic evaluation methods, only DCEA summarizes changes in health inequality that result from competing alternatives in one metric, which can be compared to a decision-maker's attitudes about the acceptable level of inequality in society in order to identify the preferred intervention.[156,160] To my knowledge, no DCEA on alcohol pricing policies has been published before.

AIMS AND CONTRIBUTION TO THE LITERATURE

This dissertation will contribute to the literature in several ways. First, <u>I developed a state-transition model of the US population and projected the future burden of ALD in the country given current rates of alcohol consumption reported in national surveys</u> before the COVID-19 pandemic. This model is the first to look at key sociodemographic groups who have experienced significant increases in high-risk drinking. The model estimates the number of cases of each type of ALD, as well as ALD-related mortality, disaggregated by age, gender, and race/ethnicity.

Second, using this microsimulation model, <u>I explored the cost-effectiveness of alcohol pricing policies in the US, specifically taxation and MUP, as interventions to reduce the burden of ALD</u>. This CEA examined the costs and health benefits of pricing policies by leveraging previously published estimates of the price elasticity of demand among low-risk, moderate, and excessive drinkers. I used healthcare and societal perspectives and employed several scenario and sensitivity analyses to understand the effect of parameter uncertainty on the cost-effectiveness estimates.

Finally, I conducted a distributional CEA, a type of equity-informative CEA, to quantitatively estimate and compare the distributional costs and health benefits of alcohol taxation policies**.** I measured changes in the relative health inequality across groups and determined, given different levels of inequality aversion, the optimal taxpolicy that is both efficient and equitable. This distributional CEA is one of the first conducted in a US setting.

Chapter 2: Estimating the Future Burden of Alcohol-related Liver Diseases

BACKGROUND

Recent studies have shown that the burden of alcohol-related liver disease (ALD) has been increasing.[161] While overall ALD prevalence may have remained stable in the US at 8%, advanced or severe forms of ALD are on the rise.[162] One study estimated that the prevalence of alcohol-related cirrhosis (AC) rose from 0.07 to 0.10% between 2009 and 2015.[9] Additionally, ALD-related mortality increased between 2-5% per year between 2007 and 2016.[18] For adults less than 34 years of age who experienced the highest relative increase in liver-related mortality between 2009-2016, the main cause was ALD.[11,17] Women, particularly women of color, experienced significant increases in ALD-related mortality and hospitalizations[16,19], and they have also been shown to die from ALD up to three years earlier than men with the same disease.[17] Alcohol has also been estimated to be responsible for 24% of all hepatocellular cancer (HCC) cases, second only to metabolic causes (37%) and higher than hepatitis B and C (28% combined).[163] The proportion of liver transplants in the US for ALD increased from 24% to 37% between 2002 and 2016, making it the most common indication for liver transplantation today.[13]

The burden of ALD is expected to increase given trends in alcohol consumption in the US. However, changes in alcohol use and misuse have been variable across sociodemographic groups. While rates of alcohol use and misuse remain highest among people who are young (≤29 years old), male, White, and have a college-level education, the steepest increases have been documented among women, older adults, racial/ethnic minorities, and people with low socioeconomic status (SES).[25] For example, the annual increase in the prevalence of binge drinking was 1% for Blacks and

Hispanics and 0.6% among Whites between 2000 and 2016.[25] While 18-29-year-olds experienced nonsignificant increases in binge drinking, individuals aged 65 and older saw a 3.4% year-to-year increase in the same period.[25] Finally, while there have been no changes in the binge drinking prevalence among men, women have seen a 2% annual increase.[25] These trends predate the COVID-19 pandemic, which has been linked to significant increases in excessive alcohol use and alcohol-related harms, including ALD.[164,165]

Given these heterogeneous trends, simulation models that aim to project the future health and economic burden of ALD must include these important differences in alcohol consumption between populations. Models should also capture varying levels of risks for ALD and ALD-related mortality, such as between men and women.[38] However, published models to date have been either static, which fail to capture important population dynamics, or single-group cohort models, which are unable to estimate ALD rates by age, gender, race/ethnicity, and their intersections.[151,166]

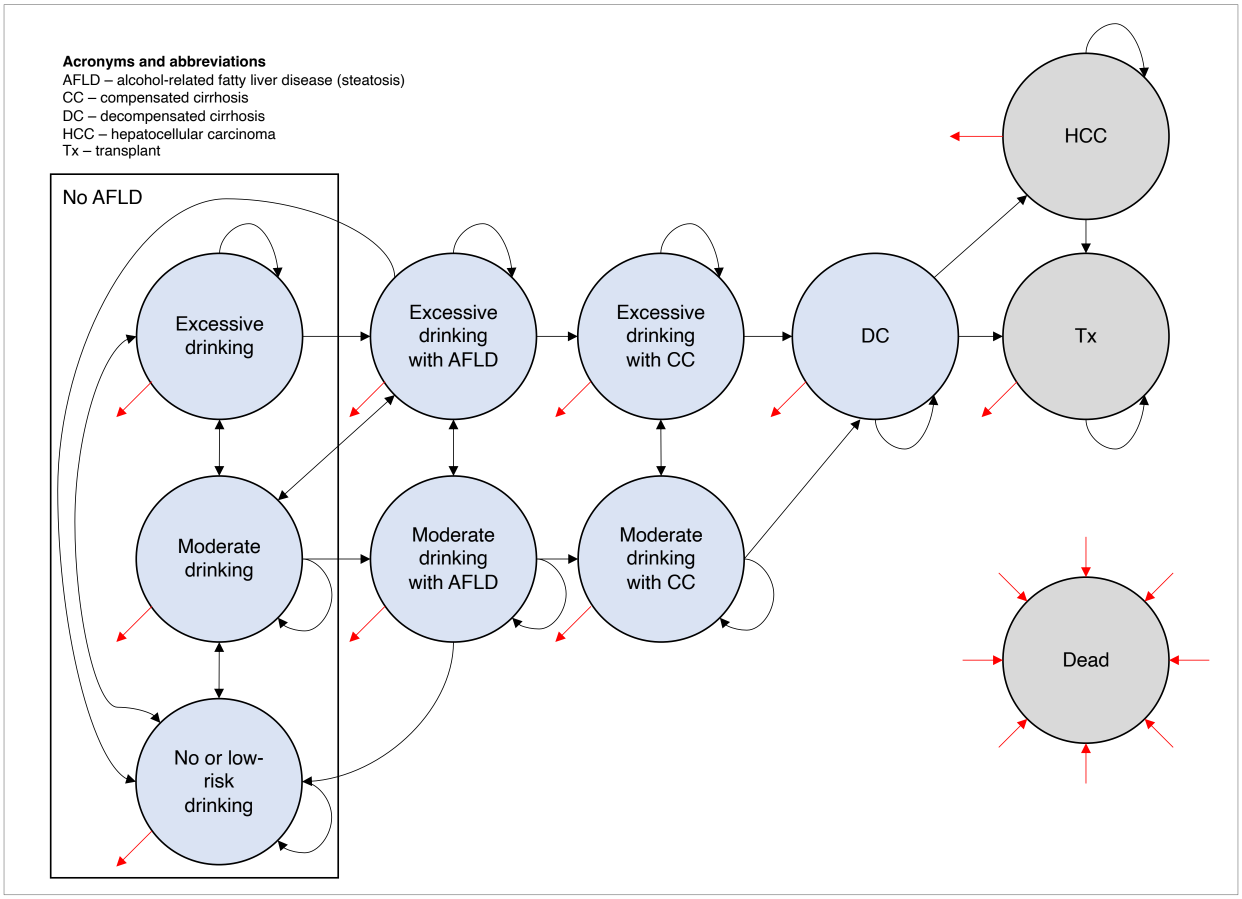
To address these limitations, I developed an individual-level, state-transition or microsimulation model of the US population. This model is the first to simulate individuals with varied sociodemographic backgrounds to produce disaggregated estimates of the ALD burden over time. This model can also be used to explore the impact of different alcohol control policies and interventions (Chapter 3), especially those with potentially heterogeneous, equity-relevant effects (Chapter 4).

METHODS

Overview

Guided by best practices in simulation modeling[167–169], I developed an open or dynamic microsimulation model that simulates US adults across different ages (18 years and older), genders, and races/ethnicities who transition between various drinking and ALD states over time (Figure 6). The model was used to estimate the number of ALD cases and ALD-related deaths under a status-quo (i.e., do-nothing) scenario. I used data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) and previously published epidemiological studies to estimate transition probabilities (Table 4). I estimated two unknown transition probabilities by calibrating modeled ALD-related death rates to reported ALD-related death rates by race/ethnicity group from the Centers from Disease Control and Prevention (CDC). The model was run for 40 annual cycles. The microsimulation was developed in R version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria) using the DARTH modeling framework.[170]

Figure 6. Microsimulation model schematic



Circles are health states, and each arrow (red and black) is a transition associated with an annual probability. The dead state was separated for clarity. Blue circles represent initialized health states, while gray circles are health states that were populated after the model was run.

Table 2. Simulation model inputs, parameters, and assumptions

Input	Base value (SD)	Range	Distribution in Monte Carlo simulation	Reference
Prevalence				
Drinking status	See aTable 1		NA	[171]
Alcohol-related fatty liver disease				
18-24 years	0.056	NA	Beta	[8]
25-44 years	0.036	NA	Beta	[8]
45-64 years	0.036	NA	Beta	[8]
≥65 years	0.01	NA	Beta	[8]
Any cirrhosis				
18-24 years	0.00003	NA	Beta	[172]
25-44 years	0.00033	NA	Beta	[172]
45-64 years	0.00082	NA	Beta	[172]
≥65 years	0.00039	NA	Beta	[172]
Decompensated cirrhosis[a]	0.28	NA	Beta	[9]
Annual transition probabilities				
Low-risk drinking[b]				
To moderate drinking	See aTable 3		Beta	[173]
To excessive drinking	See aTable 3		Beta	[173]
Moderate drinking				
To low-risk drinking	See aTable 3		Beta	[173]
To excessive drinking	See aTable 3		Beta	[173]
To moderate drinking with AFLD	0.0056 (0.001)	0.0022-0.079	Beta	[174]
To excessive drinking with AFLD	0.0056 (0.001)	0.0022-0.079	Beta	[174]
Excessive drinking				
To low-risk drinking	See aTable 3			[173]
To moderate drinking	See aTable 3			[173]
To excessive drinking with AFLD[c]	4.6 (1.58)	1.9-10.9	Log-normal	[175]
Moderate drinking with AFLD				
To low-risk drinking	See aTable 3		Beta	[173]
To excessive drinking with AFLD	See aTable 3		Beta	[173]
To moderate drinking with CC	0.062 (0.0044)	0.04-0.08	Beta	[176]
Excessive drinking with AFLD				
To low-risk drinking	See aTable 3		Beta	[173]

To moderate drinking	See aTable 3		Beta	[173]
To moderate drinking with AFLD	See aTable 3		Beta	[173]
To excessive drinking with CC	0.10 (0.0015)	0.09-0.11	Beta	[176]
Moderate drinking with CC				
To excessive drinking with CC	See aTable 3		Beta	[173]
To moderate drinking with DC	See aTable 5		Beta	[d]
Excessive drinking with CC				
To moderate drinking with CC	See aTable 3		Beta	[173]
To excessive drinking with DC	See aTable 5		Beta	[d]
Decompensated cirrhosis				
To hepatocellular carcinoma	0.0071 (0.0004)	0.0053-0.0088	Beta	[177]
To liver transplantation	0.078 (0.0033)	0.052-0.091	Beta	[13,178]
Hepatocellular carcinoma				
To liver transplantation	0.088 (0.0025)	0.077-0.10	Beta	[179,180]
Mortality rates				
Moderate drinking with CC	0.065 (0.0088)	0.03-0.10	Beta	[181]
Excessive drinking with CC	0.065 (0.0088)	0.03-0.10	Beta	[181]
Decompensated cirrhosis	0.36 (0.071)	0.17-0.64	Beta	[182]
Hepatocellular carcinoma	0.11 (0.0063)	0.091-0.11	Beta	[183]
Transplantation <1st year	0.085 (0.0025)	0.08-0.09	Beta	[13]
Transplantation ≥1st year	0.031 (0.0006)	0.03-0.0325	Beta	[13]
Other causes	See aTable 4		NA	[184]

[a] Decompensation was defined as having at least one occurrence of ascites, hepatic encephalopathy, or variceal bleeding

[b] Includes individuals who are lifetime or past-year abstainers

[c] Relative risk applied to the probability of AFLD given moderate drinking

[d] Estimated for each racial/ethnic group through calibration

AFLD, alcohol-related fatty liver disease; CC, compensated cirrhosis; DC, decompensated cirrhosis; NA, not applicable; SD, standard deviation.

Model description

Also known as a first-order Monte Carlo simulation, a microsimulation model is a type of state-transition model that simulates individuals with varied characteristics transitioning between states over time.[167,185,186] Unlike cohort or Markov state-transition models, microsimulations relax the “memoryless assumption” by allowing transitions between states to be dependent on an individual’s characteristics, such as age and gender, or the length of time an individual has been in a particular state. Microsimulations, however attractive, are computationally demanding since millions of individuals are usually required to generate stable estimates of expected value, and they also require a lot of data to be parameterized.[167]

A microsimulation was preferred for this study for several reasons. One, alcohol use behaviors vary by age, gender, and race/ethnicity in the US and elsewhere, and I am interested in estimating the future burden of ALD in these sociodemographic groups.[21119] Second, the health, social, and economic effects of alcohol misuse vary by subgroup; for example, women experience the hepatotoxic effects of alcohol at lower rates of consumption than men[38,40], and racial/ethnic minorities report more social consequences of drinking.[46–49,187–191] Finally, pricing interventions have heterogeneous effects on different sociodemographic groups, which is a phenomenon I explore in Chapter 4.

The model (Figure 6) was informed by previous decision-analytic and simulation models and developed under the guidance of experts.[152,192,193] The structure of the microsimulation model follows the established trajectory of drinking behavior and ALD progression (Figure 1 and Appendix 1), which starts with alcohol-related steatosis or fatty liver disease (AFLD) and then progresses to compensated AC, decompensated AC, and HCC which cannot be reversed. Individuals in the AFLD and compensated AC states are also assigned a drinking status, which is either moderate or excessive (Table 3). Individuals with decompensated AC and HCC may undergo transplantation, which is an absorbing state in the model; in reality, however, post-transplant patients may experience cirrhosis again if they resume alcohol use. New entrants to the model (i.e., 18-year-olds) were assumed to have the same characteristics as the 18-year-olds of the original cohort.

Table 3. Drinking status definitions from NESARC

Drinking status	Definition
Past-year drinker	Had ≥1 drinks[a] in the past year; includes low-risk, moderate, and excessive drinkers
Moderate drinker	Past-year drinker who had (1) up to 1 drink per day for men ≥65 years and women or (2) up to 2 drinks per day for men <65 years in the past year
Excessive or high-risk drinker	Past-year drinker who exceeded daily[b] and/or weekly[c] moderate drinking limits

[a] A standard drink in the US is 0.6 fl oz or 14 grams of pure ethanol

[b] (1) ≥5 drinks for men <65 years and ≥4 drinks for men ≥65 years and women on one or more occasions or (2) usual or largest ethanol intake of any beverage type >4.5 drinks for men <65 years and > 3.5 drinks for men ≥65 years and women

[c] >14 drinks per week for men <65 years and >7 drinks per week for men ≥65 years and women

NESARC, National Epidemiologic Survey on Alcohol and Related Conditions.

Starting distribution of population

The model simulates noninstitutionalized US adults aged 18 and older from 2001 onwards. An initial cohort of 1 million individuals with various ages and genders from each racial/ethnic group (i.e., White, Black, Latino or Hispanic, Asian American and Pacific Islander [AAPI], and American Indian and Alaska Native [AIAN][***]) were proportionally sampled based on their representation in the US population; data on the US population by were taken from the US Census Bureau.[194]

At the start of the model, individuals were assigned a drinking status and ALD status based on publicly available epidemiological data. Initial drinking status was based on the 2001 prevalence of past-year (i.e., current) drinking, moderate drinking, and excessive drinking in the US as reported in the 2nd wave of NESARC[171] (aTable 1); the definitions of these categories in NESARC are found in Table 3. NESARC was selected among other nationally representative surveys (e.g., National Survey on Drug Use and Health [NSDUH], National Health and Nutrition Examination Survey [NHANES]) that

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[***] Racial and ethnic categories used in the US Census were adopted for this study.

also measure drinking levels because it has sufficient representation of racial/ethnic minorities and has the most detailed questions about drinking behavior.[195,196]

The drinking status of individuals in my model are based on recommended daily limits (Table 3), as opposed to other measures of risky drinking such as binge drinking, because daily consumption of alcohol has been strongly associated with cirrhosis incidence.[197] Non-drinkers were defined as anyone who did not consume alcohol in the past year, and they were combined with other past-year drinkers who were not moderate or excessive drinkers to constitute low-risk drinkers in the model. I calculated age-, gender-, and race/ethnicity-specific drinking prevalence by assuming that drinking prevalence by age and racial/ethnic group reported in NESARC is equal to the weighted average of the drinking prevalence among men and women in each race/ethnic group (Appendix 2). Population weights were based on data from the US Census Bureau (aTable 2).[194]

I assumed that a proportion of past-year drinkers in 2001 had AFLD, compensated AC, and decompensated AC (Table 2). The prevalence of AFLD and any alcohol-related cirrhosis by age group were based on two separate retrospective analyses of NHANES.[8,172] To estimate the proportion of compensated and decompensated AC among all cirrhosis cases, I assumed that 28% of alcohol-related cirrhosis are in the decompensated state, as estimated in a previous analysis of MarketScan data.[9]

Transition probabilities

Transition probabilities for this study (Table 2) are based on previously published studies that were identified through literature reviews, citation tracking, and snowball searches conducted between July-December 2020. I estimated two unknown transition probabilities through calibration, which is described in below and in Appendix 3.

Transitions between drinking states by age, gender, and race/ethnicity were based on a previous analysis by Barbosa et al. (2019) of NESARC data that estimated long-term transition probabilities between the World Health Organization (WHO) drinking risk levels (aTable 3).[173] The results were validated by comparing calibrated transition probabilities from NESARC waves 1 and 2 with the prevalence of various drinking states from NESARC wave 3. To align WHO drinking levels from Barbosa et al. with the drinking levels in my model (Table 3), I assumed that “abstinent drinkers” and “low risk drinkers” were equivalent to my model’s low-risk and moderate drinkers, respectively, based on the definitions and drinking thresholds used by the WHO. I also assumed that excessive drinkers in my model were represented by the WHO’s “medium,” “high,” and “very high risk” drinkers.

Moderate and excessive drinkers may develop AFLD, and I based their annual risk on a historical natural history study of biopsy-confirmed AFLD in the UK.[174] For excessive drinkers, I weighted their risk of developing AFLD by the risk ratio reported in a histological study of the dose-response relationship between alcohol and cirrhosis.[175] The probability of developing cirrhosis from AFLD was based on a randomized controlled trial that tracked the outcomes of participants with biopsy-confirmed fibrosis or incomplete cirrhosis over two years[176]; this study was preferred over other sources because it disaggregated risk by level of alcohol consumption, and the probabilities derived from this study are within the range reported in a recent systematic review and meta-analysis.[181]

The probability of HCC development from compensated and decompensated cirrhosis and the probability of death from HCC are based on large population-based cohort studies of Danish patients.[177,182] For death after transplantation, we relied on a recent analysis of cohort data from the United Network for Organ Sharing database.[13] We calculated the probability of transplantation among patients with decompensated cirrhosis and HCC using waitlist rates reported from previous studies[178,179] and liver transplant rates from the Organ Procurement and Transplantation Network annual reports (Appendix 3).[180,198] All-cause mortality rates by age, gender, and race/ethnicity were taken from CDC Life Tables.[184]

Model calibration

I calibrated my model to estimate the probability of decompensation among moderate and excessive drinkers with compensated AC (Table 2). Calibration is the process of estimating unknown or uncertain model parameters by matching or “fitting” modeled results to observed data, which are referred to as calibration targets.[199] In this study, I used ALD-related mortality rates by race/ethnicity from CDC WONDER for 2005-2020 as the calibration target; thus, calibration was conducted for each race/ethnic group separately.[10] Parameter values were identified by minimizing squared differences between overall ALD-related mortality rates from my model and CDC. Detailed descriptions and results of the calibration are found in Appendix 3.

Outcomes

Using the calibrated model, I estimated the incidence rate of ALDs and ALD-related mortality for 2021-2041. The ALD incidence rate was calculated by dividing the new cases of ALD by the number of people at risk in each year. ALD-related mortality was calculated by dividing deaths from compensated AC, decompensated AC, and HCC by the number of individuals alive in each year. Results are presented in terms of overall rates and rates by age group, gender, and race/ethnicity, as well as cross sections of these sociodemographic characteristics. Using ALD rates, I also calculated the number of incident ALD cases and ALD deaths by multiplying the estimated rates by estimated population sizes from the US Census Bureau.

I employed second-order Monte Carlo simulation to understand the effect of parameter uncertainty on model estimates. In Monte Carlo simulation, I conducted 1,000 independent simulations by drawing random values of each parameter based on distributions that were assigned a priori. Transition probabilities were assigned a beta distribution, while relative risks were assigned a lognormal distribution. I based ranges and standard deviations for each input on reported figures from the literature where available; for inputs where ranges were not available, I applied ±25% on the mean estimate to generate upper and lower limits.

To incorporate the results of the calibration in the Monte Carlo simulation, I took the top 30 best-fitting estimates from the calibration of the probability of decompensation among moderate and excessive drinkers with compensated AC and randomly sampled one parameter set for every Monte Carlo trial. By sampling the calibrated parameters in pairs, I was able to capture any correlations that may exist between the two.[199]

The base-case results represent the average results of the Monte Carlo simulation, and the 95% credible interval (CI) was calculated using the normal approximation formula for a binomial distribution confidence interval (Appendix 4).

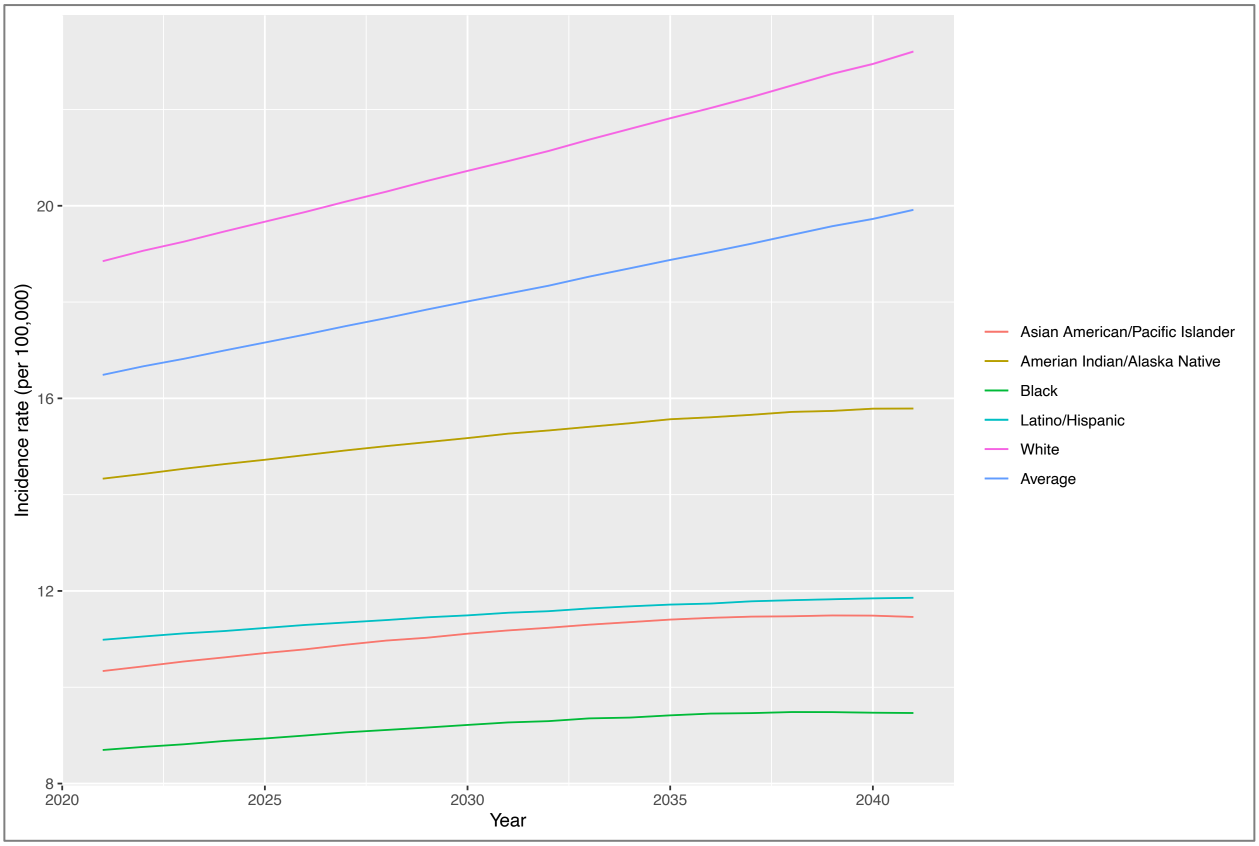
RESULTS

ALD incidence

The model projects that ALD incidence will increase from an average of 16.49 (95% CI 16.47-16.51) per 100,000 person-years in 2021 to 19.92 (95% CI 19.90-19.94) per 100,000 person-years in 2041 (

Figure 7). This represents a 17% increase over a 20-year period or roughly 0.8% per year. These rates translate to a cumulative sum of 1.3 million incident cases of compensated and decompensated alcohol-related cirrhosis in the US (Figure 8).

Figure 7. ALD incidence by racial/ethnic group



This figure shows the incidence rate of compensated and decompensated alcohol-related cirrhosis per 100,000 person-years over time. The average rate represents the weighted average across the race/ethnic groups.

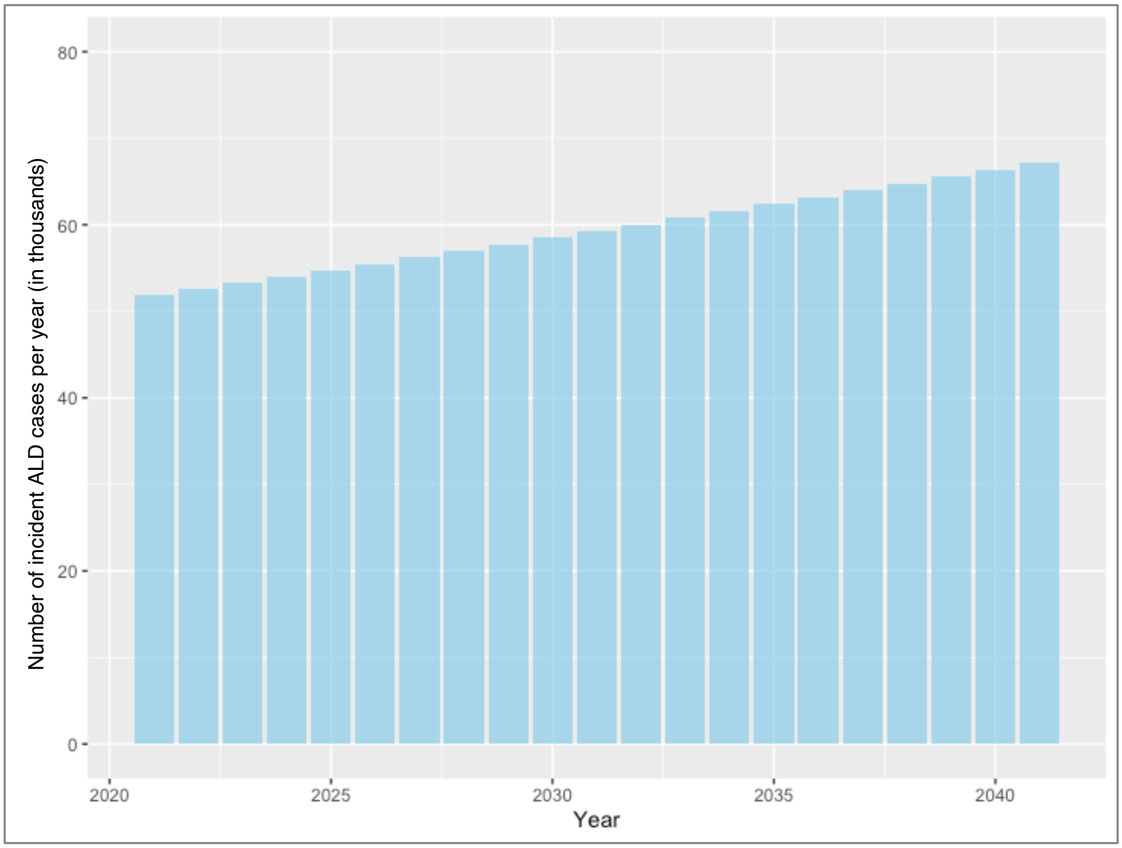
While ALD incidence is estimated to increase over time, the model found differences between racial/ethnic groups (

Figure 7). Whites had the highest incidence of ALD at 18.85 (95% CI 18.83-18.87) per 100,000 person-years in 2021, which is projected to increase to 23.20 (95% CI 23.18-23.23) per 100,000 person-years by 2041. Only Whites had an ALD incidence and ALD incidence growth rate (0.9% per year) higher than the US average. The AI/AN population had the second-highest incidence of ALD in 2021 (14. 33 per 100,000 person-years; 95% CI 14.32-14.35), followed by Latinos/Hispanics (10.99, 95% CI 10.97-11.00), AAPIs (10.34, 95% CI 10.32-10.35), and Blacks (8.69, 95% CI 8.68-8.71). The incidence of ALD for these racial/ethnic groups is estimated to increase by 9.2%, 7.4%, 9.8%, and 8.1%, respectively, over a 20-year period.

Figure 8 shows the number of ALD cases, defined as the sum of compensated and decompensated cirrhosis cases, from 2021 and 2041 that were estimated using the incidence rates in

Figure 7. The model estimated that by 2041, there will be about 67,100 new cases of ALD per year.

Figure 8. Total number of incident ALD cases by year

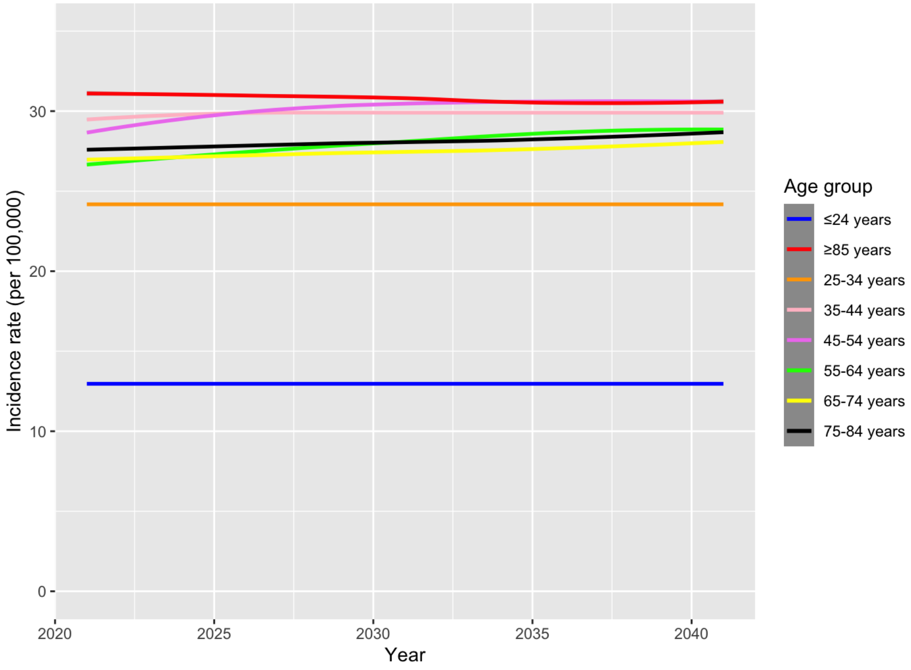


This figure plots the number of incident cases of compensated and decompensated alcohol-related cirrhosis over time.

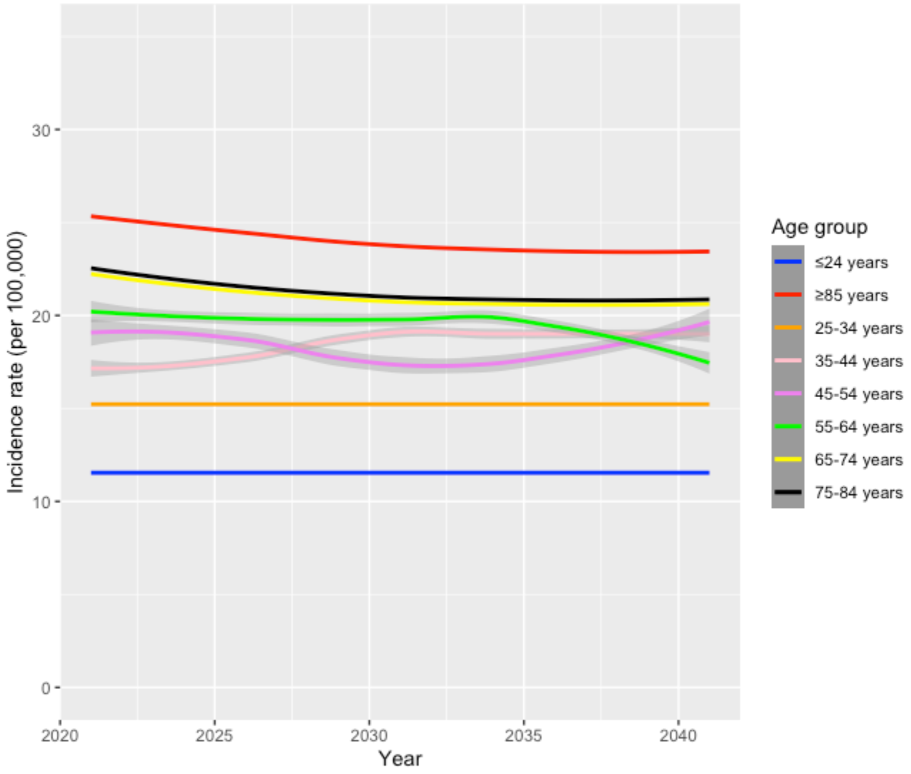
Analyzing the model's projections by age also reveals small differences that are masked by a focus on average rates (Figure 9). For example, the ALD incidence is highest among men aged 45-54, followed by 35-44-year-olds and those greater than 85 years. The incidence of ALD is roughly similar among the 55-84-year-olds. Women, who were estimated to have lower ALD incidence than men, also showed heterogeneity across age groups. However, ALD incidence rates by age do not appear to change significantly over time, largely due to the demographics of the population.

Figure 9. ALD incidence by gender and age group

A. Men



B. Women

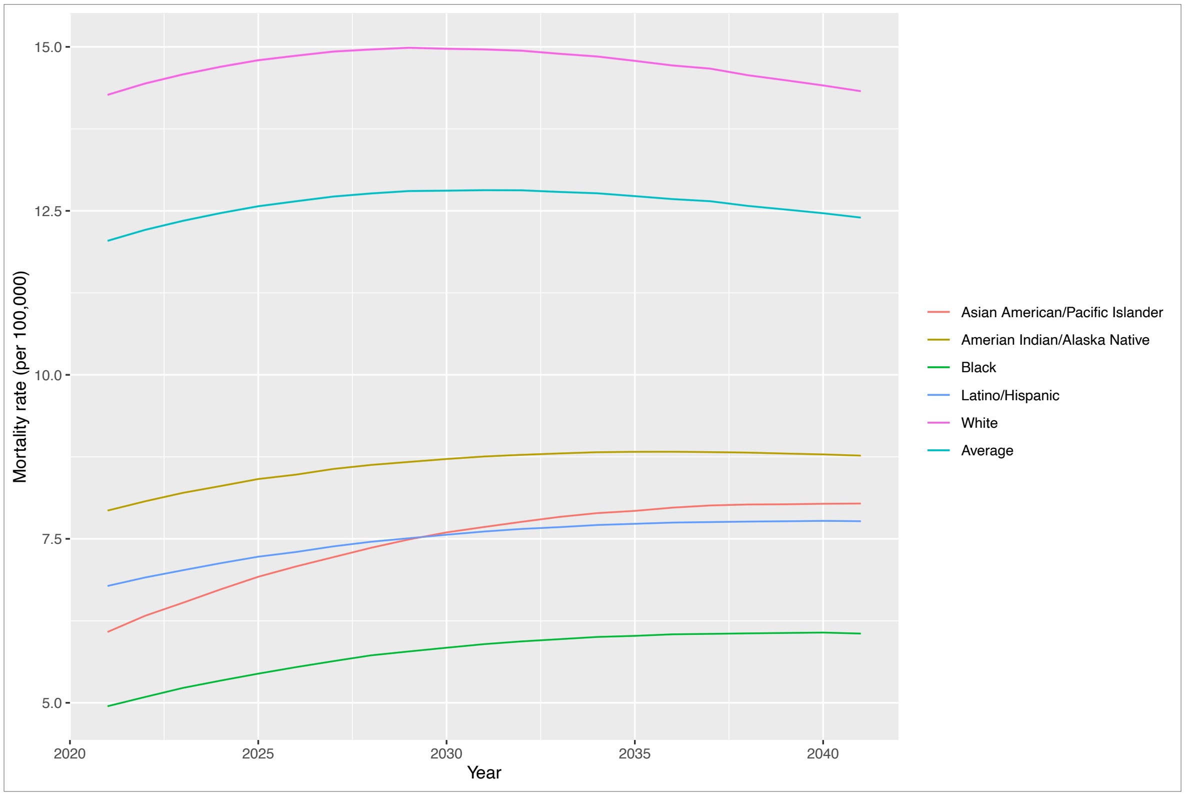


This figure shows the incidence rate of compensated and decompensated alcohol-related cirrhosis among men across various age groups per 100,000 person-years over time.

