HHS Public Access

Author manuscript

Drug Alcohol Rev. Author manuscript; available in PMC 2023 July 01.

Published in final edited form as:

Drug Alcohol Rev. 2022 July ; 41(5): 1245–1253. doi:10.1111/dar.13470.

Estimating Alcohol-Attributable Liver Disease Mortality: A Comparison of Methods

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Abstract

Introduction: Alcohol is a leading contributor to liver disease, however, estimating the proportion of liver disease deaths attributable to alcohol use can be methodologically challenging.

Methods: We compared three approaches for estimating alcohol-attributable liver disease deaths (AALDD), using the U.S. as an example. One involved summing deaths from alcoholic liver disease and a proportion from unspecified cirrhosis (direct method); two used population attributable fraction (PAF) methodology, including one that adjusted for per capita alcohol sales. For PAFs, the 2011–2015 Behavioral Risk Factor Surveillance System and per capita sales from the Alcohol Epidemiologic Data System were used to derive alcohol consumption prevalence estimates at various levels (excessive alcohol use was defined by medium and high consumption levels). Prevalence estimates were used with relative risks from two meta-analyses, and PAFs were applied to the 2011–2015 average annual number of deaths from alcoholic cirrhosis and unspecified cirrhosis (using National Vital Statistics System data) to estimate AALDD.

Results: The number of AALDD was higher using the direct method (28,345 annually) than the PAF methods, but similar when alcohol prevalence was adjusted using per capita sales and all alcohol consumption levels were considered (e.g., 25,145 AALDD). Using the PAF method, disaggregating non-drinkers into lifetime abstainers and former drinkers to incorporate relative risks for former drinkers yielded higher AALDD estimates (e.g., 27,686) than methods with all non-drinkers combined.

Discussion and Conclusions: Using PAF methods that adjust for per capita sales and model risks for former drinkers yield more complete and possibly more valid AALDD estimates.

Keywords

Alcohol; alcoholic liver disease mortality; cirrhosis; population attributable fractions

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None of the authors have any competing interests to declare, including funding from any commercial entities including alcohol companies or organizations representing the alcohol industry.

INTRODUCTION

Chronic liver disease, which typically manifests as liver cirrhosis, is an important and increasing cause of death globally, including that caused or exacerbated by alcohol consumption (1, 2). In 2016, chronic liver disease was the 11th leading cause of death worldwide, accounting for approximately two percent of all deaths. Of those deaths, approximately half are due to alcohol (2). In the U.S. in 2019, there were 24,000 deaths from alcoholic liver disease (3, 4); mortality rates from alcohol-attributable liver disease have increased particularly among women and younger age groups (5). For conditions such as alcoholic cirrhosis or alcoholic hepatitis, all deaths are fully attributable to alcohol; however, alcohol can also contribute to mortality for other emerging causes of liver disease (e.g., hepatitis C, 'non-alcoholic' fatty liver disease).

Given the rising and projected increases in liver disease mortality, including alcohol-attributable cirrhosis (6), and its contribution to declines in life expectancy (7), it is important to have valid estimates of the contribution of alcohol to all liver disease deaths. However, there is no single laboratory test to reliably indicate that alcohol may be playing a role in any particular case of liver disease, and information about alcohol consumption may not be collected or recorded reliably in medical records, potentially resulting in underestimates of alcohol involvement (8, 9).

Accurately estimating the number and proportion of liver disease deaths from alcohol use is important for public health surveillance of alcohol-attributable harm, and the estimates can be derived using two broad approaches. First, a 'direct' approach that sums deaths from fully alcohol-attributable liver disease and apportions deaths from unspecified liver disease based on an estimated proportion of unspecified cirrhosis deaths actually being alcohol-attributable (10). Second, an 'indirect' approach using population attributable fraction (PAF) methodology, which considers the prevalence of drinking at various levels of consumption and the risk of dying from a particular cause at each level of drinking.

Both approaches have advantages and limitations. In the U.S., the Centers for Disease Control and Prevention (CDC) uses the direct approach in its Alcohol-Related Disease Impact (ARDI) application, a tool that estimates the number of alcohol-related deaths in the U.S. from 58 causes relative (11). However, the most recent estimate for the proportion of unspecified cirrhosis deaths that are due to alcohol use is based on a 1986 follow-back survey of next of kin (10) and may not represent the current epidemiology of the causes of chronic liver disease.

Global endeavors, such as the World Health Organization's (WHO) Global Status Report on Alcohol and Health and the Institute for Health Metrics and Evaluation's (IHME) Global Burden of Disease study, have typically relied on indirect methods involving PAF methodology to assess alcohol-attributable mortality for chronic health conditions, such as liver disease (12, 13). These methods use meta-analyzed relative risk estimates for various levels of alcohol consumption for multiple etiologies of liver disease mortality, and combine these relative risks with alcohol use prevalence estimates to calculate alcohol-attributable fractions. However, the original studies underlying such meta-analyses may contain outdated

information, be influenced by the distribution of liver disease etiology, or both. Further, prevalence estimates for various levels of consumption are based on self-reported surveys, which underestimate alcohol consumption relative to estimates of apparent per capita consumption based on alcohol sales and tax receipt data (14, 15).

