

Health-related quality of life of alcohol use disorder with co-occurring conditions in the US population

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Abstract:

Background: Alcohol use disorder (AUD) commonly co-occurs with other health conditions or other substance use, complicating our understanding of the health-related quality of life (HRQoL) of AUD. We described the HRQoL of alcohol use disorder in the presence of co-occurring conditions and identified the contribution of each. **Methods:** Secondary analysis of National Epidemiologic Survey on Alcohol and Related Conditions III data, consisting of 36,309 non-institutionalized US adults; descriptive and regression analysis. HRQoL measured via the SF-6D; AUD via the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-5); physical, mental health, and substance use disorders/conditions as reported or assessed via AUDADIS-5. **Results:** AUD was independently associated with lower HRQoL for individuals experiencing co-occurring conditions. Compared to no AUD, past year AUD reduced SF-6D score by 0.0304 (SE = 0.0027) and prior-to-past-year AUD reduced SF-6D by 0.0163 (SE = 0.0023). AUD's co-occurring conditions were independently associated with lower HRQoL, beyond the reduction from AUD: any co-occurring physical health condition was associated with a 0.062 point reduction in SF-6D score (SE = 0.0023), any mental health condition with a 0.084 point reduction (SE = 0.0025), and any substance use disorder with a 0.038 point reduction (SE = 0.0023). **Conclusions:** AUD's association with diminished HRQoL may be explained in large part by the presence of co-occurring conditions among individuals reporting AUD, as these co-occurring conditions are associated with substantial decrements in HRQoL—often eclipsing the magnitude of the decrements associated with AUD alone. Alcohol use interventions endeavoring to improve HRQoL should consider the entirety of an individual to design patient-centered care.

Keywords: alcohol use disorder | health-related quality of life | utility | SF-6D | economic evaluation

Article:

1. Introduction

Approximately 14 % of adults in the US have experienced alcohol use disorder (AUD) within the past year and nearly 30 % reported having it anytime in their life.(Grant et al., 2015)

Individuals with AUD are substantially more likely to have any drug use disorder, major depressive disorder, and other psychiatric disorders than individuals without AUD.(Grant et al., 2015) The social costs of excessive alcohol consumption in the United States are extreme, totaling nearly \$250 billion in 2010 alone.(Sacks et al., 2015)

Because of the prevalence and societal consequences of AUD, accurate evaluations of prevention and treatment are critical to guide policy. Economic evaluation provides a measure of value for investments in health interventions—the results achieved relative to their cost. Economic evaluations can be performed from a variety of “perspectives” representing the responsible party for costs, from society to payers to the individual. Health-related quality of life (HRQoL) combined with years of life gained is the recommended outcome measure used in economic evaluation conducted from a societal perspective (Neumann et al., 2017), which when weighed against cost provides a measure of “cost-effectiveness”—the effects achieved by a particular intervention for each dollar spent compared to alternative uses of that dollar.(Hunink et al., 2014) Other outcome measures commonly used in economic evaluations of interventions targeting substance use disorders include clinical outcomes, and other perspectives (such as payer) are relevant in different contexts. In the US, the societal perspective prevails as recommended practice to ensure comparability across evaluations.

HRQoL is generally measured on a 0–1 scale, where 0 is the HRQoL assigned to being dead and 1 is the value assigned to being in full health.(Hunink et al., 2014) When combined with the years of life saved by an intervention, HRQoL can be used to estimate quality adjusted life years—i.e., QALYs—which are years of life “adjusted” for their quality. For example, one year of life lived with a serious health condition is of lesser quality than one year of life lived in full health, hence the serious condition-lived-year is “worth” something less than one QALY while the full-health-lived-year is “worth” one full QALY. Whereas clinical outcomes such as disease-specific quality of life instruments can be used to compare interventions for a specific condition, measuring outcomes in QALYs allows for interventions targeting disparate conditions to be compared on a common metric--which is useful for resource allocation decisions.

HRQoL of AUD is complicated to measure because AUD seldomly occurs in isolation. HRQoL is typically measured for an individual health state ignoring the presence of co-occurring conditions if they exist (Hunink et al., 2014); that said, it has been shown that co-occurring health conditions may affect HRQoL in a unique way, either magnifying or moderating each individual condition’s effect.(Ara and Wailoo, 2013) Co-occurring conditions are typically termed “joint” health states when measuring HRQoL or utility, while individual states are typically termed “single” states (Ara and Wailoo, 2013; Dale et al., 2008); following this convention, the presence of additional health conditions beyond those focused-upon is typically ignored, so a “joint” health state A/B consisting of state A co-occurring with state B may also have states C, D and E or may have none other than A and B, as this reflects how state A/B would occur in the population, with and without other co-occurring conditions beyond these two. Similarly, a single health state A may also occur in conjunction with state C, D, or E, unless it is specifically defined as exclusively condition A and no others, which would in practice be difficult to ascertain (i.e., it is easier to know what conditions and individual does have than what they do not have). AUD often co-occurs with other health conditions, both or all of which may diminish HRQoL. The HRQoL decrement attributable to AUD is therefore intertwined with any

HRQoL decrement that flows from the co-occurring condition, as well as any HRQoL associated with the interaction between the two (or more) conditions. QALY estimates for AUD must therefore isolate the effect on HRQoL of AUD alone or must consider the HRQoL of AUD with co-occurring conditions.

Prior research has measured the HRQoL of AUD at a mean of 0.76 on a 0–1 scale (higher is better), irrespective of co-occurring conditions.(Barbosa et al., epub August 15, 2020) Estimates of the mean HRQoL for the general population vary depending on the measurement instrument used, but generally range between 0.75–0.89 for older to younger individuals in the US respectively.(Fryback et al., 2007) HRQoL for substance use disorders can vary widely and has been reported as low as 0.574 for active injection opioid misuse (Wittenberg et al., 2016); one reported estimate of HRQoL for moderate depression was 0.672.(Wittenberg et al., 2017) Given the substantial negative decrements on HRQoL seen with these commonly co-occurring conditions, it is important to consider the presence of comorbidities when assessing the HRQoL of individuals with AUD.

The objective of this study was to describe the joint health state HRQoL for AUD and many commonly co-occurring conditions, and to describe the independent contribution of AUD to HRQoL in the presence of co-occurring conditions. Our goal was to inform economic evaluation of alcohol prevention and treatment interventions that rely on measures of health state utility/HRQoL.

2. Materials and methods

2.1. Data

We used the NESARC-III dataset for all analyses; NESARC-III is a nationally representative, face-to-face interview survey of 36,309 non-institutionalized, US adults 18 years and older residing in households and selected group quarters.(Grant et al., 2014) NESARC-III data were collected from April 2012 to June 2013 through a multistage probability sample with oversampling of racial and ethnic subgroups of the population; responses were weighted to correct for oversampling and non-response and weights were provided to users to represent the US civilian population.(Grant et al., 2014)

Included in the NESARC-III are past year and prior to past year AUD (measured using the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-5)(Grant et al., 2011)); lifetime and past year alcohol consumption (including prior years' drinking and abstaining); lifetime and past year medical conditions—self-assessed and self-reported as confirmed by a health care provider; and lifetime, past year, and prior to past year Diagnostic and Statistical Manual of Mental Disorders-defined (DSM-5(American Psychiatric Association, 2013)) mental health conditions and substance use disorders (assessed using the AUDADIS-5). NESARC-III also administered the Short-Form 12 version 2 (SF-12v2) to assess health-related quality of life (Ware et al., 1996).