ALD-related mortality

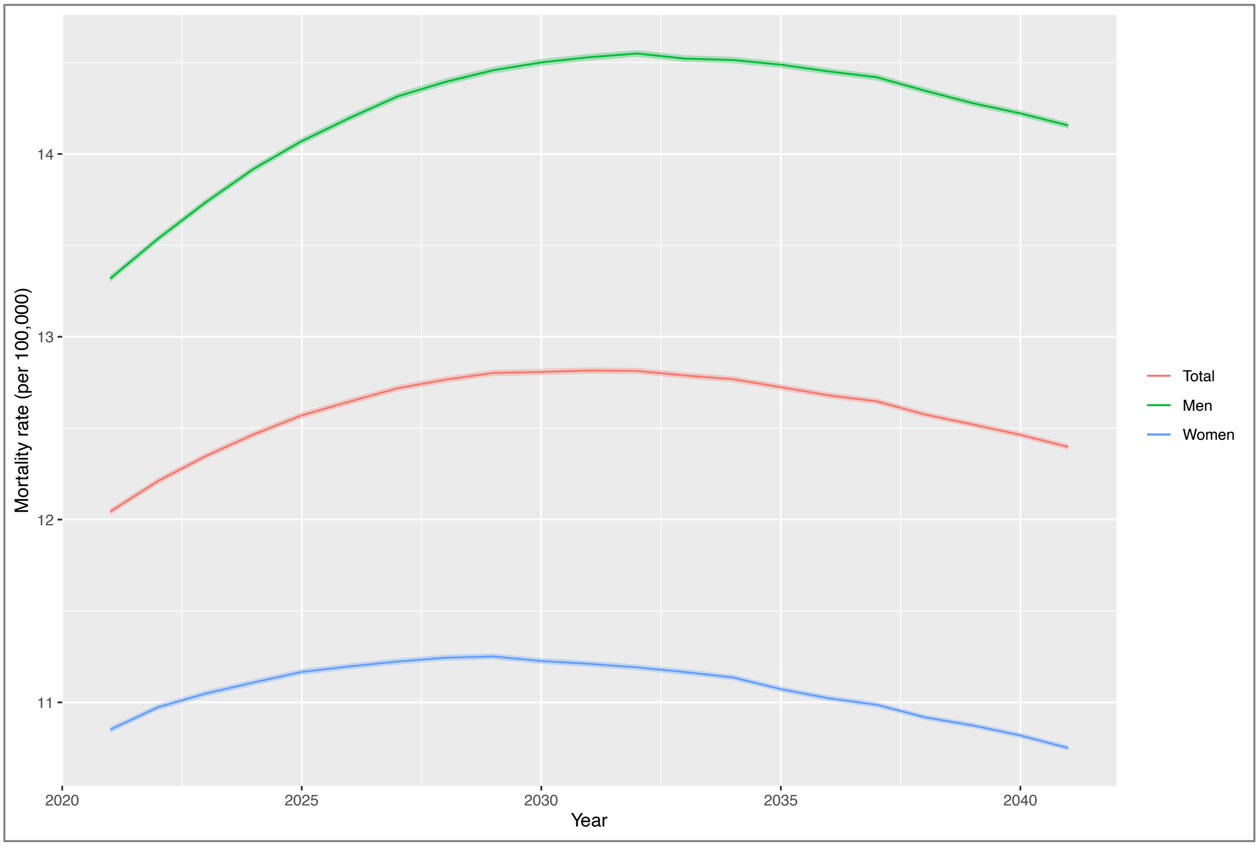
The model projects that ALD-related mortality rate will increase from 12.0 to 12.4 per 100,000 person-years between 2021 and 2041 (Figure 10). However, when analyzing ALD-related mortality rates by race/ethnicity, significant disparities are revealed. Whites have the highest ALD-related mortality at 14.3 (95% CI 14.2-14.3) per 100,000 person-years in 2021; it is the only racial group with rates that are higher than the US average. Similar to the trends found for ALD incidence, ALD-related mortality is second-highest among AIANs, followed by Latinos/Hispanics, AAPIs, and Blacks. However, the model predicts that the ALD-related mortality rate for AAPIs will supersede that of Latinos/Hispanics in year 2029, despite having a lower average ALD incidence rate from 2020-2040.

Figure 10. ALD-related mortality by racial/ethnic group



This figure shows the mortality rate from decompensated cirrhosis per 100,000 person-years over time. The average rate represents the weighted average across the race/ethnic groups.

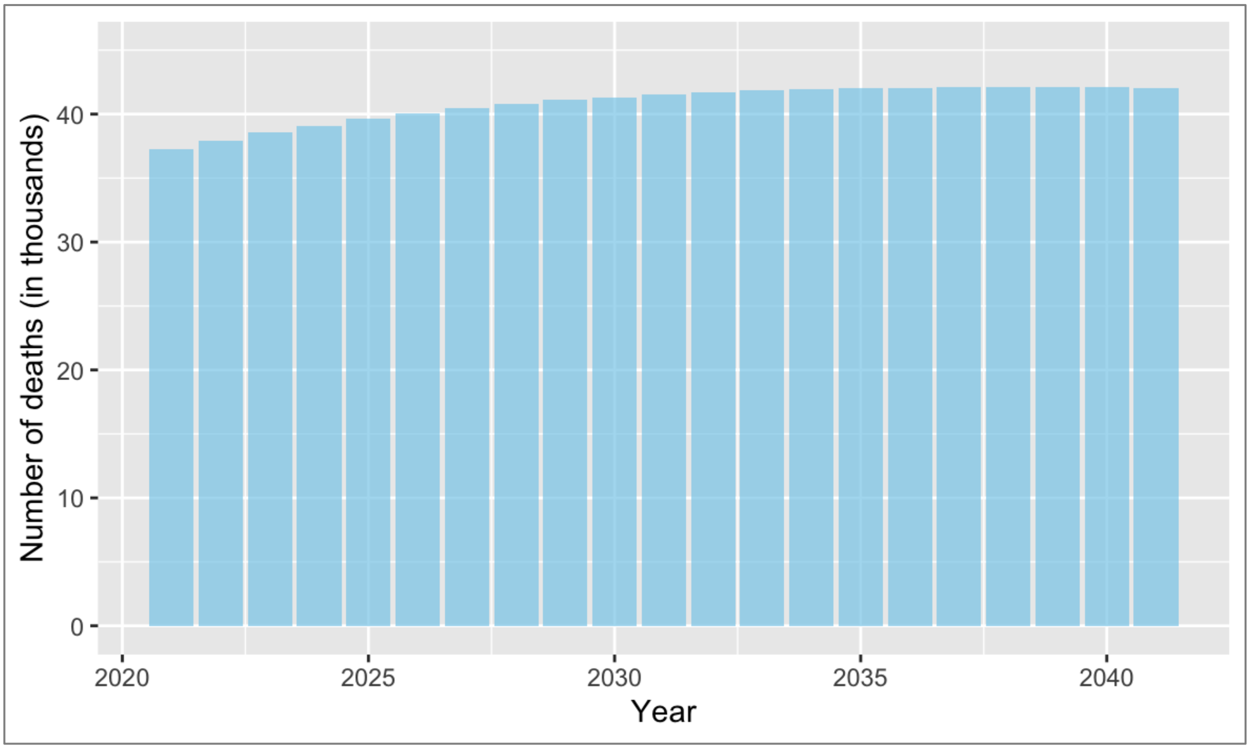
Figure 11. ALD-related mortality by gender



This figure shows the mortality rate from decompensated cirrhosis per 100,000 person-years over time. The average rate represents the weighted average across men and women.

With these estimated mortality rates, we could expect to see 30,000-40,000 deaths per year from ALD, which would lead to a total of 914,000 (95% CI 912,000-915,000) deaths after 20 years (Figure 12).

Figure 12. Number of ALD deaths by year



This figure plots the number of ALD-related deaths over time.

DISCUSSION

In this study, I projected the future burden of ALD among different sociodemographic groups in the US. I found that ALD incidence is expected to increase by 17% over 20 years, while ALD-related mortality is only expected to increase modestly in the US. This study also found that average ALD incidence and ALD-related mortality rates are masking notable disparities by age, gender, and race/ethnicity. The results of this model align with surveillance data that suggest the disproportionate impact of ALD on Whites and AIAN populations, as well as men across ages and racial/ethnic groups.[8,9,11]

ALD incidence and ALD-related mortality rates from this study differ from previous estimates using surveillance data and other modeling techniques. For example, a previous study by Julien et al. (2020) used multicohort state-transition model and estimated the incidence of decompensated AC to be 9.9 (95% CI 9.3-10.9) per 100,000 person-years in 2019, which they reported will increase to 17.5 per 100,000 in 2040.[152] By contrast, this study estimated the incidence of AC, which included both compensated and decompensated AC, to be 16 per 100,000 person-years in 2019 and 20 per 100,000 in 2040. Aside from differences in the definition of incident AC used, varied modeling approaches and data sources may have also contributed to discrepancies in the estimated long-term incidence of AC between the two studies. For example, Julien et al. assumed a flat annual increase in high-risk drinking in the US based on data from NESARC waves 2 and 3.[152] By contrast, this study did not assume year-to-year increases in drinking rates over time and instead relied on long-term transition rates from Barbosa et al., which captured some but not the same trends in drinking behavior that were reported in the NESARC. Alignment in the ways incident ALD cases and populations at risk are defined and use of similar data sources may reduce differences between model estimates, which future studies should explore.

ALD-related mortality rates also differ between this study and other sources. For example, the CDC reported a crude ALD-related mortality rate of 9 (95% CI 8.9-9.1) per 100,000 in 2020, which is 27% lower than the 11.5 per 100,000 person-years estimated from this study.[10] For 2019, the Institute for Health Metrics and Evaluation reported an even lower estimate of 5.29 per 100,000 population.[200] As with ALD incidence rates, discrepancies between these figures can be due to reasons related to the methods, data sources, and definitions of ALD-related mortality used. ALD-related mortality estimates from the CDC are based on confimed AC deaths (which may be underreported[201]) and a small proportion of unspecified cirrhosis deaths—an approach that has been critiqued for potentially undercounting ALD deaths in the country.[202] Additionally, rates from this current study reflect the weighted average across five racial/ethnic groups and excludes bi- or multi-racial individuals due to data limitations. Future studies should aim to include additional race/ethnic groups in the estimation of ALD-related mortality.

Estimates of the future burden of ALD can be used to guide resource allocation and program design and evaluation, and this study builds on a small number of previous modeling studies. For instance, the Julien et al. study mentioned previously estimated that a “strong intervention” scnenario that reduced high-risk drinking by 3.5% per year would bring down ALD-related mortality to roughly 8 per 100,000 person-years in 2040—a 50% reduction from the status-quo projection.[152] A more recent modeling study that used a microsimulation estimated that a single-year increase in alcohol misuse in the US associated with the COVID-19 pandemic could lead to 18,000 additional cirrhosis cases and 8,000 additional ALD-related deaths.[193] These findings track with empirical work that showed a 50% increase in transplant waitlist registrations and transplantations during the pandemic, primarily driven by people with alcohol-related hepatitis.[165] Outside the US, most studies have leveraged population-attributable fractions for ALD to estimate the future burden of ALD and other alcohol-related harms under different scenarios where alcohol consumption is reduced.[203,204]

This study adds to the literature by modeling different age, gender, and racial/ethnic groups in the US and providing population-specific estimates of ALD incidence and ALD-related mortality. To my knowledge, this is the first modeling study of its kind and fills a significant gap in the ALD literature. Several challenges have likely precluded the development of micosimulation and other individual-level models for ALD, particularly the paucity of data on specific subpopulations. While some model inputs in this study were specific to different age, gender, and racial/ethnic groups (e.g., drinking prevalence[171], drinking transitions[173], all-cause mortality[184]), most inputs are based on the outcomes of the general population or estimated through calibration, which may introduce significant uncertainty on the results. Additionally, ALD is challenging to model because it develops over long periods of heavy alcohol use, and long-term transition rates between ALD states under different alcohol consumption levels have not been systematically estimated before.

Historically, alcohol use, alcohol misuse, and ALD have been most common among individuals who are White, male, and have a high SES.[25] However, recent studies have revealed that women, certain racial/ethnic minorities, older adults, and people with low SES have experienced the steepest increases in alcohol use misuse in the last two decades.[21,25] These trends in alcohol consumption are likely driven by multiple factors including the increased availability and affordability of alcohol, targeted marketing efforts, and rapidly changing social and cultural norms around drinking.[21] For example, alcohol companies have focused their advertising, especially social media marketing, to women, racial/ethnic minorities, and low-SES communities in the US and around the world.[27,205,206] In terms of affordability, federal and state taxes on alcohol products in the US have not kept up with inflation or rising incomes; thus, the impact of taxes on consumption and drinking has severely waned.[71,77,83,84]

Isolation, experiences with discrimination and stigma, and economic hardship are also potential causes of increased alcohol use and misuse in the US.[19,205] Like other addictive substances, alcohol is often consumed to cope with and manage social stressors, and its wide availability and legal status allows many people to easily access it, as was seen during the COVID-19 pandemic.[164] Increased alcohol use among women has also been linked to their changing roles in society.[207] Future studies should explore the potential impact of policies that address the social determinants of alcohol use and misuse as a means of curbing the ALD burden.

The microsimulation model from this study can be used to estimate the potential costs, benefits, and distributional effects of various policy and healthcare interventions, especially in specific subgroups of interest. Research has repeatedly shown that individual- and population-level interventions such as alcohol taxation, education, and counseling have heterogeneous effects that are not often reflected in modeling studies.[131,154,155,208] (I explore the potential costs and benefits of alcohol price policies in Chapter 3.)

Study limitations

The results of this study should be interpreted with the limitations in mind. Several limitations are related to the inputs used, which introduce different degrees of uncertainty to the results. First, some inputs were not generated using data from the same population that was modeled in this study; for example, the probability of developing HCC is based on a Danish study[177], which was selected because it is the most robust and most recent natural history study of HCC risk and alcohol consumption available. Where possible, I used the most relevant and high-quality sources (e.g., meta-analyses). Second, I calibrated the model to estimate two unknown probabilities using ALD-related mortality from the CDC as the calibration target. Because I did not adjust the CDC data for potential underreporting, the calibrated parameters may be underestimated. Third, I used some inputs that reflected average outcomes for the general population instead of the subgroups that were modeled. Fourth, due to data limitations, I was not able to model racial/ethnic groups other than the five groups included in this study, such as those who identify as biracial or multiracial. The effect of parameter uncertainty introduced by these inputs was evaluated through the Monte Carlo simulation.

There are also uncertainties associated with the drinking transition rates I used. The study by Barbosa et al. (2021) estimated the most detailed drinking transition rates to date, but their results required some transformations in order for the WHO drinking levels they used to match those in my model.[173] Additionally, this study used data from two waves of NESARC to estimate drinking transitions, a survey which has been shown to have lower estimates of drinking prevalence compared to other nationally representative surveys such as the NSDUH.[195] Finally, alcohol use exhibits age, period, and cohort effects[209], and only age and period effects were reflected in the Barbosa et al. study. Cohort effects, which are age-by-period interactions or outcomes by birth year, are likely to behind ALD incidence rate crossover by age group over time observed in this study. Future research is needed to understand the influence of cohort effects on drinking behavior and future ALD burden.

There are also limitations inherent to the modeling approach used. First, state-transition models like the one used here are powerful in their simplicity but rely on several assumptions, including the “memoryless property” which assumes that the probability of transitioning to a new state is dependent only on the current state. This assumption was relaxed through the use of time- and age-dependent probabilities and the microsimulation approach. Second, the microsimulation model represents a simplified process of ALD development, and I omitted states like alcohol-related hepatitis, an acute ALD state that is associated with high mortality, due to data limitations. I also excluded liver co-morbidities (e.g., viral hepatitis infections, non-alcohol-related fatty liver disease) that have been shown to exacerbate the development of ALD and vice versa.[3,210] Future modeling studies should attempt to include these important aspects of ALD progression as they may affect estimates of ALD incidence and mortality. Third, I assumed that new entrants to the model had the same characteristics as the original cohort of 18-year-olds, which introduces significant uncertainly on longer-term estimates. Finally, the calibration process showed that model predictions match observed data closely, and the estimated probabilities likely captured both measured and unmeasured ALD dynamics.[199] The calibration can be further improved by a broader set of parameters or by adding more calibration targets, such as the incidence rate of ALD.

Conclusion

ALD cases and deaths may increase in the US alongside rising rates of alcohol misuse. A focus on average ALD incidence and ALD-related mortality rates may mask significant differences between sociodemographic groups. Populations that have been disproportionately affected by ALD in the past are estimated to continue to bear the burden of this disease. Population-level interventions are needed to address alcohol misuse and ALD.

Chapter 3: Cost-effectiveness of Alcohol Pricing Policies

BACKGROUND

Several evidence-based interventions have been shown to reduce high-risk drinking (Figure 5), and among these, pricing policies like alcohol taxes are among the most widely implemented.[2,73,77,118,211,212] Taxes work by raising the prices of alcoholic products which leads to a reduction in consumption.[89,95,98,100,102] Raising taxes on potentially unhealthy products has been the mainstay of tobacco and alcohol control and is increasingly being adopted by localities in the US and elsewhere to reduce consumption of sugar-sweetened beverages.[73–76] However, federal taxes for alcohol have not increased since 1991 and state taxes, despite some increases, have not kept up with inflation and rising incomes, which has reduced their impact.[71,77,83,84]

The effectiveness of alcohol taxes in reducing alcohol use and misuse is affected by several factors. For example, whether or not taxes are passed on to consumers and lead to price increases depends on the presence of competitors, availability of substitutes, and timing of the tax.[111] Different types of alcohol taxes (e.g., flat-rate excise taxes, volumetric taxes, and ad valorem taxes) have variable effects on prices and consumption, depending on how they are designed and implemented. When cheaper alternatives are available in the market after a tax hike, drinkers often consume cheaper beverages within their preferred category, a phenomenon known as substitution effect.[110] Substitution has been found to be more pronounced among heavy drinkers compared to light and moderate drinkers[98,104,105,107], though a few studies have reported the opposite finding.[103,106,213]

To address the limitations of alcohol taxes, another pricing policy called minimum unit pricing (MUP) has been proposed. MUP involves imposing a legal floor or minimum price below which alcohol and alcoholic beverages cannot be sold.[119] In contrast to alcohol taxes, MUP ensures that the price of the cheapest alcohol available, which is preferred overwhelmingly by the heaviest drinkers[121,128,129,131], increases by a specified amount, thereby reducing or eliminating the potential for substitution. Today, MUP is implemented in most Canadian provinces, Russia, Belarus, Moldova, Scotland and Wales in the UK, and Australia's Northern Territory where it has been associated with reductions in alcohol consumption[136–138,214,215] and various outcomes including crime, alcohol-related hospitalizations, and mortality.[139,140,143,216,217] Some control states in the US (e.g., Kansas, Ohio) have imposed minimum markups on alcohol products, effectively setting minimum prices.[121] In July 2021, Oregon, another control state, imposed a minimum price on distilled spirits ($8.95 per 750 ml bottle), which raised prices of 1-2% of products by an average of 16%.[125]

With rising alcohol misuse rates in the US that have only been exacerbated by the isolation and economic devastation of the COVID-19 pandemic[25,193], policy interventions are needed to reduce alcohol misuse and prevent alcohol-related harms, particularly the burden of alcohol-related liver diseases (ALDs). In this study, I will explore the potential cost-effectiveness of higher excise taxes on alcohol and a hypothetical MUP policy in the US as interventions to reduce ALD burden. A model-based CEA is especially suited to evaluate these pricing policies because it can use long time horizons that are required to study ALD; elucidate the impact of uncertainty on the cost and effectiveness of pricing policies; and evaluate any tradeoffs between competing alternatives. The findings of this study can inform decision-making about the optimal alcohol pricing policy in the US and can be adopted for use in other contexts.

METHODS

Overview

This cost-effectiveness analysis (CEA) adhered to the best practices proposed by the 2nd Panel on Cost-Effectiveness in Health and Medicine[218] and the 2022 Consolidated Health Economic Evaluation Reporting Standards.[219] This study leverages the microsimulation model developed in Chapter 2 to estimate the long-term cost and health benefits of alcohol excise taxes (hereafter called “alcohol taxes”) and MUP in the US. Benefits were measured in terms of quality-adjusted life years (QALYs) gained. Data on transition probabilities, costs, and health utilities (Table 4) were taken from published peer-reviewed and gray literature that were identified through literature reviews, citation tracking, and snowball searches conducted between July-December 2020.

I used healthcare and societal perspectives in this CEA. In the societal perspective, all costs and benefits are valued and included, regardless of the payer or beneficiary. In the healthcare sector perspective, only healthcare costs borne by payers and patients are included. The Impact Inventory (aTable 6) lists all the health and non-health costs and effects that were included in each perspective.[218] I discounted future benefits and costs to their present value using a 3% rate in the base case analysis, and I used a lifetime time horizon.

Model description

Chapter 2 describes the microsimulation model and the inputs used, and I discuss below some changes made to the model for this CEA. First, I used a closed version of the microsimulation model, which means that no new individuals were added to original modeled cohort. Second, I modeled fewer individuals per racial/ethnic group in the main analysis (100,000 individuals) and in the sensitivity analysis (10,000 individuals). Third, I used data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) wave 3 (2012-2013) instead of NESARC wave 2 (2000-2001) to initialize the distribution of the population by drinking and ALD status. Fourth, I used a longer (i.e., lifetime) time horizon in modeling the costs and health benefits of alcohol pricing policies. Finally, I estimated health outcomes in terms of QALYs instead of ALD incidence and mortality by assigning health utilities to each health state in the model. All analyses were conducted in R version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria) using modified CEA templates from DARTH.[170]

Table 4. CEA model inputs, parameters, and assumptions

Input	Base value (SD)	Range	Distribution in PSA	Reference
Treatment effect				
Own-price elasticity of demand[a]				
Low-risk and moderate drinkers	0.44	0.34-0.54	NA	[98]
Excessive drinkers under taxes	0.28	0-0.30	NA	[98]
Adjustment under MUP[b]	1.45	1-2[c]	NA	[110]
Cross-price elasticity of demand				[103,108]
Low-risk and moderate drinkers	0.04	0.016-0.10	NA	[103,108,109]
Adjustment for excessive drinkers[d]	2	1.5-2.5[c]	NA	[104]
Annual healthcare costs (US$)				
Moderate drinking with CC	6,756 (845)	5,067-8,445	Gamma	[220]
Excessive drinking with CC	6,756 (845)	5,067-8,445	Gamma	[220]
Decompensated cirrhosis[e]	25,956 (815)	25,539-26,374	Gamma	[221]
Hepatocellular carcinoma	58,183 (468)	57,246-59,119	Gamma	[221]
Transplantation <1st year	345,605 (43,201)	259,204-432,006	Gamma	[5]
Transplantation ≥1st year	72,284 (9,035)	54,213-90,354	Gamma	[5]
Intervention costs[f] (US$)				
Alcohol excise taxes	0	0-0.05	Gamma	See Appendix 6[222]
Minimum unit pricing				
One-time	0.51	0.13-0.9[c]	Gamma	See Appendix 7
Recurring	0.86	0.22-1.51[c]	Gamma	See Appendix 7
Health utilities				
Low-risk drinking[g]	1	NA	NA	[c]
Moderate drinking	0.94 (0.20)	0.94-1	Beta	[223]
Excessive drinking	0.84 (0.30)	0.85-1	Beta	[223]
Moderate drinking with AFLD	0.94 (0.20)	0.94-1	Beta	[223]
Excessive drinking with AFLD	0.84 (0.30)	0.85-1	Beta	[223]
Moderate drinking with CC	0.75 (0.028)	0.67-0.83	Beta	[224]
Excessive drinking with CC	0.75 (0.028)	0.67-0.83	Beta	[224]
Decompensated cirrhosis	0.672 (0.031)	0.58-0.77	Beta	[224]
Hepatocellular carcinoma	0.662 (0.019)	0.60-0.67	Beta	[225]
Transplantation <1st year	0.72 (0.07)	0.58-0.96	Beta	[226]

Transplantation ≥1st year	0.75 (0.08)	0.59-0.98	Beta	226
Death	0	NA	Beta	c
Other inputs				
Discount rate	0.03	0.02-0.08	Beta	c
Time horizon (in years)	Lifetime	NA	NA	c

The parameters listed in this table are in addition to the parameters used for the microsimulation model (Table 2).

[a] Own-price elasticities of demand for alcohol are negative; the sign has been omitted in the table for simplicity. The effect of uncertainty around these parameters were explored in scenario analyses.

[b] Adjustment factor multiplied to the own-price elasticity of demand for low-risk, moderate, and excessive drinkers under MUP

[c] Assumed by authors

[d] Adjustment factor for excessive drinkers multiplied to the cross-price elasticity of low-risk and moderate drinkers

[e] Decompensation was defined as having at least one occurrence of ascites, hepatic encephalopathy, or variceal bleeding.

[f] Alcohol tax costs are a percent of tax revenue collected, and MUP costs are per person per year. See Appendix 6 and Appendix 7 for details.

[g] Includes individuals who are lifetime or past-year abstainers

AFLD, alcohol-related fatty liver disease; CC, compensated cirrhosis; MUP, minimum unit pricing; NA, not applicable; PSA, probabilistic sensitivity analysis; SD, standard deviation.

Description of modeled scenarios

In addition to a status quo (i.e., no-intervention) scenario, I modeled five alcohol tax and MUP policies (Table 5). Taxes and MUP were selected because they represent two distinct policy proposals for reducing alcohol consumption. For example, in settings where MUP has been implemented (e.g., UK, Australia), alcohol taxes were not concurrently increased; instead, jurisdictions often select one policy over the other. In principle, both policies can be implemented simultaneously, or each policy can be applied to specific beverages.

The size of the modeled alcohol tax increases reflect previous proposals and experiences in the US[151,166,227]; for example, modeling studies have explored the potential effect of a $0.05-0.25 alcohol tax hike (roughly 4-39% increase in the average price of alcohol today)[228], as well as a tax that would increase the retail price of alcohol by 5%.[151,166] In Maryland, where state excise taxes for alcohol were raised in 2011 for the first time after 45 years, the alcohol sales tax rate was raised by 50%, from 6 to 9%.[227] The policies were also informed by research suggesting that average inflation-adjusted state excise taxes on alcohol have declined by 27-32% depending on the beverage between 1991 and 2015.[86]

Table 5. Description of modeled pricing policies

Alternative	**Description**	**Mean change in alcohol price**	**Overall change in alcohol consumption**[a]	
			Moderate	*Excessive*
Status quo	No change	None	None	None
Tax policy 1: 5% increase	5% increase in average price of alcohol	5	-2(-1, -3)	-1 (0, -2)
Tax policy 2: 15% increase	15% increase in average price of alcohol	15	-6(-4, -9)	-3 (0, -6)
Tax policy 3: 30% increase	30% increase in average price of alcohol	30	-12(-7, -18)	-6 (0, -12)
MUP policy 1: 50% increase	Price of cheapest standard drink increased by 50%	50	-30(-20, -42)	-16 (0, -27)
MUP policy 2: 100% increase	Price of cheapest standard drink increased by 100%	53	-32(-21, -44)	-17 (0, -28)

All values are in percents. Ranges in parentheses. For complete details on how changes in alcohol prices and consumption were calculated, see Appendix 5.

[a] Represents the net change in alcohol consumption, which incorporates own- and cross-price elasticities of demand.

MUP, minimum unit pricing.

In this study, I evaluated the cost-effectiveness of alcohol tax increases that raised the price of alcohol by 5%, 15%, and 30%. These price increases represent $0.03-0.60 in additional cost per standard drink of alcohol, depending on the beverage (Table 6). I assumed that the pass-through rate, or the proportion of a tax that is shifted or passed on to consumers, is 100% (i.e., a fully shifted tax).

Table 6. Estimated tax increase under each alcohol tax policy by beverage

Category	Price per standard drink (US$)[a]	Tax per standard drink (US$)[b]	Price increase in US$ (relative tax increase[c])		
			5%	*15%*	*30%*
Beer and malt beverages (5% alcohol)	1.22	0.054	0.06 (1.1)	0.18 (3.31)	0.37 (6.8)
Wine (12% alcohol)	2.00	0.042	0.10 (2.39)	0.30 (7.18)	0.60 (14.36)
Liquor (40% alcohol)	0.64	0.127	0.03 (0.24)	0.10 (0.79)	0.19 (1.5)

[a] Calculated using data from the Consumer Price Index of the US Bureau of Labor Statistics.[229]

[b] Calculated using data from the Alcohol Policy Information System of the National Institute on Alcohol Abuse and Alcoholism.[230]

[b] Based on current taxes per standard drink

For MUP, I evaluated two policies that would increase the cheapest unit of alcohol by 50% and 100%. Because MUP has not been implemented in the US at a large scale, I based these MUP scenarios on experiences of other countries. In Australia's Northern Territory, for example, the MUP implemented raised the prices of the cheapest beverages by about 85%.[119] In Scotland and Wales, the £0.50 MUP for a standard drink raised the price of the cheapest alcohol by 170% and 130%, respectively.[123,231,232]

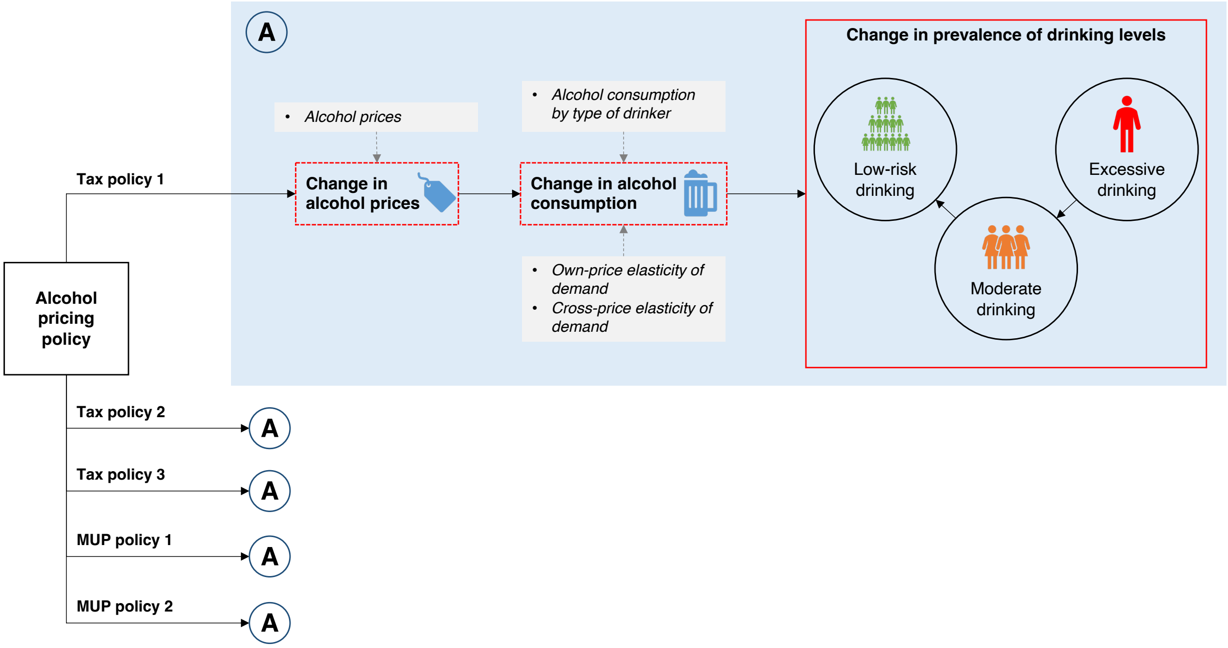
Treatment effect

The treatment effect of pricing policies was defined as the change in the initial distribution or prevalence of low-risk, moderate, and excessive drinkers. Similar to previous analyses[151], I followed a three-step process to estimate the treatment effect of pricing policies; these steps involved (1) calculating the price increase associated with each pricing policy, (2) translating price increases to changes in consumption using price elasticities of demand, and (3) applying the change in consumption to estimate the new prevalence of various drinking levels (Figure 13). All price calculations were conducted based on the price of a standard drink, which in the US is defined as a beverage with about 14g of pure ethanol (Box 1). I describe my approach in some detail below, and additional details are provided in Appendix 5.

Change in price

For the alcohol tax policies, the price increase is implied in each policy (5%, 15%, and 30%), For MUP, I determined the cheapest standard drink sold in the US using the same alcohol price data from CPI. After applying each MUP policy, I determined the new minimum price of a standard drink and calculated the average percent change in price across all beverages.

Figure 13. Estimating the treatment effect of alcohol pricing policies



This schematic summarizes the process used to estimate the effect of pricing policies on the prevalence of moderate and excessive drinking. The steps have been grouped and truncated for simplicity. The bulleted list in the gray boxes are the inputs used to conduct each step.
MUP, minimum unit pricing.

Change in consumption

To translate changes in price to changes in alcohol consumption, I used two types of price elasticities of demand. The first is called own-price elasticity of demand, which describes the change in the quantity demanded of a good relative to a percentage change in its price. Aside from varying by type of alcoholic beverage, research suggests that own-price elasticity of demand differs across drinking patterns or types of drinkers, with heavy or excessive drinkers being the least price-sensitive.[104] In this study, I used meta-analytic estimates of the own-price elasticity of demand reported by Wagenaar et al. (2009), which are -0.44 (range: -0.34 to -0.54) among low-risk and moderate drinkers and -0.28 (range: 0 to -0.30) among excessive drinkers (Table 4). The magnitude and range of these elasticities are similar to the findings of other meta-analyses.[95,98,102]

The second price elasticity I used in this study is called cross-price elasticity of demand, which relates to the degree of substitution that occurs when similar and cheaper alternatives are available. The cross-price elasticity is the change in consumption of an alternative good that results from a change in the price of a preferred good. I assumed that alcohol taxes and MUP have different effects on substitution, as previous research has demonstrated. Any price increases from alcohol taxes, which vary by type of beverage, will likely preserve existing price differences among alcohol products, leaving cheaper alternatives in the market.[233] By contrast, MUP raises the price of the lowest-cost alcohol, thereby reducing the probability that price-sensitive drinkers are able to switch to cheaper or lower-quality products; this is especially impactful for excessive drinkers who o prefer the cheapest alcohol.[121,128,129,131]

The cross-price elasticity of demand for alcohol has not been measured for the US, so for this study, I used the pooled median cross-price elasticity across all beverages for the UK and Australia (0.10, range: 0.04-0.16).[103,108,109] This estimate captures all the possible substitutions that occur when the price of different types of beverages increases. For example, a study in Australia found that a 10% increase in the price of beer sold “on premises” (e.g., in bars) led to a 6.3% reduction in consumption of beer sold in these establishments but led to a 6.9% increase in the consumption of beer sold "off premises" (e.g., in liquor stores).[103]

Since excessive drinkers are more likely to find substitutes when their preferred beverage becomes more expensive, I doubled the cross-price elasticity of demand for excessive drinkers, as suggested in the literature.[104] Under MUP, I assumed that all drinkers experience a higher (i.e., more negative) price elasticity of demand. Based on previous research, increasing the price of the lowest-cost alcohol reduced overall consumption by 145% more than increasing the price of all alcohol products[110]; thus I applied this adjustment factor on the own-price elasticity of demand for all drinker types in the MUP scenarios.

Change in drinking prevalence

I translated changes in consumption to changes in the prevalence of low-risk, moderate, and excessive drinking through several steps. I first calculated the net change in consumption, which reflects the sum of the own- and cross-price elasticities of demand (Table 5), and I applied these net changes in consumption to the daily volume of alcohol consumed by each type of drinker in the model (Figure 6). Low-risk drinkers saw no changes since any further reductions in their alcohol consumption kept them in their current drinking state. Moderate drinkers consume alcohol exactly at the gender-specific thresholds for heavy drinking (i.e., 14 grams of ethanol a day for women, 28 grams a day for men), so the net change in consumption represented the proportion of moderate drinkers who moved to the low-risk drinking state.

For excessive drinkers or individuals who consume alcohol above the heavy drinking thresholds, I applied the net change in consumption across the distribution of daily alcohol consumed by individuals in this group.[234] To calculate the proportion of excessive drinkers who move to the moderate drinking group under each policy, I fitted a log-normal distribution on the distribution of alcohol consumed by excessive drinkers, and determined the probability that excessive drinkers would fall at or below the heavy drinking thresholds after applying the net change in consumption (Appendix 5). The initial prevalence of various health states under each pricing policy is found in aFigure 3.

Costs

Various cost categories were valued and included in the analysis depending on the perspective used (see aTable 6 for Impact Inventory). I included current and future medical care costs and the costs of pricing policy implementation in the healthcare sector perspective. For the societal perspective, I included all costs in the healthcare sector perspective, as well as patient time costs, future consumption, and future productivity. All costs are in 2021 US dollars (US$); historical costs were updated using the CPI for medical care.[229]

Intervention costs

Intervention costs refer to the costs of collecting alcohol taxes and implementing MUP. I assumed in the base case that alcohol tax policies are not associated with any new costs for the public and private sectors. This is because state and local governments already routinely collect alcohol taxes, and private sector organizations, including off-premise and on-premise establishments, have existing human and capital resources to comply with any tax rate changes. This approach is similar to those taken by other CEAs of tax-based public health interventions.[235–237] In sensitivity analyses, however, I assumed that tax collection costs between 0-0.5% per $1 of alcohol tax collected, as suggested in previous analyses (Appendix 6).[222]

Since MUP has not been implemented in the US, the costs of MUP are unknown. For this study, I conducted a high-level micro-costing of the potential implementation costs of a novel MUP policy; my approach is modeled on a previous evaluation conducted by the UK government (details are found in Appendix 7).[238] The main cost categories included one-time costs for dissemination and training for public and private employees and annual enforcement costs at the state and local levels. I applied ±75% from the base value to establish range of possible per-capita costs (Table 4).