We are not aware of previous studies directly comparing indirect and direct methods of assessing the burden of alcohol-attributable liver disease. Therefore, the purpose of this study was to compare these approaches for calculating the average annual number of alcohol-attributable liver disease deaths (AALDD), using the U.S. as an example. We examined differences in AALDD by sex, level of alcohol consumption (all consumption levels versus excessive drinking), selection of relative risk estimates, the inclusion of risk estimates for former drinkers, and the type of relative risk function (categorical versus continuous).

METHODS

Overview

We compared several approaches for estimating AALDD in the U.S. Method 1, which is currently used in the CDC's ARDI application, involves summing all deaths from alcoholic liver disease and adding 40% of deaths from unspecified cirrhosis; the 40% alcohol-attributable proportion is based on a study that conducted interviews with next of kin for people who died by liver disease (10, 11). Method 2 involves PAF methodology in which prevalence estimates for low, medium, and high levels of alcohol consumption were calculated using the 2011–2015 Behavioral Risk Factor Surveillance System (BRFSS) after 'indexing'. This indexing procedure is a survey-based adjustment, described elsewhere (16), which adjusts each respondent's self-reported consumption to account for the number of drinks consumed during binge drinking occasions, if those quantities exceed usual consumption on days when alcohol is consumed. Method 3 also uses PAF methodology using BRFSS-based alcohol consumption prevalence estimates, but each respondents' average daily alcohol consumption prevalence estimates were calculated after adjusting so that population-weighted consumption accounted for 73% of presumed alcohol per capita consumption (17) based on alcohol sales and tax data from Alcohol Epidemiological Data System (18). This 73% level was chosen to align with alcohol consumption reported in U.S.-based epidemiological cohort studies used to derive relative risk estimates for alcohol consumption (17, 19). For each method, we also examined the percentage of all liver disease deaths that were attributable to alcohol, using the same ICD-10 codes in the denominator as used to calculate AALDD in the study.

In Method 1, it is not possible to determine the contribution of various levels of alcohol consumption to AALDD because it does not rely on PAF calculations; however, in ARDI these deaths are considered to be from excessive drinking. For Methods 2 and 3, we examined AALDD for any level of average daily alcohol consumption (low, medium, and high) and for excessive drinking (medium and high consumption). In Methods 2 and 3, low average daily consumption was defined as an average of >0–≤1 standard drinks/day (women) or >0–≤2 drinks/day (men), medium consumption was defined as >1–≤2 drinks/day (women) or >2–≤4 drinks/day (men), and high consumption was defined as

>2 drinks/day (women) or >4 drinks/day (men) (17). To determine the number of deaths from excessive drinking, relative risks were calculated in two ways. First, relative risks for medium and high consumption were rescaled such that they were divided by the relative risk for low consumption, so the risk of AALDD among excessive drinkers was relative to the risk among people who drink low levels of alcohol (20). Second, we also used relative risks for excessive drinking that were not rescaled for which the non-drinkers were the reference group.

Data Sources Used to Calculate the Prevalence of Alcohol Consumption

Self-reported alcohol consumption from the BRFSS was used as the foundation for calculating average daily consumption prevalence estimates for Methods 2 and 3. The BRFSS is a state-based telephone survey of approximately 400,000 non-institutionalized, U.S. adults aged ≥18 years, conducted in all states, the District of Columbia, and U.S. territories (though data from U.S. territories were not included in this analysis) (4). It is conducted via random-digit-dialing. The 2011–2015 BRFSS data (median response rate range: 45.2–49.7%) were used to align with the years of data in CDC's ARDI application at the time of this study.

U.S. data for population-level apparent consumption (referred to as "per capita sales" and used in Method 3 to adjust prevalence estimates) were obtained from the National Institute of Alcohol Abuse and Alcoholism's Alcohol Epidemiologic Data System (18). The data are based on the volume of each alcoholic beverage type sold annually in each state from sales receipts reports and shipment data from state government and industry sources. Per capita sales were derived by summing beverage-specific consumption and dividing by the number of persons in the U.S. ≥18 years.

Relative Risk Estimates for Mortality

Methods 2 and 3 use PAF methodology in which the prevalence estimate for each level of consumption is combined with its corresponding relative risk estimate. For these methods, we compared AALDD using relative risk estimates from two meta-analyses (see relative risk estimates in Supplementary Table 1). One relative risk function is currently used by the WHO from Rehm et al. (12, 21) and a second relative risk function is from the Institute of Health Metrics and Evaluation (IHME) Global Burden of Disease study (13). Both meta-analyses present continuous relative risk functions. To create categorical relative risk estimates corresponding to the low, medium, and high levels of average daily consumption used in the CDC's ARDI application, the relative risk at the midpoint for the low and medium consumption groups was used (11, 20); for the high volume group, we calculated the risk corresponding to the median consumption value given that this group has no upper bound and the distribution is highly skewed.

We also assessed differences in the estimated number of AALDD with categorical relative risks versus continuous functions using the WHO relative risks. AALDD based on categorical relative risks were estimated using the three levels of average daily consumption (low, medium, and high) from the ARDI application. AALDD based on continuous risks were calculated using the WHO continuous risk functions (21), which were described in

the International Model of Alcohol Harms and Policies (InterMAHP) application (22, 23). To compare categorical and continuous relative risks, deaths from all levels of alcohol consumption were estimated (not deaths from excessive drinking).