2.2. Variables

We used the NESARC-III past year and prior to past year variables to create an additional “lifetime AUD” variable defined as any AUD reported at any point in time (i.e., the union of past year and prior to past year). We also created variables measuring alcohol consumption based on the WHO alcohol consumption risk levels, as indicators of quality of life in individuals with AUD (Witkiewitz et al., 2018; World Health Organization, 2000): we converted ounces of alcohol consumed as reported in NESARC-III to grams of ethanol consumed; we defined five risk categories consisting of “no risk: lifetime abstinence” if no reported lifetime consumption of alcohol; “no risk: former drinker” if less than 1 g of daily ethanol consumption reported within the past year but more than 1 g prior to past year; “low risk” if male and 1–40 grams of daily ethanol consumption reported within the past year or female and 1–20 grams; “medium risk” if male and 40–60 grams reported daily or female and 20–40 g; “high risk” if male and more than 60 g reported daily or female and more than 40 g (we combined WHO high and very high risk consumption levels due to small sample size).

We calculated the corresponding SF-6D scores from SF-12v2 responses using an established algorithm.(Brazier and Roberts, 2004) NESARC-III imputed SF-12v2 data under specific conditions (National Institute on Alcohol Abuse and Alcoholism, 2020); we excluded from analysis all observations with missing SF-12v2 data after NESARC imputation (n = 146).

We included all physical health, mental health, and substance use disorders/conditions included in NESARC-III as individual variables if the sample size was 50 or greater; we created grouped condition variables for those with samples of less than 50 and for some clinically similar conditions. For physical health conditions we included those reported as confirmed by a physician or health professional; for mental health conditions and substance use disorders we included those as measured by the AUDADIS-5. Grouped condition variables included all cancers (other than breast due to its large sample size and clinical association with alcohol consumption), lung conditions, bipolar disorders, depressive disorders, eating disorders, generalized anxiety, and personality disorders. We grouped cocaine and stimulant use, heroin and opioid use, and other drugs (see Table 1 notes). We also created grouped variables for at least one reported physical health condition, mental health condition, and substance use disorder (notably, nicotine use disorder constituted the vast majority of this category at over 90 %). Grouped condition variables included at least one condition that met the category criterion(a)-- and could include either more than one condition that met the criteria or an additional condition/disorder that did not meet those criteria or both. Within individual condition variables we excluded observations with missing data (i.e., neither reported as present nor absent); within grouped condition variables we excluded observations in which data were missing for all conditions within the group.

Table 1. Sample Characteristics: unweighted sample sizes and proportions weighted to reflect US population.

	Total Sample Unweighted n (weighted %)	Never AUD ¹ Unweighted n (weighted %)	Lifetime AUD Unweighted n (weighted %)
Age (years)	36,163	26,189 (71)	9,974 (29)
< 21	1,591 (5)	1,206 (5)	385 (5)
21 - 45	17,260 (44)	11,469 (39)	5,791 (55)
46 - 65	12,047 (35)	8,883 (36)	3,164 (33)

	Total Sample Unweighted n (weighted %)	Never AUD¹ Unweighted n (weighted %)	Lifetime AUD Unweighted n (weighted %)
> 65	5,265 (16)	4,631 (20)	634 (7)
Gender			
Female	20,357 (52)	15,950 (57)	4,407 (40)
Race/Ethnicity			
White, non-Hispanic	19,118 (66)	12,938 (63)	6,180 (74)
Black, non-Hispanic	7,747 (12)	6,032 (13)	1,715 (9)
American Indian/Alaskan	508 (1)	296 (1)	212 (2)
Asian/Native Hawaiian	1,789 (6)	1,510 (7)	279 (3)
Hispanic, any race	7,001 (15)	5,413 (16)	1,588 (12)
Education			
No college	15,205 (39)	11,478 (40)	3,727 (35)
Some college	7,964 (22)	5,461 (21)	2,503 (25)
Degree ²	12,994 (39)	9,250 (39)	3,744 (40)
WHO alcohol consumption risk level ³			
No risk: lifetime abstinence ⁴	4,513 (11)	4,513 (16)	
No risk: former drinkers ⁵	14,722 (40)	12,259 (46)	2,463 (26)
Low risk	13,397 (40)	8,409 (34)	4,988 (52)
Medium risk	1,599 (4)	625 (3)	974 (9)
High risk ⁶	1,932 (5)	383 (1)	1,549 (13)
Physical health conditions			
Any physical health condition [§]	18,679 (54)	13,582 (54)	5,097 (53)
Anemia	1,974 (5)	1,421 (5)	553 (5)
Arthritis	6,464 (19)	4,910 (20)	1,554 (16)
Bowel condition ^a	1,256 (4)	855 (4)	401 (4)
Breast cancer	208 (1)	171 (1)	37 (<1)
Cancers ^b	1,107 (4)	818 (4)	289 (3)
Chest pain	1,527 (4)	1,048 (4)	479 (5)
Cirrhosis	130 (<1)	72 (<1)	58 (<1)
Diabetes	3,501 (9)	2,834 (10)	667 (7)
Difficulty sleeping	2,770 (8)	1,811 (7)	959 (9)
Epilepsy	317 (1)	200 (1)	117 (1)
Fibromyalgia	728 (2)	515 (2)	213 (2)
Hardening of arteries	459 (1)	333 (1)	126 (1)
Heart attack	308 (1)	229 (1)	79 (1)
High blood pressure	8,946 (25)	6,858 (27)	2,088 (21)
High cholesterol	6,682 (20)	5,072 (21)	1,610 (17)
High triglycerides	2,555 (8)	1,875 (9)	680 (8)
Human Immunodeficiency Virus	233 (1)	147 (<1)	86 (1)
Lung condition ^c	1,953 (5)	1,308 (5)	645 (6)
Nerve condition ^d	297 (1)	210 (1)	87 (1)
Osteoporosis	1,313 (4)	1,088 (5)	225 (2)
Other heart condition ^e	1,522 (5)	1,140 (5)	382 (4)
Other liver condition ^f	365 (1)	194 (1)	171 (2)
Other nerve condition ^g	3,432 (10)	2,363 (9)	1,069 (11)
Pancreatitis	125 (<1)	76 (<1)	49 (<1)
Rapid heartbeat	1,635 (5)	1,112 (5)	523 (5)
Sexually transmitted disease	324 (1)	162 (<1)	162 (1)

	Total Sample Unweighted n (weighted %)	Never AUD ¹ Unweighted n (weighted %)	Lifetime AUD Unweighted n (weighted %)
Stomach ulcer	936 (2)	599 (2)	337 (3)
Stroke	296 (1)	242 (1)	54 (1)
Traumatic brain injury	173 (<1)	107 (<1)	66 (1)
Mental health conditions			
Any mental health condition §	10,824 (29)	6,085 (23)	4,739 (45)
Bipolar disorders ^h	951 (3)	367 (1)	584 (6)
Depressive disorders ⁱ	4,772 (13)	2,705 (10)	2,067 (19)
Eating disorders ^j	383 (1)	196 (1)	187 (2)
Generalized anxiety ^k	2,874 (8)	1,552 (6)	1,322 (13)
Personality disorders ^l	5,217 (14)	2,288 (8)	2,929 (28)
Phobias ^m	2,669 (8)	1,540 (6)	1,129 (11)
Post-traumatic stress disorder	1,767 (5)	836 (3)	931 (9)
Schizotypal disorders	2,420 (6)	1,147 (4)	1,273 (12)
Substance use disorders			
Any substance use disorder ^s	7,889 (22)	3,756 (14)	4,133 (40)
Cannabis	971 (3)	250 (1)	721 (6)
Cocaine and stimulants	245 (1)	45 (<1)	200 (2)
Heroin and opioids	356 (1)	119 (<1)	237 (2)
Nicotine	7,278 (20)	3,522 (13)	3,756 (37)
Other drugs ⁿ	73 (<1)	18 (<1)	55 (1)
Sedative	132 (<1)	40 (<1)	92 (1)
Multiple conditions/disorders			
Physical and mental health condition	6,704 (19)	3,892 (10)	2,812 (8)
Physical health and substance use disorder	4,266 (12)	2,136 (6)	2,130 (6)
Mental health and substance use disorder	3,832 (10)	1,418 (4)	2,404 (7)
Physical, mental health, and substance use disorder	2,397 (7)	961 (3)	1,436 (4)

¹ **AUD:** Alcohol Use Disorder **Never AUD:** No Alcohol Use Disorder diagnosis in past year, prior to past year, and lifetime.