Related and unrelated medical costs

The routine costs of care for compensated and decompensated AC were based on a costing analysis conducted for a previous CEA[220] and a study on the costs of treating US veterans with cirrhosis[221], respectively. All costs associated with liver transplantation are based on a claims-based analysis of a commercially insured population in the US.[5] Future unrelated medical costs based on healthcare expenses by age from the 2019 Consumer Expenditure Survey of the US Bureau of Labor Statistics (Appendix 8).

Other societal costs

For the societal perspective, I included lifetime productivity and consumption costs. I also valued and included time costs or foregone productivity of patients using published estimates of time spent on alcohol use treatments and ALD treatments multiplied by average daily wages (Appendix 8).

Health outcomes

Health outcomes were measured in terms of QALYs gained. A QALY represents a year that a person is alive weighted by that person's health-related quality of life.[239] QALYs, which have their limitations, are a preferred measure of health in CEAs because they are (1) preference-based, (2) combine quantity and quality of life in one metric, and (3) provide a common and consistent metric that can be used to compare different interventions.[240]

The weights used to calculate QALYs are based on health utilities that typically range from 1 (a year in perfect health) to 0 (death). I took health utility estimates for the various states in the model from the literature (Table 4).[224–226,241]

Analysis

Cost-effectiveness analysis

The summary statistic of CEAs is the incremental cost-effectiveness ratio (ICER), defined as the cost per unit of health outcome gained. The ICER is calculated using the formula

$$ICER = \frac{\Delta Costs}{\Delta Effectiveness} = \frac{C_b - C_a}{E_b - E_a} \qquad \textbf{Eq. 1}$$

where C refers to costs and E refers to effectiveness of two alternatives, which are denoted by the indices a and b. An intervention is typically considered cost-effective if its ICER is equal to or less than a cost-effectiveness threshold, which represents the health opportunity costs of additional spending in the health sector. (From a demand-side perspective, the cost-effectiveness threshold represents a decision-maker's willingness to pay for an additional unit of benefit.) In this study, I used a cost-effectiveness threshold range of $100,000-150,000 per QALY gained.[240]

The base-case analysis used the base values of each model input (Table 2 and Table 4). Since I modeled individuals from five racial/ethnic groups, I weighted the average outcomes of each racial/ethnic group by their share of the total US population to generate overall results. Data on the US population used to calculate population weights by were taken from the US Census Bureau.[194] I calculated ICERs by comparing each pricing policy with the status quo. I also ordered the policies by increasing effectiveness and compared each one to the next effective, undominated intervention, which is a standard dominance test in CEAs where there are multiple alternatives. These incremental analyses assumes that the interventions are mutually exclusive and independent, though they may be implemented at the same time and have interactions which I do not explore in this study.

Sensitivity analysis

To explore the effect of uncertainty on the cost-effectiveness of the pricing policies, I conducted three types of sensitivity analyses. The first is one-way sensitivity analysis where each transition probability, cost input, and health utility was varied one at a time from their lowest to highest value, while keeping other parameters at their base value, to determine how extreme values affect the cost-effectiveness of pricing policies. Ranges for each input (Table 4) were based on the literature where available; for inputs where ranges were not available, I applied ±25% on the base or mean estimate to generate upper and lower limits. Results of one-way sensitivity analyses were summarized in tornado diagrams.

The second type of sensitivity analysis is called scenario analysis, where I deterministically changed specific assumptions in the model. In one set of scenario analyses, I used upper and lower limits of the net change in consumption (Table 4), which created “optimistic” and “conservative” scenarios of the potential effect of pricing policies on the prevalence of moderate and excessive drinking. In a second set of analyses, I used high and low values of the probability of transitioning between drinking states to create two additional scenarios (aTable 3). In the “low drinking” scenario, excessive and moderate drinkers experienced a higher probability of transitioning to moderate and low-risk drinking, respectively, and low-risk and moderate drinkers experienced a lower probability of transitioning to moderate and excessive drinking, respectively. These assumptions were reversed in the “high drinking” scenario.

The third and final type of sensitivity analysis I conducted is probabilistic sensitivity analysis (PSA), where parameters were varied simultaneously over 1,000 independent or Monte Carlo trials. In each trial, a random value of each parameter was drawn from the pre-assigned distributions and used in the model (Table 4). Transition probabilities and health utilities were assigned beta distributions, while costs were assigned a gamma distribution. I summarized the results of the PSA in cost-effectiveness acceptability frontiers, which show the uncertainty around the optimal choice at each cost-effectiveness threshold. A cost-effectiveness acceptability frontier plots the probability that the most economically preferred intervention (i.e., intervention with the highest net monetary value) is the optimal choice compared to other alternatives over a range of ICER thresholds.[242]

RESULTS

Base case

The base-case results are shown in

Table 7. Under a healthcare sector perspective, when interventions were compared to the next more effective and undominated intervention, only MUP policy 2 was found to be dominant; all other policies were extendedly dominated, which means that they have ICERs that were higher than MUP policy 2, which is the most effective intervention. This finding is shown graphically in the cost-effectiveness plane in Figure 14.

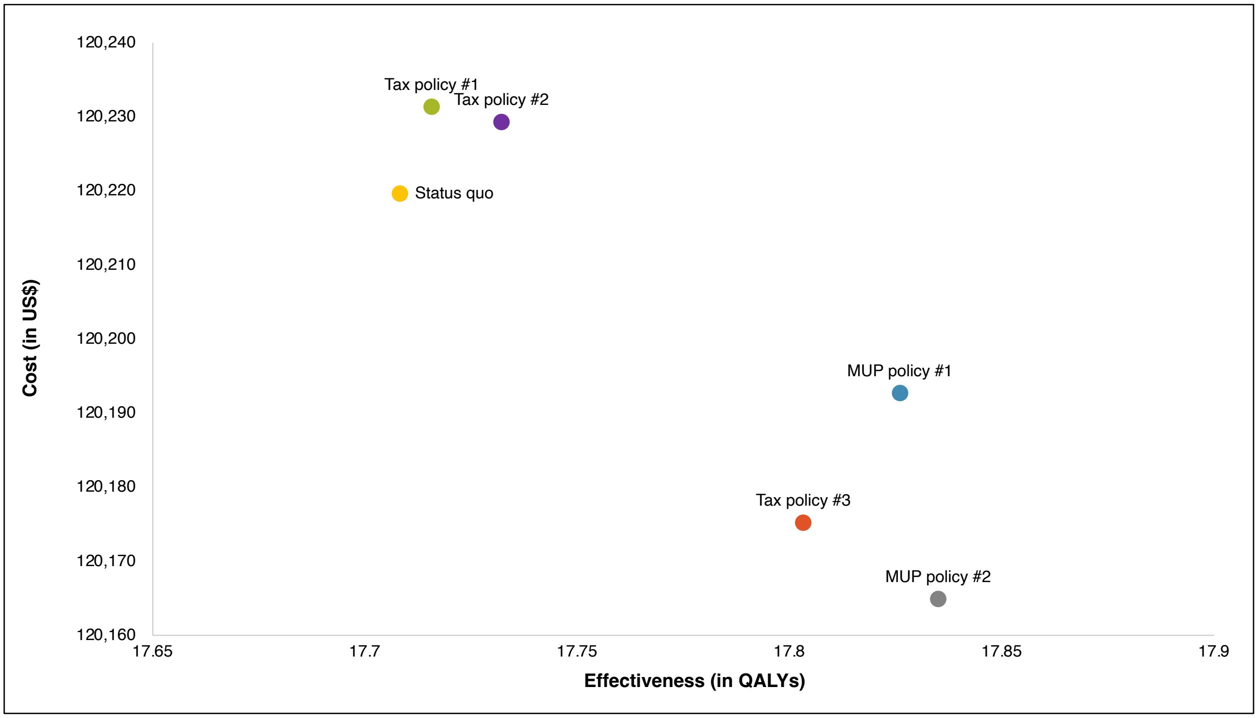
Table 7. Cost-effectiveness analysis of alcohol pricing policies using a healthcare sector perspective

			ICER (in cost per QALY gained)	
Intervention	**Average cost (in US$)**	**Average effectiveness (in QALYs)**	*Compared to next effective, undominated intervention*	*Compared to status quo*
Status quo	120,220	17.71	NA	NA
Tax policy 1: 5% increase	120,231	17.72	Dominated	1,548
Tax policy 2: 15% increase	120,229	17.73	Dominated	403
Tax policy 3: 30% increase	120,175	17.80	Dominated	Dominant
MUP policy 1: 50% increase	120,193	17.83	Dominated	Dominant
MUP policy 2: 100% increase	120,165	17.84	Dominant	Dominant

ICERs were calculated by comparing each strategy with each strategy to the next more effective and undominated option. This type of incremental analysis assumes that the strategies are mutually exclusive and independent. The final column compares to the status quo which would be more apporoprate if the strategies were not mutually exclusive.

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

Figure 14. Cost-effectiveness plane of pricing policies using a healthcare perspective



A cost-effectiveness plane plots the average total costs (in US$) and average total effectiveness (in QALYs) of each evaluated strategy. The dotted red line represents the efficiency frontier, which is defined by the most efficient interventions at increasing levels of health benefit. Interventions to the left of the efficiency frontier are "extendedly dominated," which means that these interventions are less efficient than combinations of other strategies.
QALY, quality-adjusted life expectancy.

If compared only to the status quo, Tax policy 1 and 2 had positive ICERs, while Tax policy 3 and two MUP policies were dominant or "cost-saving," which means that they produced more QALYs at a lower cost than the status quo. Tax policies 1-3 were associated with incremental benefits of 0.01, 0.02, and 0.10 QALYs respectively, while the largest incremental benefit was associated with MUP policies 1 and 2 (0.12 and 0.13, respectively).

Under a societal perspective (Table 8), none of the interventions remained dominant compared to the status quo. All five pricing policies had positive ICERs that were below the cost-effectiveness threshold range of $100,000-150,000 per QALY gained, which suggests that they are cost-effective interventions. When subjected to dominance analysis, MUP policy 2 was the only policy that remained cost-effective, while the other policies were extendedly dominated.

Table 8. Cost-effectiveness analysis of alcohol pricing policies using a societal perspective

			ICER (in cost per QALY gained)	
Intervention	**Average cost (in US$)**	**Average effectiveness (in QALYs)**	*Compared to status quo*	*Compared to next effective, undominated intervention*
Status quo	90,392	17.71	NA	NA
Tax policy 1: 5% increase	90,454	17.72	8,146	Dominated
Tax policy 2: 15% increase	90,400	17.73	302	Dominated
Tax policy 3: 30% increase	90,616	17.80	2,357	Dominated
MUP policy 1: 50% increase	90,606	17.83	1,816	Dominated
MUP policy 2: 100% increase	90,570	17.84	1,401	1,401

ICERs were calculated by comparing each strategy with the status quo and each strategy to the next more effective and undominated option. This type of incremental analysis assumes that the strategies are mutually exclusive and independent.
ICER, incremental cost-effectiveness ratio; MUP, minimum unit pricing; NA, not applicable; QALY, quality-adjusted life year.

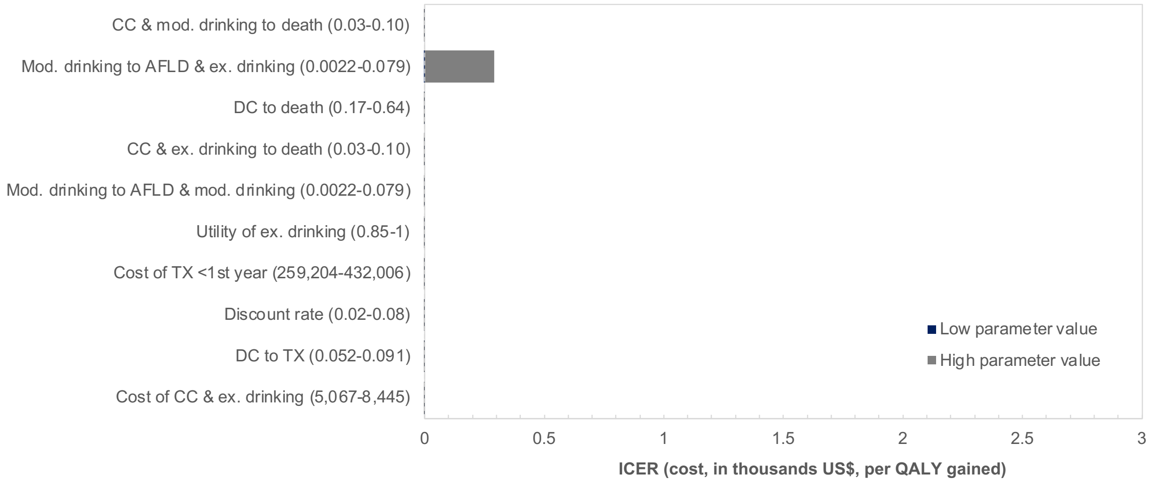
Deterministic sensitivity analysis

The results of the deterministic sensitivity analysis are shown in Figure 15-Figure 16 and aFigure 6-aFigure 7. Using a healthcare perspective, all five pricing policies remained dominant compared to the status quo except when high values of one transition probability was used (Figure 15 and aFigure 6). When the probability of transitioning from moderate drinking to AFLD and excessive drinking was at its highest (0.079), the ICERs of the pricing policies were equal to $291 per QALY gained.

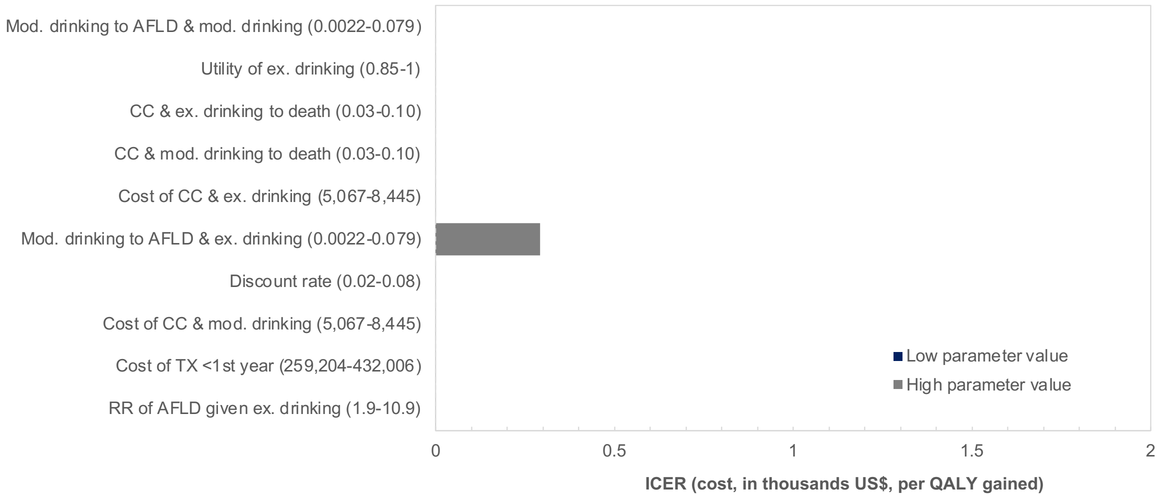
A similar pattern was seen for the societal perspective analysis. High values of the probability of transitioning from moderate drinking to AFLD and excessive drinking led to the highest ICERs among the pricing policies. However, values of other inputs also influenced whether a pricing policy was cost-saving or cost-increasing. For example, the discount rate was an influential across all five pricing policies (Figure 16 and aFigure 7).

Figure 15. Deterministic sensitivity analysis for selected policies using a healthcare sector perspective

A. Tax policy 1



B. MUP policy 1

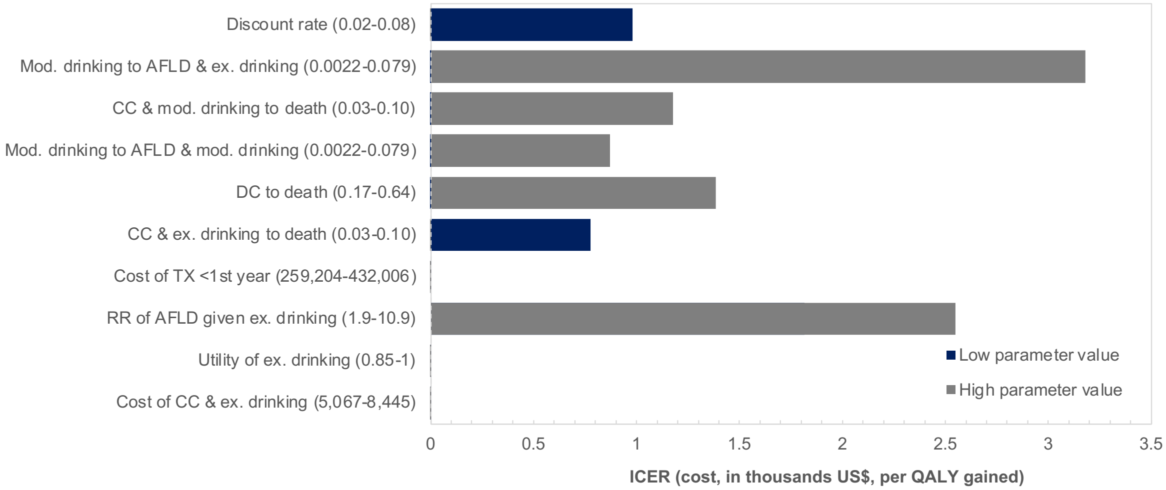


Tornado diagrams show the range of ICERs that result from using the lowest and highest values of selected model inputs, which are shown in the parentheses. The tornado diagrams shown here are for Tax policy 1 (A) and MUP policy 1 (B); only the 10 most influential inputs were included here. Negative ICERs, which represent cases where an intervention is dominant or cost-saving, were excluded from these graphs.

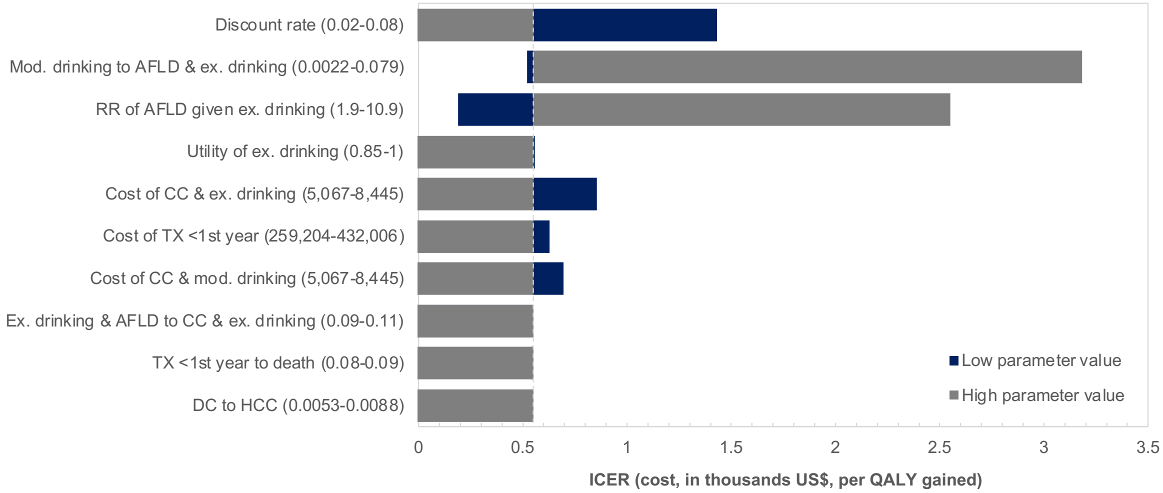
AFLD, alcohol-related fatty liver disease; CC, compensated cirrhosis; ex., excessive; ICER, incremental cost-effectiveness ratio; mod., moderate; MUP, minimum unit pricing; RR, relative risk; TX, transplantation.

Figure 16. Deterministic sensitivity analysis for selected policies using a societal perspective

A. Tax policy 1



B. MUP policy 1



Tornado diagrams show the range of ICERs that result from using the lowest and highest values of selected model inputs, which are shown in the parentheses. The tornado diagrams shown here are for Tax policy 1 (A) and MUP policy 1 (B); only the 10 most influential inputs were included here. Negative ICERs, which represent cases where an intervention is dominant or cost-saving, were excluded from these graphs. The dashed vertical line represents the ICER from the base-case results.

AFLD, alcohol-related fatty liver disease; CC, compensated cirrhosis; ex., excessive; ICER, incremental cost-effectiveness ratio; mod., moderate; MUP, minimum unit pricing; RR, relative risk; TX, transplantation.

Scenario analysis

Changing effect of policies: optimistic and conservative scenarios

In a conservative scenario where the assumed effect of alcohol pricing policies on consumption was smaller compared to the base case (aTable 14), all but Tax policy 2 were dominant compared to the status quo under a healthcare sector perspective. When the effect of pricing policies on alcohol consumption was increased in the optimistic scenario, all pricing policies were dominant compared to the status quo (aTable 14). The incremental benefits in the optimistic scenario were also higher compared to the base-case results. For example, the incremental benefits of the MUP policies, were 1.5 times higher and the tax policies had incremental benefits that were 1.4-2.7 times higher.

Under a societal perspective and conservative scenario, only Tax policy 1 was dominant compared to the status quo, though the rest of the four pricing policies had ICERs that were still significantly lower than the cost-effectiveness threshold range of $100,000-150,000 per QALY gained (aTable 15). The results were similar for the optimistic scenario under the societal perspective.

Changing drinking probabilities: low and high drinking scenarios

In the low drinking scenario where low-risk and moderate drinkers were less likely to increase their drinking and moderate and excessive drinkers were more likely to reduce their drinking, Tax policy 3 and the two MUP policies were dominant to the status quo using a healthcare sector perspective (aTable 16). Using a societal perspective, all five pricing policies had positive ICERs that were below the $100,000-150,000 per QALY threshold range (aTable 17).

In the high drinking scenario, low-risk and moderate drinkers were assumed to be more likely to increase their drinking, while moderate and excessive drinkers were less likely to reduce their drinking. Using a healthcare sector perspective, only Tax policy 3 and the two MUP policies were dominant to the status quo (aTable 16). Using a societal perspective, all five pricing policies had positive ICERs that were still below the

$100,000-150,000 per QALY threshold range (aTable 17), with the MUP policy 2 having the lowest ICER ($1,300 per QALY gained).

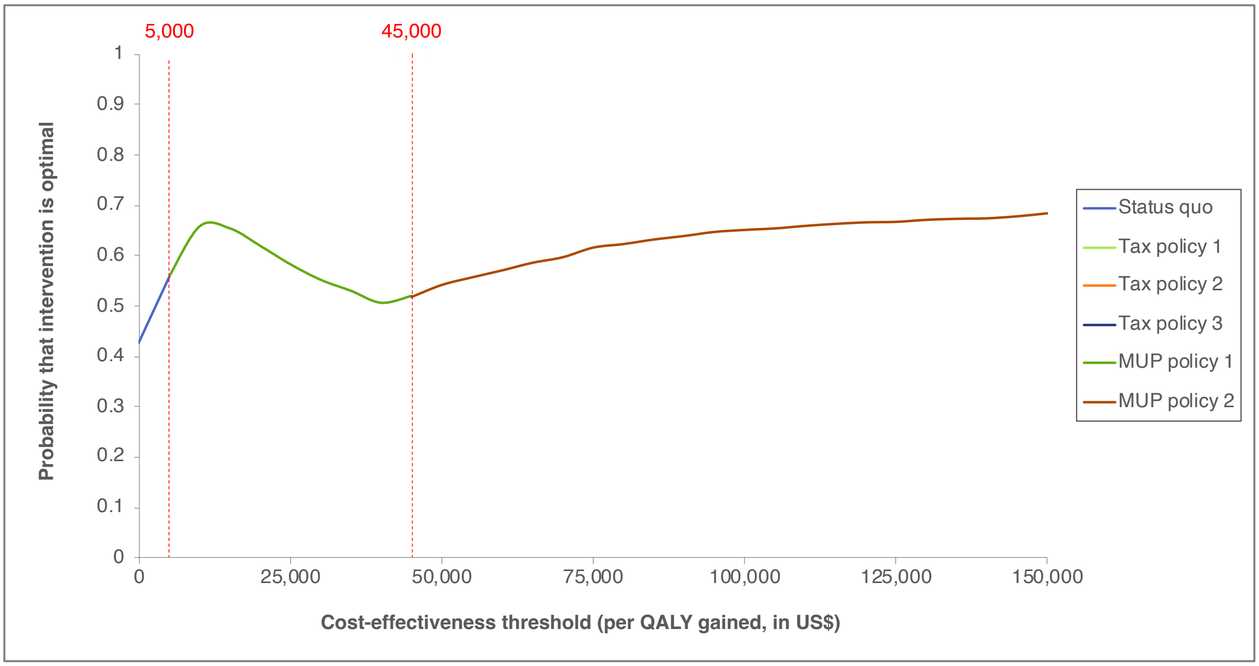
Two-way analyses were also conducted that combined all the different scenarios, and the results are shown in aTable 16 and aTable 17. The results suggest that modifying the assumptions around the effects of pricing policies on alcohol consumption and drinking transition probabilities affected whether certain policies were cost-effective or not. For example, Tax policy 2 was dominated by the status quo under the conservative and high-drinking scenarios.

Probabilistic sensitivity analysis

The results of the PSA are summarized in cost-effectiveness acceptability frontiers in Figure 17 and Figure 18. Overall, MUP policies 1 and 2 were most often identified as optimal strategies, especially with cost-effectiveness thresholds above $0. However, the PSA also revealed uncertainty around the optimal intervention across different cost-effectiveness thresholds, particularly when assumptions around the effect of pricing policies on alcohol consumption were varied.

Under a healthcare sector perspective and using the base-case estimates of the effect of pricing policies, the PSA found that the status quo is the optimal choice when the cost-effectiveness threshold is $0 or when a decision-maker prefers a cost-saving intervention (Figure 17). However, the probability that the status quo is optimal is only 43%, which was followed by Tax policy 1 at 40%. With thresholds between $5,000 and $45,000 per QALY gained, MUP policy 1 was the optimal policy with 50-66% probability. For thresholds above $45,000 per QALY gained, the optimal intervention is MUP policy 2 with a probability approaching 70%.

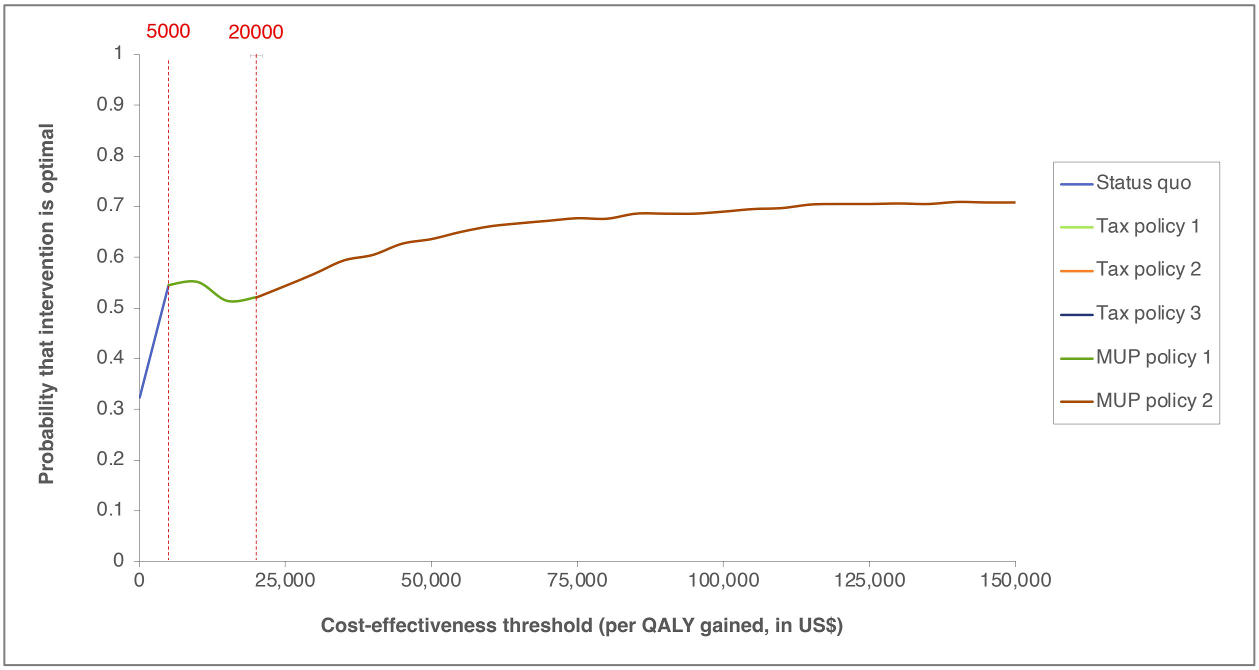
Figure 17. Cost-effectiveness acceptability frontier using base-case treatment effects and healthcare sector perspective



This cost-effectiveness acceptability frontier shows the uncertainty around the optimal intervention across a range of cost-effectiveness thresholds. The red dashed line denotes the cost-effectiveness threshold where the optimal strategy changes. These results were generated using the base-case effects of the pricing policies on alcohol consumption and a healthcare sector perspective.

Under a societal perspective (Figure 18), The status quo is the optimal choice with 43% probability when the cost-effectiveness threshold is $0. With a threshold between $5,000 and $40,000 per QALY gained, MUP policy 1 is the optimal choice with about 60% probability. MUP policy 2 is the optimal choice at threshold values at or above $45,000 per QALY gained.

Figure 18. Cost-effectiveness acceptability frontier using base-case treatment effects and societal perspective



This cost-effectiveness acceptability frontier shows the uncertainty around the optimal intervention across a range of cost-effectiveness thresholds. The red dashed line denotes the cost-effectiveness threshold where the optimal strategy changes. These results were generated using the base-case effects of the pricing policies on alcohol consumption and a societal perspective.

When effect of pricing policies on alcohol consumption were varied from the conservative to the optimistic scenario, the optimal policy changed as well. As shown in aFigure 4, under a conservative scenario and healthcare sector perspective, the optimal solution was MUP policy 2 at thresholds below $90,000 per QALY gained, while MUP policy 1 was the optimal choice at higher threshold values. However, the probability that either MUP policy 1 or MUP policy 2 is the optimal solution was roughly 50%, which suggests that either intervention has an equal chance of being the optimal choice under these assumptions and when parameter uncertainty is accounted for. The same outcome was seen when a societal perspective was used (aFigure 5); MUP policy 1 was the optimal choice but at a probability slightly above 50%.

Under the optimistic scenario where the effects of pricing policies on alcohol consumption are assumed to be higher, MUP policy 1 was the optimal choice at low cost-effectiveness thresholds (i.e., below $5,000 per QALY gained), while MUP policy 2 was the optimal choice with a probability of about 70% under healthcare sector (aFigure 4) or societal perspectives (aFigure 5).

DISCUSSION

This study evaluated the cost-effectiveness of different alcohol pricing policies to reduce the burden of ALD in the US. I found that increases to current alcohol excise taxes and a novel MUP policy are cost-saving or cost-effective interventions compared to the status quo, even when the most conservative assumptions were made about the potential effects of these policies on alcohol consumption. However, varying both drinking rates and the treatment effectiveness of pricing policies together influenced whether tax increases were cost-effective. By contrast, under all circumstances considered, MUP policies were found to be cost-effective or cost-saving versus the status quo based on commonly used cost-effectiveness thresholds in the US.

More importantly, I found that an MUP policy that increased the price of the cheapest alcohol beverage by 100% was most likely to be cost-effective than a smaller MUP that raised the price of the cheapest alcohol by 50% or any alcohol tax increase. This finding held even when the perspective of the analysis was changed (healthcare sector vs. societal) or when parameter uncertainty was accounted for in sensitivity analyses. However, this analysis also found that the status quo and tax policies may be the economically preferable choice at cost-effectiveness thresholds below $5,000 per QALY gained, though there was significant uncertainty around these results which suggests that other policies may also be optimal at low thresholds.

MUP has been implemented in several jurisdictions, most recently in the Scotland (2018), the Northern Territory of Australia (2018), and Wales (2020). Research from these settings has shown that MUP has been successful in achieving most intended outcomes. For example, in Scotland prices of alcohol sold in off-premise establishments rose across the board, and the volume of alcohol sold to adults decreased just one year after the implementation of MUP[136,144–146]; more recent analyses revealed that price increases and purchase decreases were sustained in the 2nd year of implementation.[147]

Data also suggest that MUP may be encouraging current drinkers to switch to lower-strength beers, a positive sign towards harm reduction.[243] In Australia, the MUP coincided with significant decreases in wine consumption, as well as alcohol-related assaults, ambulance attendances, hospital admissions, and crash injuries and fatalities.[217,244]

Some unintended consequences from MUP have also been documented. For example, in Scotland there is some evidence that spending on alcohol among low-income heavy drinkers rose more quickly than their high-income counterparts, suggesting that MUP may have regressive effects.[147] Additionally, MUP may have not led to a reduction in emergency department visits as intended, and many stakeholders reported no changes in consumption or crime in a qualitative evaluation.[245] Non-compliance was also documented, especially among small alcohol retail stores.[246] Finally, while off-premise alcohol prices have increased, the prices of on-premise alcohol did not change.[144] In Australia, the per-capita consumption of beverages other than bottled or cask (i.e., “boxed”) wine was unchanged following the implementation of MUP, and the impact of MUP was not uniform throughout the Northern Territory.[217,244]

MUP may be the most optimal alcohol pricing policy, but its implementation will likely depend on other factors.[125] For example, alcohol tax increases, which this study also found to be cost-effective compared to the status quo, are easier to adopt since laws, systems, and infrastructures already exist to routinely collect these duties from alcohol producers and retailers. By contrast, if implemented, MUP is a new policy that will require significant public and private investment before the health and economic benefits estimated in this study can be realized. Additionally, excise taxes are often preferred by federal and state governments since tax increases automatically become revenue; with MUP, additional spending on alcohol will go to producers and retailers unless a jurisdiction controls the sale of alcohol (e.g., control states). In Scotland for instance, additional spending from MUP go to manufacturers and retailers because the government does not have a state monopoly on alcohol wholesaling or retailing.[247] Finally, the feasibility of MUP or tax increases will be dependent on political considerations, especially since opposition from industries and consumers has been formidable.[248]

In this study, I assumed that alcohol tax increases and MUP are mutually exclusive interventions, though they may be implemented concurrently in the real world. If taxes and MUP are implemented together, tax increases may lead to price increases among some beverages that will cause their new prices to meet or exceed the MUP. These effects were not explored in this study, and future studies can evaluate the joint or combined effects of pricing policies if decisionmakers are interested in implementing both types of pricing policies. However, to date tax increases and MUP are seen as distinct policy options that have not been simultaneously adopted.

This study is one of very few CEAs that have evaluated alcohol taxes and MUP and is, to my knowledge, the first to focus on the US context. While there have been many simulation modeling studies that explored the potential health benefits of alcohol pricing policies in the US[151,166] and elsewhere[84,132,203,204,249], the number of economic evaluations that considered healthcare or societal costs have been limited. CEAs by the World Health Organization found that a 25% or 50% alcohol excise tax increase is cost-effective in low-, middle-, and high-income countries and provides more value for money than other interventions such as bans on alcohol advertising, restrictions on the availability of retail alcohol, or brief interventions from physicians.[116,117,250] However, these analyses have many limitations, including their use of static models, limited focus on heavy drinkers, and direct translation of tax increases to mortality benefits, which overlooks the relationship between prices and alcohol consumption or intermediate outcomes like ALD. Studies from Australia have also shown that volumetric and excise taxes on alcohol are cost-saving interventions to avert alcohol-related harm including injuries.[114,115,251]

One study by Dutch researchers reported that increasing taxes on all alcohol products produced more QALYs than increasing the tax on beer alone, although the ICERs were very similar (€5,300 vs €5,100 per QALY gained) from a healthcare perspective.[252] The authors explained that reductions in alcohol-related diseases from alcohol taxes may increase the prevalence of other diseases unrelated to alcohol, and that any cost savings may be outweighed by future medical expenses. Their findings highlight the need to include future unrelated medical costs and to use long-term time horizons to capture downstream effects of alcohol pricing policies in CEAs, which were both done in this study. Like the Dutch study, I found that the inclusion of other outcomes changed the results of the analysis; for example, in the healthcare sector perspective, all five pricing policies were cost-saving compared to the status quo in the base-case analysis, but only two—Tax policy 1 and MUP policy 2—remained cost-saving after the inclusion of patient time costs and future consumption and productivity in the societal perspective.

Two previous analyses have explored the cost-effectiveness of MUP. One analysis conducted by the UK government found that MUP is cost-saving compared to a no-intervention scenario.[238] Another study in South Africa used an extended CEA framework and found that a 10-rand ($1 = 13.2 rand) MUP could avert 22,600 deaths over a 20-year time horizon, 56% of which would be among the lowest two wealth quintiles; MUP was also estimated to save $4.2 billion in public and private costs.[253] However, that study found that MUP would increase spending on alcohol by about $26 million, which would disproportionately affect the poorest households, suggesting that MUP may be regressive.