To assess the impact of including information on former drinkers in estimates of AALDD, we conducted an additional analysis to reclassify non-drinkers into former drinkers versus lifetime abstainers, and recalculated deaths for Methods 2 and 3 after incorporating relative risk estimates for former drinkers. However, former drinkers may have drunk excessively and may have stopped drinking because of an alcohol-related health condition, including liver disease (24). We estimated the percentage of non-drinkers who were former drinkers versus lifetime abstainers based on U.S. adult respondents from the 2015 National Survey on Drug Use and Health (25). Non-drinkers were those who reported no alcohol consumption in past year, former drinkers were defined as non-drinkers who reported a history of lifetime alcohol consumption, and lifetime abstainers were non-drinkers who reported no history of lifetime alcohol consumption. The relative risk for former drinkers and developing liver disease was obtained from another meta-analysis (26).

Data Source for Mortality

Mortality data for 2011–2015 were from CDC's National Vital Statistics System based on ICD-10 codes for deaths from alcoholic liver disease and unspecified liver cirrhosis (27). Alcoholic liver disease (i.e., fully alcohol-attributable) included ICD-10 codes K70.0-K70.4 and K70.9, and unspecified liver cirrhosis (partially attributable to alcohol) included K74.0-K74.2, K74.6, K76.0, K76.7 and K76.9 (20, 28).

RESULTS

Compared with the survey-based adjustment that adjusts consumption data to account for binge drinking (Method 2), adjusting consumption data to account for 73% of per capita sales (Method 3) resulted in higher prevalence estimates of medium and high average daily consumption, and lower prevalence estimates for low average daily consumption (Table 1). For example, for men, the prevalence of medium consumption was 11.0% and high consumption was 10.6% using Method 3, compared with 6.4% for medium consumption and 3.5% for high consumption using Method 2. Among men, 40.7% were non-drinkers, of which 15.6% were classified as lifetime abstainers and 25.1% as former drinkers; among women, 53.4% were non-drinkers who were similarly distributed between lifetime abstainers (27.2%) and former drinkers (26.2%).

Method 1 does not estimate deaths based on consumption levels, so results do not vary by alcohol consumption levels or relative risks (Table 2), although CDC's ARDI application considers all 28,345/year deaths as due to excessive consumption. For AALDD estimates from excessive drinking in reference to low levels of alcohol consumption (rather than non-drinking), Method 3 that adjusted to 73% of per capita sales resulted in almost twice the number of AALDD compared to Method 2 that used the survey-based adjustment (WHO relative risk estimates: 15,633 versus 7,696; IHME: 19,280 versus 10,527). However, because low average daily drinking increases the risk of liver disease, the number of AALDD from excessive consumption was substantially higher in reference to non-drinking

(rather than low consumption). For example, using Method 3 and WHO's relative risk function, there were 15,633 AALDD deaths from excessive drinking using low consumption as the reference group, but 22,837 AALDD deaths with non-drinking as the reference group, a 46.1% relative difference. Using the IHME relative risk function, the relative difference was 12.0% (21,921 versus 19,280). Using WHO relative risk function, compared with AALDD from any level of drinking for Method 3, excessive drinking accounted for 90.1% (97.1% if using IHME risks) when non-drinking was the referent, but only for 62.2% (85.4% if using IHME risks) when low consumption was the referent.

For deaths from any consumption (i.e., all levels of consumption), Method 1 yielded the largest estimate of average annual AALDD (28,345), while Method 2 yielded the lowest estimates (e.g., 18,789 using WHO's relative risks) (Table 2).. Estimated AALDD using Method 2 yielded a total number of AALDD that barely exceeded the approximately 18,000 deaths from just the deaths coded as alcoholic liver disease deaths in the vital statistics data, which are fully alcohol-attributable (data n him him ot shown). For any drinking, Method 3 using WHO's relative risks yielded approximately 33% higher total estimates (25,145 AALDD) than Method 2, and approximately 11% lower estimates than Method 1.

For any drinking, the different relative risk functions only modestly affected AALDD estimates (Table 2). The WHO relative risks resulted in slightly higher AALDD estimates associated with any drinking than from the IHME relative risks (e.g., 25,145 versus 22,578 using Method 3), particularly for women. Conversely, compared to the WHO relative risks, the IHME relative risks resulted in higher AALDD estimates associated with excessive drinking when using low drinking as the referent (e.g., 19,280 versus 15,633 using Method 3), with relative differences more pronounced among men.

Stratifying non-drinkers into former drinkers and lifetime abstainers, and incorporating risk estimates for former drinkers into estimates using WHO relative risks, resulted in higher estimated total AALDD for both sexes, regardless of whether categorical or continuous relative risks were used (Table 3). For example, based on Method 3 including risks for former drinkers resulted in 2,541 additional AALDD (27,686 versus 25,145 with categorical relative risks) compared to not including risks for former drinkers. Compared to using continuous relative risks, categorical relative risks yielded higher AALDD estimates for men and women (both with and without modeling risks for former drinkers).

Method 1 yielded the greatest proportion of alcohol-attributable deaths relative to all liver disease deaths (65.8%), followed by Method 3 when accounting for risks from former drinkers (64.3%); Method 2 yielded the lowest proportion (43.6%) of liver disease deaths that were alcohol-attributable (Figure 1).