² **Degree:** Associate, technical, bachelor's, or higher.

³ **WHO alcohol consumption risk levels:** World Health Organization's criteria for risk of consumption on a single drinking day: World Health Organization International Guide for Alcohol Consumption and Related Harm, WHO, Geneva, 2000.

⁴ **No risk: lifetime abstinence:** no alcohol consumption in the past year and prior to past year.

⁵ **No risk: former drinkers:** no alcohol consumption in the past year but reported alcohol consumption prior to past year.

⁶ **High risk:** high risk and very high risk WHO consumption risk levels.

^a **Bowel condition:** NESARC variable that includes: inflammatory bowel disease, irritable bowel syndrome.

^b **Cancers:** Combined variable created from the following NESARC variables: liver; mouth, tongue, throat, and esophagus; other (unspecified) cancer.

^c **Lung condition:** Combined variable created from the following NESARC variables: bronchitis; emphysema; pneumonia; influenza; tuberculosis.

^d **Nerve condition:** NESARC variable that includes: reflex sympathetic dystrophy, complex regional pain syndrome.

^e **Other heart condition:** Any heart disease not specifically queried in NESARC-III.

^f **Other liver condition:** Any liver disease not specifically queried in NESARC-III.

^g **Other nerve condition:** NESARC variable that includes: nerve pain in back, arms, or legs.

^h **Bipolar disorders:** Combined variable created from the following NESARC variables: manic or hypomanic bipolar disorders; other bipolar disorders.

ⁱ **Depressive disorders:** Combined variable created from the following NESARC variables: major or episodic depressive disorder; dysthymic; manic or hypomanic depressive disorder.

^j **Eating disorders:** Combined variable created from the following NESARC variables: bulimia; anorexia nervosa; binge eating.

^k **Generalized anxiety:** Combined variable created from the following NESARC variables: generalized anxiety disorder; agoraphobia; panic disorder.

^l **Personality disorders:** Combined variable created from the following NESARC variables: borderline personality; conduct disorder; antisocial disorder.

^m **Phobias:** Combined variable created from the following NESARC variables: specific phobia; social phobia.

ⁿ **Other drugs:** Combined variable created from the following NESARC variables on substance use: hallucinogens, solvents, club drugs, all other not queried in NESARC-III.

[§] **Any (physical, mental, substance):** All (physical, mental, substance) conditions appearing in the NESARC-III.

Finally, we created categorical variables for sociodemographic characteristics, with age as < 21 (18–20), 21–45, 46–65, and > 65 years; education as high school or less education (“no college”), some college education (“some college”), and some post-high school degree (associate, technical school, bachelor’s or higher; “degree”); race and ethnicity used NESARC-III categories of white non-Hispanic, Black non-Hispanic, American Indian/Alaskan native non-Hispanic, Asian/native Hawaiian/other pacific Islander non-Hispanic, and Hispanic any race.

Ethics approval for the study was obtained from the University of North Carolina Greensboro (UNCG) Institutional Review Board; NESARC-III data were subject to a limited access data agreement between UNCG and the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

2.3. Analysis

We described the sample using unweighted frequencies and the final weighted proportions representing the US population, on AUD status, demographic characteristics, WHO alcohol consumption risk level, and physical health, mental health, and substance use conditions/disorders. We applied NESARC-III population weights for all subsequent analyses. Using the NESARC-III population weights, we calculated mean SF-6D scores and standard deviations (SD) for the individual (i.e., “single”) health states of lifetime AUD, past year AUD, and prior to past year AUD, and for all individual physical, mental, and substance use disorders/conditions, as well as for the grouped categories of any physical, mental, or substance use disorder/condition. We defined “single” states as any individual reporting that condition regardless of any other condition they may or may not have reported—in other words, the population of individuals with a condition as they exist in the larger population. We also calculated the mean SF-6D score and SD for all joint health states consisting of the co-occurrence of one of the AUD categories and at least one of the health condition/disorder categories: lifetime, past year, or prior to past year AUD, and at least one physical condition, mental health condition, or substance use disorder. Each of these joint states included at least the two identified states and could include other states as well: for example, past year AUD and physical health condition was defined as *at least* the presence of these two states in tandem, not excluding any other AUD or any mental health condition or substance use disorder.

Finally, to isolate the HRQoL associated with AUD, we estimated linear regression models to predict SF-6D score as a function of AUD status controlling for co-occurring conditions, WHO

alcohol consumption risk level, and respondent demographic characteristics (gender, age, education, race/ethnicity). We used ordinary least squares (OLS), adjusted for survey sampling strata and weights, and tested the significance of regression coefficients at a p-value of 0.01 due to the precision afforded by our large sample size; OLS is commonly used to model utility scores despite the range being limited to 0–1.(Pullenayegum et al., 2010) We included alcohol consumption measures because prior research suggests the HRQoL associated with AUD health states may vary with consumption levels (Barbosa et al., epub August 15, 2020), and we included consumption by AUD status interaction terms to assess the possible mitigating effect of consumption level on AUD status or the converse. We tested models with all co-occurring conditions included as individual dummy variables and with co-occurring conditions grouped as physical health conditions, mental health conditions, and substance use disorders. Finally, we used Wald tests to assess the statistical significance of multiple comparisons: all interaction terms as a group, medium versus high alcohol consumption risk level, former drinkers versus lifetime abstainers, and past year versus prior to past year AUD. We used Stata 16.1 for all analyses (StataCorp, LLC, College Station, TX).

3. Results

The analytic sample included 36,163 individuals; descriptive statistics are presented in Table 1 (frequencies presented are for the unweighted sample, proportions are weighted to reflect the US population). Of these, 9,974 individuals (29 %) reported AUD at some point in their lifetime. Eleven percent (4,513) reported never drinking, 40 % were currently abstinent, 40 % were low risk per WHO alcohol consumption risk level, 4% were medium risk, and 5% were high or very high risk.(World Health Organization, 2000) About half (54 %) reported at least one physical health condition, roughly the same among those reporting never and lifetime AUD (54 % and 53 % respectively); 29 % reported at least one mental health condition with 45 % of those with lifetime AUD and 23 % of those who never experienced AUD; and 22 % reported any substance use disorder—with nicotine comprising the most common type (20 %), and all substance use disorders were more commonly reported among individuals experiencing lifetime AUD than those not (40 % versus 14 % respectively). Combinations of physical and mental health conditions were slightly less prevalent among individuals with lifetime AUD compared with individuals never reporting AUD (8% versus 10 %, respectively), while combinations of mental health and substance use disorders were slightly more likely (7% versus 4%), and other combinations were about the same.