Limitations

In addition to the limitations of the microsimulation model used (see Chapter 2), this CEA has several limitations that are worth noting. First and most importantly, I likely underestimated the health benefits of alcohol pricing policies. I only estimated ALD-related morbidity and mortality, yet alcohol is linked to other diseases and outcomes such as violence and crime (Figure 4). Future analyses should include other health, social, and economic consequences of alcohol use. Additionally, I assumed that alcohol pricing policies only affected the initial distribution of low-risk, moderate, and excessive drinkers. In practice, the implementation of pricing policies may also reduce the probability of transitioning from low-risk and moderate drinking to excessive drinking;

however, data on this is lacking. The findings in this study, therefore, represent an underestimate of the potential benefits of alcohol pricing policies.

Second, I used average alcohol prices from the CPI when estimating changes in alcohol consumption, which may have masked the vast heterogeneity in alcohol prices across brands, categories, and locations[254]; future studies can use retail "scanner" data and product-level pricing analysis to understand the range of product prices, as previous research has done.[255] Third, this CEA simulated a representative US population, and future studies should focus on subnational contexts since alcohol pricing policies like excise taxes and MUP are local interventions. Fourth, I assumed a 100% pass-through rate for alcohol excise taxes, which means that any tax increases are fully passed on to consumers. However, taxes may be undershifted or overshifted, and research suggests that pass-through rates depend to some extent on the type of beverage.[256] This study found that the size of the price change associated with a tax increase influences the potential magnitude of health benefits, so an overshifted tax may lead to a higher impact; the opposite would be true for an undershifted tax.

Fifth, due to data limitations, I income was not a sociodemographic characteristic that I was able to include in the model. However, the inclusion of income in future studies can facilitate important analyses that are relevant to the evaluation of pricing policies. For instance, future work can incorporate the income elasticity of demand, which is the change in consumption that is associated with changes in income. As people age and potentially earn more income, the effect of alcohol price increases may wane and affect the long-term cost-effectiveness of pricing policies. Additionally, with information on the income level and drinking status of individuals over time, the potential regressivenes of alcohol pricing policies may be evaluated. Previous modeling studies suggest that MUP is less regressive than alcohol taxes since the heaviest drinkers are often economically better off[119,130,132–135], though limited empirical evidence from the implementation of MUP in the UK suggests that MUP may still have regressive effects.

Conclusions

This study evaluated the long-term cost-effectiveness of alcohol pricing policies to reduce the burden of ALD in the US. Both alcohol excise tax increases and a novel MUP were found to be cost-saving or cost-effective interventions, with the highest MUP being more likely to provide the most value for money. Various assumptions, including the magnitude of the price change associated with each policy, influenced the cost-effectiveness of excise taxes and MUP. Because of the narrow focus of this study on ALD, the health benefits of pricing policies have likely been underestimated, and future studies should include the other health and social consequences of alcohol use.

Chapter 4: Distributional Cost-effectiveness of Alcohol Pricing Policies

BACKGROUND

Alcohol pricing policies that raise the price of alcohol are effective and cost-effective interventions to reduce alcohol consumption and misuse. Previous research has consistently demonstrated a negative or inverse relationship between alcohol prices and consumption[89,95,98,100,102], and higher alcohol prices have been associated with lower rates of various outcomes including sexually transmitted diseases, injuries, accidents, and alcohol-related liver diseases (ALD).[77,79,83,87–89,257] The previous chapter also found that alcohol excise taxes and minimum unit pricing (MUP), a policy which sets a price floor for a standard drink, are cost-effective if not cost-saving interventions in the US compared to the status quo; the results were robust even under the most conservative assumptions about the effectiveness of taxes and MUP.

However, the effectiveness of pricing policies is unlikely to be uniform across the population. For example, most studies reveal that the price elasticity of demand for alcohol, which describes the reduction in consumption following an increase in price, is larger for light and moderate drinkers compared to heavy drinkers.[98,104,105,107] Research has also shown that women (compared to men)[131,258,259] and older people (compared to younger people)[44,260] are more sensitive to changes in alcohol prices. Finally, a couple of studies have suggested that racial and ethnic groups respond differently to alcohol taxes, and even starker differences between racial/ethnic minorities are seen when analyzed by gender or across different beverage-specific taxes.[154,155]

Capturing these heterogeneous effects is important when evaluating pricing policies to ensure that they are effective, efficient, and equitable. For instance, though most racial and ethnic minorities report less or comparable alcohol misuse than their White counterparts[21,45], these groups experience higher rates of death from ALD, greater alcohol-related harms, and more severe social consequences of alcohol use. This phenomenon, which is called the "alcohol harm paradox" [46–52], may exacerbate existing health and socioeconomic inequities when left unaddressed. (In this study, inequity is defined as any unjust difference or inequality in health outcomes.) Gender is also an important factor since women are more likely to experience the negative effects of alcohol on the liver at lower levels of consumption than men. These equity-related considerations have become more salient since racial/ethnic minorities and women faced the steepest increases in high-risk drinking and alcohol use disorder in the last decade (Figure 3).[21,261]

Building on the previous chapter, I conducted a distributional cost-effectiveness analysis (DCEA) to estimate the costs, effects, and distributional impact of two beverage-specific alcohol tax policies in the US as interventions to reduce the burden of ALDs. This study price elasticities of demand by race/ethnicity and gender and evaluated distributions of health using a social welfare function.

METHODS

This DCEA evaluated the cost-effectiveness and health equity effects of hypothetical increases to current beer and liquor (i.e., spirit) taxes compared to the status quo. Like the previous chapter, this study used the microsimulation model from Chapter 2 and generated results from healthcare and societal perspectives (see Impact Inventory in aTable 6). Data on transition probabilities, costs, and health utilities (Table 9) were taken from published peer-reviewed and gray literature that were identified through literature reviews, citation tracking, and snowball searches conducted between July-December 2020. Health benefits were measured in terms of quality-adjusted life years (QALYs) gained, and health equity effects were measured in terms of the Atkinson index, a social welfare function, and a related metric called the equally distributed equivalent level of health (EDEH). I discounted future health benefits and costs to their present value using a 3% rate in the base case analysis, and I used a lifetime time horizon.

Table 9. DCEA model inputs, parameters, and assumptions

Input	Base value (SD)	Range	Distribution in PSA	Reference
Treatment effect				
Price elasticity of demand[a]	See Table 10	See Table 10	Normal	154
Costs				
Intervention costs[b]	0	0-0.05	Gamma	222
Healthcare costs (US$)				
Moderate drinking with CC	6,756 (845)	5,067-8,445	Gamma	220
Excessive drinking with CC	6,756 (845)	5,067-8,445	Gamma	220
Decompensated cirrhosis[c]	25,956 (815)	25,539-26,374	Gamma	221
Hepatocellular carcinoma	58,183 (468)	57,246-59,119	Gamma	221
Transplantation <1st year	345,605 (43,201)	259,204-432,006	Gamma	5
Transplantation ≥1st year	72,284 (9,035)	54,213-90,354	Gamma	5
Health utilities				
Low-risk drinking[e]	1	NA	NA	d
Moderate drinking	0.94 (0.20)	0.94-1	Beta	223
Excessive drinking	0.84 (0.30)	0.85-1	Beta	223
Moderate drinking with AFLD	0.94 (0.20)	0.94-1	Beta	223
Excessive drinking with AFLD	0.84 (0.30)	0.85-1	Beta	223
Moderate drinking with CC	0.75 (0.028)	0.67-0.83	Beta	224
Excessive drinking with CC	0.75 (0.028)	0.67-0.83	Beta	224
Decompensated cirrhosis	0.672 (0.031)	0.58-0.77	Beta	224
Hepatocellular carcinoma	0.662 (0.019)	0.60-0.67	Beta	225
Transplantation <1st year	0.72 (0.07)	0.58-0.96	Beta	226
Transplantation ≥1st year	0.75 (0.08)	0.59-0.98	Beta	226
Death	0	NA	Beta	d
Other inputs				
Discount rate	0.03	0.02-0.08	Beta	d
Time horizon (in years)	Lifetime	NA	NA	d

The parameters listed are in addition to the parameters used for the microsimulation model (Table 2).

[a] Varies by race/ethnicity and gender

[b] Percent of tax value

[c] Decompensation was defined as having at least one occurrence of ascites, hepatic encephalopathy, or variceal bleeding.

[d] Assumed by authors

[e] Includes individuals who are lifetime or past-year abstainers

AFLD, alcohol-related fatty liver disease; CC, compensated cirrhosis; MUP, minimum unit pricing; NA, not applicable; PSA, probabilistic sensitivity analysis; SD, standard deviation.

Overview of distributional CEA

In conventional CEA, which is grounded on utilitarianism, health gains and losses between different individuals are treated equally. For example, a 0.10 QALY gain in people with the common cold is equivalent to a 0.10 QALY gain in people with a severe or debilitating illness. Additionally, extending the life of a person with a severe condition, which is associated with a lower health-related quality of life, is worth fewer QALYs than extending the life of a healthy person. Thus, the assumption that a “QALY is a QALY is a QALY” goes against concerns for health equity, which is defined as the absence of unjust differences in health.[262] Achieving health equity requires treating populations differently based on need or disadvantage, and it implies prioritizing certain groups over others when resources are scarce.[263]

To address the equity-related limitations of CEA, equity-informative economic evaluation methods have been developed; one such method is DCEA.[157,158] DCEA extends the traditional CEA framework by quantifying the distributional effects of health interventions based on different equity-relevant characteristics like socioeconomic status, race/ethnicity, geography, and disease burden. One of the benefits of DCEA compared to other equity-informative methods is its ability to summarize the distributional impact of interventions in one metric, which can be compared to a decision-maker’s aversion to inequality. Thus, the results of a DCEA can identify the preferred intervention and quantify any equity-efficiency tradeoffs.[156,160] Efficiency-equity tradeoffs are especially relevant in alcohol pricing policies because of their potential to impact population subgroups in different ways.

Because DCEA is a nascent technique, no checklist or reporting standards have been developed to inform or guide DCEAs. Instead, I relied on existing best practices for conventional CEAs[218,219], as well as the first main text on DCEAs[264], in conducting this study and reporting its results.

Model description

This DCEA used the same microsimulation model in Chapter 2 and adopted the same changes to the model that were listed in Chapter 3. To briefly recall, the microsimulation model simulates US adults aged 18-85 years old with various ages, genders, and race/ethnicities. Individuals with various sociodemographic characteristics were proportionally sampled based on their representation in the US population.[194] Data from the National Epidemiologic Survey on Alcohol and Related Conditions wave 3, the largest, nationally representative epidemiological survey on alcohol and drug use conducted by the National Institutes of Health (NIH), were used to determine the initial distribution of the population by drinking status.[265] Additional data from published literature were used to determine the prevalence of alcohol-related fatty liver disease, compensated cirrhosis, and decompensated cirrhosis.[8,9]

For this DCEA, I simulated individuals from three racial/ethnic groups, namely White, Black, and Latino/Hispanic; these groups were selected based on the availability of evidence on the effectiveness of alcohol taxes. In addition to estimating the costs and health benefits in terms of QALYs of the tax policies, I also calculated the average quality-adjusted life expectancy (QALE) at birth for each racial/ethnic group pre- and post-intervention. QALEs were used to calculate the Atkinson index and the EDEH, which measures total health and its distribution.

Description of modeled scenarios

In addition to the status quo or no-intervention scenario, I modeled two alcohol tax increases on beer and liquor (

Table 10). Beer and liquor were chosen because the most recent evidence on the heterogeneous effects of alcohol tax increases on overall consumption by race/ethnicity and gender involve these two beverages.[154] The magnitude of the tax increases (5% and 30%) is similar to the ones modeled in Chapter 3, which were found to be cost-effective and cost-saving interventions compared to the status quo.

Table 10. Description of modeled alcohol tax policies

Category	Price per standard drink (US$)[a]	Tax per standard drink (US$)[b]	Price increase in US$ (relative tax increase)	
			5%	*30%*
Beer and malt beverages (5% alcohol)	1.22	0.054	0.06 (1.1)	0.37 (6.8)
Liquor (40% alcohol)	0.64	0.127	0.03 (0.24)	0.19 (1.5)

[a] Calculated using data from the Consumer Price Index of the US Bureau of Labor Statistics.[266]
[b] Calculated using data from the Alcohol Policy Information System of the National Institute on Alcohol Abuse and Alcoholism.[230]

Treatment effect

As in Chapter 3, the treatment effect of alcohol taxes was defined as the change in the initial distribution of low-risk, moderate, and excessive drinkers. Similar to previous analyses[151], I followed a two-step process to estimate the treatment effect of pricing policies; these steps involved (1) translating price increases to changes in alcohol consumption using price elasticities of demand and (2) applying the change in consumption to estimate the new prevalence of various drinking levels (Figure 13). All price calculations were conducted based on the price of a standard drink, which in the US is defined as a beverage with about 14g of pure ethanol (Box 1). I describe my approach in some detail below, and additional details are provided in Appendix 9.

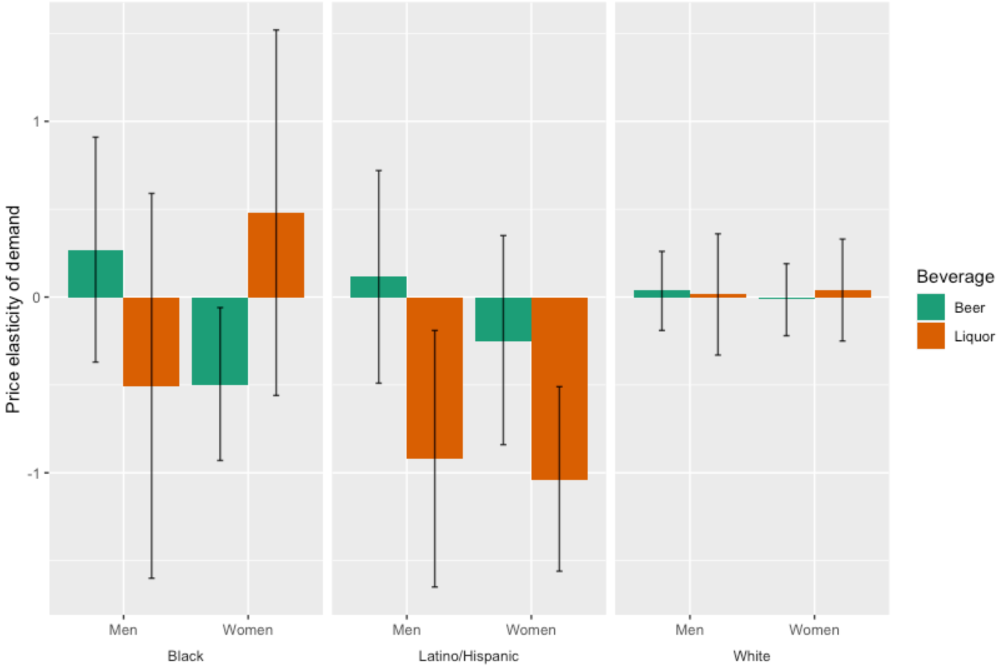
Change in consumption

To translate changes in price to changes in alcohol consumption, I used previously estimated price elasticities of demand, which describe the change in consumption following a change in price of a good. Specifically, this study leveraged the work by Subbaraman et al. (2020), which estimated the effect of state-level beer and liquor taxes, which include excise and ad valorem taxes, on the total volume of alcohol consumed in the past 12 months by race/ethnicity and gender.[154] Using self-reported alcohol consumption data from four waves (2000-2015) of the US National Alcohol Surveys and state tax data from Alcohol Policy Information System, the study found that White, Black, and Hispanic women showed negative price elasticities of demand for beer, which means that beer price increases were may lead to lower alcohol consumption in these groups (Figure 19). On the other hand, White, Black, and

Hispanic men showed positive price elasticities of demand for beer, which suggests that these groups increase their overall alcohol consumption when beer prices increase. The price elasticities of demand for liquor show different responses among these groups; Black and Hispanic men and Hispanic women reduce their total alcohol consumption when the price of liquor increases, while White and Black women and White men increase their total alcohol consumption.

It is worth nothing that only three of the price elasticities of demand estimated by Subbaraman et al. were statistically different from 0, as denoted by the confidence intervals in Figure 19. Because of a lack of statistical significance and the wide ranges for most results, I assumed a 0 or null price elasticity of demand for all racial/ethnic and gender groups whose results were not statistically significant. In sensitivity analysis, I used the ranges for each subgroup's price elasticity of demand to construct distributions for these parameters, as is recommended for economic evaluations that use nonsignificant results.[267–269]

Figure 19. Price elasticities of demand for beer and liquor by race/ethnicity and gender



Graph constructed based on findings from Subbaraman et al. (2020).[154] Shaded bars are the average estimate, and the lines are the 95% confidence interval.

Change in drinking prevalence

Changes in alcohol consumption were translated to changes in the prevalence of low-risk, moderate, and excessive drinking for each racial/ethnic and gender group. For low-risk and moderate drinkers, the change in consumption (aTable 18) represented the proportional increase or decrease in prevalence, making the estimation straightforward (Appendix 9).

For excessive drinkers, which are individuals who consume alcohol above daily drinking thresholds, I applied the change in consumption across the distribution of daily alcohol consumed by individuals in this group.[234] To calculate the proportion of excessive drinkers who move to the moderate drinking group under each policy, I fitted a log-normal distribution on the distribution of alcohol consumed by excessive drinkers, and determined the probability that excessive drinkers would fall at or below the heavy drinking thresholds; this procedure was done for each racial/ethnic and gender group (Appendix 9). The initial prevalence of various health states under each tax policy is found in aFigure 9.

Costs

As in Chapter 3, I included current and future medical care costs and intervention costs in the healthcare sector perspective. For the societal perspective, I included all costs in the healthcare sector perspective, as well as patient time costs, future consumption, and future productivity. All costs are in 2021 US dollars (US$); historical costs were updated using the CPI for medical care.[229]

Intervention costs

Intervention costs refer to the costs of collecting alcohol excise taxes. In the base case, I assumed that the alcohol tax policies I modeled are not associated with any new costs for the public and private sectors. This is because state and local governments routinely collect alcohol taxes, and alcohol producers and retailers will likely use existing resources to comply with any tax rate changes. This assumption is also made by previous CEAs of tax-based public health interventions.[235–237]

However, in sensitivity analyses, I assumed that the alcohol tax increases I modeled are associated with an annual per-person cost between 0-0.05% of each additional dollar of excise tax collected, as suggested in previous studies.[222]

Related and unrelated medical costs

The routine costs of care for compensated and decompensated AC were based on a costing analysis conducted for a previous CEA[220] and a study on the costs of treating US veterans with cirrhosis[221], respectively. All costs associated with liver transplantation are based on a claims-based analysis of a commercially insured population in the US.[5] Future unrelated medical costs based on healthcare expenses by age from the 2019 Consumer Expenditure Survey of the US Bureau of Labor Statistics (Appendix 8).

Other societal costs

For the societal perspective, I included lifetime productivity and consumption costs. I also valued and included time costs or foregone productivity of patients using published estimates of time spent on alcohol use treatments and ALD treatments multiplied by average daily wages (Appendix 8).

Health outcomes

Health outcomes were measured in terms of QALYs gained. The weights used to calculate QALYs are based on health utilities that typically range from 1 (a year in perfect health) to 0 (death). I took health utility estimates for the various states in the model from the literature (Table 9).[224–226,241]

Analysis

Due to the significant uncertainty in model parameters, particularly the price elasticities of demand by race/ethnicity and gender, I conducted probabilistic sensitivity analysis (PSA) and used the results to calculate the base-case findings. In PSA, I ran 1,000 independent simulations of 10,000 individuals from every racial/ethnic group by drawing random values of each parameter based on distributions that were assigned a priori. Transition probabilities were assigned a beta distribution, relative risks were assigned a lognormal distribution, and the price elasticities of demand by race/ethnic and gender groups were assigned normal distributions. I based ranges and standard deviations for each input on reported figures from the literature where available; for inputs where ranges were not available, I applied ±25% on the mean estimate to generate upper and lower limits.

In the base-case, I assumed that only Black women responded to beer tax increases and only Latino/Hispanic men and women responded to liquor tax increases, while all other racial/ethnic and gender groups did not respond to changes in alcohol taxes (Figure 19). In supplemental analyses, however, I assigned distributions to the price elasticities of demand of all racial/ethnic and gender groups to understand the effect of uncertainty around the treatment effectiveness of tax policies from the Subbaraman et al. study.

Cost-effectiveness

I calculated the incremental cost-effectiveness ratio (ICER), which is defined as the cost per unit of health outcome gained. An intervention is typically considered cost-effective or efficient if its ICER is equal to or less than a cost-effectiveness threshold, which represents the health opportunity costs of additional spending in the health sector. In this study, I used a cost-effectiveness threshold range of $100,000-150,000 per QALY gained[240], which I assumed to be uniform across racial/ethnic groups. In practice, however, different populations may face higher opportunity costs from foregone or displaced resources; for example, a study in the UK found that the lowest socioeconomic group disproportionately bear the opportunity costs of changes in health spending.[270]

To calculate ICERs, I took the average costs and effectiveness from the PSA and used the results in Eq. 1.

Equity impact

To measure the health equity impacts of tax policies, I calculated the Atkinson index (A_{ε}), one of many social welfare functions that focuses on relative inequality in the distribution of societal resources, such as income or health.[156,160] The Atkinson index was calculated using the formula

$$A_{\varepsilon} = \begin{cases} 1 - \left[\frac{1}{n}\sum_{i=1}^{n}\left(\frac{QALE_i}{\overline{QALE}}\right)^{1-\varepsilon}\right]^{\frac{1}{1-\varepsilon}} & for\ 0 \leq \varepsilon \neq 1 \\ 1 - \left[\prod_{i=1}^{n}\left(\frac{QALE_i}{\overline{QALE}}\right)\right]^{\frac{1}{n}} & for\ \varepsilon = 1 \end{cases} \quad \textbf{Eq. 2}$$

where n is the number of racial/ethnic groups, $QALE_i$ is the average QALE of racial/ethnic group i, $\overline{QALE}$ is the average QALE of the total population, and ε is the inequality aversion parameter. Health outcomes other than QALE can be used in the calculation of the Atkinson index, though QALE was selected for this study because it captures lifetime or overall health, which varies by racial/ethnic group and is a widely recognized health inequity. For instance, the average life expectancy at birth of Black people is about 3.7 years lower than White people, and this disparity has been linked to higher death rates among Black people for conditions like diabetes and heart disease which are socially driven and rooted in historical and persistent racism.[271,272]

The Atkinson index was selected because it most closely reflects the definition of health equity. First, it measures relative inequality in health, which is the difference between one group's health compared to the overall health of the population. Second, the Atkinson index is a "prioritarian" social welfare function that gives more weight to the health and health gains of individuals with less health or those who are worst-off. (The degree of prioritization is further adjusted using the inequality aversion parameter, which is discussed below.)

A_ε takes on a value between 0 (complete equality) to 1 (complete inequality) and can be interpreted as the proportion of QALE that could be forgone without any losses in social welfare, if the remainder were distributed equally.[273] For example, when A_ε = 0.20, then the same level of social welfare can be achieved as the current level and distribution of QALEs if only 80% of QALEs existed in the population and were distributed equally.

The inequality aversion parameter (ε) for health represents a decision-maker's attitude or judgment about the distribution of health in society.[274] This parameter varies from 0 (i.e., indifference about inequality or a perfect utilitarian perspective) to infinity; higher parameter values denote a preference for improvements among the worse off, which reflects a stronger prioritarian ethic.[274,275] Empirical measures of the inequality aversion parameter are available in the literature, though none to date have been specific to the US. In the UK, the inequality aversion parameter for health was estimated in 2017 study to be around 10.95 (95% CI: 9.23-13.54)[276], which is significantly higher than historical estimates of the inequality aversion parameter for income ($1 < \varepsilon < 2$).[273] In this study, I varied ε between 1 and 30, as previously published DCEAs have done.[156,160,277,278]

To translate the A_ε on the same scale as individual health, I also calculated the EDEH. The EDEH, for each value of ε, represents the level of health each person in the population would receive that would (1) make the health distribution equal and (2) make society indifferent between an equal distribution of health and the actual unequal distribution of health.[156] In other words, the EDEH serves as the equity-adjusted health benefit of each intervention. The EDEH, given the Atkinson index A_ε, was calculated using the formula

$$EDEH = (1 - A_\varepsilon)\overline{QALE} \qquad \textbf{Eq. 3}$$

Additional analyses were conducted using the EDEH of each intervention. The EDEH of each tax policy was subtracted from the EDEH of the status quo, and the difference is referred to as the change in EDEH which represents the change in health-related social welfare. If the change in EDEH is positive, then an intervention improves population health and reduces inequality; the opposite is true when the change in EDEH is negative.[279] When EDEH is subtracted from $\overline{QALE}$, the difference represents the average amount of health per person that a decision-maker is willing to forego to achieve full equality in health; it can also be interpreted as the cost of health inequity.[279]

Sensitivity analyses

In the base case, I assumed that racial/ethnic and gender groups whose price elasticity of demand were not statistically significant in the Subbaraman et al. study was 0. In sensitivity analysis, I used the estimated average price elasticity of demand and ranges for each group to construct normal distributions for these parameters. As a result, some groups may have positive or negative price elasticities of demand, depending on the parameters of the distribution. As in the base case, I took 1,000 values of the price elasticity of demand and conducted PSA to generate the average results.

RESULTS

Cost-effectiveness analysis

The cost-effectiveness results, which were generated through the PSA, are shown in Table 11 for the healthcare sector perspective and in aTable 20 for the societal perspective. The model found that compared to the status quo, all four tax policies were dominant or cost-saving using a healthcare sector perspective (Table 11), which means that they produce more health and less costs than the status quo.

Table 11. Cost-effectiveness of alcohol tax policies using a healthcare sector perspective

			ICER (in cost per QALY gained)	
Intervention	**Cost (in US$)**	**Benefit (in QALYs)**	*Compared to status quo*	*Compared to next expensive, undominated intervention*
30% liquor	41,668.95	6.27963	Dominant	NA
5% liquor	41,670.39	6.27763	Dominant	Dominated
30% beer	41,671.49	6.27787	Dominant	Dominated
5% beer	41,671.97	6.27744	Dominant	Dominated

Status quo	41,672.38	6.27730	NA	Dominated

Interventions are ordered by increasing cost. ICERs were calculated by comparing each strategy with the status quo and each strategy to the next more effective and undominated option. This type of incremental analysis assumes that the strategies are mutually exclusive and independent.
ICER, incremental cost-effectiveness ratio; NA, not applicable. QALY, quality-adjusted life year.

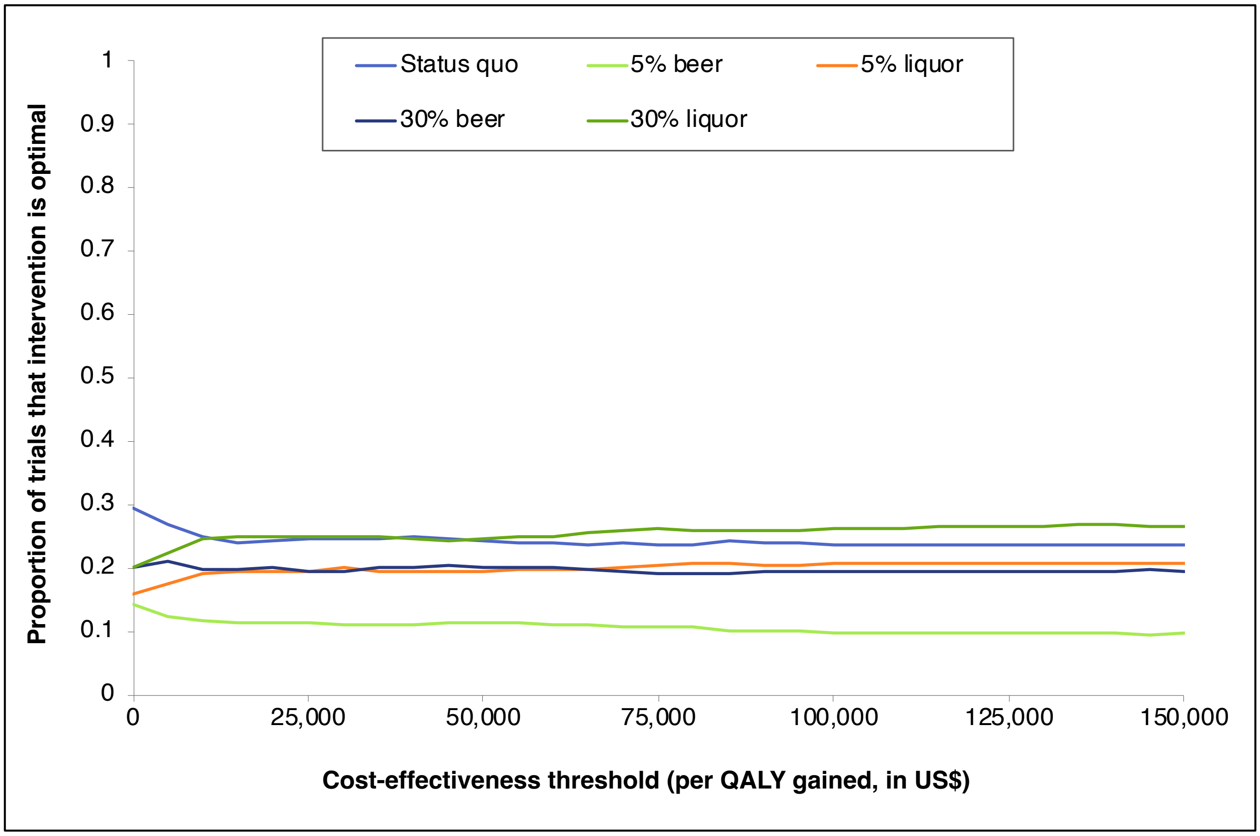
However, when interventions were ordered by increasing cost and compared to the next expensive, undominated intervention (a standard dominance test in CEAs), only the 30% liquor tax was found to be cost-effective. All three other tax policies—5% liquor tax, 30% beer tax, and 5% beer tax—were dominated because these interventions were more expensive and produced fewer QALYs than the 30% liquor tax (Table 11).

Similar results were found using a societal perspective (aTable 20). The 30% liquor tax was associated with the lowest ICER when compared to the status quo at $2,350 per QALY gained. Dominance analysis also found that only the 30% liquor tax was cost-effective using a societal perspective with an ICER of $1,193 per QALY gained.

Cost-effectiveness acceptability curves in

Figure 20 and aFigure 10 further summarize the results of the PSA. The results suggest that there is significant uncertainty associated with the optimal intervention across all cost-effectiveness thresholds. For example, the status quo was found to be the optimal intervention at cost-effectiveness thresholds below $10,000 per QALY gained and between $35,000-45,000 per QALY gained using the healthcare sector perspective. For all other cost-effectiveness thresholds, the 30% liquor tax was the optimal choice. However, the probability that either the status quo or 30% liquor tax was the optimal choice was less than 30% across all cost-effectiveness thresholds. Other tax policies such as the 5% liquor tax and 30% beer tax had 20% probability of being the optimal choice across all thresholds.

Figure 20. Cost-effectiveness acceptability curves using a healthcare sector perspective



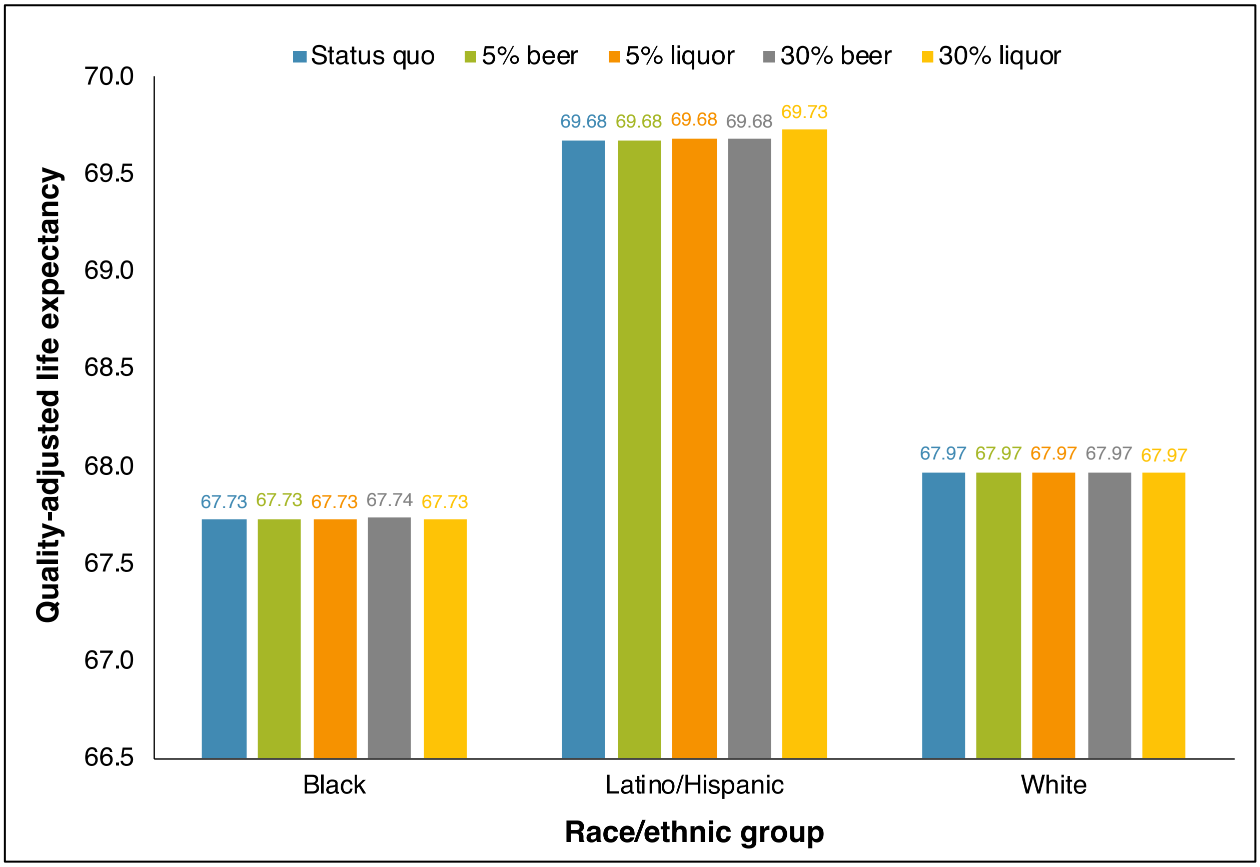
Cost-effectiveness acceptability curves plot the probability that an intervention is the optimal choice across a range of cost-effectiveness thresholds.
QALY, quality-adjusted life year.

From a societal perspective, the status quo was the optimal choice for cost-effectiveness thresholds below $20,000 per QALY gained, while the 5% liquor tax was the optimal choice for all other thresholds (aFigure 10). However, there was significant uncertainty around these results as well, with probabilities at 30% or less.

Equity impact

Average QALEs for each intervention are shown in Figure 21. Black individuals had the lowest average QALE, followed by Whites and Latinos/Hispanics at baseline and under each policy. The order of QALEs by race/ethnicity estimated by the model are similar to the order of life expectancy by race/ethnicity reported in the US.[271]

Figure 21. Quality-adjusted life expectancy by race/ethnicity under each intervention

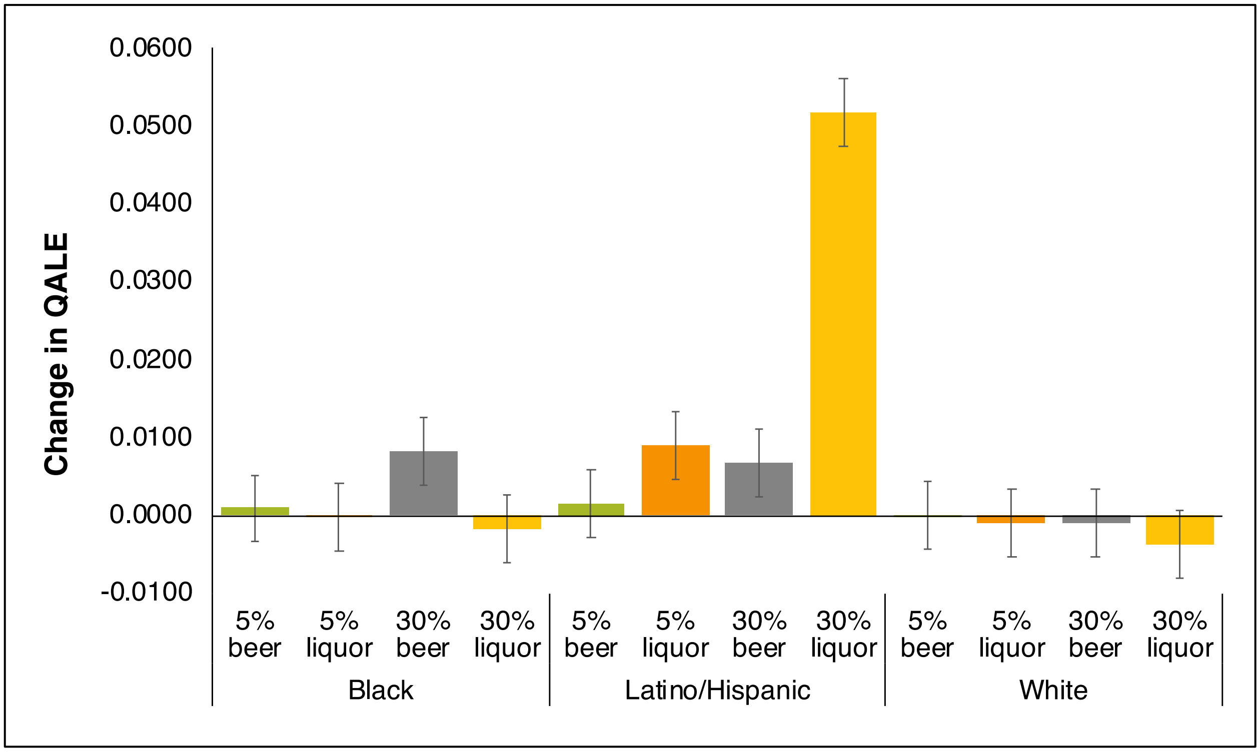


The quality-adjusted life expectancy under the status quo and 5% liquor tax have been labeled for comparison. Differences between policies are small and may not be visible in this graph.