DISCUSSION

Given the large and increasing burden of chronic liver disease, sufficiently accounting for the contribution of alcohol can inform the use of evidence-based strategies to combat it (29). To our knowledge, this is one of the only studies comparing a 'direct' method (summing deaths from alcoholic cirrhosis plus a proportion from unspecified cirrhosis) with

an ‘indirect’ approach using PAF methodology. We found that the two methods yielded similar estimates of AALDD, but only when the indirect method incorporated risks from all levels of alcohol consumption (including low volume consumption), when survey-based prevalence estimates were adjusted to more closely correspond with consumption based on sales and tax data, and when modeling risk estimates for former drinkers.

Going forward, the indirect approach using PAF methodology has practical and scientific attributes that may favor its use to better capture the full contribution of alcohol to liver disease deaths, particularly given the limitations with the coding of alcohol in liver disease deaths. First, indirect methods allow for estimating alcohol involvement in liver disease deaths at various levels of alcohol use (e.g., low, medium, high). Second, using PAF methodology allows one to capture the contribution of alcohol to liver diseases for various conditions to which alcohol contributes, but is not the sole or principal cause and for which alcohol’s attribution in any single death would be difficult to estimate on clinical grounds (e.g., the progression of cirrhosis from hepatitis C).

However, PAF-based estimates can be limited by their reliance on survey data, which typically substantially underestimate population-level consumption compared to that based on alcohol sales and tax receipt data (14). In this study, when we applied a more modest survey-based adjustment (rather than one based on sales data) to calculate alcohol consumption prevalence estimates, the findings were similar to just the number of deaths from alcoholic liver disease). This suggests that the survey-based adjustment to account for the underreporting of alcohol use was not robust enough and emphasizes the importance of using sales data, tax data, or both, as the ideal method for adjusting self-reported alcohol consumption when using PAF methods (17).

Such data on alcohol from surveys, sales records, and taxes is generally available in higher income countries and increasingly available in lower- and middle-income countries as well. If country-specific data are not available, supplemental data can be obtained from global systems such as the WHO’s Global Information System on Alcohol and Health or the IHME’s Global Burden of Disease. While the indirect approach can be used in various jurisdictions, the accuracy of the results will depend on the quality of the jurisdiction-specific data and the number of data sources informed by global-level supplemental data. Overall, it is most important to undertake at least some type of surveillance for alcohol-caused liver disease, and this paper illustrates that comparable estimates can be achieved with either a direct or indirect approach.

Disaggregating nondrinkers into lifetime abstainers and former drinkers, and incorporating risk estimates for former drinkers, resulted in increased estimates of AALDD. This is consistent with research indicating that many former drinkers had drunk excessively and are at increased risk for liver disease, suggesting it would be problematic to assign them the same risk of dying as never drinkers (24, 30). However, estimates of risk for former drinkers may not address the issue of “former drinker bias” in those studies included in meta-analyses in which the reference group was comprised of nondrinkers, rather than lifetime abstainers (31). Because former drinkers might have elevated risks for several diseases, including liver disease, removing former drinkers from the nondrinking reference

group would produce less biased relative risks related to alcohol and would likely result in increased risk estimates at all levels of consumption (32). However, many data sources that assess alcohol consumption do not assess whether non-drinkers are former drinkers or lifetime abstainers, making it challenging to estimate how former drinkers contribute to the alcohol-related public health impact in states. Finally, studies show that a substantial proportion of those who report being lifetime abstainers were in fact former drinkers, highlighting the need for better surveillance of lifetime drinking measures (33).

We also found that categorical relative risks yielded higher AALDD estimates than those based on continuous risk functions. In this study, categorical risks for low and medium average daily consumption were derived from continuous functions by evaluating the function at the midpoint of the consumption boundaries (for the high consumption level, the median was used). It is possible that categorical risk estimates exceeded continuous ones for low and medium consumption levels because the consumption level represented by the midpoints could be higher than the median consumption of respondents in the level ranges. AALDD estimates based on categorical or continuous relative risks might be more similar if points below the range midpoints were used as the basis for selecting the relative risks, or if the median observed values within each consumption level range were calculated from survey data.

When calculating the contribution of excessive drinking to AALDD, the choice of the reference group (low consumption or non-drinking) for the relative risk estimates makes a considerable difference. Since alcohol use increases the risk of liver disease, even at low consumption levels (13, 21), estimating the risk of AALDD from excessive drinking at medium and high consumption levels is underestimated when low consumption is used as the referent.

This work is subject to caveats and limitations. First, in addition to the former drinker bias discussed above, AALDD estimates were conservative because some liver disease-related diagnoses that alcohol contributes to were not included in either meta-analyses used for determining the relative risks; examples include deaths from esophageal varices and portal hypertension, which are almost exclusively sequelae of liver cirrhosis, and hepatitis C and ‘non-alcoholic’ fatty liver disease for which alcohol consumption can be a contributing factor (34, 35). For Method 3, our estimates were also conservative because we did not adjust prevalence estimates to account for unrecorded consumption (e.g., home-produced alcohol) in the U.S. population, which is estimated to be approximately 10% of total consumption (12). Second, all three methods relied on some older data (e.g., the proportion of unspecified cirrhosis deaths from alcohol in Method 1, and some of the studies in the meta-analyses used for Methods 2 and 3); therefore, differences in the current distribution of specific diagnoses within the category of liver disease might yield different pooled relative risks compared to existing ones. Third, Methods 2 and 3 were based on cross-sectional relationships between alcohol consumption and liver disease mortality. However, this is unlikely to have a substantial impact on the findings, given both the relative stability of alcohol consumption in the U.S. and the ‘reservoir’ effect regarding population alcohol use and cirrhosis (36, 37). Fourth, although we used the same ICD-10 codes to define deaths for all three methods, there were slight differences in the ICD-10 codes used in the

meta-analyses that were used to determine the relative risks, so we included the two sets of relative risks to facilitate comparisons of the resulting AALDD estimates.