SF-6D utilities for the joint health states of each AUD status with each physical health condition, mental health condition, and substance use disorder are presented in Table 2, as well as the SF-6D utilities for the single health states of each AUD status and each health condition/disorder (meaning the utility for anyone who reported at least that AUD status or at least that health condition/disorder regardless of whatever other health condition they may have had). The mean SF-6D utilities for all AUD states were similar: lifetime AUD was 0.7623 (SD = 0.1436), past year AUD was 0.7625 (0.1377), and only prior to past year AUD was 0.7622 (0.1488). Overall, mean SF-6D utilities for the population with conditions other than AUD were generally lower than mean SF-6D utilities for AUD (lower score equates with worse HRQoL), meaning that the utility decrement associated with other-than-AUD conditions was larger than that for AUD, or the HRQoL associated with AUD was better than the HRQoL of other conditions/disorders. For

example, the mean SF-6D utility associated with any physical health condition was 0.7480 (0.1523) compared to 0.7623 (0.1436) for lifetime AUD. Similarly, the mean SF-6D utility associated with any mental health condition was 0.7119 (0.1483) and any substance use disorder was 0.7370 (0.1561), both lower than that for lifetime, past year, and prior to past year AUD (Table 2).

Table 2. SF-6D utilities for AUD joint health states with physical and mental health conditions and substance use disorders.

Physical health conditions	General Population with Health Condition Mean (SD) n	Lifetime AUD ¹	Past Year AUD	Only Prior to Past Year AUD
		0.7623 (0.1436) 9,974	0.7625 (0.1377) 5,123	0.7622 (0.1488) 4,851
		AUD Population with Health Condition Mean (SD) n		
Any Physical health condition ^s	0.7480 (0.1523) 18,679	0.7234 (0.1494) 5,097	0.7225 (0.1355) 2,236	0.7240 (0.1536) 2,861
Anemia	0.6998 (0.1525) 1,974	0.6791 (0.1402) 553	0.6815 (0.1317) 259	0.6776 (0.1459) 294
Arthritis	0.7022 (0.1588) 6,464	0.6719 (0.1553) 1,554	0.6667 (0.1487) 528	0.6740 (0.1580) 1,026
Bowel condition ^a	0.6728 (0.1588) 1,256	0.6369 (0.1517) 401	0.6694 (0.1337) 156	0.6187 (0.1583) 245
Breast Cancer	0.7191 (0.1475) 208	0.6660 (0.1515) 37	0.6892 (0.1777) 14	0.6505 (0.1336) 23
Cancers ^b	0.7216 (0.1598) 1,107	0.7130 (0.1659) 289	0.7222 (0.1504) 99	0.7093 (0.1720) 190
Chest Pain	0.6473 (0.1643) 1,527	0.6402 (0.1640) 479	0.6512 (0.1500) 212	0.6325 (0.1730) 267
Cirrhosis	0.6407 (0.1663) 130	0.6215 (0.1610) 58	0.5730 (0.1127) 30	0.6731 (0.1886) 28
Diabetes	0.7213 (0.1588) 3,501	0.7092 (0.1551) 667	0.7067 (0.1623) 212	0.7101 (0.1525) 455
Difficulty Sleeping	0.6605 (0.1574) 2,770	0.6454 (0.1531) 959	0.6575 (0.1505) 420	0.6372 (0.1544) 539
Epilepsy	0.6608 (0.1504) 317	0.6312 (0.1538) 117	0.6538 (0.1474) 58	0.6087 (0.1581) 59
Fibromyalgia	0.6047 (0.1499) 728	0.5863 (0.1387) 213	0.5767 (0.1222) 59	0.5893 (0.1437) 154
Hardening of Arteries	0.6763 (0.1524) 459	0.6714 (0.1609) 126	0.6293 (0.1292) 39	0.6879 (0.1696) 87
Heart Attack	0.6711 (0.0125) 308	0.6793 (0.1646) 79	0.6694 (0.0981) 34	0.6850 (0.1934) 45
High Blood Pressure	0.7365 (0.1569) 8,946	0.7159 (0.1557) 2,088	0.7140 (0.1501) 843	0.7169 (0.1587) 1,245
High Cholesterol	0.7444 (0.1564) 6,682	0.7250 (0.1552) 1,610	0.7223 (0.1488) 615	0.7265 (0.1587) 995
High Triglycerides	0.7411 (0.1550) 2,555	0.7269 (0.1571) 680	0.7214 (0.1520) 255	0.7300 (0.1600) 425
	0.7238 (0.1559)	0.6887 (0.1483)	0.6928 (0.1597)	0.6826 (0.1319)

		Lifetime AUD^l	Past Year AUD	Only Prior to Past Year AUD
Human Immunodeficiency Virus	233	86	49	37
Lung Condition ^c	0.6746 (0.1586) 1,953	0.6530 (0.1551) 645	0.6619 (0.1525) 260	0.6479 (0.1565) 385
Nerve Condition ^d	0.6580 (0.1679) 297	0.6246 (0.1737) 87	0.6171 (0.1337) 24	0.6270 (0.1855) 63
Osteoporosis	0.6962 (0.1645) 1,313	0.6403 (0.1623) 225	0.6540 (0.1575) 68	0.6351 (0.1643) 157
Other Heart Condition ^e	0.6945 (0.1573) 1,522	0.6902 (0.1587) 382	0.6880 (0.1392) 126	0.6911 (0.1666) 256
Other Liver Condition ^f	0.6827 (0.1665) 365	0.6696 (0.1699) 171	0.6677 (0.1499) 72	0.6709 (0.1836) 99
Other Nerve Condition ^g	0.6574 (0.1597) 3,432	0.6438 (0.1572) 1,069	0.6639 (0.1565) 411	0.6339 (0.1567) 658
Pancreatitis	0.6538 (0.1666) 125	0.6129 (0.1859) 49	0.6152 (0.1432) 21	0.6116 (0.2086) 28
Rapid Heartbeat	0.6688 (0.1570) 1,635	0.6507 (0.1544) 523	0.6616 (0.1387) 207	0.6449 (0.1621) 316
Sexually Transmitted Disease	0.7334 (0.1439) 324	0.7137 (0.1412) 162	0.7271 (0.1381) 103	0.6896 (0.1446) 59
Stomach Ulcer	0.6737 (0.1678) 936	0.6638 (0.1591) 337	0.6766 (0.1495) 151	0.6551 (0.1651) 186
Stroke	0.6313 (0.1595) 296	0.5488 (0.1595) 54	0.5673 (0.1751) 18	0.5411 (0.1541) 36
Traumatic Brain Injury	0.6584 (0.1503) 173	0.6559 (0.1569) 66	0.6973 (0.1453) 40	0.5984 (0.1568) 26
Mental health conditions	General Population with Health Condition	Lifetime AUD	Any Past Year AUD	Only Prior to Past Year AUD
Any Mental health condition ^s	0.7119 (0.1483) 10,824	0.7049 (0.1429) 4,739	0.7130 (0.1355) 2,520	0.6969 (0.1496) 2,219
Bipolar Disorders ^h	0.6913 (0.1502) 951	0.6766 (0.1432) 584	0.6797 (0.1383) 332	0.6732 (0.1484) 252
Depressive Disorders ⁱ	0.6703 (0.1398) 4,772	0.6592 (0.1304) 2,067	0.6681 (0.1237) 1,135	0.6494 (0.1367) 932
Eating Disorders ^j	0.7028 (0.1484) 383	0.6812 (0.1355) 187	0.6909 (0.1220) 102	0.6696 (0.1500) 85
Generalized Anxiety ^k	0.6662 (0.1485) 2,874	0.6548 (0.1396) 1,322	0.6716 (0.1317) 668	0.6396 (0.1449) 654
Personality Disorders ^l	0.6948 (0.1493) 5,217	0.6936 (0.1442) 2,929	0.7042 (0.1348) 1,639	0.6820 (0.1531) 1,290
Phobias ^m	0.7061 (0.1523) 2,669	0.6922 (0.1481) 1,129	0.7061 (0.1405) 550	0.6808 (0.1514) 579
Post-Traumatic Stress Disorder	0.6528 (0.1494) 1,767	0.6467 (0.1432) 931	0.6583 (0.1370) 465	0.6367 (0.1477) 466
Schizotypal Disorder	0.6752 (0.1502) 2,420	0.6658 (0.1428) 1,273	0.6859 (0.1343) 729	0.6422 (0.1488) 544