QALE changes associated with each tax policy by racial/ethnic group are shown in

Figure 22. Several tax policies were associated with QALE gains across racial/ethnic groups. The largest QALE gains were found among Latinos/Hispanics under liquor taxes (0.009 and 0.05 for 5% and 30%, respectively), and these changes were robust based on the PSA. Small decreases in QALE were observed for Whites and Blacks under five policies, those these changes were likely due to randomness in the model, as indicated by the error bars which cross 0.

Figure 22. Change in quality-adjusted life expectancy by race/ethnicity under each intervention

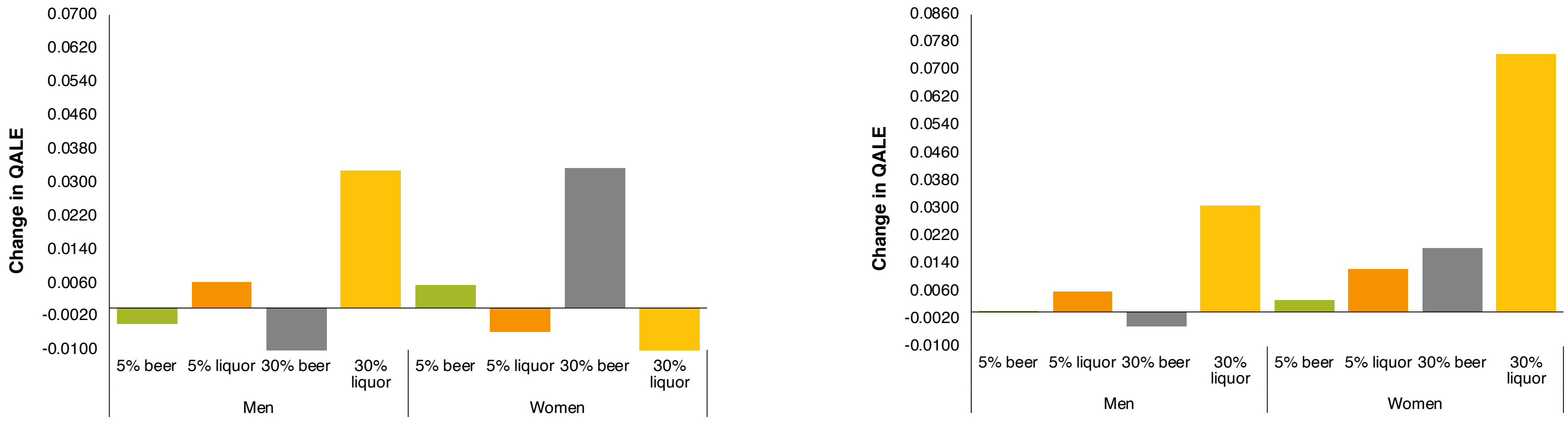


Changes in QALE were calculated by subtracting the QALE associated with each policy with the QALE associated with the status quo. QALE, quality-adjusted life expectancy.

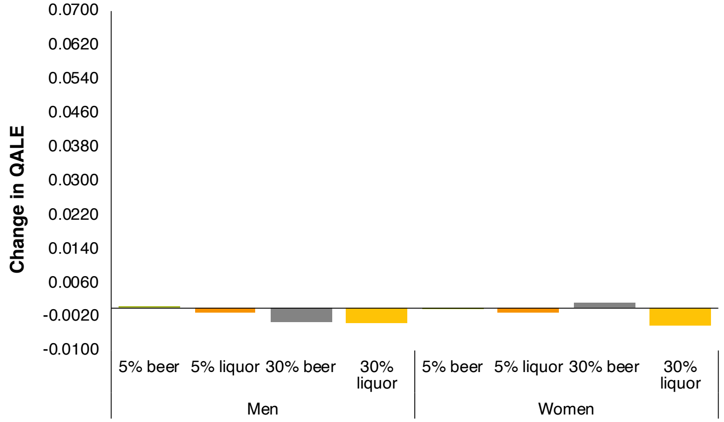
Estimated QALE gains and losses were not uniform between genders in each racial/ethnic group. For example, Black men saw QALE losses under beer taxes and QALE gains under liquor taxes; the opposite was observed for Black women (experienced QALE losses for all policies except for the 30% beer tax.

Figure 23). Latino/Hispanic men and women, on the other hand, saw QALE gains for all tax policies, except for the beer taxes which led to small QALE losses among Latino/Hispanic men. Finally, White men experienced QALE losses across all four tax policies except the 5% beer tax, while White women experienced QALE losses for all policies except for the 30% beer tax.

Figure 23. Change in quality-adjusted life expectancy among racial/ethnic and gender groups under each intervention


A. Black

B. Latino/Hispanic


C. White

Changes in QALE were calculated by subtracting the QALE associated with each policy with the QALE associated with the status quo.
QALE, quality-adjusted life expectancy.

When these estimated QALEs were used to calculate Atkinson indices for each intervention, this study found that the status quo was associated with the lowest Atkinson index for any value of the inequality aversion parameter, which means that it leads to the lowest level of inequality in health (Table 12). The 30% liquor tax, on the other hand, had the highest Atkinson index, which means that the distribution of health under this policy is the most unequal.

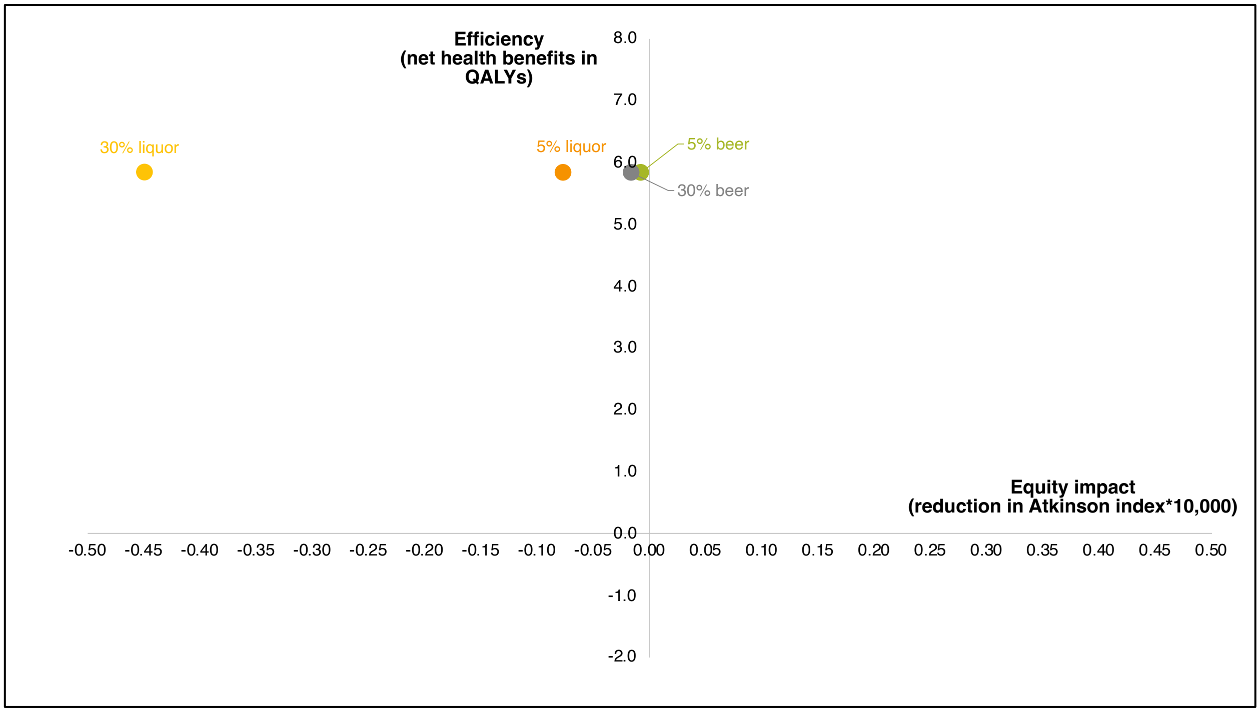
Table 12. Atkinson index across interventions

Inequality aversion parameter (ε)	Status quo	5% beer	5% liquor	30% beer	30% liquor
0	0	0	0	0	0
1	0.000066*	0.00033	0.00065	0.00126	0.00183†
5	0.000066*	0.00033	0.00065	0.00126	0.00183†
10	0.000069*	0.00034	0.00068	0.00131	0.00191†
20	0.000066*	0.00033	0.00065	0.00126	0.00183†
30	0.000070*	0.00035	0.00068	0.00133	0.00192†

Asterisk (*) denotes the intervention with the lowest Atkinson index at each inequality aversion parameter value, which represents the lowest inequality. The cross (†) marks the intervention with the highest Atkinson index, which represents the highest inequality.

Figure 24 summarizes the efficiency and equity effects of the tax policies, which are shown in Table 11 and Table 12 respectively. Using a cost-effectiveness threshold of $100,000 per QALY gained, the model found that all four tax policies have positive net health benefits. All four tax policies were associated with negative Atkinson index changes, which means that the tax policies may lead to more inequality than the status quo.

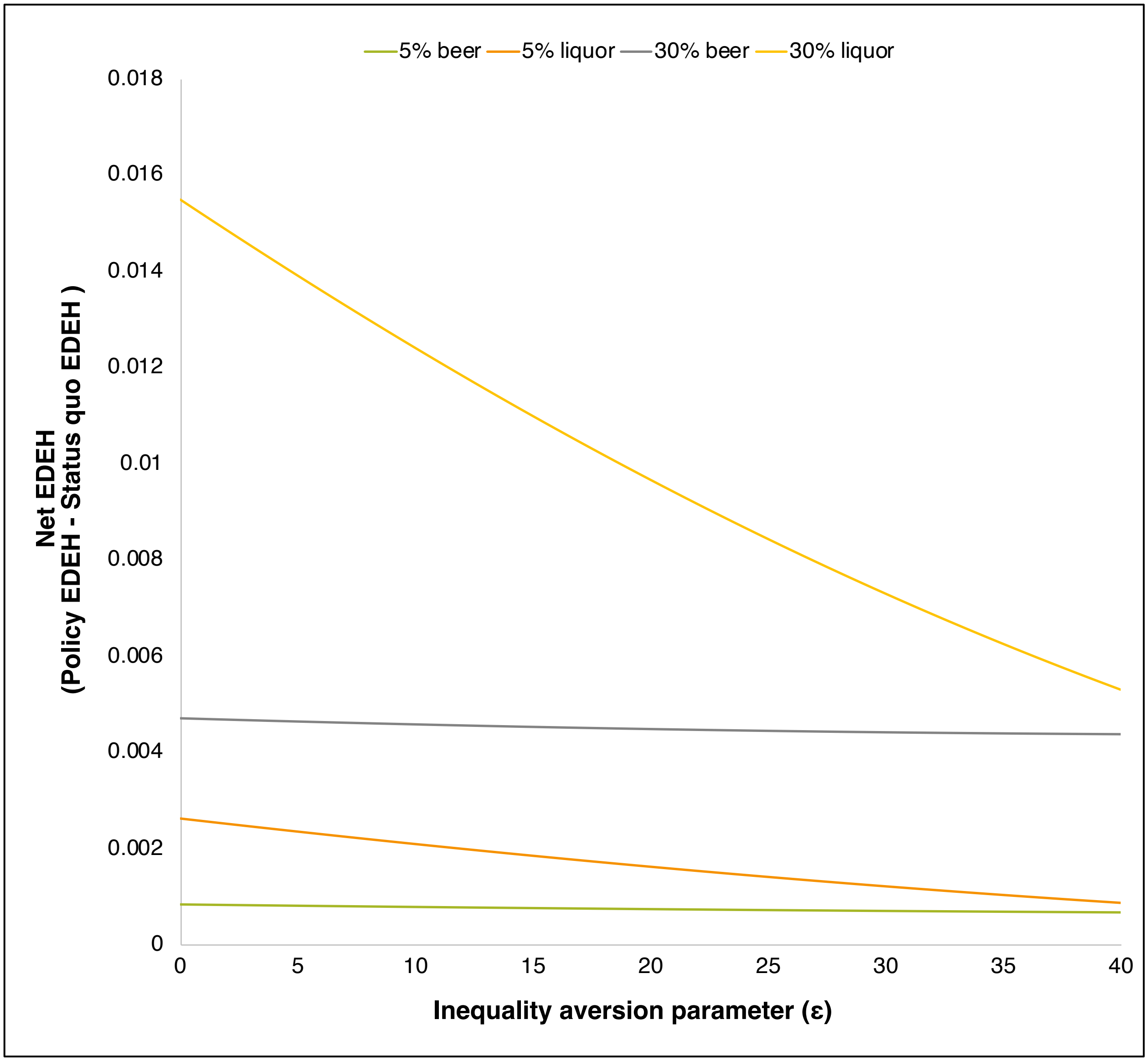
Figure 24. Equity-efficiency impact plane



The equity-efficiency impact plane plots the efficiency, in terms of net health benefits, and equity impact, in terms of a reduction in the Atkinson index, of each tax policy. The net health benefits were calculated using a cost-effectiveness threshold of $100,000 per QALY gained and using a healthcare perspective. The Atkinson index was calculated using an inequality aversion parameter equal to 10 and by comparing each policy with the status quo.
QALY, quality-adjusted life years.

Figure 25 shows the results of the equity trade-off analysis using EDEH. Across all inequality aversion parameter values, the 30% liquor tax had a higher net EDEH when interventions were compared to the status quo. Since EDEH increases with total population health and decreases with inequality in the distribution of health, the results suggest that the population health gains associated with the 30% liquor tax may outweigh the inequality in the distribution of health; this finding was robust across all values of the inequality aversion parameter including 0, which denotes a perfectly utilitarian perspective (i.e., indifference towards inequality and preference for largest total health). The 30% beer tax had the second highest net EDEH, followed by the 5% liquor tax.

Figure 25. Equity trade-off analysis



EDEH is the level of health per person, if distributed equally, that would produce the same level of social welfare as the distribution of health in the status quo; thus, a higher EDEH is always preferred. The net EDEH was calculated by subtracting each policy's EDEH with the status quo EDEH. A higher inequality aversion parameter denotes a stronger preference for equality.
EDEH, equally distributed equivalent of health.

Sensitivity analyses

When uncertainty in the price elasticities of demand for all racial/ethnic and gender groups were incorporated in the PSA (and including elasticities that did not have statistically-significant effects), similar results to the base case were found. The 30% tax was estimated to be the most cost-effective option, while other tax policies were extendedly dominated (aFigure 11). QALE changes also varied by racial/ethnic and gender groups (aFigure 12), which caused the 30% liquor tax to have the highest Atkinson index or the highest inequality in the distribution of health (aTable 21). The equity-efficiency impact analysis (aFigure 13) found that while liquor taxes were still associated with higher Atkinson indices than the status quo, beer taxes may in fact reduce health inequity. Finally, the equity tradeoff analysis (aFigure 14) revealed that the 30% liquor tax had the highest net EDEH, which suggests that gains in health may outweigh any inequalities in the distribution of health associated with this policy.

DISCUSSION

This study was the first application of a DCEA framework to evaluate alcohol tax policies in the US. The results suggest that on average, beer and liquor taxes can be cost-effective or cost-saving interventions, though the efficiency of each intervention depends in part on the perspective and comparator used. For example, beer and liquor taxes were cost-saving using a healthcare sector perspective and cost-effective using a societal perspective and when compared to the status quo.

When interventions were ordered by increasing cost and compared against the nearest undominated option—a standard dominance analysis in CEAs—only the 30% liquor tax was found to be cost-effective in both healthcare sector and societal perspectives. All other tax policies were extendedly dominated, which means that they produce less health and higher cost than the 30% liquor tax. The PSA also revealed that the 30% liquor tax was most likely to be the efficient choice at cost-effectiveness thresholds above $45,000 per QALY gained, though there was significant uncertainty around this result. Findings from this study, therefore, should be interpreted cautiously. The sizeable influence of parameter or second-order uncertainty should be evaluated in future analyses using parameter estimates with greater precision.

The dominance of the 30% liquor tax among all other strategies was likely driven by the large gains in health observed among most racial/ethnic and gender groups. This study found that a 30% liquor tax was associated with larger QALE gains among Black men and Latino/Hispanic men and women and smaller QALE losses among Black women and White men and women. The QALE gains under a 30% liquor tax among Latinos/Hispanics were especially large that the average QALE rose in this group (from 69.67 to 69.73), while the QALE of Blacks and Whites were virtually unchanged. This finding aligns with previous empirical research that found a negative association between state-level liquor taxes and chronic alcohol-attributable mortality[280]; the same study also found that beer taxes were negatively associated with mortality, but only among Black males.

Because the 30% liquor tax was associated with large gains in some groups but not others, the Atkinson index, a measure of relative inequality in the population, was also highest for this intervention. The Atkinson index for the 30% liquor tax was significantly influenced by the fact that the largest gains accrued among Latinos/Hispanics, who had the highest QALE at baseline and had a higher QALE than the post-intervention population average. The 30% liquor tax was also associated with a small decrease in QALE among Blacks (-0.00173). By contrast, the status quo, had the lowest Atkinson index across all inequality aversion parameter values used. This was likely influenced by variable changes in QALY under different tax policies across racial/ethnic and gender groups.

Despite the higher inequality (i.e., larger Atkinson index) associated with the 30% liquor tax, the equity tradeoff analysis revealed that this policy’s net EDEH was higher than any other intervention. Because the EDEH captures both total health and its distribution, this finding suggests that overall population health gains may outweigh the inequality in the distribution of health that results from the implementation of a 30% liquor tax. This finding was found to be robust even after uncertainty around the true effectiveness of pricing policies for all racial/ethnic groups was incorporated in sensitivity analyses.

This analysis relied on previous estimates of the price elasticity of demand for alcohol that had significant uncertainty. Research by Subbaraman et al. found that changes to total alcohol consumption varied by race/ethnicity and gender, though only two elasticities were statistically shown to be statistically different from 0.[154] Previously, An and Sturm (2011) analyzed Behavioral Risk Factor Surveillance System data from 1984-2009 and found that alcohol taxes had varied effects on light, moderate, and heavy drinking, rejecting the null hypothesis that all racial/ethnic groups have similar responses to alcohol taxes and potentially other pricing policies.[155]

Like Subbaraman et al., An and Sturm found that some racial/ethnic groups may increase their consumption when alcohol taxes increase, particularly among excessive drinkers. This finding, which contradicts most studies on alcohol prices and consumption that have found a negative relationship, is a likely outcome given the price variability that alcohol taxes create. Research by Shang et al. (2018), for example, suggest that a “mixed” alcohol tax structure that result from the use of multiple types of alcohol taxes (e.g., beverage-specific, ad valorem, and volumetric) can lead to significant price variability that promotes tax avoidance and product substitution.[233] The same phenomenon has been observed for excise taxes for tobacco, which suggests that volume-based taxes or minimum unit pricing may be more effective policies to reduce consumption since they are more likely to reduce price variability at the lower (i.e., cheaper) end of the distribution.

This study joins a growing number of DCEAs that have evaluated healthcare and public health interventions in various settings.[158,159] Only one study to my knowledge has focused on the US context, which estimated the efficiency and equity effects of two HIV prevention and treatment strategies in six major cities.[281] The authors found that an equity-focused approach that allocated HIV services based on a population’s need (i.e., HIV incidence rate) was the most efficient and equitable approach that reduced the incidence of health disparities in all but one city. No other DCEA has evaluated alcohol taxes before, though previous modeling and cost-effectiveness studies have explored the distributional impacts of alcohol taxes. Work by the Centers for Disease Control and Prevention, for instance, found that a $25-cent-per-drink would reduce overall alcohol consumption by 9% and excessive drinking by 11%.[151] That study also found that the tax increase would affect excessive drinkers the most—a finding that a more recent study has also reported.[166]

Limitations

The findings of this study should be interpreted with its limitations in mind. Several limitations related to the model, inputs, and various assumptions that were discussed in detail in Chapters 2 and 3 also apply to this DCEA. For example, this study also underestimated the potential health benefits of alcohol taxes due to its narrow focus on ALD morbidity and mortality. Also, I assumed that tax policies only affected the initial distribution of drinking levels, though in practice alcohol taxes policies may also reduce the probability of transitioning from low-risk and moderate drinking to excessive drinking. This data, however, is currently lacking.

There are also additional limitations associated with this study specifically. First, the price elasticities of demand by race/ethnicity and gender have significant uncertainty intervals. I incorporated and evaluated the effect of parameter uncertainty through the PSA, which found that the probability that the optimal decision is the right one was less than 30% across a range of cost-effectiveness threshold values. This finding suggests that parameter uncertainty has a significant effect on the cost-effectiveness results, and future studies should use more precise estimates of the price elasticity of demand. Additionally, only two price elasticities of demand were statistically different from 0. Though the lack of statistical significance in these estimates does not preclude their use in economic evaluation[267–269], additional research is needed to estimate the true effect of prices on alcohol consumption using larger samples.

Second, while this study incorporated two equity-relevant characteristics, namely race/ethnicity and gender, it omitted other variables that are also relevant to the evaluation of alcohol control polices like taxation. Future research should include these variables given that price elasticities of demand for alcohol have been shown to vary by level of drinking[104], gender[131,258,259], age[44,260], and race/ethnicity[154,155], and focusing on average effects may mask important differences between groups. However, additional empirical work is needed to estimate the heterogeneous effects of alcohol prices on consumption among intersectional groups like the ones included in this DCEA.

Third, due to lack of data, I excluded other race/ethnic and gender groups from this study. For example, I did not model Asian American and Pacific lander, American Indian and Alaska Natives, and other biracial or multiracial groups since their price elasticities of demand were not estimated in the same study as Whites, Latinos/Hispanics, and Blacks. Additionally, only men and women were included in the gender category, thereby excluding transgender and nonbinary individuals who face higher risks for alcohol and other substance use disorders.[39]

Fourth, this study measured inequality in the distribution of health using the Atkinson index, which focuses on relative health. The Atkinson index is considered a prioritarian social welfare function since it gives more weight to the health of individuals with less health relative to the average population health. In this study, Black men and women had the lowest estimated QALE compared to Whites and Latinos/Hispanics, which is also what official life expectancy statistics have found.[271] Other measures of inequality are available, such as the Gini index, standard concentration index, and the Kolm index, which measure absolute inequality in health.[156,160] Future studies can use these inequality metrics if they reflect the preferred ethical framework to estimate the equity impacts of health interventions. However, like the Atkinson index, the Kolm index is a social welfare function that relies on the inequality aversion parameter for health, which has not been estimated for the US. Additional work in this area is needed if methods like DCEA are to be formally used in decision-making.

Finally, this study assumed that the health opportunity cost, which was represented by the cost-effectiveness threshold range, is uniform across racial/ethnic groups. However, different populations may face higher opportunity costs from foregone or displaced resources. For example, a study in the UK found that the lowest socioeconomic group disproportionately bear the opportunity costs of changes in health spending.[270]

Conclusion

Alcohol tax policies may have heterogeneous effects across equity-relevant populations such as racial/ethnic minorities and gender groups. This study found that a 30% liquor tax increase was the most economically efficient intervention compared to the status quo or to other liquor and beer taxes included in the analysis. However, the 30% liquor tax was associated with the highest health inequality, due to its higher impact among Latinos/Hispanics who already have the highest baseline health when measured in QALEs. By contrast, the status quo had the lowest health inequality. Equity tradeoff analysis suggests that the total population health gains associated with a 30% liquor tax may outweigh any inequality in the distribution of health. This exploratory study highlights the need to incorporate the distributional effects of alcohol control policies to ensure that interventions advance population health without harming equity.

Chapter 5: Conclusion

CONTEXT

The burden of alcohol-related liver diseases (ALD) is increasing in the US amidst rising rates of alcohol use and misuse. While the prevalence of mild ALD has remained stable[8,162], an analysis found that the prevalence of severe ALD rose from 2.2% in 2002 to 6.6% in 2016, and the proportion of hospitalizations due to severe alcohol-related cirrhosis (AC) more than doubled from 11.6% to 25.8%.[162] During this period, alcohol use and misuse were steadily increasing in the US; a meta-analysis found that the prevalence of alcohol use and binge drinking have been increasing by 0.30% and 0.72% per year since 2000.[25] AC is now the underlying cause of half of all liver cirrhosis-related deaths in the US[20], and ALD has become the main indication for liver transplantation among adults less than 40 years.[13,14]

Several trends suggest that the burden of ALD is shifting in the population. For example, ALD-related discharges are increasing more rapidly among women compared to men.[16] The gap in ALD mortality between men and women has also been decreasing, especially among 25-34-year-olds.[17] While ALD mortality rates have been historically highest among older adults[17], adults less than 35 years have faced the steepest increases in ALD deaths; between 2009 and 2016, ALD mortality rose by 10% per year (from 8.9% to 12.2%) among 25-34-year-olds.[11] Finally, racial/ethnic groups have experienced different changes in ALD mortality. One study estimated that annual changes in ALD mortality were 3.7%, 1.2%, 2.5%, and 2.1% for Whites, Blacks, Asian Americans, and Hispanics, respectively, between 2017-2016.[18] However, when analyzed by race/ethnicity and gender, starker differences are revealed. In one study, black men and women and Hispanic men saw decreases in ALD mortality rates, while

White men and women and Hispanic men have seen 2-5% annual percent changes across all ages.[17,19]

CONTRIBUTIONS

These trends inspired and informed this dissertation. I conducted three studies that focused on the distribution of ALD burden and the heterogeneous effects of policies to reduce drinking and prevent ALD. The aim was to contribute to our understanding of ALD and the potential impact of our evidence-based public health interventions.

In the first study (Chapter 2), I developed a novel microsimulation model that projected the future burden of ALD in the US. Unlike previous models, I included various individual sociodemographic characteristics (i.e., age, gender, and race/ethnicity) to understand the disparities in ALD burden over time. I estimated that ALD cases and deaths may increase in the US alongside rising rates of alcohol misuse. Average ALD incidence and ALD-related mortality rates masked stark differences between sociodemographic groups. I also found that groups that have been disproportionately affected by ALD in the past are likely to continue bearing the health burden.

The second and third studies were focused on interventions, specifically alcohol pricing policies, which have been shown to be effective tools in reducing alcohol use and misuse. In Chapter 3, I compared the costs, health benefits, and cost-effectiveness of three hypothetical alcohol tax increases and two minimum unit pricing (MUP) policies. I found that alcohol tax increases and MUP are cost-saving or cost-effective interventions when compared to the status quo. Among all interventions, an MUP that increased the price of the cheapest alcohol by 100% had the highest probability of providing the most value for money. Like previous economic evaluations, this study supports the implementation of pricing policies to reduce drinking and ALD. This study likely underestimated the benefits of pricing policies due to its focus on ALD alone.

Finally, in the third study (Chapter 4), I applied a distributional cost-effectiveness analysis (DCEA) framework to evaluate the cost-effectiveness and equity impacts of beer and liquor taxes. I leveraged previous estimates of the heterogeneous effects of pricing policies across racial/ethnic and gender groups. I found that a 30% liquor tax increase was the most economically efficient intervention compared to the status quo or to other liquor and beer taxes included in the analysis. However, the 30% liquor tax was associated with the highest health inequality, due to its higher impact on populations who already have the highest baseline health when measured in QALEs. By contrast, the status quo had the lowest health inequality. Equity tradeoff analysis suggests that the total population health gains associated with a 30% liquor tax may outweigh any inequality in the distribution of health. This exploratory study highlighted the need to incorporate the distributional effects of alcohol control policies to ensure that interventions advance population health without harming equity.

FUTURE WORK

These studies highlight important areas of future work. First, additional research is needed to estimate several population-specific parameters. In my model, only all-cause mortality rates, the starting prevalence of health states, and drinking transitions were available by race/ethnicity and gender. All other inputs were based on averages from the best-available literature. Estimating population-specific parameters may be challenging due to data limitations, including small numbers of individuals from intersectional groups of interest.

Similarly, for lack of data my model excluded key demographic and socioeconomic variables that are relevant to the evaluation of pricing policies. Among these, socioeconomic status is the most important, given that pricing policies may disproportionately impact low-income individuals and families, which would introduce a new equity concern. Empirical research is needed to estimate effects of pricing policies on different income groups in the US.

The microsimulation model can be adapted to estimate the burden of ALD in smaller contexts, such as states or cities. Future studies should focus on subnational contexts since alcohol control interventions like taxes are under local jurisdiction.

This dissertation was exclusively focused on ALD, so it excluded any other health, social, and economic consequences of alcohol. However, this choice has underestimated the health benefits of pricing policies. Future studies should aim to include these other alcohol-related outcomes such as alcohol use disorder, violence and crime, other cancers, and injuries.

Pricing policies, especially taxation, are the most common policy intervention used to control alcohol use, and they are also the intervention with the most robust evidence base. However, other policies and interventions (Table 13) have been shown to be effective in reducing alcohol use and misuse. For example, restricting the sale of alcohol, such as by limiting hours and banning promotions, has been linked to reductions in drinking, though the quality of evidence is moderate to low and only available in specific settings.[68,84] The microsimulation model I developed can be adapted to evaluate whether other alcohol control interventions are cost-effective and/or equity-improving.

While alcohol has been increasing in the US even before the COVID-19 pandemic, research has shown that alcohol use and misuse may have worsened for specific populations but not others.[282] Alcohol is often consumed to cope with and manage social stressors, and its wide availability and legal status allows many people to easily access it, as was seen during the COVID-19 pandemic.[164] Future modeling studies should estimate the effect that the pandemic may have on the long-term burden of ALD and other alcohol-related harms. For example, work by Julien et al. (2022) estimated that a single-year increase in alcohol misuse in the US following the COVID-19 pandemic could lead to 18,000 additional cirrhosis cases and 8,000 additional ALD-related deaths [193]

DCEA is a novel technique that incorporates equity considerations in economic evaluation. It is a welcome development at a time where research and analytical methods are needed to ensure that health interventions are effective, efficient, and equitable. Several parameters required for DCEA have not been estimated for the US context, such as the inequality aversion parameter, which precludes its broader use and application. Future research should empirically estimate these parameters.

Table 13. Population-level policy interventions to control alcohol

Category and type of policy intervention	GRADE rating[†]	Summary of evidence
Taxation and price regulation		
Taxation	High	Increasing tax is a highly effective and cost-effective approach to health improvement
Minimum unit pricing (MUP)	Moderate	Minimum prices effectively reduce health and other harms, is targeted at the heaviest drinkers who experience the greatest harm, and is cost-effective
Relative and combined impact of taxation and other pricing policies	Low	Combined taxation plus MUP increases impact and improves cost-effectiveness compared with MUP alone
Ban on sales of alcohol below the cost of taxation	Low	The ban on selling alcohol below the cost of taxation had minimal impact
Bans or restrictions on price promotions	Moderate	Restrictions on price promotions may reduce consumption, but more evidence is needed
Regulating marketing		
Advertising bans	Moderate	Complete advertising bans are a highly effective and cost-effective approach to health improvement
Industry self-regulation of alcohol marketing	Low	Industry self-regulation is unlikely to be effective; little evidence of beneficial effect
Specific actions to protect children from exposure to alcohol marketing	Very low	Reducing child exposure to alcohol marketing would theoretically impact alcohol consumption by children
Regulating availability		
Density of alcohol outlets	Low/moderate	Reducing the density of alcohol outlets may reduce social disorder and road traffic crashes
Hours and days of sale	Moderate	Reducing hours of sale may reduce alcohol-related harm
Responsibility deal pledge	Very low	Public-private partnerships are not shown to bring about effective changes which benefit public health
Education and information		
Mass media campaigns which aim to change alcohol consumption	Low	Non-industry sponsored campaigns increase knowledge and awareness, little direct impact on behavior, not cost-effective

Social marketing approaches	Low	No firm conclusions can be made
Social norm approaches	Very low/low	No firm conclusions can be made
Alcohol education programs	Very low/low	Little lasting evidence of effectiveness or cost-effectiveness
Labeling of alcoholic beverages	Low	Labels increase knowledge and awareness
Managing the drinking environment		
Multicomponent community programs	Low/moderate	Small reductions in acute harms, cost-effective, cost-saving and can be scaled up
Server training	Very low/low	Impact is small and the research is characterized by self-reported measurements
Server liability	Moderate	Impacts are small and predominantly focus on acute harms
Replacing glassware with safer alternatives	Very low	Replacing glassware with safer alternatives is based on sound principle and may reduce injuries
Voluntary removal or the sale of high-strength alcohol	Very low	Voluntary removals of high strength alcohol may reduce acute alcohol-related harm but easily undermined
Policing and enforcement approached (including minimum drinking age)	Low/moderate	Resource intensive interventions with possible short-term reductions in acute harm
Public drinking bans	Very low	Negatively impact marginalized groups, such as the homeless with little benefit

Adopted from Public Health England, 2016[84] and Burton *et al.*, 2017[68]

[a] GRADE, which stands for Grading of Recommendations Assessment, Development and Evaluation, is an approach to appraising the quality and strength of evidence supporting health policy recommendations. The 4-level GRADE ratings are based on an assessment of studies done in high-income countries that are members of the Organisation for Economic Co-operation and Development (OECD).

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Appendices

Appendix 1. Etiology of Alcohol-related Liver Disease

The natural progression of alcohol-related liver disease (ALD), which results from repeated injury to the liver, is well-understood (Figure 1).[1,2] When alcohol is consumed, it is first metabolized to acetaldehyde, a highly toxic, reactive, and carcinogenic substance, then oxidized to acetate in liver cells or hepatocytes. Alcohol metabolism changes the “cellular redox potential” of liver cells that, along with other mechanisms, leads to fat synthesis and accumulation of fat in the liver.[3] The alcohol metabolic pathway also leads to the production of reactive oxygen species, which can cause oxidative stress and a cascade of negative events that contribute to ALD such as DNA damage.[1]

Steatosis or alcohol-related fatty liver disease (AFLD) is the first stage in ALD, which occurs commonly in high-risk drinkers, including binge drinkers. Steatosis is the deposition of fat in liver cells and is a reversible condition if a person stops drinking.[3] Continuous alcohol consumption, however, causes AFLD to progress to hepatic inflammation or alcoholic steatohepatitis (ASH), a prerequisite of fibrosis. Over a long period of time, fibrosis can occur, which is the formation of an “extracellular matrix” in the liver after repeated wound-healing responses to ASH.[1] Fibrosis is staged, from F0 (no fibrosis) to F4 (severe cirrhosis), using noninvasive elastographic techniques such as FibroScan®.

Alcohol-related cirrhosis (AC) is divided into two types, compensated and decompensated. Compensated AC is a phase where a part of the liver remains functional and “compensates” for the damaged portions. On the other hand, decompensated AC occurs when scar tissue has taken over the liver. When the decompensation phase has been reached, patients experience one or more of several signature symptoms, including ascites (accumulation of fluid in abdominal cavity), hepatic encephalopathy (brain dysfunction), jaundice (yellowing of the skin), portal hypertension (high blood pressure in the portal venous system), and variceal bleeding (bleeding from dilated blood vessels in the esophagus).[283] With continued alcohol use, AC can further progress to hepatocellular cancer (HCC) due to hepatic inflammation and oxidative stress that contributes to tumor initiation.[1] Throughout these ALD stages, a separate but related acute clinical syndrome called alcohol-related hepatitis (AH) may occur, which is characterized by rapid onset of jaundice and subsequent liver failure. AH is associated with extremely high mortality rates of up to 60%.[4–6]

Treatment

Alcohol cessation is a key therapeutic goal in treating patients with ALD (discussed in detail in Appendix 2). While steatosis is reversible, more advanced forms of ALD are not; thus, only cessation of alcohol consumption can arrest the progression of liver disease. Different medications may be indicated for specific patients; for example, patients with AH can be prescribed corticosteroids, provided nutrition therapy, and even hospitalized, while those with infections due to decompensated AC complications are treated with antimicrobials.[2,210,212] For patients with decompensated AC and HCC, only liver transplantation is the long-term solution.