CONCLUSIONS

We found that direct and PAF methods can yield similar estimates of AALDD. However, when using PAF methods to derive estimates of AALDD, it is important to consider the contribution of all levels of alcohol consumption and to adjust survey-based prevalence estimates of alcohol consumption to account for per capita alcohol sales. In addition, since about half of non-drinkers are former drinkers including some who drank excessively in the past, it is also important to model the risks of former drinkers. If valid relative risks are available to calculate PAF, estimates of AALDD can also capture other causes of liver disease mortality including viral hepatitis and so-called 'nonalcoholic' fatty liver disease (38).

Regardless of methodologic approach, alcohol consumption remains a predominant contributor to chronic liver disease (5). It is also noteworthy that alcohol consumption, and excessive consumption in particular, can cause or exacerbate multiple types of liver disease conditions, in addition to those caused solely by alcohol (39). Therefore, effective population-level alcohol control strategies can help to address the large burden of chronic liver disease (29, 40). The implementation of stronger evidence-based alcohol policies (e.g., increasing alcohol taxes, regulating alcohol outlet density) has been associated with lower rates of death from alcohol-related liver diseases (41, 42).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgement:

This project is supported by the Centers for Disease Control and Prevention (CDC) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award totaling $81,777 with 100 percent funded by CDC/HHS. The findings and conclusions of this study are those of the authors and do not necessarily represent the official position of the CDC or HHS. This work was funded by research agreement 75D30120P09906.

REFERENCES

1. Cheemerla S, Balakrishnan M. Global epidemiology of chronic liver disease. Clinical Liver Disease. 2021;17(5):365. [PubMed: 34136143]
2. Rehm J, Shield KD. Global burden of alcohol use disorders and alcohol liver disease. Biomedicines. 2019;7(4):99.
3. Centers for Disease Control and Prevention. Chronic Liver Disease and Cirrhosis [Available from: https://www.cdc.gov/nchs/fastats/liver-disease.htm.
4. Centers for Disease Control and Prevention. Alcohol Use [Available from: https://www.cdc.gov/nchs/fastats/alcohol.htm.
5. Yoon Y, Chen C. Liver cirrhosis mortality in the United States: national, state, and regional trends 2000–2017 [cited 2021 April 7]. Available from: https://pubs.niaaa.nih.gov/publications/surveillance114/Cirr17.htm.

6. Julien J, Ayer T, Bethea ED, Tapper EB, Chhatwal J. Projected prevalence and mortality associated with alcohol-related liver disease in the USA, 2019–40: a modelling study. Lancet Public Health. 2020;5(6):e316–e23. [PubMed: 32504584]
7. Arias E, Tejada-Vera B, Ahmad F, Kochanek KD. Provisional Life Expectancy Estimates for 2020. 2021.
8. Manos MM, Leyden WA, Murphy RC, Terrault NA, Bell BP. Limitations of conventionally derived chronic liver disease mortality rates: results of a comprehensive assessment. Hepatology. 2008;47(4):1150–7. [PubMed: 18264998]
9. Sofair AN, Barry V, Manos MM, Thomas A, Zaman A, Terrault NA, et al. The epidemiology and clinical characteristics of patients with newly diagnosed alcohol-related liver disease: results from population-based surveillance. Journal of Clinical Gastroenterology. 2010;44(4):301–7. [PubMed: 19745759]
10. Parrish KM, Dufour MC. Drinking patterns and liver cirrhosis mortality. Alcohol and Alcoholism. 1991;Suppl 1:331–4.
11. Centers for Disease Control and Prevention. Alcohol-Related Disease Impact (ARDI) 2020 [Available from: https://www.cdc.gov/ARDI/.
12. World Health Organization. Global Status Report on Alcohol and Health Geneva, Switzerland: World Health Organization; 2018 [Available from: https://www.who.int/substance_abuse/publications/global_alcohol_report/en/.
13. Global Burden of Disease 2016 Collaborators. Alcohol use and burden for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2018;392:1015–35. [PubMed: 30146330]
14. Nelson DE, Naimi TS, Brewer RD, Roeber J. US state alcohol sales compared to survey data, 1993–2006. Addiction. 2010;105(9):1589–96. [PubMed: 20626370]
15. Stockwell T, Zhao J, Macdonald S. Who under-reports their alcohol consumption in telephone surveys and by how much? An application of the 'yesterday method'in a national Canadian substance use survey. Addiction. 2014;109(10):1657–66. [PubMed: 24825591]
16. Stahre M, Naimi T, Brewer R, Holt J. Measuring average alcohol consumption: the impact of including binge drinks in quantity–frequency calculations. Addiction. 2006;101(12):1711–8. [PubMed: 17156170]
17. Esser M, Sherk A, Sabina Subbaraman M, Martinez P, Karriker-Jaffe K, Sacks J, et al. Improving estimates of alcohol-attributable deaths in the United States: the impact of adjusting for the underreporting of alcohol consumption. Journal of Studies on Alcohol and Drugs. 2022;83:134–44. [PubMed: 35040769]
18. Slater M, Alpert H. Apparent per capita alcohol consumtion: national, state and regional trends, 1977–2018 [cited 2021 April 12]. Available from: https://pubs.niaaa.nih.gov/publications/surveillance115/CONS18.htm.
19. Stockwell T, Zhao J, Sherk A, Rehm J, Shield K, Naimi T. Underestimation of alcohol consumption in cohort studies and implications for alcohol's contribution to the global burden of disease. Addiction. 2018;113(12):2245–9. [PubMed: 30014539]
20. Centers for Disease Control and Prevention. ARDI methods 2020 [Available from: https://www.cdc.gov/alcohol/ardi/methods.html.
21. Rehm J, Taylor B, Mohapatra S, Irving H, Baliunas D, Patra J, et al. Alcohol as a risk factor for liver cirrhosis: A systematic review and meta-analysis. Drug and Alcohol Review. 2010;29:437–45. [PubMed: 20636661]
22. Sherk A, Stockwell T, Rehm J, Dorocicz J, Shield KD, Churchill S. The international model of alcohol harms and policies: a new method for estimating alcohol health harms with application to alcohol-attributable mortality in Canada. Journal of studies on alcohol and drugs. 2020;81(3):339–51. [PubMed: 32527386]
23. Sherk A, Stockwell T, Rehm J, Dorocicz J, Shield KD. The International Model of Alcohol Harms and Policies (InterMAHP): A comprehensive guide to the estimation of alcohol-attributable morbidity and mortality. Version 1.0: December 2017. British Columbia, Canada.2017 [Available from: https://www.uvic.ca/research/centres/cisur/projects/intermahp/index.php.