		Lifetime AUD ¹	Past Year AUD	Only Prior to Past Year AUD
Substance Use Disorders	General Population with Health Condition	Lifetime AUD	Any Past Year AUD	Only Prior to Past Year AUD
Any Substance Use Disorder [§]	0.7370 (0.1561) 7,889	0.7277 (0.1493) 4,133	0.7360 (0.1420) 2,445	0.7173 (0.1574) 1,688
Cannabis	0.7302 (0.1432) 971	0.7225 (0.1397) 721	0.7260 (0.1358) 593	0.7084 (0.1542) 128
Cocaine and Stimulants	0.6861 (0.1313) 245	0.6791 (0.1267) 200	0.6910 (0.1253) 158	0.6420 (0.1253) 42
Heroin and Opioids	0.6165 (0.1422) 356	0.6179 (0.1403) 237	0.6377 (0.1453) 155	0.5837 (0.1247) 82
Nicotine	0.7383 (0.1563) 7,278	0.7276 (0.1499) 3,756	0.7341 (0.1432) 2,153	0.7201 (0.1570) 1,603
Other Drugs ⁿ	0.6900 (0.1474) 73	0.6938 (0.1467) 55	0.6939 (0.1463) 50	0.6916 (0.1710) 5
Sedative	0.6352 (0.1307) 132	0.6348 (0.1243) 92	0.6445 (0.1172) 61	0.6144 (0.1377) 31

¹ **AUD:** Alcohol Use Disorder.

^a **Bowel condition:** NESARC variable that includes: inflammatory bowel disease, irritable bowel syndrome.

^b **Cancers:** Combined variable created from the following NESARC variables: liver; mouth, tongue, throat, and esophagus; other (unspecified) cancer.

^c **Lung condition:** Combined variable created from the following NESARC variables: bronchitis; emphysema; pneumonia; influenza; tuberculosis.

^d **Nerve condition:** NESARC variable that includes: reflex sympathetic dystrophy, complex regional pain syndrome.

^e **Other heart condition:** Any heart disease not specifically queried in NESARC-III.

^f **Other liver condition:** Any liver disease not specifically queried in NESARC-III.

^g **Other nerve condition:** NESARC variable that includes: nerve pain in back, arms, or legs.

^h **Bipolar disorders:** Combined variable created from the following NESARC variables: manic or hypomanic bipolar disorders; other bipolar disorders.

ⁱ **Depressive disorders:** Combined variable created from the following NESARC variables: major or episodic depressive disorder; dysthymic; manic or hypomanic depressive disorder.

^j **Eating disorders:** Combined variable created from the following NESARC variables: bulimia; anorexia nervosa; binge eating.

^k **Generalized anxiety:** Combined variable created from the following NESARC variables: generalized anxiety disorder; agoraphobia; panic disorder.

^l **Personality disorders:** Combined variable created from the following NESARC variables: borderline personality; conduct disorder; antisocial disorder.

^m **Phobias:** Combined variable created from the following NESARC variables: specific phobia; social phobia.

ⁿ **Other drugs:** Combined variable created from the following NESARC variables on substance use: hallucinogens, solvents, club drugs, all other not queried in NESARC-III.

[§] **Any (physical, mental, substance):** All (physical, mental, substance) conditions appearing in the NESARC-III.

Mean SF-6D utilities for AUD with co-occurring conditions were generally—but not always—lower than SF-6D utilities for either AUD alone or the health condition/disorder without AUD (Table 2). In other words, SF-6D utilities for joint health states of AUD and a co-occurring condition were oftentimes lower—worse—than the SF-6D utility for either of the contributing health states. For example, the joint health state of any AUD status and any physical health condition was lower than either component state: combined utility was approximately 0.72 while separately they were approximately 0.76 and 0.74 for AUD and physical health conditions respectively. A similar pattern was seen for the joint state of AUD and any mental health

condition and AUD and any substance use disorder, wherein the mean SF-6D utility for the joint health state was lower than that for the component health states (Table 2).

Our regression model results, shown in Table 3, revealed the independent contribution of AUD and co-occurring conditions to SF-6D utility scores, controlling for alcohol consumption risk level and demographic characteristics. Compared to never having AUD, individuals with past year or prior to past year AUD had slightly worse HRQoL: prior to past year AUD was associated with a 0.0163 (standard error—SE = 0.0023; $p < 0.01$) lower SF-6D score, and past year AUD was associated with a 0.0304 point lower SF-6D score (0.0027; $p < 0.01$; Wald test, $F = 17.92$, $p < 0.01$). By comparison, having had any physical health condition was associated with a 0.0621 point decrement in SF-6D score (0.0023; $p < 0.01$), any mental health condition with a 0.0843 point decrement (0.0025; $p < 0.01$), and any substance use disorder with a 0.0380 point decrement (0.0023; $p < 0.01$). Compared to low-risk alcohol consumption, non-drinking, whether lifelong abstinence or “former” drinking (i.e., abstinence following prior year(s) consumption), was associated with a 0.02 point decrease in SF-6D score (0.0028 and 0.0017 respectively, $p < 0.01$; Wald test, $F = 0.11$, $p = 0.7448$); the SF-6D scores associated with higher consumption risk levels were not statistically different from low-risk consumption (Table 3). Interaction terms between AUD health states and alcohol risk consumption levels were non-significant collectively (Wald test, $F = 1.28$, $p = 0.2711$; on-line supplementary material (supplementary material can be found by accessing the online version of this paper at <http://dx.doi.org> and by entering doi: ...)) and not included in model; a full model with all co-occurring conditions included individually and interaction terms is included in the same on-line supplementary material.

Table 3. Linear regression model predicting SF-6D scores as a function of AUD and co-occurring condition categories.