Costs

ALD exacts significant economic and social costs to patients, families, and the larger society. Patients with advanced forms of ALD lose days at work due to their illness, which lead to income losses.[284–287] Since people who develop ALD are older and experience severe symptoms (e.g., cognitive and physical changes in patients with hepatic encephalopathy), they often have informal caregivers such as spouses or children who provide support and whose own health and quality of life are negatively impacted.[288,289] Research has shown, for example, that care for older adults with cirrhosis can be taxing on families and caregivers as they require more healthcare services and informal caregiving than those without cirrhosis.[290] The costs of treatment for AC and HCC are expensive and can impact a family's finances. The costs of AH treatment and liver transplantation, in particular, are more than US$100,000 per patient[5,221,291], and limited research suggests that costs for AC care have increased over time even as mean length of hospital stay among AC patients decreased.[9,292,293]

Appendix 2. Initial Health State of Population

Drinking status of starting population

The prevalence of past-year drinking, moderate drinking, and excessive drinking from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; aTable 1) are reported separately by race/ethnicity (i), age group (j), and gender (k). Thus, to calculate drinking prevalence in each intersection of race/ethnicity, age group, and gender (pD_{ijk}), I assumed that drinking prevalence by race/ethnicity and age (pD_{ij}) from NESARC is equal to the weighted average of the drinking prevalence among men and women, as in Eq. 4:

$$pD_{ij} = \frac{\sum pD_{ik} * w_{ijk}}{\sum w_{ijk}} \qquad \textbf{Eq. 4}$$

Population weights (w_{ijk}) were calculated using population estimates in 2000 from the US Census Bureau (aTable 2).[194] Because the sum of the weights equals 1, the denominator in Eq. 4 is dropped, and only the numerator remains. I also assumed that the drinking prevalence by race/ethnicity and gender (pD_{ik}) is the product of the average drinking prevalence between genders (pD_k) and the ratio of the drinking prevalence between men and women (r_k). Thus, the numerator in Eq. 4 is transformed to:

$$pD_{ij} = (pD_{ij} * r_{k=1} * w_{ij|k=1}) + (pD_{ij} * r_{k=2} * w_{ij|k=2}) \qquad \textbf{Eq. 5}$$

Solving for pD_{ijk} in Eq. 5 gives the final equation:

$$pD_{ij} = \frac{pD_{ij}}{(r_{k=1} * w_{ij|k=1}) + (r_{k=2} * w_{ij|k=2})} \qquad \textbf{Eq. 6}$$

I then used pD_{ijk} from Eq. 6 and the drinking prevalence ratio between men and women to calculate drinking prevalence by race/ethnicity, age, and gender. For example, to calculate the prevalence of past-year drinking among 18-year-old White men $pD_{i=White|j=18|k=men}$, I used the following formula:

$$pD_{i=White|j=18|k=men} = pD_{i=White|j=18} * r_{k=men} \qquad \textbf{Eq. 7}$$

aTable 1. Distribution of past-year drinking status by gender, age group, and race/ethnicity, 2001-2002

Drinking status	**All**	**Gender**		**Age**			
Total		*Male*	*Female*	*18-24*	*25-44*	*45-64*	*≥65*
Past-year drinker	65.44 (0.59)	72.82 (0.59)	59.67 (0.77)	70.79 (1.04)	72.93 (0.71)	64.28 (0.72)	45.07 (0.88)
Moderate drinker	21.34 (0.31)	29.68 (0.5)	12.09 (0.35)	21.16 (0.83)	21.84 (0.49)	20.93 (0.54)	20.72 (0.8)
Excessive drinker	15.68 (0.34)	17.84 (0.51)	13.29 (0.4)	20.42 (0.83)	14.65 (0.46)	15.64 (0.54)	13.91 (0.68)
White							
Past-year drinker	69.51 (0.67)	74.27 (0.73)	65.1 (0.79)	77.05 (1.31)	78.52 (0.8)	68.95 (0.82)	48.29 (1)
Moderate drinker	21.83 (0.39)	30.45 (0.61)	12.73 (0.39)	22.21 (1.11)	22.2 (0.61)	21.52 (0.61)	21.09 (0.88)
Excessive drinker	16.25 (0.39)	18.51 (0.55)	13.85 (0.47)	22.47 (1.04)	15.34 (0.57)	15.72 (0.62)	14.45 (0.76)
Black							
Past-year drinker	53.23 (0.85)	62.62 (1.25)	45.92 (1.01)	60.1 (1.9)	61.2 (1.3)	49.63 (1.52)	23.43 (1.4)
Moderate drinker	19.91 (0.73)	29.26 (1.27)	9.99 (0.72)	17.72 (2.08)	21.34 (1.13)	19.9 (1.48)	13.66 (2.15)
Excessive drinker	16.38 (0.8)	19.88 (1.1)	12.67 (0.96)	14.87 (1.94)	16.21 (1.04)	18.58 (1.56)	11.7 (1.81)
AIAN							
Past-year drinker	58.24 (2.64)	65.48 (3.5)	51.66 (3.23)	70.66 (6.39)	65.78 (4.09)	53.27 (3.99)	37.93 (5.07)
Moderate drinker	18.49 (1.91)	25.26 (3.13)	10.67 (2.48)	16.29 (5.63)	20.25 (3.13)	16.74 (3.42)	18.57 (4.16)
Excessive drinker	21.89 (2.57)	21.63 (3.52)	22.19 (3.75)	38.71 (8.1)	19.86 (3.62)	19.65 (3.63)	15.62 (7.11)
AAPI							
Past-year drinker	48.36 (2.07)	61.51 (2.58)	36.11 (2.67)	59.06 (4.34)	52.54 (2.33)	40.84 (3.29)	32.7 (4.28)
Moderate drinker	16.48 (1.37)	20.43 (2.02)	10.19 (1.59)	13.37 (2.98)	18.68 (1.99)	12.93 (2.83)	21.49 (9.69)
Excessive drinker	9.83 (1.2)	10.83 (1.79)	8.24 (1.9)	17.76 (3.85)	7.64 (1.5)	9.97 (3.25)	2.76 (1.87)
Latino/Hispanic							
Past-year drinker	59.93 (0.92)	69.99 (1.2)	49.52 (1.51)	60.42 (1.79)	65.68 (1.09)	54.35 (1.74)	36.63 (1.96)
Moderate drinker	21.07 (1)	28.87 (1.46)	9.65 (0.86)	21.91 (2.05)	21.45 (1.24)	19.33 (2.06)	20.4 (2.86)
Excessive drinker	11.75 (0.72)	13.76 (1.04)	8.81 (0.92)	14.01 (1.49)	10.94 (0.92)	12.31 (1.5)	9.54 (2.26)

Numbers are percents with standard errors in parentheses. Data are from the 2nd wave of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).

AAPI, Asian American and Pacific Islander; AIAN, American Indian and Alaska Native

aTable 2. Population weights used to calculate drinking prevalence

Race/ethnicity	Gender	Age	Weight[a]
White	Men	18-24	0.51
		25-44	0.50
		45-64	0.49
		≥65	0.43
	Women	18-24	0.49
		25-44	0.50
		45-64	0.51
		≥65	0.57
Black	Men	18-24	0.50
		25-44	0.47
		45-64	0.45
		≥65	0.41
	Women	18-24	0.50
		25-44	0.53
		45-64	0.55
		≥65	0.59
AAPI	Men	18-24	0.49
		25-44	0.46
		45-64	0.46
		≥65	0.42
	Women	18-24	0.51
		25-44	0.54
		45-64	0.54
		≥65	0.58
AIAN	Men	18-24	0.50
		25-44	0.50
		45-64	0.47
		≥65	0.44
	Women	18-24	0.50
		25-44	0.50
		45-64	0.53
		≥65	0.56
Latino/Hispanic	Men	18-24	0.52
		25-44	0.51
		45-64	0.48
		≥65	0.43

Women	18-24	0.48
	25-44	0.49
	45-64	0.52
	≥65	0.57

[a] Weights were calculated by dividing the number of people men and women in each age group by the total number of people in the age group.

AAPI, Asian American and Pacific Islander; AIAN, American Indian and Alaska Native

ALD status of starting population

The prevalence of AFLD in 2001 was taken from a retrospective analysis of the 2001-2016 National Health and Nutrition Examination Survey (NHANES), which are nationally representative, repeated cross-sectional surveys of the noninstitutionalized US population.[8] The prevalence of any cirrhosis by age group in 2001 was based on another analysis of 1994-2004 NHANES data, which also estimated that 17.9% of all cirrhosis cases were attributable primarily to alcohol use.[172] To estimate the prevalence of CC and DC, I assumed that 28% of all alcohol-related cirrhosis cases are in the decompensated state, as reported in a previous analysis of MarketScan data.[9]

Transitions between drinking states

I based transition probabilities between drinking states on a study by Barbosa et al. which used several procedures to estimate long-term transition probabilities by age group, gender, and race/ethnicity.[173] First, the authors used data from NESARC waves 1 and 2, which are panel data collected in 2001 and 2004, to estimate one-year transition probabilities between World Health Organization (WHO) drinking levels. They then calibrated their results using a 16-year study of treatment-seeking individuals with alcohol use disorder (AUD) in California to estimate two sets of long-term transition probabilities (i.e., 3-8 years and 8-16 years). Finally, they validated their results by comparing the distribution of their predicted drinking levels with those reported in the NESARC wave 3, which is a cross-sectional survey conducted in 2012.

The final set of transition probabilities between drinking states I used in this study are shown in aTable 3. I used transition probabilities for the 3-8-year time horizon estimated by Barbosa et al. To match the WHO drinking levels to the drinking categories in my model, I assumed that WHO's "abstinent drinkers" (<1 g of alcohol per day) and "low risk drinkers" (1-40 g of alcohol per day for men, 1-20 g per day for women) corresponded to my model's low-risk and moderate drinking groups, respectively. I then used the average results for the WHO's "medium risk" (41-60 g of alcohol per day for men, 21-40 g for women), "high risk" (61-100 g of alcohol per day for men, 41-60 g for women), and "very high risk" (>100 g of alcohol per day for men, >60 g for women) drinking levels for my excessive drinking category.

aTable 3. Annual transition probabilities for drinking states by age, gender, and race/ethnic groups

White		*Low-risk*	*Moderate*	*Excessive*
18-35 years	*Low-risk*	0.86 (0.83-0.88)	0.12 (0.1-0.15)	0.02 (0.01-0.04)
	Moderate	0.03 (0.02-0.05)	0.86 (0.83-0.89)	0.1 (0.06-0.16)
	Excessive	0.1 (0.05-0.16)	0.06 (0.03-0.12)	0.84 (0.64-1.06)
36-50 years	*Low-risk*	0.93 (0.91-0.95)	0.05 (0.03-0.06)	0.02 (0.01-0.04)
	Moderate	0.06 (0.04-0.08)	0.81 (0.77-0.85)	0.13 (0.08-0.2)
	Excessive	0.05 (0.02-0.1)	0.08 (0.04-0.14)	0.86 (0.65-1.1)
≥51 years	*Low-risk*	0.96 (0.95-0.98)	0.02 (0.01-0.03)	0.02 (0.01-0.04)
	Moderate	0.04 (0.02-0.06)	0.87 (0.83-0.9)	0.1 (0.05-0.15)
	Excessive	0.05 (0.02-0.1)	0.08 (0.04-0.14)	0.86 (0.65-1.1)
Black		*Low-risk*	*Moderate*	*Excessive*
18-35 years	*Low-risk*	0.93 (0.9-0.94)	0.05 (0.04-0.07)	0.02 (0.01-0.04)
	Moderate	0.04 (0.03-0.07)	0.83 (0.79-0.86)	0.13 (0.08-0.19)
	Excessive	0.06 (0.03-0.11)	0.26 (0.2-0.34)	0.68 (0.49-0.89)
36-50 years	*Low-risk*	0.96 (0.95-0.98)	0.02 (0.01-0.03)	0.02 (0.01-0.04)
	Moderate	0.07 (0.04-0.09)	0.79 (0.74-0.82)	0.15 (0.1-0.21)
	Excessive	0.05 (0.02-0.1)	0.24 (0.19-0.31)	0.7 (0.53-0.91)
≥51 years	*Low-risk*	0.96 (0.95-0.98)	0.02 (0.01-0.03)	0.02 (0.01-0.04)
	Moderate	0.05 (0.03-0.08)	0.82 (0.78-0.85)	0.13 (0.08-0.18)
	Excessive	0.04 (0.01-0.08)	0.27 (0.21-0.33)	0.7 (0.53-0.91)
Hispanic		*Low-risk*	*Moderate*	*Excessive*
18-35 years	*Low-risk*	0.91 (0.89-0.94)	0.07 (0.05-0.09)	0.02 (0.01-0.04)
	Moderate	0.05 (0.03-0.07)	0.83 (0.79-0.86)	0.13 (0.08-0.18)
	Excessive	0.06 (0.03-0.12)	0.26 (0.2-0.34)	0.67 (0.49-0.88)
36-50 years	*Low-risk*	0.96 (0.95-0.98)	0.02 (0.01-0.03)	0.02 (0.01-0.04)

	Moderate	0.07 (0.04-0.09)	0.79 (0.74-0.82)	0.15 (0.1-0.21)
	Excessive	0.05 (0.03-0.1)	0.24 (0.19-0.31)	0.7 (0.53-0.9)
≥51 years	*Low-risk*	0.96 (0.95-0.98)	0.02 (0.01-0.03)	0.02 (0.01-0.04)
	Moderate	0.05 (0.03-0.08)	0.82 (0.78-0.85)	0.13 (0.08-0.19)
	Excessive	0.04 (0.02-0.08)	0.27 (0.22-0.33)	0.7 (0.53-0.9)
Others[a]		*Low-risk*	*Moderate*	*Excessive*
18-35 years	*Low-risk*	0.8 (0.77-0.83)	0.18 (0.15-0.21)	0.02 (0.01-0.04)
	Moderate	0.05 (0.04-0.08)	0.82 (0.78-0.85)	0.12 (0.08-0.18)
	Excessive	0.07 (0.03-0.12)	0.26 (0.19-0.33)	0.68 (0.49-0.89)
36-50 years	*Low-risk*	0.91 (0.89-0.93)	0.07 (0.05-0.09)	0.02 (0.01-0.04)
	Moderate	0.07 (0.05-0.09)	0.78 (0.74-0.82)	0.15 (0.1-0.21)
	Excessive	0.05 (0.02-0.1)	0.24 (0.19-0.3)	0.7 (0.53-0.91)
≥51 years	*Low-risk*	0.96 (0.95-0.98)	0.02 (0.01-0.03)	0.02 (0.01-0.04)
	Moderate	0.06 (0.04-0.08)	0.82 (0.78-0.85)	0.13 (0.08-0.19)
	Excessive	0.04 (0.01-0.08)	0.27 (0.21-0.32)	0.7 (0.53-0.91)

Starting drinking state are listed in the columns while ending drinking state are listed in the rows. Some probabilities may not add up to 1 due to rounding.

[a] Inputs used for Asian American and Pacific Islander and American Indian and Alaska Native groups

Appendix 3. Estimating 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%).[178] Based on data from United Network for Organ Sharing, the total waitlisted population was 3,712 in 2016 (the most recent year available).[198] 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 annual probability of transplantation among decompensated AC liver patients is 0.0778 (range: 0.0523-0.0903).[198]

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).[179] 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.[180]

Probability of death from all causes

Probability of death by age, gender, and race/ethnicity from all causes (i.e., all-cause mortality) were taken from 2018 CDC Life Tables.[184] Unlike metabolic causes of liver disease (e.g., non-alcoholic fatty liver disease), research suggests that presence of ALD may not affect all-cause mortality[294,295]; thus, mortality rates were not adjusted or modified before being used in the model. Probability of death by race/ethnicity was only available for Whites, Blacks, and Hispanics, so overall rates for the US population were used for Asian American and Pacific Islander (AAPI) and American Indian and Alaska Native (AIAN) populations (aTable 4).

aTable 4. Probability of death by age and gender for the US population

Age	Mortality among men	Mortality among women
0	0.00621335	0.005061193
5	1.60E-04	0.000122656
18	0.00081146	0.00032858
25	0.00153075	0.000597521
35	0.00211938	0.00109676
45	0.00331756	0.002001822
55	0.00776535	0.004746125
65	0.01607784	0.00963815
75	0.03432165	0.023929337
85	0.09448869	0.072861724
100	1	1

These probabilities reflect the risk of dying from any cause between the age that is listed and the next age. For brevity, only selected ages are shown.

Model calibration

I used calibration to estimate the probability of decompensation among moderate and excessive drinkers with CC by racial/ethnic group. Crude ALD-related mortality rates among adults 18 years and older were used as the calibration target. Observed data were based on the Underlying Cause of Death data retrieved from the CDC WONDER database; detailed descriptions of the sources and methods behind this data are available elsewhere.[296] The underlying cause of death is based on the WHO definition and is determined using information entered by physicians on death certificates. If multiple conditions are provided, the underlying cause is based on the sequence of conditions on the certificate.

In this study, I defined ALD-related mortality as any deaths that were caused by diseases with the following ICD-10 codes: K70.0 (alcoholic fatty liver); K70.1 (alcoholic hepatitis); K70.2 (alcoholic fibrosis and sclerosis of liver); K70.3 (alcoholic cirrhosis of liver); K70.4 (alcoholic hepatic failure); and K70.9 (alcoholic liver disease, unspecified). I used the same formula (Eq. 8), as in CDC WONDER, to calculate yearly crude ALD-related mortality rates (rM) for each racial/ethnic group (i) using output from my model.

$$rM_i = \frac{\sum nM_{jk}}{\sum nP_{jk}} \qquad \textbf{Eq. 8}$$

nM refers to the number of ALD-related deaths and nP is the number of individuals at risk for each age (j) and gender (k) group.

I used sum of squared errors (SSE) as the goodness of fit measure, which was calculated by squaring the difference between modeled ($M_h(\theta)$) and observed (y_h) ALD-related mortality rates for each year (y) in 2005-2020 (Eq. 9). I initialized the model with drinking prevalence data from 2001 and calibrated the model after a four-year delay or initialization period.

$$SSE = \sum_{h=2005}^{2020} (y_h - M_h(\theta))^2 \qquad \textbf{Eq. 9}$$

I used differential evolution algorithm via the DEoptim package in R[297] to search parameter values (θ) that minimized SSE. Differential evolution is a type of metaheuristic or evolutionary algorithm that is ideal for nonlinear and multi-modal constrained optimization problems.[298,299] Convergence was achieved when the smallest

SSE or the stopping rule (i.e., 1,000 procedure iterations) was reached, whichever came first, as recommended by best practices in calibration.[199]

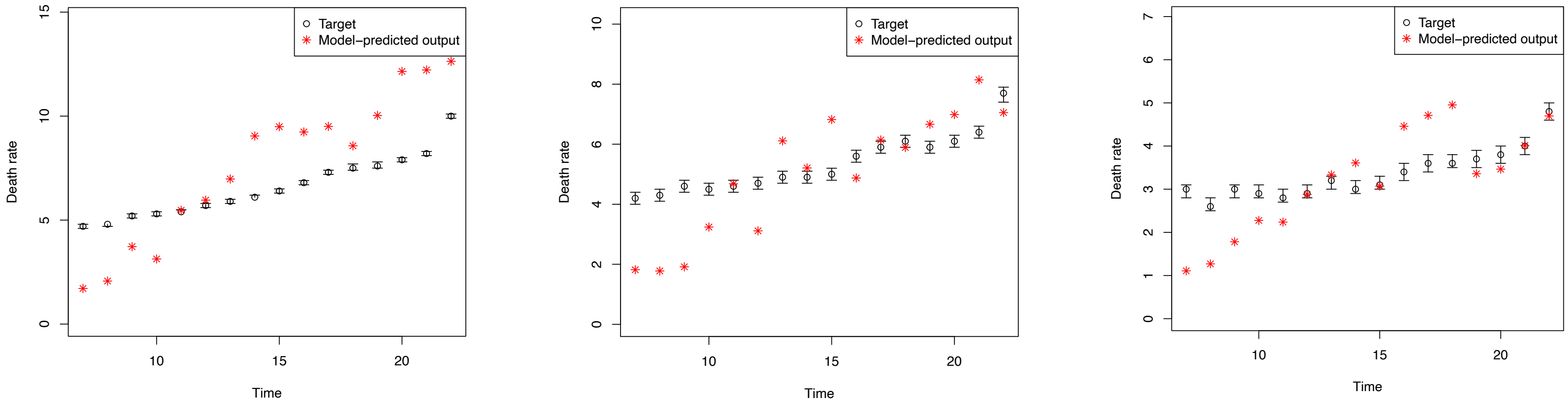
The plots of the calibration results are shown in aFigure 1. The model-predicted ALD-related mortality rates were generated using the best-fitting probabilities from the calibration, which are shown in aTable 5. The calibration plots show that model-predicted outcomes track closely but not perfectly with observed data from the CDC. The SSEs associated with the estimated probabilities are shown in aTable 5.

aTable 5. Calibration results

Racial/ethnic group	Decompensation among moderate drinkers	Decompensation among excessive drinkers	Goodness of fit (SSE)
White	0.0111	0.00881	50.943
Black	0.00156	0.0135	12.347
Latino/Hispanic	0.00826	0.00968	27.279
AIAN	0.00238	0.0528	0.0128
AAPI	0.00267	0.00153	3.977

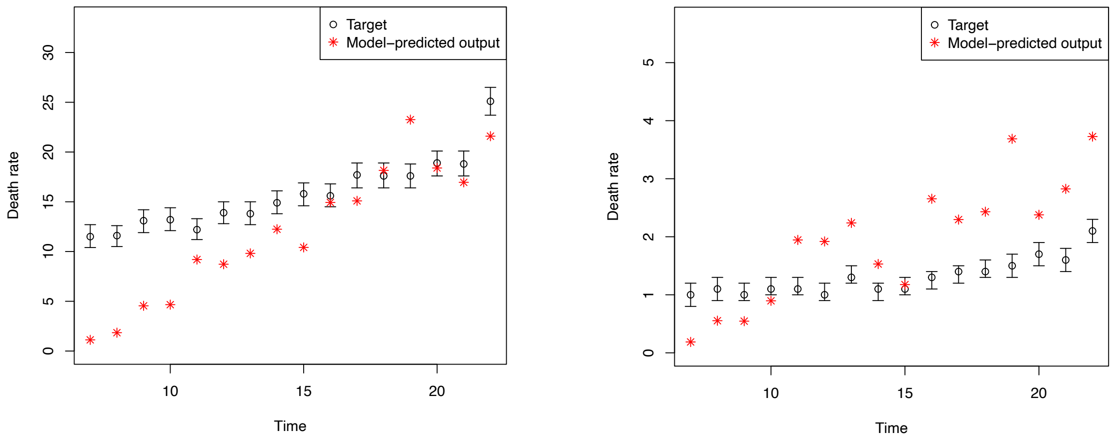
The numbers shown here are annual probabilities.
AAPI, Asian American and Pacific Islander; AIAN, American Indian and Alaska Native; SSE, sum of squared errors.

aFigure 1. Calibration result plots


A. White

B. Latino/Hispanic

C. Black


D. AIAN

E. AAPI

These graphs plot model-predicted ALD-related mortality rate with calibration targets from the CDC by each race/ethnic group. Model outcomes were generated using the best-fitting parameters.

AAPI, Asian American and Pacific Islander; AIAN, American Indian and Alaska Native; ALD, alcohol-related liver disease; CDC, Centers for Disease Control and Prevention.

Appendix 4. Calculating Credible Intervals

To calculate 95% credible intervals (CIs) for the mean estimates from the probabilistic sensitivity analysis (PSA), I used the normal approximation method for a binomial random variable or proportion. By the central limit theorem, the means of a large number of samples are normally distributed, regardless of their underlying distribution; thus, the confidence interval of a sample mean probability, $\hat{p}$, calculated from a binomially distributed variable can be approximated using the formula (Eq. 10)

$$\hat{p} \pm z * \sqrt{\frac{\hat{p}\ (1-\hat{p})}{n}} \qquad \textbf{Eq. 10}$$

where n is the number of trials, which is equal to the total number of simulated individuals in each PSA simulation, and z is the quantile from the standard normal distribution. z is associated with a target error rate, α, as shown in the equation (Eq. 11).

$$z = 1 - \frac{\alpha}{2} \qquad \textbf{Eq. 11}$$

To calculate the 95% CI, z was set to 1.96 (where α = 1 - 0.95 = 0.05).

aTable 6. Impact Inventory

Sector	Type of Impact	Healthcare sector 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	
	Medical costs paid for by patients out-of-pocket	X	X	
	Future related medical costs	X	X	
	Future unrelated medical costs	X	X	
Informal healthcare sector				
Health	Patient costs		X	
	Unpaid caregiver time costs			
	Transportation costs			Excluded due to lack of data
Non-healthcare sectors				
Productivity	Formal labor market earnings lost		X	
	Cost of unpaid lost productivity due to illness		X	
	Cost of uncompensated household production		X	
Consumption	Future consumption unrelated to health		X	
Social services				Excluded due to lack of data
Legal/criminal justice				Excluded
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.

Appendix 5. Estimating the Effect of Taxes and MUP on Alcohol Prices and Consumption

The treatment effect of pricing policies in this study was represented by the immediate or instantaneous change in the prevalence of low-risk, moderate, and excessive drinking that results from a change in alcohol consumption (Figure 13). The change in alcohol consumption (δ) is a function of the change in alcohol prices (α) and the net elasticity of demand, which describes the total change in alcohol consumption following a change in its price. The net elasticity of demand was the difference between own-price (β) and cross-price (γ) elasticities of demand. This is represented in the following formula (Eq. 12):

$$\delta_{pd} = \alpha_p * (\beta_d - \gamma_d) \qquad \textbf{Eq. 12}$$

The indices p and d, respectively, refer to pricing policy and drinking level, which can be moderate or excessive. In practice, price elasticities of demand vary by type of beverage, but due to a lack of data on volume of each beverage consumed by different types of drinkers, average or generic elasticities were used.

To estimate the treatment effect under each pricing policy, the following steps were carried out.

Step 1: The first step was calculating the price of a standard drink of beer, wine, and liquor. Alcohol price data for this study were taken from the Consumer Price Index (CPI) of US Bureau of Labor Statistics (aTable 7).[228] I calculated the price of a standard drink of beer, wine, and liquor by using the volume of a standard drink for each beverage, which varies due to alcohol content.

aTable 7. Average alcohol prices

Category	Average price (in US$) per volume (in mL)	Volume of standard drink (in mL)	Standard drinks per unit	Price per standard drink (US$)
Beer and malt beverages (5% alcohol)	1.63 per 473	355	1.33	1.22

Wine (12% alcohol)	13.50 per 1,000	148	6.76	2.00
Liquor (40% alcohol)	14.48 per 1,000	44	22.54	0.64

Data from the Consumer Price Index of the US Bureau of Labor Statistics.[229]

Step 2: The second step was calculating the percent change in price under each policy. For alcohol taxes, the price increase is implied in each policy (5%, 15%, and 30%), and these percent changes were used as the α in Eq. 12.

For MUP, I assumed that the cheapest standard drink sold in the US is hard liquor at $0.64 per unit (aTable 7), and I used this as the basis for calculating the price increase of the hypothetical MUPs. For example, an MUP that increases the price of the cheapest alcohol by 100% would yield an MUP equal to $1.28 (2*$0.64). Any standard drink sold below this price will also experience a price change, while beverages that are already priced above the MUP are not affected. For example, a standard drink of beer and malt beverages ($1.22) must now be sold with a 5% increase in price, while the cost of wine ($2.00) can remain unchanged. The average price increase for liquor and beer (100% and 5%, respectively) was used as the α in Eq. 12. (With better data, the calculation of the average price increase under MUP can be weighted by the share of each beverage of total alcohol consumption in the US.)

Step 3: The third step was translating percent changes in price to changes in consumption. To do this, I relied on two price elasticities of demand. The own-price elasticity of demand (β) describes the change in the quantity demanded of a good relative to a percentage change in its price, while cross-price elasticity of demand (γ) is the change in consumption of an alternative good that results from a change in the price of a preferred good. For this study, I used pooled median cross-price elasticity across all beverages for the UK and Australia (0.10, range: 0.04-0.16)[103,108,109]; this estimate captures all the possible substitutions that occur when the price of different types of beverages increases. The difference between these two elasticities of demand represents the net change in consumption, which varies by drinking level (aTable 8).

Step 4: The fourth and final step in estimating the treatment effect was calculating the prevalence of low-risk, moderate, and excessive drinking under each policy using the net change in consumption.

Since low-risk drinkers already fall into the lowest-drinking category, any reduction in their alcohol consumption would keep them in their current state. For moderate drinkers, who consume alcohol exactly at the gender-specific thresholds for heavy drinking (i.e., 14 grams of ethanol a day for women, 28 grams a day for men), I assumed the net change in consumption represented the proportion of moderate drinkers who moved to the low-risk drinking category.

For excessive drinkers, I applied the net change in consumption across the distribution of daily alcohol consumed by people in this group and determined the proportion of people who moved to the moderate drinking category. For the distribution of daily alcohol consumed by excessive drinkers, I relied on the analysis of Jiang et al. (2021) who measured the distribution of daily drinking volume among men and women using the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) waves 1 and 2.[234] That study found that the mean consumption of women with DSM-IV alcohol dependence was around 63 grams of ethanol per day, while among men it was significantly higher at around 105 grams; both distributions were left-skewed. I fitted a log-normal distribution on the distribution of alcohol consumed by excessive drinkers (aFigure 2) and, after applying the net change in consumption under each pricing policy, determined the probability that excessive drinkers would fall at or below the heavy drinking thresholds using the probability density function.

As aFigure 2 shows, the excise tax policies (represented by the orange, yellow, and purple curves) were associated with slight shifts in the distribution of alcohol consumed, while MUP policies (represented by the blue and green curves) were associated with more significant changes in the distribution of alcohol consumed. For example, the mean of daily alcohol consumed among men was reduced to 102 grams under tax policy 1 and to 88 grams under MUP policy 1.

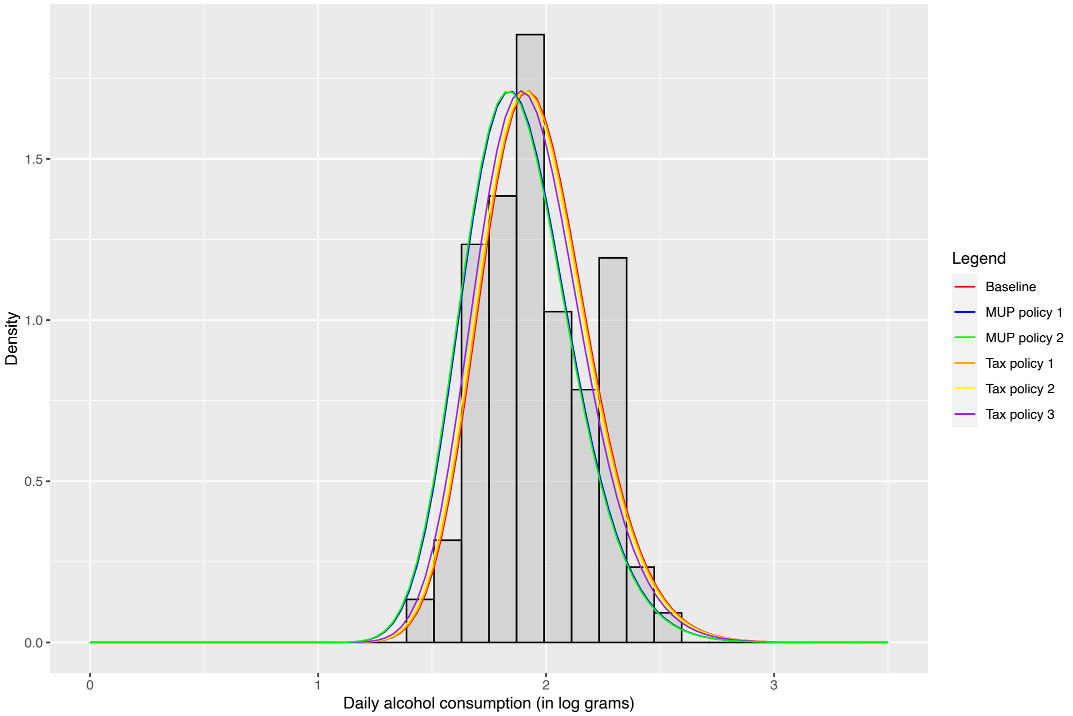
aTable 8. Potential effect of pricing policies

Scenario	Description	Mean change in alcohol price	Gross change in alcohol consumption (range)		Substitution (range)		Net change in alcohol consumption (range)	
			Moderate	*Excessive*	*Moderate*	*Excessive*	*Moderate*	*Excessive*
Status quo	No change in pricing policy	None	None	None	None	None	None	None
Tax policy 1: 5% increase	5% increase in average alcohol tax	5%	-2 (-2, -3)	-1 (0, -2)	0 (0, 1)	0 (0, 1)	-2(-1, -3)	-1 (0, -2)
Tax policy 2: 15% increase	15% increase in average alcohol tax	15%	-7 (-5, -8)	-4 (0, -5)	1 (0, 2)	1 (0, 3)	-6(-4, -9)	-3 (0, -6)
Tax policy 3: 30% increase	30% increase in average alcohol tax	30%	-13 (-10, -16)	-8 (0, -9)	1 (0, 3)	2 (0, 6)	-12(-7, -18)	-6 (0, -12)
MUP policy 1: 50% increase	Price of cheapest standard drink increased by 50%	50%	-32 (-25, -39)	-20 (-1, -22)	2 (0, 5)	4 (0, 10)	-30(-20, -42)	-16 (0, -27)
MUP policy 2: 100% increase	Price of cheapest standard drink increased by 100%	53%	-34 (-26, -41)	-21 (-1, -23)	2 (0, 5)	4 (0, 11)	-32(-21, -44)	-17 (0, -28)

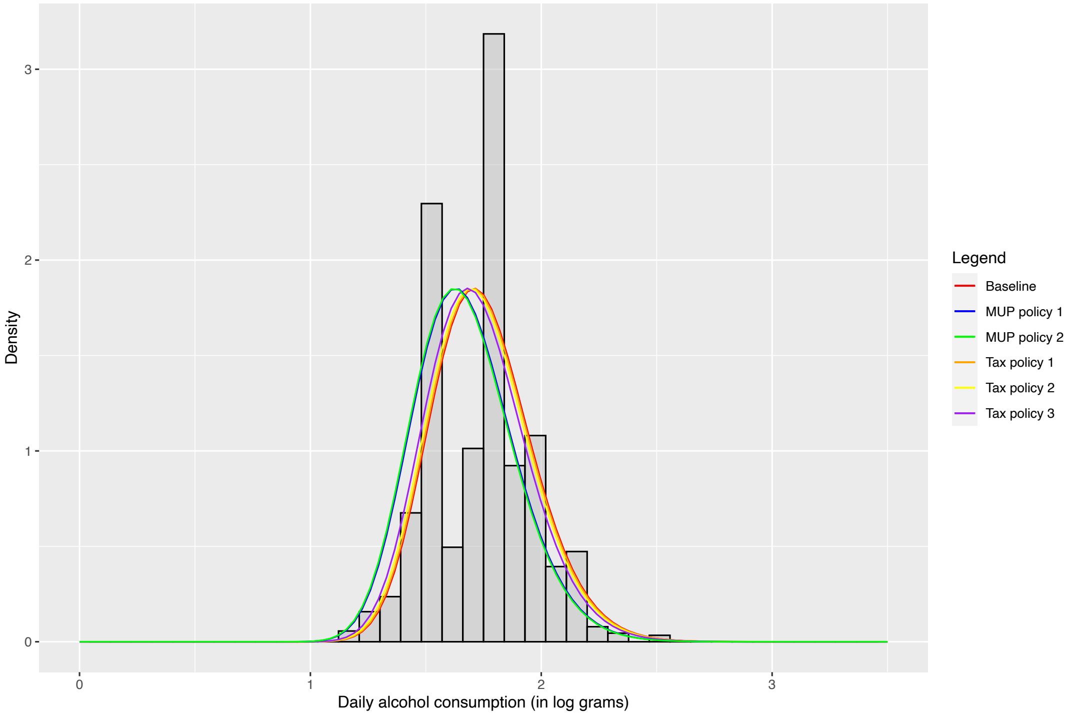
Values are all in percents. Ranges in parentheses.
MUP, minimum unit pricing.

aFigure 2. Distribution of daily alcohol drinking volume

A. Men



B. Women



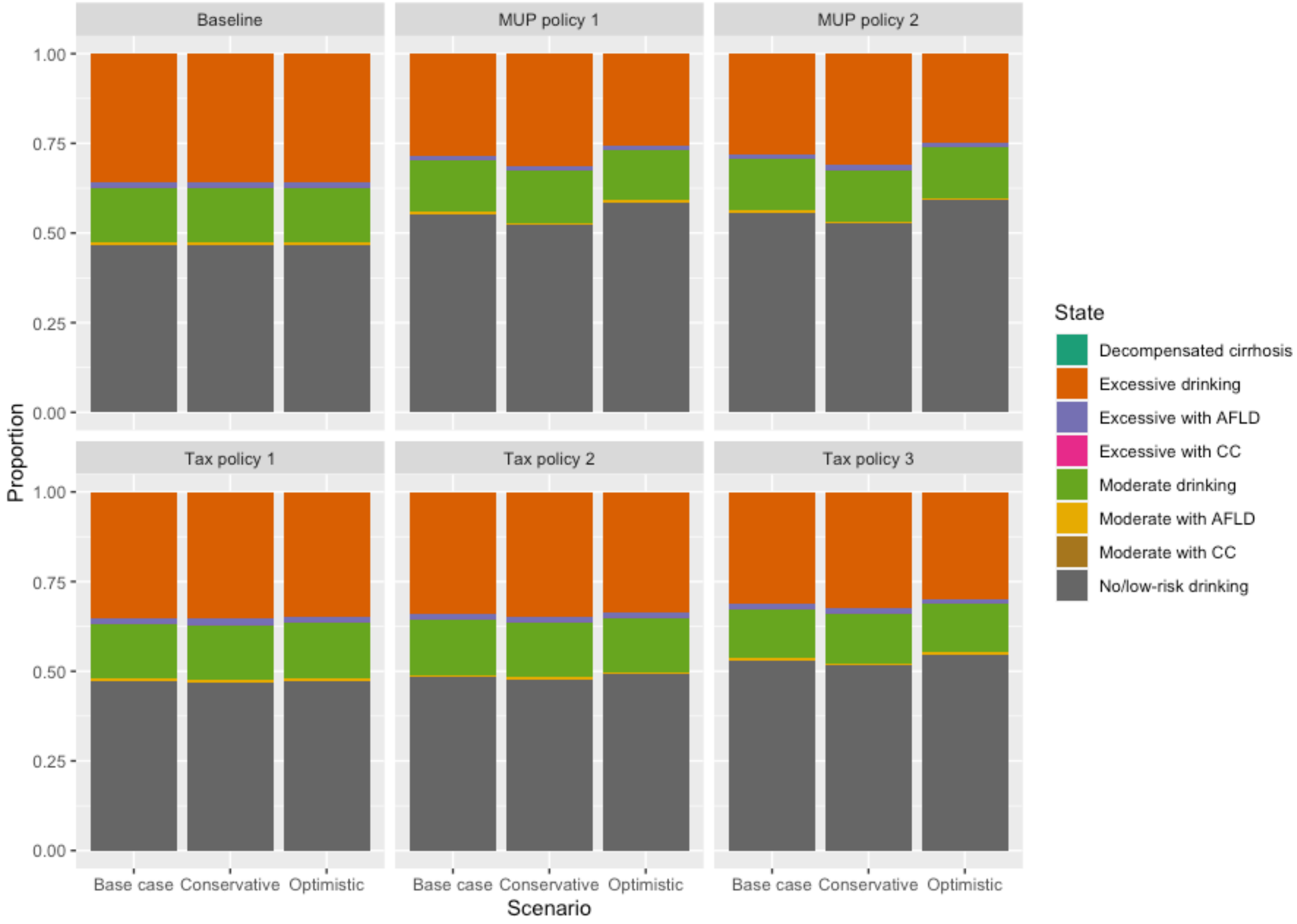
The histograms represent the distribution of alcohol consumed by (A) men and (B) women with DSM-IV alcohol dependence using data from NESARC waves 1 and 2, and the red curve represents the probability density function of the log-normal distribution fitted to log-transformed data. Applying the net change in consumption of each pricing policy reduced the daily alcohol consumed by individuals, and the blue, green, orange, yellow, and purple curves represent the log-normal distribution fitted for the five pricing policies that were evaluated in this study. Curves for the alcohol tax policies are partially

obstructed from view due to overlap with the baseline red curve, which signifies minimal change in the distribution of alcohol volume consumed.
DSM, Diagnostic and Statistical Manual of Mental Disorders; MUP, minimum unit pricing; NESARC, National Epidemiologic Survey on Alcohol and Related Conditions.