24. Hasin DS, Grant BF. AA and other helpseeking for alcohol problems: former drinkers in the US general population. Journal of Substance Abuse. 1995;7(3):281–92. [PubMed: 8749788]
25. Substance Abuse and Mental Health Services Administration. Results from the 2015 National Survey on Drug Use and Health: Detailed Tables (table 2–43b) [Available from: https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015.htm#tab2-43b.
26. Roerecke M, Vafaei A, Hasan OS, Chrystoja BR, Cruz M, Lee R, et al. Alcohol consumption and risk of liver cirrhosis: a systematic review and meta-analysis. American Journal of Gastroenterology 2019;114(10):1574–86. [PubMed: 31464740]
27. Centers for Disease Control and Prevention. CDC WONDER [Available from: https://wonder.cdc.gov/.
28. Centers for Disease Control & Prevention. Alcohol-Related Disease Impact (ARDI) International Classification of Diseases (ICD) Codes and Alcohol-Attributable Fraction (AAF) Sources 2021 [updated July 6. Available from: https://www.cdc.gov/alcohol/ardi/alcohol-related-icd-codes.html.
29. Hydes T, Gilmore W, Sheron N, Gilmore I. Treating alcohol-related liver disease from a public health perspective. Journal of Hepatology. 2019;70(2):223–36. [PubMed: 30658724]
30. Dawson DA. Drinking patterns among individuals with and without DSM-IV alcohol use disorders. Journal of Studies on Alcohol. 2000;61:111–20. [PubMed: 10627104]
31. Naimi TS, Stockwell T, Zhao J, Xuan Z, Dangardt F, Saitz R, et al. Selection biases in observational studies affect associations between 'moderate'alcohol consumption and mortality. Addiction. 2017;112:207–14. [PubMed: 27316346]
32. Schutte KK, Nichols KA, Brennan PL, Moos RH. A ten-year follow-up of older former problem drinkers: Risk of relapse and implications of successfully sustained remission. Journal of Studies on Alcohol and Drugs. 2003;64:367.
33. Callinan S, Chikritzhs T, Livingston M. Consistency of drinker status over time: drinking patterns of ex-drinkers who describe themselves as lifetime abstainers. Journal of studies on alcohol and drugs. 2019;80(5):552–6. [PubMed: 31603757]
34. Long MT, Massaro JM, Hoffmann U, Benjamin EJ, Naimi TS. Alcohol use is associated with hepatic steatosis among persons with presumed non-alcoholic fatty liver disease. Clinical Gastroenterology and Hepatology. 2019.
35. Schwarzinger M, Baillot S, Yazdanpanah Y, Rehm J, Mallet V. Contribution of alcohol use disorders on the burden of chronic hepatitis C in France, 2008–2013: A nationwide retrospective cohort study. Journal of Hepatology. 2017;67(3):454–61. [PubMed: 28396173]
36. Norström T The use of aggregate data in alcohol epidemiology. British Journal of Addiction. 1989;84(9):969–77. [PubMed: 2624626]
37. Skog O-J. The risk function for liver cirrhosis from lifetime alcohol consumption. Journal of Studies on Alcohol. 1984;45(3):199–208. [PubMed: 6748660]
38. Rehm J, Patra J, Brennan A, Buckley C, Greenfield TK, Kerr WC, et al. The role of alcohol use in the aetiology and progression of liver disease: A narrative review and a quantification. Drug and Alcohol Review. 2021.
39. Fuster D, Samet JH. Alcohol use in patients with chronic liver disease. New England Journal of Medicine. 2018;379(13):1251–61. [PubMed: 30257164]
40. Babor T, Caetano R, Casswell S, Edwards G, Giesbrecht N, Graham K, et al. Alcohol: No Ordinary Commodity: Research and Public Policy. New York: Oxford University Press; 2010.
41. Hadland SE, Xuan Z, Blanchette J, Heeren TC, Swahn MH, Naimi TS Alcohol policies and alcoholic cirrhosis mortality in the United States. Preventing Chronic Disease. 2015;12:1–11.
42. Parikh N, Chung G, Mellinger J, Blanchette J, Naimi T, Tapper E. Alcohol policies and alcohol-related liver disease mortality. Gastroenterology. 2021;161:350–2. [PubMed: 33753104]