Alcohol Use Disorder (ref = no AUD)	Coefficient (SE)
Prior to past year AUD ¹	-0.0163* (0.0023)
Past Year AUD	-0.0304* (0.0027)
Co-occurring conditions (ref = condition category not reported)	
Any physical health condition [§]	-0.0621* (0.0023) ^{ss}
Any mental health condition [§]	-0.0843* (0.0025)
Any substance use disorder [§]	-0.0380* (0.0023)
WHO alcohol consumption risk level ³ (ref = low risk)	
No Risk: Lifetime abstinence ⁴	-0.0209* (0.0028)
No Risk: Former drinkers ⁵	-0.0200* (0.0017)
Medium risk	0.0059 (0.0040)
High risk ⁶	-0.0060 (0.0044)
Demographic characteristics	
Female (ref = male)	-0.0254* (0.0018)
Age (years; ref=<21): 21–45	-0.0268* (0.0036)
46–65	-0.0418* (0.0041)
66+	-0.0504* (0.0045)
Educational attainment (ref = no college):	
Some College	0.0127* (0.0024)
Degree ²	0.0292* (0.0021)
Race/ethnicity (ref = White, non-Hispanic):	
Black, non-Hispanic	-0.0111* (0.0030)

Alcohol Use Disorder (ref = no AUD)	Coefficient (SE)
American Indian/Alaskan native, non-Hispanic	-0.0151 (0.0079)
Asian/Native Hawaiian/other Pacific Islander, non-Hispanic	-0.0045 (0.0038)
Hispanic, any race	0.0071* (0.0025)
_constant	0.9052* (0.0039)
Wald Tests	F-Statistic (p-value)
Former Drinkers = Lifetime Abstinence	0.1100 (0.7448)
Medium Risk Consumption = High Risk Consumption	4.63 (0.0335)
Past year AUD = Prior to past year AUD	17.92* (0.0000)

* = significant at $p < 0.01$; Ref = reference group.

¹ **AUD:** Alcohol Use Disorder; SE = standard error.

² **Degree:** Associate, technical, bachelor's, or higher.

³ **WHO alcohol consumption risk levels:** World Health Organization's criteria for risk of consumption on a single drinking day: World Health Organization International Guide for Alcohol Consumption and Related Harm, WHO, Geneva, 2000.

⁴ **No risk: lifetime abstinence:** no alcohol consumption in the past year and prior to past year.

⁵ **No risk: former drinkers:** no alcohol consumption in the past year but reported alcohol consumption prior to past year.

⁶ **High risk:** high risk and very high risk WHO consumption risk levels.

[§] **Any (physical, mental, substance):** All (physical, mental, substance) conditions appearing in the National Epidemiological Survey on Alcohol and Related Conditions-III (NESARC-III).

4. Discussion

HRQoL is an important input to economic evaluation, as it is the quality adjustment factor of quality adjusted life years—QALYs—which are the outcome measure used in cost-effectiveness analysis. (Hunink et al., 2014) Estimating QALYs for AUD is complicated by the prevalence of co-occurring health conditions. We found that about half of individuals in the US with a lifetime history of AUD report at least one physical health condition and 40 % or more report co-occurring mental health or substance use disorders. To understand the impact of AUD interventions on HRQoL we must therefore understand the HRQoL of the dual conditions experienced by many individuals with AUD. This descriptive study of the NESARC-III database, a US population survey, demonstrates the HRQoL of AUD as it commonly occurs among the population with other physical, mental health, and substance use conditions. AUD is associated with diminished HRQoL, but to a somewhat lesser extent than the other physical, mental health, or substance use disorders with which it is commonly observed. In fact, among all conditions reported in NESARC-III, mental health conditions as a group are associated with the largest decrement in HRQoL, followed by physical health conditions, any substance use disorder, and then past year AUD. Our results suggest that the impact of AUD on HRQoL may be intertwined with the conditions with which it commonly co-occurs, potentially limiting the benefit accrued by AUD interventions when other conditions are simultaneously present—unless interventions target these co-occurring conditions as well.

Co-occurring mental health conditions and substance use disorders are generally more common among individuals reporting AUD than in the general population, while physical health conditions occur at about the same rate. Economic evaluations of AUD would therefore benefit from including joint health states when assessing the value of interventions; such a perspective would more accurately address the entirety of an individual's health status than limiting the perspective to AUD alone (or any single condition when others may be present). The multitude

of possible combinations of AUD status and other conditions is large, and becomes vast when considering AUD plus more than one additional condition. Hence the availability of utilities for such joint states is quite valuable for calculating QALYs—which we present in this paper to facilitate their inclusion in analyses. Our comprehensive catalog of utilities for health states of AUD plus co-occurring conditions provides researchers and analysts with population-level data for decision analytic and cost-effectiveness modeling, meaning utilities for all individuals included in the national NESARC-III database, which is generally larger and more diverse than samples included in trials, not to mention more convenient than empiric data collection.

The importance of understanding the role of joint health conditions for HRQoL of AUD is highlighted by contrasting the HRQoL decrements associated with past year AUD with prior to past year AUD in our simple means and regression models. Our simple means suggest that former (i.e., prior to past year) AUD may be associated with the same HRQoL as current (i.e., past year) AUD, implying that resolving symptoms of AUD may not be associated with any improvement in HRQoL. This result does not control for any co-occurring health conditions, however, which when accounted for show a somewhat different picture. After controlling for physical and mental health conditions and any substance use disorder, prior to past year AUD was associated with a small but statistically significant improvement in HRQoL relative to past year AUD. In other words, resolution of (current) AUD symptoms was associated with improved HRQoL once the confounding effects of co-occurring conditions were considered. Our regression models further suggested that low levels of alcohol use were associated with improved HRQoL relative to abstinence, even after controlling for AUD and other health conditions. These results extend previous findings on the low HRQoL of abstinence (Barbosa et al., epub August 15, 2020) by controlling for possible explanatory confounders, thereby suggesting that abstinence may be an undesirable state from a HRQoL perspective regardless of its clinical benefit. Our findings have potentially important implications for evolving definitions of AUD recovery that focus on resolution of AUD symptoms and non-abstinent levels of alcohol consumption.(Witkiewitz and Tucker, 2020)

Beyond informing revised concepts of recovery, it is important to understand the dynamics of HRQoL in the context of AUD and co-occurring conditions. While AUD is associated with worse HRQoL, as are nearly all health conditions, we found that AUD plays a relatively minor role in diminished HRQoL because of the prevalence of co-occurring conditions that have a more substantial impact. While controlling for alcohol consumption risk level and co-occurring conditions, we found that past year AUD was associated with a decrease in HRQoL on par with any substance use disorder—of about 0.03 on a 0–1.0 utility scale, while physical and mental health conditions were associated with a decrease of about 0.06 and 0.08 points respectively, approximately double the magnitude of past year AUD. More distant AUD—prior to the past year—was associated with an even smaller HRQoL decrement, of 0.016 points. These results suggest that the diminution in HRQoL reported by individuals with AUD may be masking a more complex dynamic, wherein co-occurring conditions may in fact be driving much of the HRQoL decrement commonly associated with AUD—at least among those individuals with co-occurring conditions. And consequently, interventions targeting AUD alone may not fully “recover” an individual’s HRQoL if solely the AUD is resolved while the co-occurring condition remains. That said, we do not know the temporal relationship between AUD and any co-occurring condition, nor could we explore it in this data set, so it’s unclear whether one

precipitated the other or they existed independently. Capturing the HRQoL of the joint health state of AUD and any co-occurring condition is important to accurately assess the cost-effectiveness AUD-targeted interventions.

As usual, there are caveats to consider in our analysis. Our use of the NESARC-III database limited us to the data collected in the survey: NESARC-III sampled only individuals in non-institutional settings, excluding individuals who are incarcerated and living in long-term institutional settings for whom HRQoL may be different. We cannot extend our conclusions to those populations. Moreover, we were limited to the physical, mental health, and substance use disorders included in NESARC-III, and we cannot report on others nor are we certain that our conclusions would hold if they were included in our analysis. All data in NESARC-III are self-reported, with the accompanying caveats of self-reported data. That said, the NESARC-III survey asked for confirmation of the existence of physical health conditions by a medical professional, adding validity to those reports. And they used the AUDADIS-5 to establish AUD and mental health and substance use disorders, which is not included in many other surveys. We are relatively confident of data quality in NESARC-III because of the infrastructure surrounding the survey administration and data cleaning, and the large, population-based sample adds validity to our results. Our results are based on UK preference weights applied to the collected SF-6D scores, as these are the most currently-available scores although are likely to differ from US preferences; our analysis should be updated when US preference weights are available for the SF-6D. And lastly, utilities are known to differ across measurement instruments, including the SF-6D relative to others. Research shows that the SF-6D is more sensitive to mild conditions as could be the case with AUD, and that it performs better in alcohol disorders than alternatives (the EQ-5D for example). (Brazier et al., 2004; Essex et al., 2014; Kontodimopoulos et al., 2009; McCrone et al., 2009) That said, replication of our results with other utility measures would add validity to our conclusions.