Scenario analysis

I constructed optimistic and conservative scenarios for each policy by using the upper and lower values of the net change in consumption (aTable 8). These scenarios represent how the initial distribution of drinkers shift when policies have a higher effect (i.e., optimistic) or lower effect (i.e., pessimistic) on drinking compared to the base case. The distribution of the starting population under each scenario and policy is shown in aFigure 3.

aFigure 3. Initial distribution of population under different scenarios



This figure shows the distribution of the starting population in each health state under the base case, conservative and optimistic scenarios. Each panel represents a policy that was modeled.
AFLD, alcohol-related fatty liver disease; CC, compensated cirrhosis.

Appendix 6. Estimating the Costs of Alcohol Tax Collection

I assumed in the base case that increases in alcohol taxes do not impose additional costs to the public and private sectors. This assumption follows from the fact that state and local governments routinely collect alcohol taxes, and alcohol producers and retailers may use existing resources to comply with any tax rate changes. This assumption is also made by previous CEAs of tax-based public health interventions.[235–237]

In sensitivity analysis, I assumed that alcohol tax collection can cost up to 0.5% of every additional tax dollar collected, based on historical estimates from the US Government Accountability Office (formerly the US General Accounting Office).[222] I grossly estimated the annual per-capita costs using publicly available data.

aTable 9 shows the cost of tax collection used in this study. I based the total amount of alcohol excise taxes collected by state and local governments ($7.7 billion in 2019) on data from the Tax Policy Center of the Urban Institute and Brookings Institution.[300] After applying each policy's tax increase (i.e., 5%, 15%, and 30%) and estimating the total revenue, I divided the result by the number of adults 18 years and older in the US (258 million in 2020) based on data from the US Census Bureau.[301]

aTable 9. Estimated costs of alcohol tax collection

Tax policy	Additional tax revenue (in billions US$)	Annual cost of tax collection per capita (US$)[a]
5% increase	8.1	0-0.16 (0.019)
15% increase	8.9	0-0.17 (0.021)
30% increase	10.0	0-0.19 (0.024)

[a] Upper limit of the range is based on 0.5% cost per $1 tax revenue collected. $0 was assumed to be the base-case value and lower limit of the range. Values in parentheses are the standard deviation.

This approach makes several assumptions. First, I assumed that alcohol tax revenue would increase proportionally based on the tax increase under each policy. Additionally, I did not calculate the cost of increased alcohol taxes on the private sector, which may include costs associated with compliance and lost revenue from a reduction in consumption.

Appendix 7. Estimating the Intervention Costs of MUP

To estimate the cost of implementing MUP in the US, I conducted an ingredients-based micro-costing similar to the approach used by the UK government in its official impact assessment of a national MUP policy.[238] The UK government consulted various stakeholders to understand the potential costs to the public and private sectors of a novel MUP policy.

The main private sector or business costs identified were (1) familiarization costs, or the costs associated with re-pricing goods, amending bar codes, changing prices on shelves, shop displays, and websites; and (2) implementation costs, or the costs associated with identifying and cross-checking the new sales price of goods across different markets or geographies. (Implementation costs are only likely to affect small retailers who do not use centralized pricing systems.) Familiarization was estimated to take up to 1 staff hour per retailer, while implementation costs were estimated to take 8 staff hours per retailer.

The public sector costs include (1) one-off transition costs and (2) annual enforcement costs. Transition costs include the costs of producing and disseminating/communicating guidance to retailers and local alcohol beverage authorities about the new MUP policy; these costs were estimated to be £500 ($630) per authority in the UK. Additional transition costs were also estimated for all enforcement staff who will need to become familiar with the new MUP policy; this cost was estimated at 0.5-1 hour per staff member. On the other hand, enforcement costs include staff time and resources devoted to a range of enforcement activities such as citation of non-complying retailers, review and revocation of licenses, and imposition of penalties (from fines, site closures, to imprisonment). As in the UK, enforcement of MUP in the US will be the responsibility of local alcohol beverage authorities or boards and police departments. Enforcement was estimated to be between 1-3 staff hours per week per local authority, which includes police officers responsible for ensuring compliance with MUP. aTable 10 shows the inputs used to calculate MUP implementation costs for the US. I took the number of off-premise and on-premise retailers from IBISWorld, a market research data company.[302,303] The number of state alcohol beverage authorities is based on the roster maintained by the Alcohol and Tobacco Tax and Trade Bureau of the US Department of Treasury[304], and I took the number of local police departments from a US Department of Justice survey.[305] The number of state and local enforcement officers is based on estimates from a previous study that evaluated the resources devoted to underage drinking compliance checks.[306] I based hourly wages for private and public sector employees on data from the US Bureau of Labor Statistics.[307] Absent any empirical estimates, I assumed that transition costs associated with disseminating MUP guidance is $2,000 per agency, which is 3.1 times higher than the UK value, making it a pessimistic estimate.

aTable 10. Inputs used in costing MUP in the US

Input	Value	Reference
Number of retailers		
Off-premise	44,307	302,303
On-premise	149,339	302,303
Alcohol beverage authorities		
Number of state authorities	62	304
Number of local law enforcement agencies	17,398	305
Enforcement officers per 100,000 population[a]	330.72	306
Wages (US$)[b]		
Public sector	38.07	307
Private sector	54.96	307

[a] Includes state and local enforcement officers
[b] Average wages and includes salaries and fringe benefits

The results of the costing exercise, which are shown in aTable 11, are meant to represent high-level estimates of the costs of implementing MUP in the US. I calculated per-capita costs by dividing the total costs by the number of adults 18 years old and older. The total first-year costs are $1.32 (range: $0.33-2.31) per person, while annual recurring costs are $0.83 (range: $0.21-1.45) per person.

aTable 11. Final MUP intervention costs used in the model

Type	Category	Total cost (US$)	Cost per capita (US$)
One-time private sector	Familiarization[a]	7,372,065	0.03
	Implementation[b]	13,494,140	0.05
One-time public sector	Transition[c]	106,262,257	0.41
Recurring public sector	Enforcement	214,026,771	0.83

[a] Off- and on-premise retailers and establishments
[b] Off-premise retailers and establishments only
[c] Includes personnel costs and dissemination costs for each alcohol beverage authority

Appendix 8. Estimating Societal Costs

Patient time costs

Alcohol-related liver disease (ALD) patients spend significant amounts of time for routine care and hospitalizations. I thus calculated the time costs or forgone productivity for each ALD state by multiplying the median daily earnings of full-time working adults (disaggregated by age) reported by the US Bureau of Labor Statistics[308] by the annual average length of disease and/or length of hospitalization reported in the literature[187,284–286] (in days) for various health states included in the model (aTable 12).

aTable 12. Patient time costs for various health states

Input	CC	DC	HCC	TX <12 months	TX ≥12 months
Time spent (in days)	4	4	5.6	17.6	21
Time cost (in US$) by age group					
<25	56	56	79	248	296
25-34	87	87	122	382	456
35-44	106	106	148	465	554
45-54	107	107	149	469	560
55-64	110	110	154	484	577
65-74	97	97	136	426	509

C, compensated cirrhosis; DC, decompensated cirrhosis; HCC, hepatocellular carcinoma, TX, liver transplantation.

Future productivity

I relied on productivity estimates by age from Grosse et al. (2019), which used gross human capital approach to estimate market (i.e., earnings) and non-market (i.e., household) productivity (aTable 13).[309]

aTable 13. Productivity and consumption by age group (in 2021 US$)

Age	Productivity[a]	Consumption[b]	Health care consumption[c]	Net productivity
<25	22,767	41,648	1,600	-18,880
25-34	73,030	60,551	3,351	12,479
35-44	98,249	79,378	5,111	18,871
45-54	94,106	81,991	5,665	12,115
55-64	76,761	73,658	6,315	3,102
65-74	43,471	53,229	7,242	-9,758

≥75	18,083	58,388	7,253	-40,305

[a] Updated data from Grosse et al. (2019)[309]

[b] Data from Consumer Expenditure Survey of the US Bureau of Labor Statistics.[310]

[c] Healthcare expenditures from the Consumer Expenditure Survey

Consumption costs

Future consumption was based on expenditure data from the US Bureau of Labor Statistics 2019 Consumer Expenditure Survey (aTable 13).[310] Though more recent versions of the Consumer Expenditure Survey are available, I used the year just prior to the COVID-19 pandemic. The expenditure data includes healthcare spending, so I did not value those separately and assumed that those capture any future unrelated medical care costs.

aTable 14. Scenario analysis using a healthcare sector perspective

Alternative	Conservative scenario			Optimistic scenario		
	Average cost (in US$)	*Average effectiveness (in QALYs)*	*ICERs (in US$ per QALY gained)*[a]	*Average cost (in US$)*	*Average effectiveness (in QALYs)*	*ICERs (in US$ per QALY gained)*[a]
Status quo	120,370	17.73	NA (NA)	120,260	17.73	NA
Tax policy 1: 5% increase	120,327	17.73	Dominant (Dominated)	120,178	17.73	Dominant (Dominated)
Tax policy 2: 15% increase	120,377	17.74	1,204 (Dominated)	120,209	17.76	Dominant (Dominated)
Tax policy 3: 30% increase	120,230	17.80	Dominant (Dominated)	120,191	17.84	Dominant (Dominated)
MUP policy 1: 50% increase	120,368	17.90	Dominant (Dominated)	120,056	17.90	Dominant (Dominated)
MUP policy 2: 100% increase	120,301	17.90	Dominant (10,965)	120,103	17.90	Dominant (7,671)

The conservative scenario used the lowest estimated net change in consumption for each policy, and the optimistic scenario used the highest estimated net change in consumption (aTable 8).

[a] Values in parentheses are ICERs from comparing each policy to the next more effective and undominated alternative.

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

aTable 15. Scenario analysis using a societal perspective

Alternative	Conservative scenario			Optimistic scenario		
	Average cost (in US$)	*Average effectiveness (in QALYs)*	*ICER (in US$ per QALY gained)*[a]	*Average cost (in US$)*	*Average effectiveness (in QALYs)*	*ICER (in US$ per QALY gained)*[a]
Status quo	90,208	17.73	NA (NA)	90,435	17.73	NA (NA)
Tax policy 1: 5% increase	90,133	17.73	Dominant (Dominated)	90,334	17.73	Dominant (Dominated)
Tax policy 2: 15% increase	90,331	17.74	20,234 (Dominated)	90,490	17.76	Dominated (Dominated)
Tax policy 3: 30% increase	90,292	17.80	1,280 (Dominated)	90,613	17.84	1,527 (Dominated)
MUP policy 1: 50% increase	90,374	17.90	971 (779)	90,607	17.90	1,011 (Dominated)
MUP policy 2: 100% increase	90,358	17.90	909 (2,624)	90,657	17.90	1,260 (8,200)

The conservative scenario used the lowest estimated net change in consumption for each policy, and the optimistic scenario used the highest estimated net change in consumption (aTable 8).

[a] Values in parentheses are ICERs from comparing each policy to the next more effective and undominated alternative.

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

aTable 16. Two-way scenario analysis using a healthcare sector perspective

Alternative	Base-case		Conservative scenario		Optimistic scenario	
	Low drinking	*High drinking*	*Low drinking*	*High drinking*	*Low drinking*	*High drinking*
Tax policy 1: 5% increase	1,767	9,128	88,716[a]	2,732	Dominant	742,095[a]
Tax policy 2: 15% increase	1,690	2,125	17,205	26,026[a]	Dominant	Dominant
Tax policy 3: 30% increase	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant
MUP policy 1: 50% increase	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant
MUP policy 2: 100% increase	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant

Numbers in this table are ICERs (US$ per QALY gained) comparing each pricing policy with the status quo. The conservative scenario used the lowest estimated net change in consumption for each policy, and the optimistic scenario used the highest estimated net change in consumption (aTable 8). The low drinking scenario assumed that excessive and moderate drinkers were more likely to reduce their consumption and moderate and low-risk drinkers were less likely to increase their consumption; in the high drinking scenario, excessive and moderate drinkers were less likely to reduce their consumption and moderate and low-risk drinkers were more likely to increase their consumption (aTable 3).

[a] Negative incremental costs and negative incremental benefit compared to the status quo

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

aTable 17. Two-way scenario analysis using a societal perspective

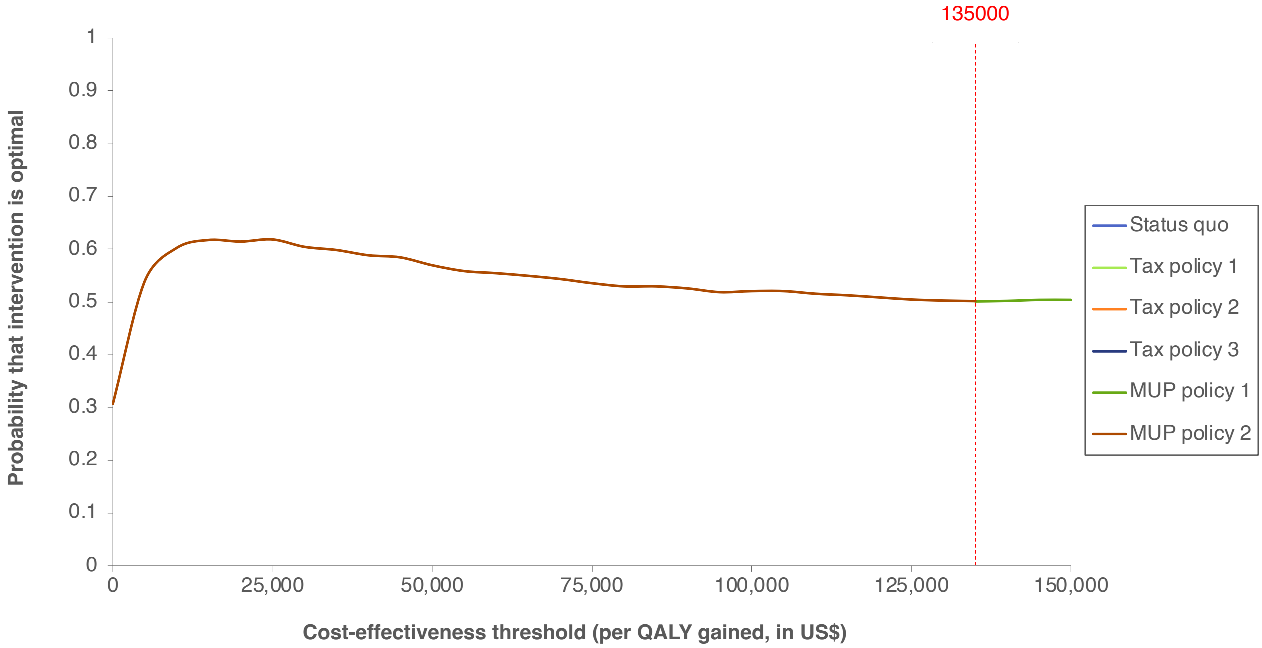
Alternative	Base-case		Conservative scenario		Optimistic scenario	
	Low drinking	*High drinking*	*Low drinking*	*High drinking*	*Low drinking*	*High drinking*
Tax policy 1: 5% increase	29,792	10,971	67,721[a]	11,374[a]	(5,515)	595,776[a]
Tax policy 2: 15% increase	3,255	3,547	42,868	Dominated	506	1,370
Tax policy 3: 30% increase	1,656	1,370	409	1,723	1,185	1,327
MUP policy 1: 50% increase	1,437	1,947	1,888	2,484	522	898
MUP policy 2: 100% increase	847	1,300	1,543	2,730	986	870

Numbers in this table are ICERs (US$ per QALY gained) comparing each pricing policy with the status quo. The conservative scenario used the lowest estimated net change in consumption for each policy, and the optimistic scenario used the highest estimated net change in consumption (aTable 8). The low drinking scenario assumed that excessive and moderate drinkers were more likely to reduce their consumption and moderate and low-risk drinkers were less likely to increase their consumption; in the high drinking scenario, excessive and moderate drinkers were less likely to reduce their consumption and moderate and low-risk drinkers were more likely to increase their consumption (aTable 3).

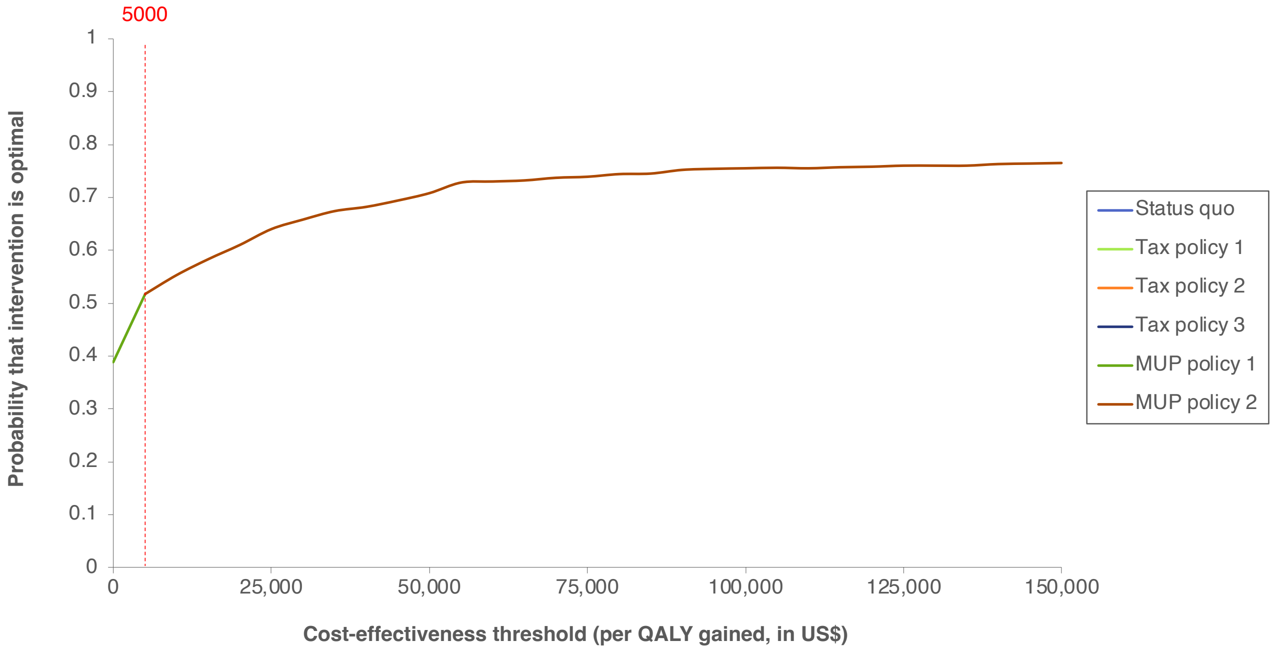
[a] Negative incremental costs and negative incremental benefit compared to the status quo
ICER, incremental cost-effectiveness ratio; MUP, minimum unit pricing; NA, not applicable; QALY, quality-adjusted life year.

aFigure 4. Cost-effectiveness acceptability frontier using conservative and optimistic estimates of the treatment effect and healthcare sector perspective

A. Conservative scenario



B. Optimistic scenario

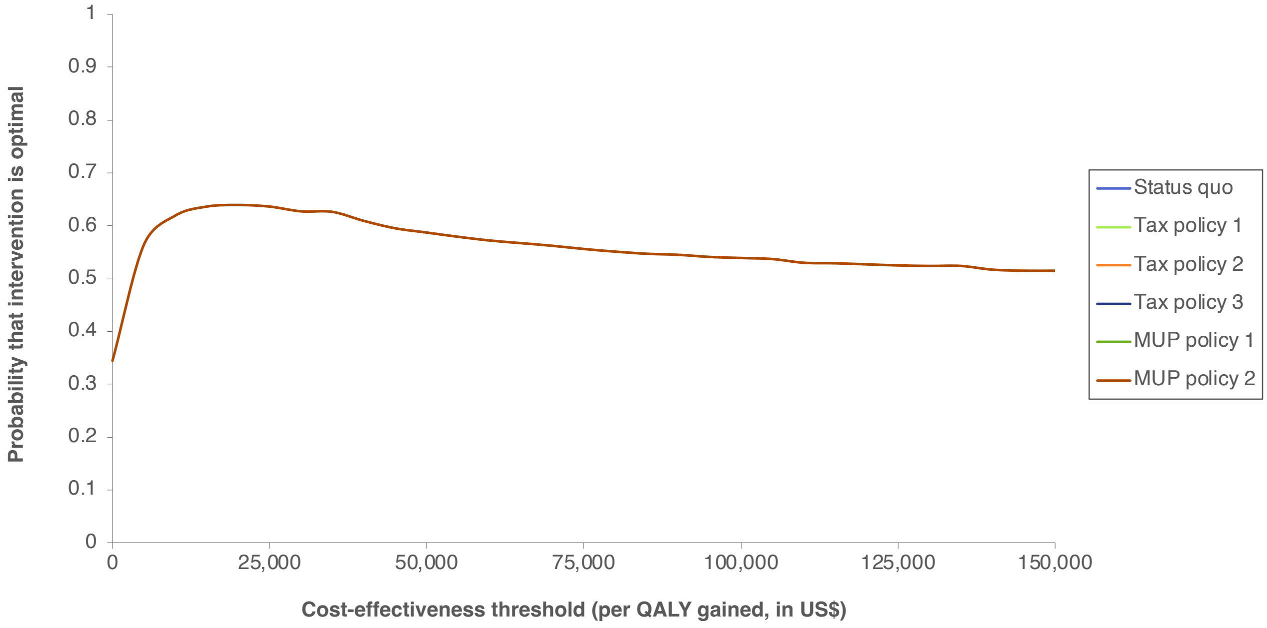


These cost-effectiveness acceptability frontiers show the uncertainty around the optimal intervention across a range of cost-effectiveness thresholds and under different assumptions. The red dashed line denotes the cost-effectiveness threshold where the optimal strategy changes from policy to another. These results were generated using the conservative (A) and optimistic (B) scenario assumptions for the effect of pricing policies on alcohol consumption and a healthcare sector perspective. The conservative scenario used the lowest estimated net change in consumption for each policy, and the optimistic scenario used the highest estimated net change in consumption (aTable 8).

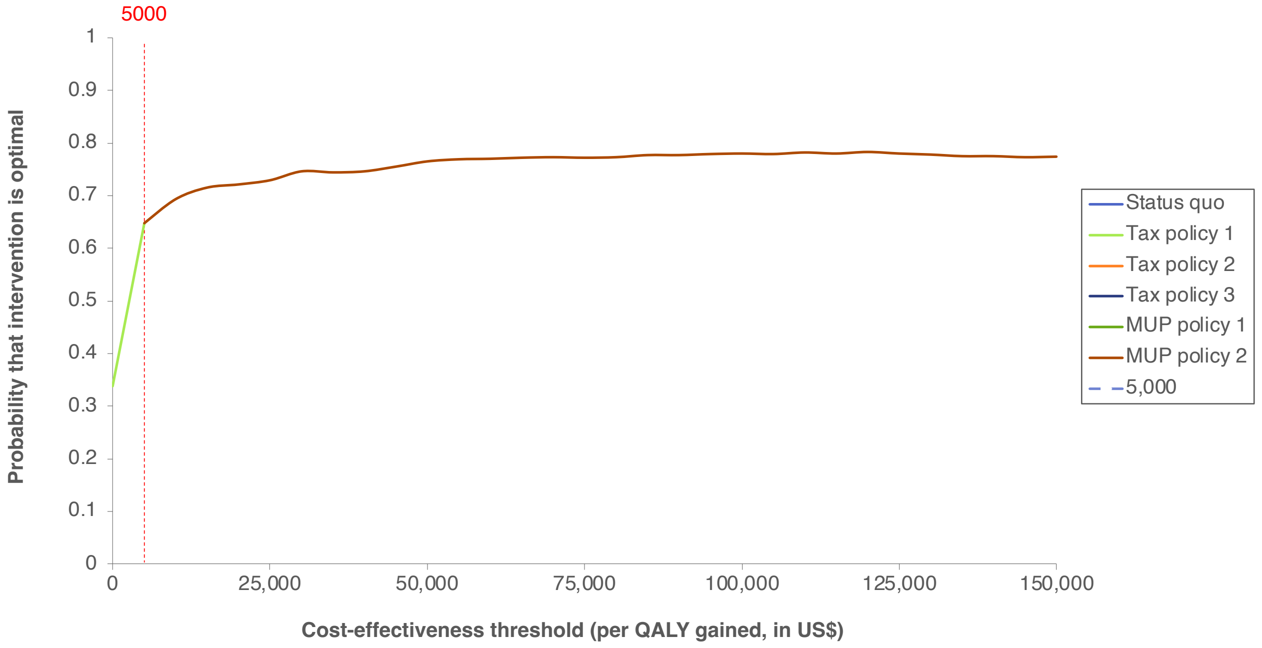
MUP, minimum unit pricing.

aFigure 5. Cost-effectiveness acceptability frontier using conservative and optimistic estimates of the treatment effect and societal perspective

A. Conservative scenario

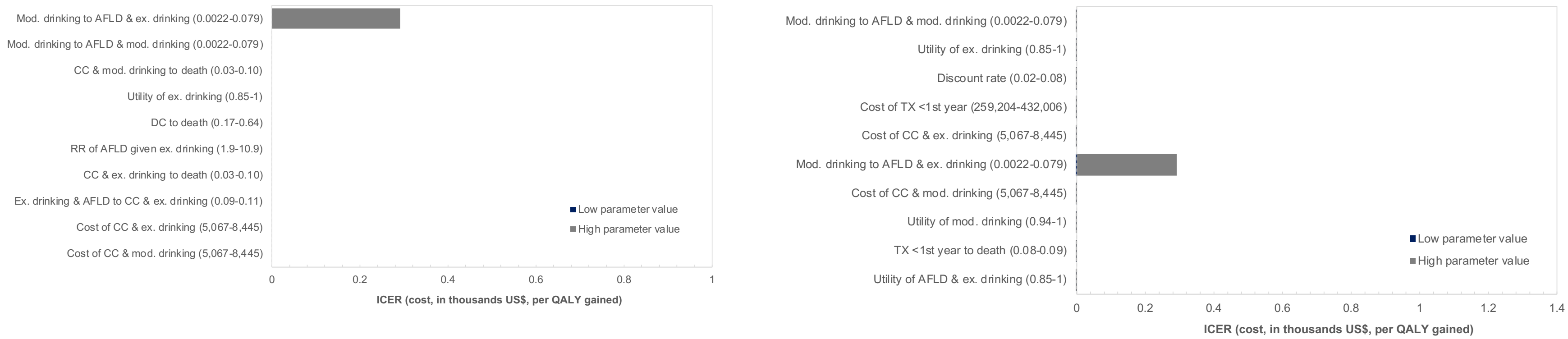


B. Optimistic scenario



These cost-effectiveness acceptability frontiers show the uncertainty around the optimal intervention across a range of cost-effectiveness thresholds and under different assumptions. These results were generated using the conservative (A) and optimistic (B) scenario assumptions for the effect of pricing policies on alcohol consumption and a societal perspective. The conservative scenario used the lowest estimated net change in consumption for each policy, and the optimistic scenario used the highest estimated net change in consumption (aTable 8). At a cost-effectiveness threshold of 0, both Tax policy 1 and MUP 1 were the optimal choice 32% of the time under the optimistic scenario.
MUP, minimum unit pricing.

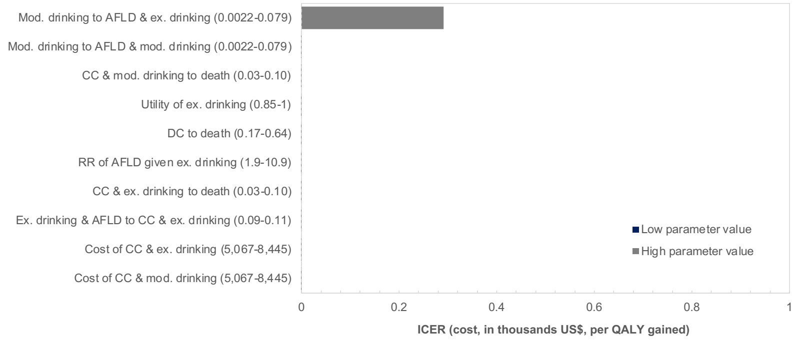
aFigure 6. Deterministic sensitivity analysis for selected policies using a healthcare sector perspective



A. Tax policy 2

B. Tax policy 3

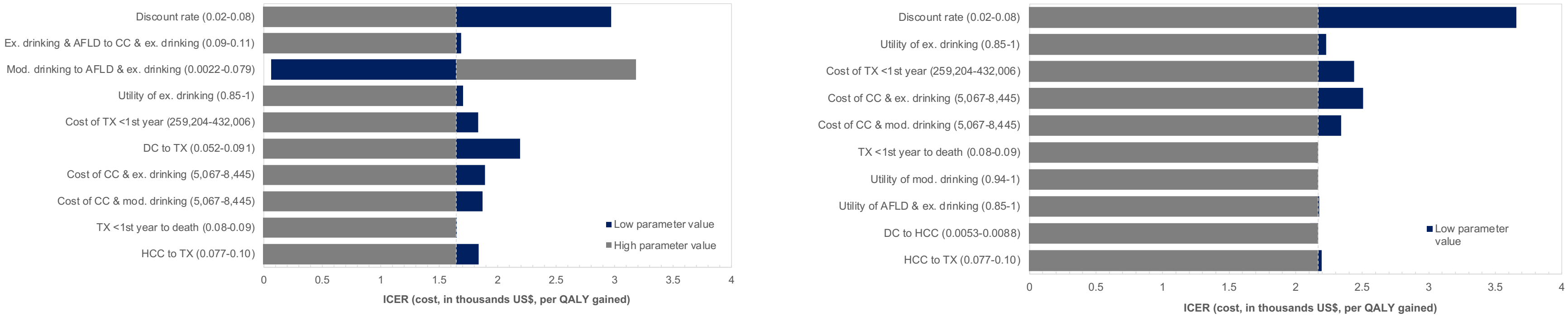
C. MUP policy 2



Tornado diagrams show the range of ICERs that result from using the lowest and highest values of selected model inputs, which are shown in the parentheses. Only the 10 most influential inputs were included here. Negative ICERs, which represent cases where an intervention is dominant or cost-saving, were excluded from these graphs.

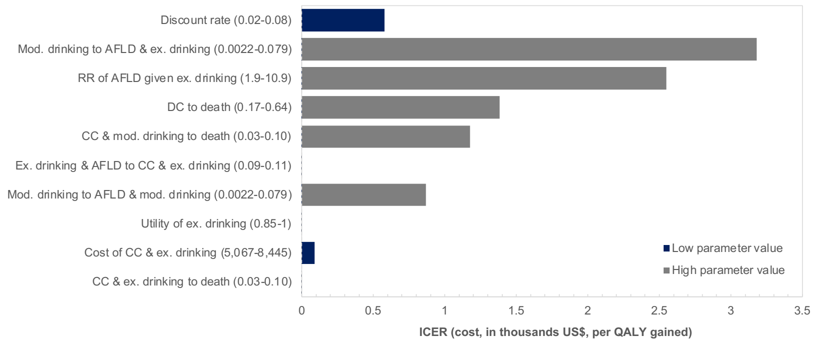
AFLD, alcohol-related fatty liver disease; CC, compensated cirrhosis; ex., excessive; ICER, incremental cost-effectiveness ratio; mod., moderate; MUP, minimum unit pricing; RR, relative risk; TX, transplantation.

aFigure 7. Deterministic sensitivity analysis for selected policies using a societal perspective


A. Tax policy 2

B. Tax policy 3

C. MUP policy 2



Tornado diagrams show the range of ICERs that result from using the lowest and highest values of selected model inputs, which are shown in the parentheses. Only the 10 most influential inputs were included here. Negative ICERs, which represent cases where an intervention is dominant or cost-saving, were excluded from these graphs. The dashed vertical line represents the ICER from the base-case results.

AFLD, alcohol-related fatty liver disease; CC, compensated cirrhosis; ex., excessive; ICER, incremental cost-effectiveness ratio; mod., moderate; MUP, minimum unit pricing; RR, relative risk; TX, transplantation.

Appendix 9. Estimating the Treatment Effect of Modeled Alcohol Tax Policies

As in Chapter 3, the treatment effect of the modeled alcohol tax policies was operationalized as the change in the initial distribution of low-risk, moderate, and excessive drinkers in the model. The process followed to estimate the treatment effect of each modeled tax policy was also the same as in Chapter 3 (see Figure 13 and Appendix 5). The steps are reiterated below.

Step 1: The first step was translating changes in price to changes in consumption for each tax policy using Eq. 12. Each percent change in price (5% and 30%) was multiplied to price elasticities of demand by race/ethnicity and gender from the literature (Figure 19).

Step 2: The second step was estimating the change in the starting prevalence of various drinking states by race/ethnicity and gender given the changes in consumption estimated in Step 1 (aTable 18). The change in prevalence for low-risk (L), moderate (M), and excessive drinking (E) was calculated using the following formulas

$$L_{ikp} = \begin{cases} L_{ik|p=0} - \left(L_{ik|p=0} * \delta_{ikp}\right) \; \forall \; \delta \geq 0 \\ L_{ik|p=0} - \left(M_{ik|p=0} * \delta_{ikp}\right) \; \forall \; \delta < 0 \end{cases} \quad \textbf{Eq. 13}$$

$$M_{ikp} = \begin{cases} M_{ik|p=0} - \left(M_{ik|p=0} * \delta_{ikp}\right) + \left(L_{ik|p=0} * \delta_{ikp}\right) \; \forall \; \delta \geq 0 \\ M_{ik|p=0} + \left(M_{ik|p=0} * \delta_{ikp}\right) - \left(E_{ik|p=0} * \delta_{ikp}\right) \; \forall \; \delta < 0 \end{cases} \quad \textbf{Eq. 14}$$

$$E_{ikp} = \begin{cases} E_{ik|p=0} + \left(M_{ik|p=0} * \delta_{ikp}\right) \; \forall \; \delta \geq 0 \\ E_{ik|p=0} + \left(E_{ik|p=0} * \delta_{ikp}\right) \; \forall \; \delta < 0 \end{cases} \quad \textbf{Eq. 15}$$

where δ is the change in consumption (aTable 18), and the indices i, k, and p refer to race/ethnicity, gender, and tax policy, respectively ($p = 0$ refers to the baseline). Equations Eq. 13-Eq. 15 are conditional on the sign of δ, which determines whether the prevalence of each drinking state increases or decreases. For example, if $\delta < 0$, then consumption decreases, which leads some moderate and excessive drinkers to move to low-risk and moderate drinking, respectively.

For low-risk and moderate drinkers, δ is equal to the values in aTable 18. Moderate drinkers consume alcohol equal to the gender-specific thresholds for heavy drinking (i.e., 14 grams of ethanol a day for women, 28 grams a day for men), so the change in consumption represents the proportion of moderate drinkers who either move to the low-risk or excessive drinking state, depending on the sign of δ. (A similar proportion of low-risk drinkers also reduce their consumption, but they remain in the low-risk drinking state.)

As with moderate drinkers, a proportion of low-risk drinkers, which include abstainers and people who consume alcohol below the daily drinking thresholds, increase their consumption when $\delta \geq 0$. In this study, I assumed that any increases in the consumption of low-risk drinkers will only move them to the moderate drinking state since $1 > \delta > 0$ for race/ethnic groups, genders, and policies, which means no low-risk drinker may increase their consumption high enough to move to the excessive drinking state.

For excessive drinkers, I applied the change in consumption to the distribution of daily alcohol consumed by people in this group, and from the result I determined the proportion of people who moved to the moderate drinking category based on the gender-specific thresholds for heavy drinking. For the distribution of daily alcohol consumed by excessive drinkers, I relied on the analysis of Jiang et al. (2021) who measured the distribution of daily drinking volume among men and women with DSM-IV alcohol dependence using National Epidemiologic Survey on Alcohol and Related Conditions waves 1 and 2.[234] After applying the change in consumption under each pricing policy to the data from Jiang et al., I fitted log-normal distributions for men and women separately and used the probability density function to estimate the probability that excessive drinkers would fall at or below the heavy drinking thresholds.