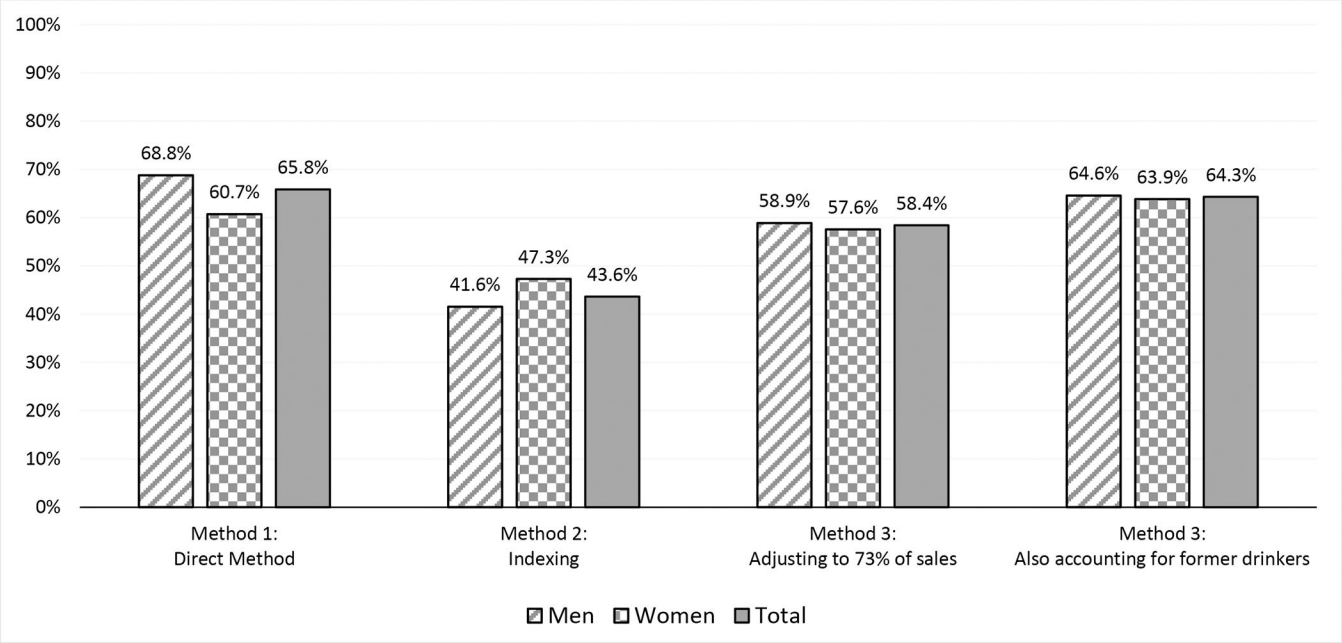

Figure 1.

Proportion of alcohol-attributable deaths relative to total deaths from assessed types of liver disease[a] from all levels of alcohol consumption, by sex and method,[b] U.S. population, 2011–2015

[a] To calculate the proportion of liver deaths due to alcohol, the denominator (i.e., total deaths from liver disease) was based on the same ICD-10 codes as used to determine the numerator (i.e., deaths that were alcohol-attributable.)

[b] Method 1 involves summing all deaths from alcoholic cirrhosis and 40% of deaths from unspecified cirrhosis; the current approach used in the Centers for Disease Control Prevention Alcohol-Related Disease Impact application. Method 2 adjusts average daily consumption by indexing the number of drinks consumed during binge drinking occasions, if those quantities exceed usual consumption on days when alcohol is consumed (16). Method 3 adjusts the self-reported alcohol consumption to account for 73% of per capita alcohol sales (17). Method 3 accounting for former drinkers is the same as method 3, except non-drinkers were divided into lifetime abstainers and never drinkers, and relative risk estimates for former drinkers were also incorporated in estimates of deaths.

Table 1.

Prevalence estimates for various levels of alcohol consumption based on method of calculation, non-drinker classification method, and sex, U.S. population, 2011–2015

Method[b]	Non-drinker Classification Method[c]	Sex	Alcohol Consumption Status[a]						
			Non-drinkers			Average daily consumption			
			Lifetime abstainers (%)	Former drinkers (%)	All non-drinkers (%)	Low (%)	Medium (%)	High (%)	Total (%)
Direct Method (Method 1)	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Indexing (Method 2)	Not accounting for former drinker status	Men	-	-	40.7	49.4	6.4	3.5	100.0
		Women	-	-	53.4	40.0	4.4	2.2	100.0
	Accounting for former drinker status	Men	15.6	25.1	-	49.4	6.4	3.5	100.0
		Women	27.2	26.2	-	40.0	4.4	2.2	100.0
Adjusted to 73% of per capita sales (Method 3)	Not accounting for former drinker status	Men	-	-	40.7	37.7	11.0	10.6	100.0
		Women	-	-	53.4	30.2	7.6	8.8	100.0
	Accounting for former drinker status	Men	15.6	25.1	-	37.7	11.0	10.6	100.0
		Women	27.2	26.2	-	30.2	7.6	8.8	100.0

[a] Non-drinkers were divided into former drinkers and lifetime abstainers using proportions from the 2015 National Survey on Drug Use and Health. Low consumption was defined as an average of >0–≤1 standard drinks per day (women) or >0–≤2 drinks/day (men), medium consumption was defined as >1–≤2 drinks/day (women) or >2–≤4 drinks/day (men), and high consumption was defined as >2 drinks/day (women) or >4 drinks/day (men).