5. Conclusions

In conclusion, consideration of co-occurring conditions in assessing HRQoL of AUD is critical because of the prevalence of such conditions and their outsized influence on HRQoL compared to AUD. Empiric estimation of AUD joint health states allows for inclusion of accurate values in economic evaluation, using values presented in this paper. Consideration of the full person—including all conditions an individual may be experiencing—is a goal of patient-centeredness. Including joint health states in economic evaluations is a step in toward acknowledging the entirety of individuals and integrating a patient-centered perspective into economic analyses.

Contributors

Eve Wittenberg, PhD [*corresponding author*]: conceived of study, directed analysis, interpreted results, wrote first draft of manuscript, approved final version.

Carolina Barbosa, PhD: conceived of study, directed analysis, interpreted results, edited first draft of manuscript, approved final version.

Riley Hein: conducted data analysis, edited first draft of manuscript, approved final version.

Emma Hudson: conducted data analysis, edited first draft of manuscript, approved final version.

Benjamin Thornburg: conducted data analysis, edited first draft of manuscript, approved final version.

Jeremy W. Bray, PhD: conceived of study, directed analysis, interpreted results, edited first draft of manuscript, approved final version.

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Declaration of Competing Interest

The authors have no conflicts to disclose.

References

- American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders, 5th ed. 5th ed., Arlington, VA.
- Ara, R., Wailoo, A.J., 2013. Estimating health state utility values for joint health conditions: a conceptual review and critique of the current evidence. *Med. Decis. Making* 33, 139–153.
- Barbosa, C., Bray, J.W., Dowd, W.N., Barnosky, A., Wittenberg, E., epub August 15, 2020. SF-6D utility scores for alcohol use disorder status and alcohol consumption risk levels in the US population. *Addiction*.
- Brazier, J.E., Roberts, J., 2004. The estimation of a preference-based measure of health from the SF-12. *Med. Care* 42, 851–859.
- Brazier, J., Roberts, J., Tsuchiya, A., Busschbach, J., 2004. A comparison of the EQ-5D and SF-6D across seven patient groups. *Health Econ.* 13, 873–884.
- Dale, W., Basu, A., Elstein, A., Meltzer, D., 2008. Predicting utility ratings for joint health States from single health States in prostate cancer: empirical testing of 3 alternative theories. *Med. Decis. Making* 28, 102–112.
- Essex, H.N., White, I.R., Khadjesari, Z., Linke, S., McCambridge, J., Murray, E., Parrott, S., Godfrey, C., 2014. Quality of life among hazardous and harmful drinkers: EQ-5D over a 1-year follow-up period. *Qual. Life Res.* 23, 733–743.

- Fryback, D.G., Dunham, N.C., Palta, M., Hanmer, J., Buechner, J., Cherepanov, D., Herrington, S.A., Hays, R.D., Kaplan, R.M., Ganiats, T.G., Feeny, D., Kind, P., 2007. US norms for six generic health-related quality-of-life indexes from the National Health Measurement study. *Med. Care* 45, 1162–1170.
- Grant, B.F., Goldstein, R.B., Chou, S.P., Saha, T.D., Ruan, W.J., Huang, B., Smith, S.M., Zhang, H., Jung, J., Pickering, R.P., Aivadyan, C., Greenstein, E., Hasin, D.S., 2011. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-Diagnostic and Statistical Manual of Mental Disorders, fifth edition. Version (AUDADIS-5). National Institute on Alcohol Abuse and Alcoholism, Rockville, MD.
- Grant, B.F., Chu, A., Sigman, R., Amsbury, M., Kali, J., Sugawara, Y., Jiao, R., Ren, W., Goldstein, R., 2014. Source and Accuracy Statement: National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III). National Institute on Alcohol Abuse and Alcoholism, Rockville, MD.
- Grant, B.F., Goldstein, R.B., Saha, T.D., Chou, S.P., Jung, J., Zhang, H., Pickering, R.P., Ruan, W.J., Smith, S.M., Huang, B., Hasin, D.S., 2015. Epidemiology of DSM-5 alcohol use disorder: results from the national epidemiologic survey on alcohol and related conditions III. *JAMA Psychiatry* 72, 757–766.
- Hunink, M., Weinstein, M., Wittenberg, E., et al., 2014. *Decision Making in Health and Medicine: Integrating Evidence and Values*. Cambridge University Press, Cambridge, UK.
- Kontodimopoulos, N., Pappa, E., Papadopoulos, A.A., Tountas, Y., Niakas, D., 2009. Comparing SF-6D and EQ-5D utilities across groups differing in health status. *Qual. Life Res.* 18, 87–97.
- McCrone, P., Patel, A., Knapp, M., Schene, A., Koeter, M., Amaddeo, F., Ruggeri, M., Giessler, A., Puschner, B., Thornicroft, G., 2009. A comparison of SF-6D and EQ-5D utility scores in a study of patients with schizophrenia. *J. Ment. Health Policy Econ.* 12, 27–31.
- National Institute on Alcohol Abuse and Alcoholism, 2020. NESARC-III Data Notes (Accessed July 8 2020). <https://www.niaaa.nih.gov/research/nesarc-iii/data-notes>.
- Neumann, P., Sanders, G., Russel, L., et al., 2017. *Cost-Effectiveness in Health and Medicine*, 2nd ed. Oxford University Press, New York.
- Pullenayegum, E.M., Tarride, J.E., Xie, F., Goeree, R., Gerstein, H.C., O'Reilly, D., 2010. Analysis of health utility data when some subjects attain the upper bound of 1: are Tobit and CLAD models appropriate? *Value Health* 13, 487–494.
- Sacks, J.J., Gonzales, K.R., Bouchery, E.E., Tomedi, L.E., Brewer, R.D., 2015. 2010 national and state costs of excessive alcohol consumption. *Am. J. Prev. Med.* 49, e73–e79.
- Ware Jr., J., Kosinski, M., Keller, S.D., 1996. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med. Care* 34, 220–233.
- Witkiewitz, K., Tucker, J.A., 2020. Abstinence not required: expanding the definition of recovery from alcohol use disorder. *Alcohol. Clin. Exp. Res.* 44, 36–40.

- Witkiewitz, K., Kranzler, H.R., Hallgren, K.A., O'Malley, S.S., Falk, D.E., Litten, R.Z., Hasin, D.S., Mann, K.F., Anton, R.F., 2018. Drinking risk level reductions associated with improvements in physical health and quality of life among individuals with alcohol use disorder. *Alcohol. Clin. Exp. Res.* 42, 2453–2465.
- Wittenberg, E., Bray, J.W., Aden, B., Gebremariam, A., Nosyk, B., Schackman, B.R., 2016. Measuring benefits of opioid misuse treatment for economic evaluation: health-related quality of life of opioid-dependent individuals and their spouses as assessed by a sample of the US population. *Addiction* 111, 675–684.
- Wittenberg, E., Bray, J.W., Gebremariam, A., Aden, B., Nosyk, B., Schackman, B.R., 2017. Joint utility estimators in substance use disorders. *Value Health* 20, 458–465. World Health Organization, 2000. *International Guide for Monitoring Alcohol Consumption and Related Harm*. World Health Organization, Geneva, Switzerland.