As aFigure 8 shows, very small changes were seen in the drinking volume of men and women when beer taxes were increased by 5%, as depicted by the overlapping curves. However, when liquor taxes were increased by 5%, Latino/Hispanic and Black men and Latino/Hispanic and White women experienced reductions in drinking volume, while White men and Black women saw very little change in consumption. The final changes in the prevalence of excessive drinking by race/ethnicity and gender are found in aTable 19.

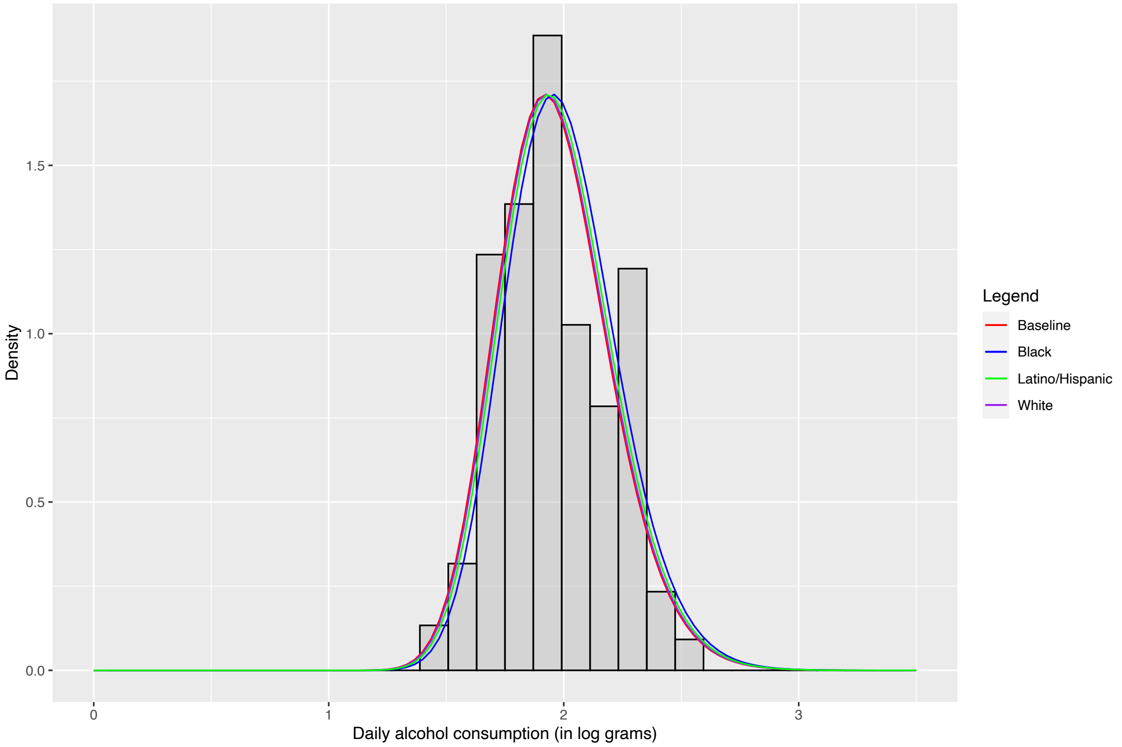
aTable 18. Change in consumption by race/ethnicity and gender for beer and liquor

Race/ethnicity	Gender	Beer		Liquor	
		5%	*30%*	*5%*	*30%*
White	Women	-0.0005 (-0.011, 0.0095)	-0.003 (-0.066, 0.057)	0.002 (-0.0125, 0.0165)	0.012 (-0.075, 0.099)
	Men	0.002 (-0.0095, 0.013)	0.012 (-0.057, 0.078)	0.001 (-0.0165, 0.018)	0.006 (-0.099, 0.108)
Black	Women	-0.025 (-0.0465, -0.003)	-0.15 (-0.279, -0.018)	0.024 (-0.028, 0.076)	0.144 (-0.168, 0.456)
	Men	0.0135 (-0.0185, 0.0455)	0.081 (-0.111, 0.273)	-0.0255 (-0.08, 0.0295)	-0.153 (-0.48, 0.177)
Latino/Hispanic	Women	-0.0125 (-0.042, 0.0175)	-0.075 (-0.252, 0.105)	-0.052 (-0.078, -0.0255)	-0.312 (-0.468, -0.153)
	Men	0.006 (-0.0245, 0.036)	0.036 (-0.147, 0.216)	-0.046 (-0.0825, -0.0095)	-0.276 (-0.495, -0.057)

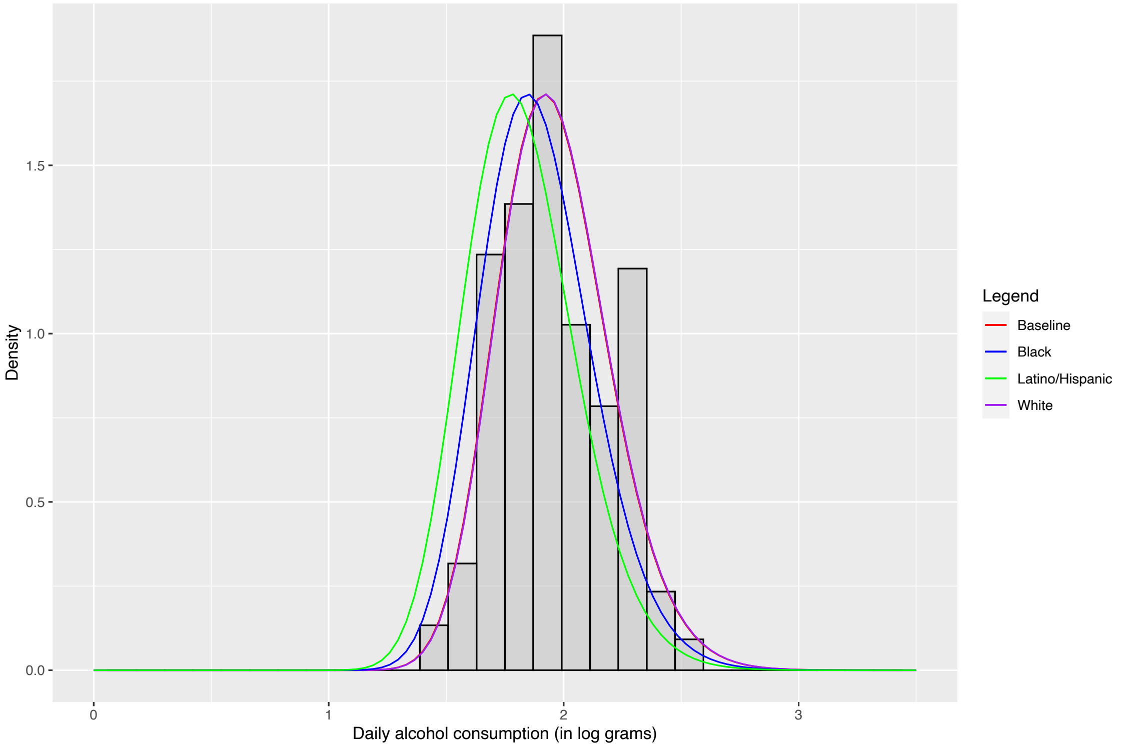
Base values and range in parentheses.

aFigure 8. Distribution of daily alcohol drinking volume among excessive drinkers after 30% price increase in beer and liquor

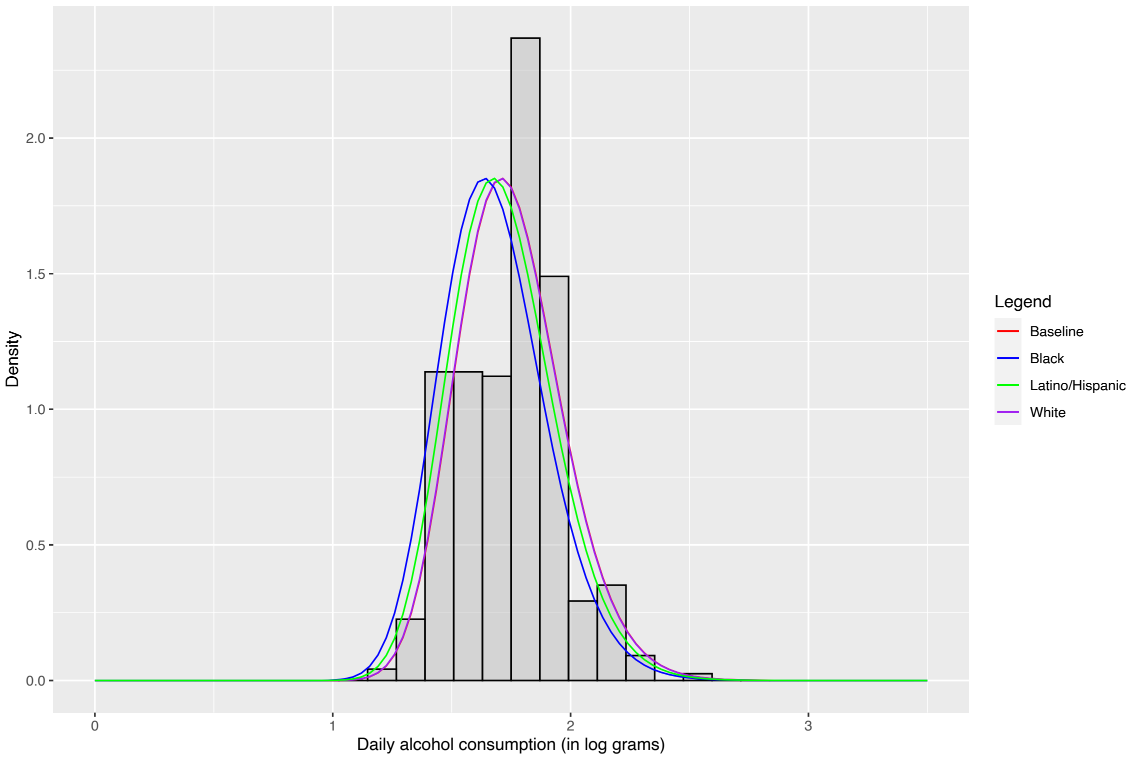
A. Beer: Men



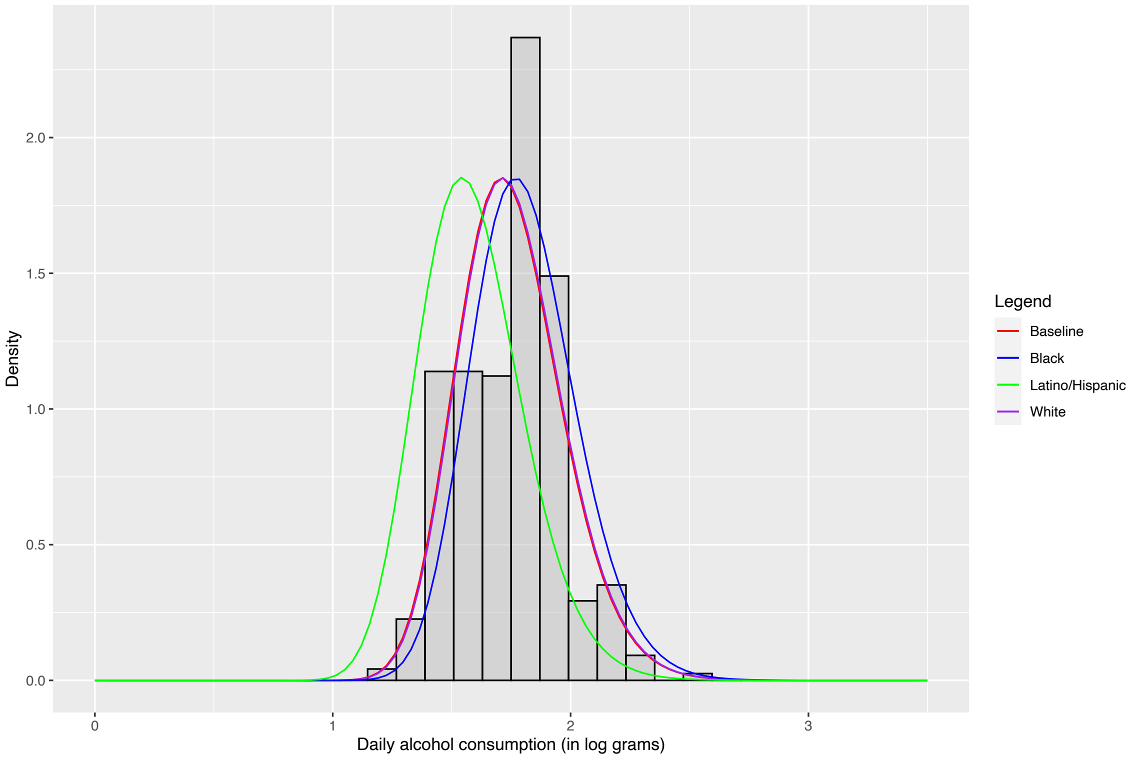
B. Liquor: Men



C. Beer: Women



D. Liquor: Women



The histograms represent the distribution of alcohol consumed by (A and C) men and (B and D) women with DSM-IV alcohol dependence using data from NESARC waves 1 and 2, and the red curves (which are obstructed from view due to overlap with other curves) represents the probability density function of the log-normal distribution fitted to log-transformed data.

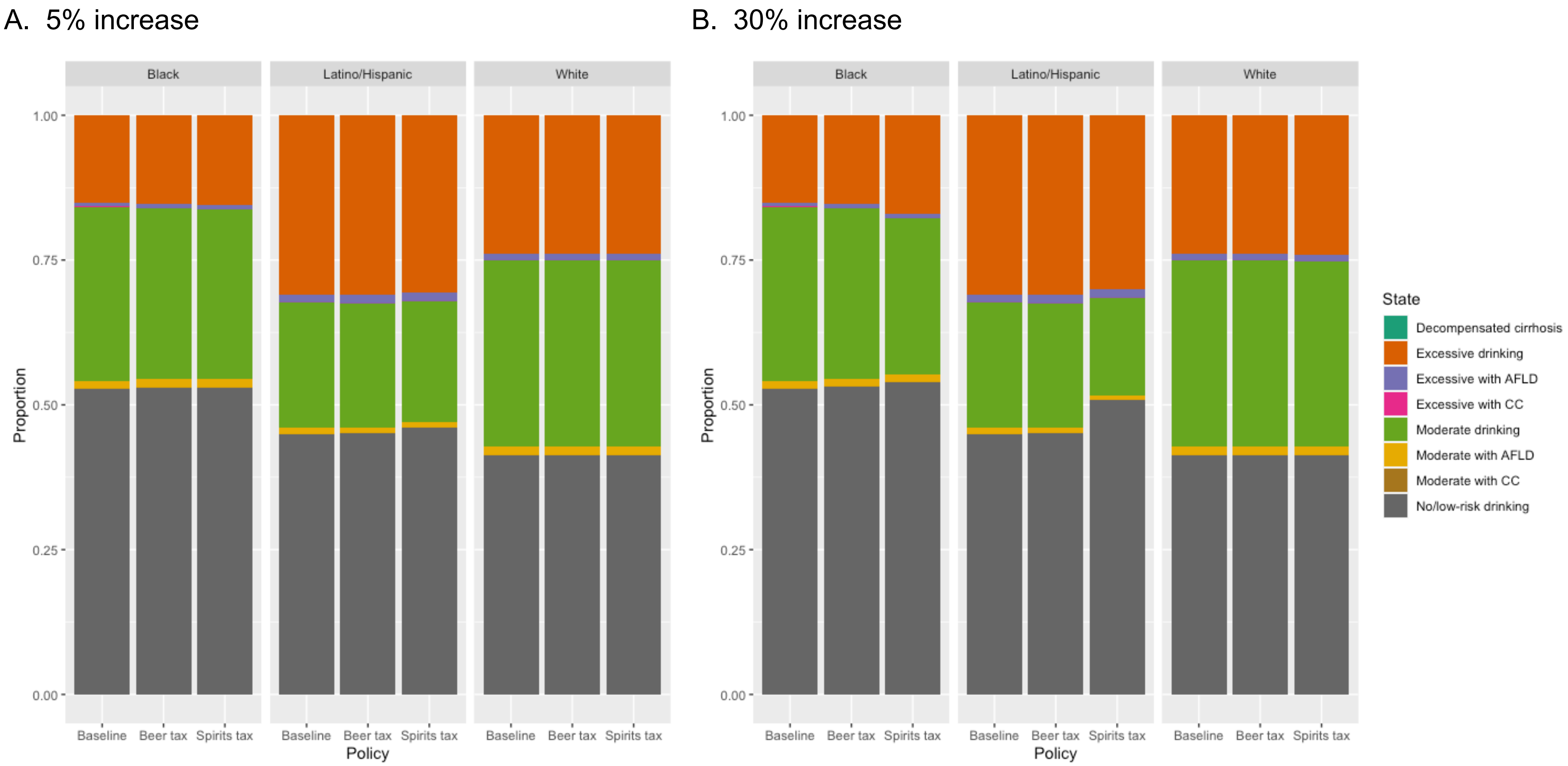
After applying the change in consumption to the original data for men and women separately, new log-normal distributions were fitted to the data to generate the race/ethnicity-specific curves (blue for Black, green for Latino/Hispanic, and purple for White) which represent daily alcohol consumption among excessive drinkers when Tax policy 1 is applied to beer (A and B) or to liquor (C and D).

aTable 19. Change in prevalence of excessive drinking by race/ethnicity and gender

Race/ethnicity	**Gender**	**Beer**		**Liquor**	
		5%	*30%*	*5%*	*Liquor*
White	Women	-0.0004	-0.0003	0.0002	0.0004
		(-0.0005, 0.0005)	(-0.004, 0.0005)	(-0.0033, 0.0005)	(-0.0005, 0.0005)
	Men	0.0063	0.004	0.0033	0.0061
		(-0.0073, 0.0068)	(-0.0101, 0.0063)	(-0.0134, 0.0063)	(-0.0077, 0.0068)
Black	Women	-0.0005	-0.0005	0.000005	0.00021
		(-0.0007, -0.0006)	(-0.0011, -0.0021)	(-0.0021, 0.0021)	(-0.0006, 0.0006)
	Men	0.005	0.0011	-0.0021	-0.0056
		(-0.0078, 0.0062)	(-0.0145, 0.004)	(-0.1646, 0.004)	(-0.0118, 0.0062)
Latino/Hispanic	Women	-0.0004	-0.0002	-0.0022	-0.0006
		(-0.0007, 0.0005)	(-0.0016, 0.001)	(-0.0101, -0.001)	(-0.001, -0.0005)
	Men	0.0054	0.0016	-0.0101	-0.0073
		(-0.0081, 0.0066)	(-0.0185, 0.0054)	(-0.1804, -0.0054)	(-0.012, -0.0066)

Base values and range in parentheses.

aFigure 9. Initial distribution of population by race/ethnicity



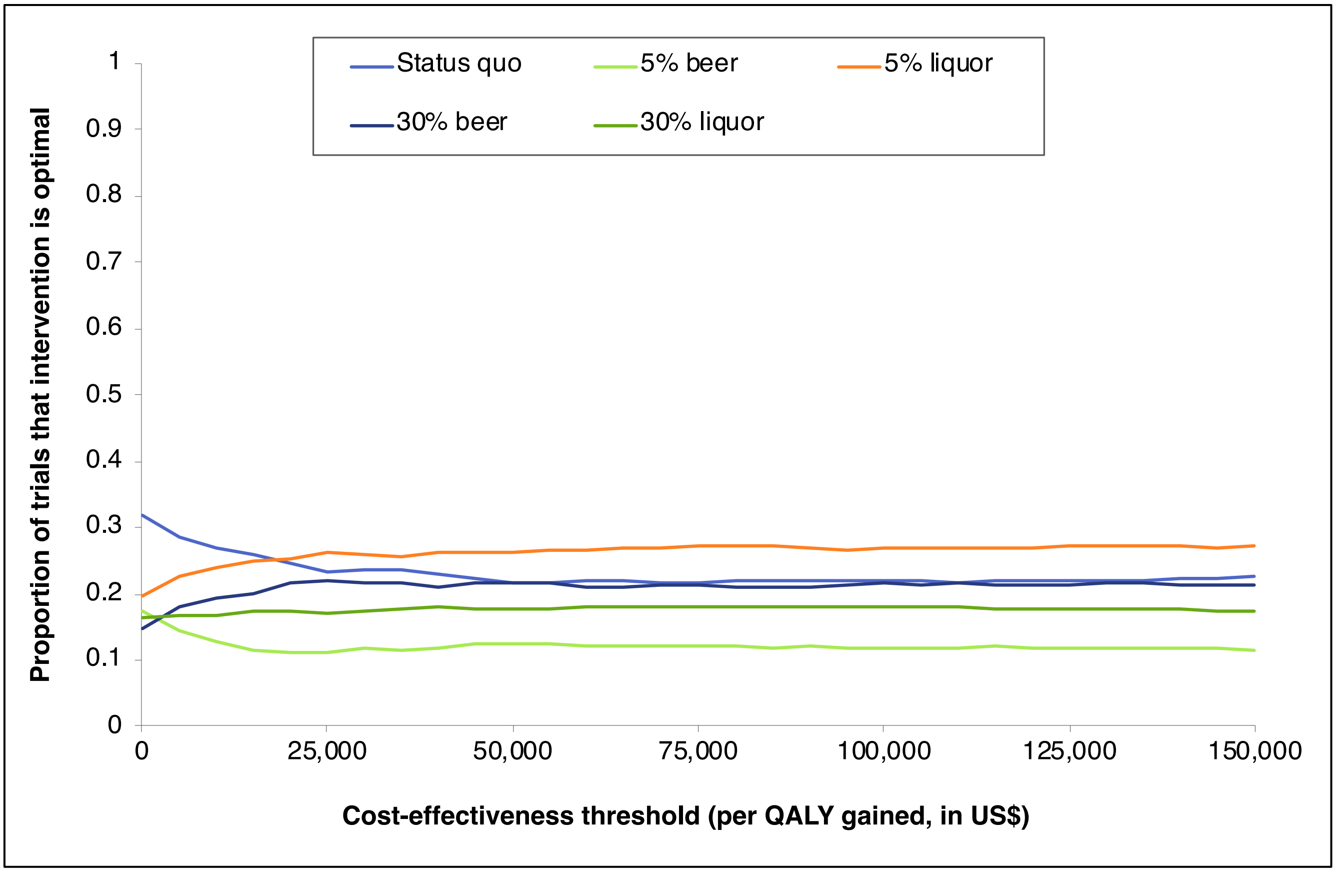
This figure shows the distribution of the starting population in each health state under (A) Tax policy 1 and (B) Tax policy 2 for each racial/ethnic group
AFLD, alcohol-related fatty liver disease; CC, compensated cirrhosis.

aTable 20. Cost-effectiveness of alcohol tax policies using a societal perspective

			ICER (in cost per QALY gained)	
Intervention	**Cost (in US$)**	**Benefit (in QALYs)**	*Compared to status quo*	*Compared to next expensive, undominated intervention*
Status quo	31,626.51	6.2135	NA	NA
5% liquor	31,628.86	6.2138	8,599	Dominated
5% beer	31,629.10	6.2138	7,324	Dominated
30% beer	31,630.10	6.2142	4,773	Dominated
30% liquor	31,631.98	6.2158	2,350	1,193

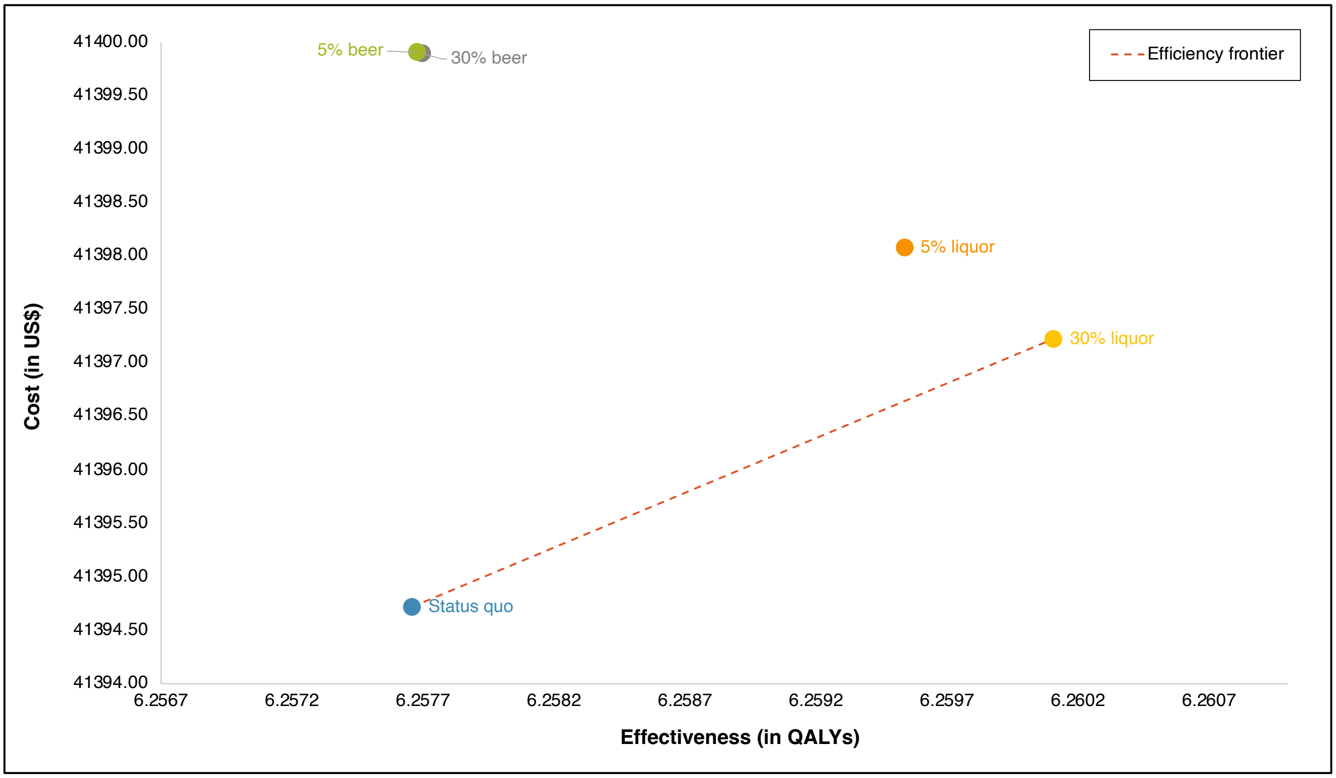
Interventions are listed in ascending order of average costs.
ICER, incremental cost-effectiveness ratio; NA, not applicable. QALY, quality-adjusted life year.

aFigure 10. Cost-effectiveness acceptability frontier using a societal perspective



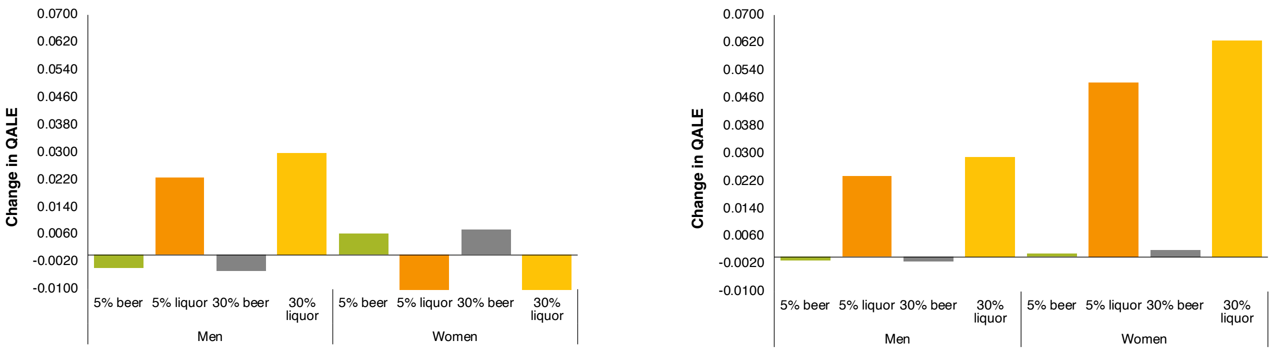
A cost-effectiveness acceptability frontier shows the uncertainty around the optimal intervention across a range of cost-effectiveness thresholds. The red dashed line denotes the cost-effectiveness threshold where the optimal strategy changes from one policy to another.
QALY, quality-adjusted life year.

aFigure 11. Cost-effectiveness plane using a healthcare perspective



A cost-effectiveness plane plots the average total costs (in US$) and average total effectiveness (in QALYs) of each evaluated strategy. The dotted red line represents the efficiency frontier, which is defined by the most efficient interventions at increasing levels of health benefit. Interventions to the left of the efficiency frontier are "extendedly dominated," which means that these interventions are less efficient than combinations of other strategies.
QALY, quality-adjusted life expectancy.

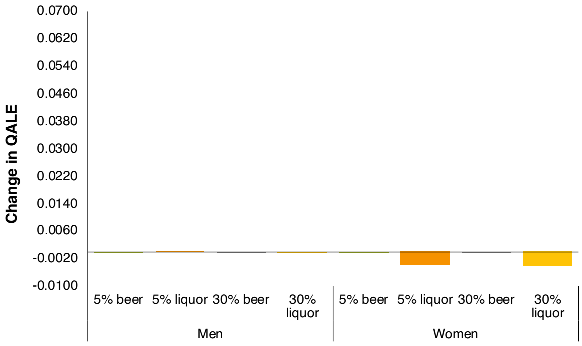
aFigure 12. Change in quality-adjusted life expectancy among racial/ethnic and gender groups under each intervention



D. Black

E. Latino/Hispanic

F. White



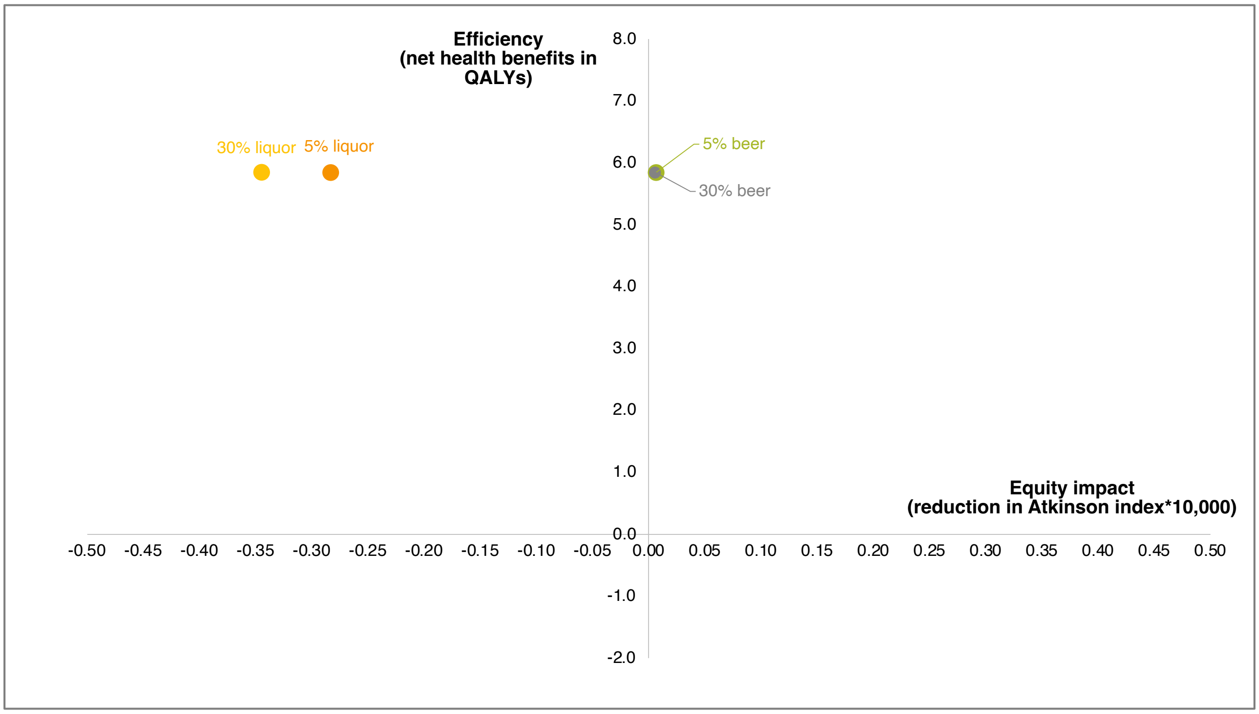
Changes in QALE were calculated by subtracting the QALE associated with each policy with the QALE associated with the status quo. QALE, quality-adjusted life expectancy.

aTable 21. Atkinson index across interventions

Inequality aversion parameter (ε)	Status quo	5% beer	5% liquor	30% beer	30% liquor
0	0	0	0	0	0
1	0.0000664	0.0000663*	0.0000694	0.0000663	0.0000700†
5	0.0003287	0.0003284*	0.0003432	0.0003284	0.0003463†
10	0.0006487	0.0006480*	0.0006770	0.0006481	0.0006831†
20	0.0012598	0.0012585*	0.0013136	0.0012586	0.0013252†
30	0.0018297	0.0018277*	0.0019059	0.0018280	0.0019223†

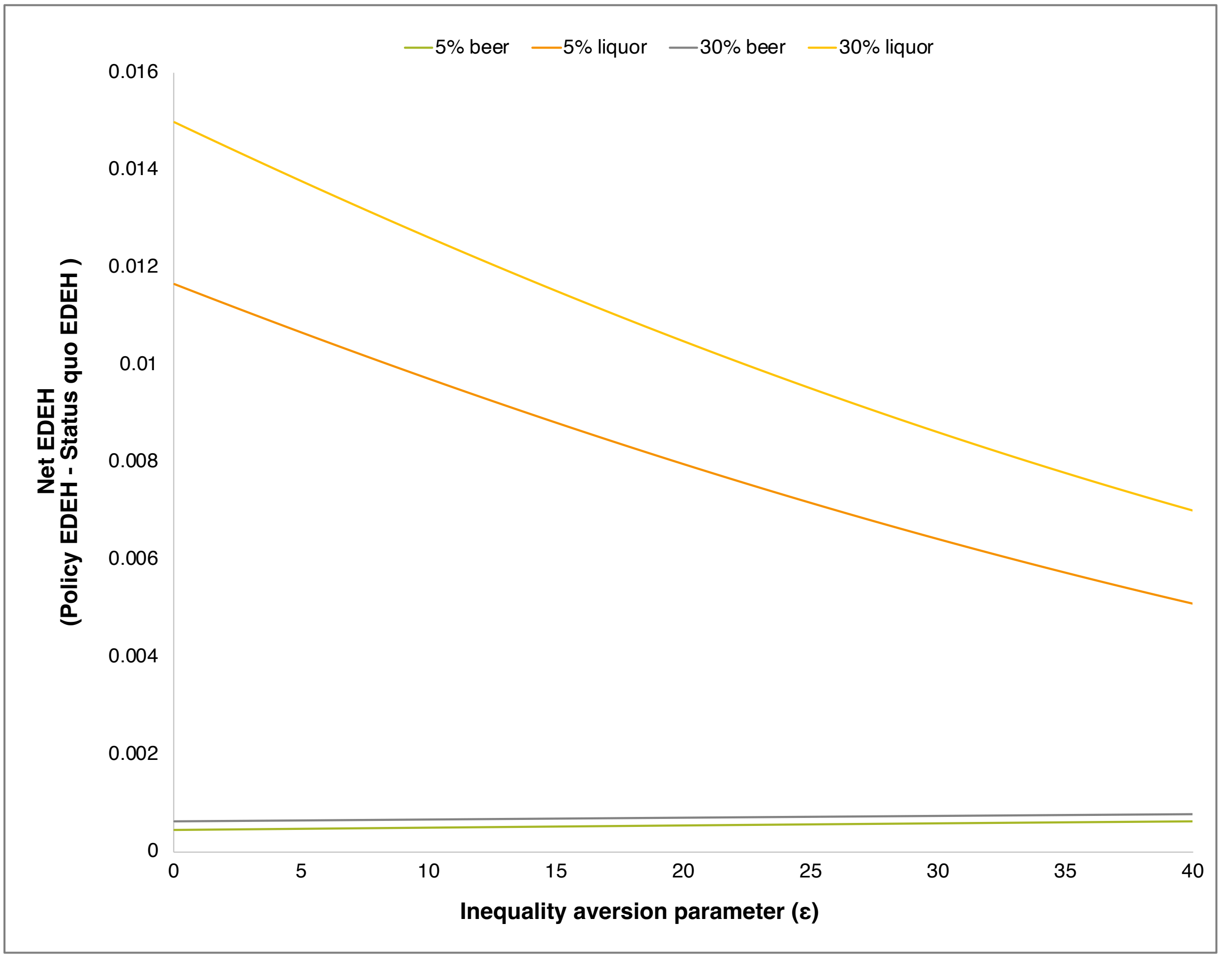
Asterisk (*) denotes the intervention with the lowest Atkinson index at each inequality aversion parameter value, which represents the lowest inequality. The cross (†) marks the intervention with the highest Atkinson index, which represents the highest inequality.

aFigure 13. Equity-efficiency impact plane



The equity-efficiency impact plane plots the efficiency, in terms of net health benefits, and equity impact, in terms of a reduction in the Atkinson index, of each tax policy. The net health benefits were calculated using a cost-effectiveness threshold of $100,000 per QALY gained and using a healthcare perspective. The Atkinson index was calculated using an inequality aversion parameter equal to 10 and by comparing each policy with the status quo.
QALY, quality-adjusted life years.

aFigure 14. Equity trade-off analysis



EDEH is the level of health per person, if distributed equally, that would produce the same level of social welfare as the distribution of health in the status quo; thus, a higher EDEH is always preferred. The net EDEH was calculated by subtracting each policy's EDEH with the status quo EDEH. A higher inequality aversion parameter denotes a stronger preference for equality.

EDEH, equally distributed equivalent of health