[b] Method 1 does not use alcohol consumption prevalence estimates so they are not applicable (n/a). Method 2 adjusts average daily consumption by indexing the number of drinks consumed during binge drinking occasions, if those quantities exceed usual consumption on days when alcohol is consumed (16). Method 3 adjusts the self-reported alcohol consumption to account for 73% of per capita sales (17).

[c] Non-drinkers can be considered as a group or divided into never-drinkers (i.e., lifetime abstainers) and former drinkers; therefore, the prevalence estimates for 'Not accounting for former drinker status' are restricted to the prevalence of non-drinkers and the prevalence estimates for 'Accounting for former drinker status' are for former drinkers and lifetime abstainers.

Table 2.

Average annual number of deaths from alcohol-attributable liver disease, by method of calculation, source of relative risk estimates, level of alcohol consumption and sex, U.S. population, 2011–2015

Source of Relative Risk Estimates[a]	Level of Alcohol Consumption and Reference Group[b]	Sex	Method		
			Direct Method (Method 1)[c]	Indexing (Method 2)[d]	Adjusted to 73% of per capita sales (Method 3)[e]
World Health Organization	Excessive drinking vs. Low	Men	18,822	6,121	11,953
		Women	9,523	1,575	3,681
		Total	28,345	7,696	15,633
	Excessive drinking vs. None	Men	18,822	8,801	15,212
		Women	9,523	4,095	7,625
		Total	28,345	12,896	22,837
	Any drinking vs. None	Men	18,822	11,373	16,115
		Women	9,523	7,416	9,030
		Total	28,345	18,789	25,145
Institute for Health Metrics and Evaluation	Excessive drinking vs. Low	Men	18,822	9,010	15,617
		Women	9,523	1,517	3,663
		Total	28,345	10,527	19,280
	Excessive drinking vs. None	Men	18,822	11,299	17,883
		Women	9,523	1,714	4,039
		Total	28,345	13,013	21,921
	Any drinking vs. None	Men	18,822	12,818	18,308
		Women	9,523	2,148	4,269

Source of Relative Risk Estimates[a]	Level of Alcohol Consumption and Reference Group[b]	Sex	Method		
			Direct Method (Method 1)[c]	Indexing (Method 2)[d]	Adjusted to 73% of per capita sales (Method 3)[e]
		Total	28,345	14,966	22,578

Totals may not sum due to rounding.

[a]The relative risk estimates from these two sources are presented in Supplementary Table 1.

[b]Excessive alcohol consumption includes medium and high levels of consumption. Medium consumption was defined as >1–≤2 drinks/day for women or >2–≤4 drinks/day for men, and high consumption was defined as >2 drinks/day for women or >4 drinks/day for men. The ‘excessive drinking vs. low’ comparison is the number of alcohol-attributable liver disease deaths caused by excessive consumption in excess of what would be expected were excessive drinkers to consume at low levels of consumption, whereas the ‘excessive drinking vs. none’ comparison represents the number of alcohol-attributable liver disease deaths caused by excessive consumption in excess of what would be expected were drinkers (including those who consumed at low levels) to consume no alcohol. ‘Any’ drinking refers to all levels of consumption (low, medium, and high) combined.

[c]This method involves summing deaths from alcoholic cirrhosis and a fixed proportion of deaths from unspecified cirrhosis, and does not involve prevalence or relative risk estimates. Therefore, results presented in the table for men, women, and total are identical irrespective of level of consumption or choice of relative risk estimates.

[d]Method 2 adjusts average daily consumption by indexing the number of drinks consumed during binge drinking occasions, if those quantities exceed usual consumption on days when alcohol is consumed.

[e]Method 3 adjusts self-reported alcohol consumption to account for 73% of per capita sales.

Table 3.

Average annual number of deaths from alcohol-attributable liver disease from all levels of alcohol consumption, with and without incorporating risk estimates for former drinkers and by type of risk function, U.S. population, 2011–2015[a]

Type of relative risks	Sex	Incorporate former drinker risk?[b]	
		No	Yes
Categorical[c]	Men	16,115	17,673
	Women	9,030	10,013
	Total	25,145	27,686
Continuous[c]	Men	12,423	15,476
	Women	6,427	8,665
	Total	18,850	24,142

[a]Prevalence estimates were calculated using Method 3, based on self-reported alcohol consumption in the 2011–2015 Behavioral Risk Factor Surveillance System, adjusted to account for 73% of per capita alcohol sales based on tax and shipment data from the Alcohol Epidemiologic Data System.

[b]Risks for former drinkers came from Roerecke et al. (26)

[c]Categorical and continuous risk estimates came from Rehm et al. (21), which are also used by the World Health Organization.