Health-related quality of life of alcohol use disorder with co-occurring conditions in the US population

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On-line Supplementary Information

This material supplements, but does not replace, the peer-reviewed paper in *Drug and Alcohol Dependence*

Linear regression model predicting SF-6D scores as a function of AUD and individual co-occurring conditions present in NESARC-III

	Coefficient (SE)
Alcohol Use Disorder (ref=no AUD)	
Prior to past year AUD ¹	-0.0174* (0.0033)
Past Year AUD	-0.0290* (0.0027)
Physical health condition (ref=condition not reported)	
Anemia	-0.0192* (0.0040)
Arthritis	-0.0392* (0.0022)
Bowel condition ^a	-0.0208* (0.0048)
Breast cancer	-0.0162 (0.0116)
Cancers ^b	-0.0184 (0.0051)
Chest pain	-0.0279* (0.0057)
Cirrhosis	-0.0319 (0.0167)
Diabetes	-0.0201* (0.0029)
Difficulty sleeping	-0.0371* (0.0035)
Epilepsy	-0.0446* (0.0089)
Fibromyalgia	-0.0595* (0.0072)
Hardening of arteries	-0.0165 (0.0082)
Heart attack	-0.0087 (0.0106)
High blood pressure	-0.0184* (0.0023)
High cholesterol	-0.0049 (0.0027)
High triglycerides	0.0037 (0.0036)
Human immunodeficiency virus	-0.0157 (0.0129)
Lung condition ^c	-0.0301* (0.0038)
Nerve condition ^d	-0.0089 (0.0118)
Osteoporosis	-0.0124 (0.0053)
Other heart condition ^e	-0.0175* (0.0039)
Other liver condition ^f	-0.0121 (0.0094)
Other nerve condition ^g	-0.0687* (0.0040)
Pancreatitis	-0.0222 (0.0142)
Rapid heartbeat	-0.0143* (0.0049)
Sexually transmitted disease	-0.0050 (0.0096)
Stomach ulcer	-0.0131* (0.0055)
Stroke	-0.0535* (0.0095)
Traumatic brain injury	-0.0232 (0.0151)
Mental health condition (ref=condition not reported)	
Bipolar disorders ^h	0.0021 (0.0048)

Depressive disorders ⁱ	-0.0724* (0.0027)
Eating disorders ^j	0.0008 (0.0081)
Generalized anxiety ^k	-0.0367* (0.0038)
Personality disorders ^l	-0.0273* (0.0030)
Phobias ^m	-0.0195* (0.0034)
Post-traumatic stress disorder	-0.0257* (0.0046)
Schizotypal disorder	-0.0131* (0.0043)
Substance use disorder (ref=disorder not reported)	
Cannabis	-0.0066 (0.0062)
Cocaine and stimulants	-0.0168 (0.0094)
Heroin and opioids	-0.0557* (0.0090)
Nicotine	-0.0229* (0.0022)
Other drugs ⁿ	-0.0042 (0.0185)
Sedative	0.0009 (0.0127)
WHO alcohol consumption risk level³ (ref=low risk)	
No risk: lifetime abstinence ⁴	-0.0129* (0.0026)
No risk: former drinkers ⁵	-0.0138* (0.0020)
Medium risk	0.0101 (0.0063)
High risk ⁶	-0.0038 (0.0081)
Demographic characteristics	
Female (ref=male)	-0.0186* (0.0017)
Age (years; ref=<21): 21 to 45	-0.0205* (0.0034)
46 to 65	-0.0280* (0.0038)
66+	-0.0273* (0.0043)
Educational attainment (ref=no college): Some College	0.0108* (0.0023)
Degree ²	0.0243* (0.0020)
Race/ethnicity (ref=White, non-Hispanic):	
Black, non-Hispanic	-0.0145* (0.0029)
American Indian/Alaskan native, non-Hispanic	0.0005 (0.0067)
Asian/Native Hawaiian/other Pacific Islander, non-Hispanic	-0.0098 (0.0038)
Hispanic, any race	0.0046 (0.0026)
Interaction variables (WHO Risk * AUD)	
Former Drinkers*Prior to Past Year AUD	0.0090 (0.0046)
Former Drinkers*Past Year AUD	-0.0016 (0.0111)
Medium Risk*Prior to Past Year AUD	-0.0140 (0.0129)
Medium Risk*Past Year AUD	-0.0127 (0.0086)
High Risk*Prior to Past Year AUD	0.0071 (0.0161)
High Risk*Past Year AUD	-0.0028 (0.0095)
_constant	0.8835* (0.0039)

Wald Tests	F-Statistic (p-value)
Former Drinkers = Lifetime Abstinence	0.1500 (0.6971)
Medium Risk Consumption = High Risk Consumption	1.8900 (0.1724)
Prior to past year AUD = past year AUD	8.3100* (0.0047)
Joint Significance of Interaction Variables	1.2900 (0.2681)

* = significant at $p < 0.01$; Ref=reference group

¹**AUD:** Alcohol Use Disorder; SE=standard error

²**Degree:** Associate, technical, bachelor's, or higher

³**WHO alcohol consumption risk levels:** World Health Organization's criteria for risk of consumption on a single drinking day: World Health Organization International Guide for Alcohol Consumption and Related Harm, WHO, Geneva, 2000.

⁴**No risk: lifetime abstinence:** no alcohol consumption in the past year and prior to past year

⁵**No risk: former drinkers:** no alcohol consumption in the past year but reported alcohol consumption prior to past year

⁶**High risk:** high risk and very high risk WHO consumption risk levels

^a**Bowel condition:** NESARC variable that includes inflammatory bowel disease, irritable bowel syndrome

^b**Cancers:** Combined variable created from the following NESARC variables: liver; mouth, tongue, throat, and esophagus; other (unspecified) cancer

^c**Lung condition:** Combined variable created from the following NESARC variables: bronchitis, emphysema, pneumonia, influenza, tuberculosis

^d**Nerve condition:** NESARC variable that includes reflex sympathetic dystrophy, complex regional pain syndrome

^e**Other heart condition:** Any heart disease not specifically queried in NESARC-III

^f**Other liver condition:** Any liver disease not specifically queried in NESARC-III

^g**Other nerve condition:** NESARC variable that includes nerve pain in back, arms, or legs

^h**Bipolar disorders:** Combined variable created from the following NESARC variables: manic or hypomanic bipolar disorders; other bipolar disorders

ⁱ**Depressive disorders:** Combined variable created from the following NESARC variables: major or episodic depressive disorder, dysthymic, manic or hypomanic depressive disorder

^j**Eating disorders:** Combined variable created from the following NESARC variables: bulimia, anorexia nervosa, binge eating

^k**Generalized anxiety:** Combined variable created from the following NESARC variables: generalized anxiety disorder, agoraphobia, panic disorder

^l**Personality disorders:** Combined variable created from the following NESARC variables: borderline personality, conduct disorder, antisocial disorder

^m**Phobias:** Combined variable created from the following NESARC variables: specific phobia, social phobia

ⁿ**Other drugs:** Combined variable created from the following NESARC variables on substance use: hallucinogens, solvents, club drugs, all other not queried in NESARC-III