

# Global burden of alcoholic liver diseases

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## Summary

Liver diseases contribute markedly to the global burden of mortality and disease. This paper provides an overview from a global perspective of the contribution of alcohol to liver diseases.

The Global Burden of Disease study methodology was used to estimate the burden of alcohol-attributable liver cirrhosis and alcohol-attributable liver cancer in 2010 as measured by deaths and disability adjusted life years (DALYs). This methodology estimates attributable fractions based on alcohol exposure distribution and relative risks associated with different levels of drinking.

Globally, in 2010, alcohol-attributable liver cirrhosis was responsible for 493,300 deaths (156,900 female deaths and 336,400 male deaths) and 14,544,000 DALYs (4,112,000 DALYs for women and 10,432,000 DALYs for men), representing 0.9% (0.7% for women and 1.2% for men) of all global deaths and 0.6% (0.4% for women and 0.8% for men) of all global DALYs, and 47.9% of all liver cirrhosis deaths (46.5% for women and 48.5% for men) and 46.9% of all liver cirrhosis DALYs (44.5% for women and 47.9% for men). Alcohol-attributable liver cancer was responsible for 80,600 deaths (14,800 female deaths and 65,900 male deaths) and 2,142,000 DALYs (335,000 DALYs for women and 1,807,000 DALYs for men).

The burden of alcohol-attributable liver cirrhosis and liver cancer is high and entirely preventable. Interventions to reduce alcohol consumption are recommended as a population health priority and may range from taxation increases for alcoholic beverages to increases in screening and treatment rates for alcohol use disorders.

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**Abbreviations:** ALD, alcoholic liver disease; DALYs, disability adjusted life years; ICD, international classification of diseases; GBD, global burden of disease; PYLL, potential years of life lost; YLD, years lived with disability; AAF, alcohol-attributable fraction; RR, relative risk; USD, US dollars.



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## Introduction

### *The global burden of liver diseases*

Liver diseases have been found to contribute markedly to the global burden of mortality and morbidity [1,2]. In the 2010 Global Burden of Disease (GBD) study, more than one million deaths (1,030,800 deaths representing 2.0% of all deaths, 1.4% of all deaths of women and 2.4% of all deaths of men) and 31,027,000 Disability Adjusted Life Years (DALYs) (1.2% of all DALYs, 0.8% of all DALYs for women, 1.6% of all DALYs for men) were due to liver cirrhosis. A DALY here denotes a summary measure for burden of disease, which is composed of the addition of years of life lost to premature mortality and years of life lost to disability. Another 752,100 deaths (representing 1.4% of all deaths, 1.0% of all deaths of women and 1.8% of all deaths of men) and 19,111,000 DALYs (0.8% of all DALYs, 0.5% of all DALYs for women and 1.0% of all DALYs for men) were due to liver cancer. The health burden for both diseases is considerably more pronounced in men with 67% of liver cirrhosis deaths and 69% of liver cancer deaths involving men, and 70% of DALYs due to liver cirrhosis and 73% of DALYs due to liver cancer in each case for men.

### *Alcohol and liver disease*

Alcohol is consumed widely in most parts of the world and has long been identified as a major risk factor for all liver diseases [3]; for modern overviews see [4–6]. Even though the majority of adults are still abstainers, almost half of the world's population consumed alcohol in the past year [7]. It is the aim of this paper to provide an overview from a global perspective of the contribution of alcohol to liver diseases.

### *Alcoholic liver disease – pathology and biological pathways*

The International Classification of Diseases (ICD-10) recognizes several forms of alcoholic liver disease (ALD; see ICD-10, K70), sometimes considered stages [8], that range from relatively mild and reversible alcoholic hepatic steatosis (fatty liver) (K70.0) and alcoholic hepatitis (K70.1), to alcoholic fibrosis and sclerosis of the liver (K70.2), and further to severe and irreversible stages of ALD, such as alcoholic liver cirrhosis (K70.3) and alcoholic hepatic failure (K70.4).

Pathogenesis of specific forms of ALD is covered extensively in the EASL Clinical Practical Guidelines for the management of ALD [9]. In short, alcohol consumption, especially heavy consumption, induces changes in lipid metabolism (increases lipogenesis and mobilization of lipids and simultaneously decreases hepatic lipid catabolism), resulting in accumulation of lipids in hepatocytes called fatty liver. In some cases, alcohol consumption causes an inflammatory response, known as alcoholic hepatitis or steatohepatitis if it is accompanied by hepatic lipid deposition. Though hepatic steatosis and alcoholic hepatitis do not normally cause irreversible hepatocellular changes, persistence and severity of these conditions eventually lead to fibrosis and sclerotic changes in the liver that result in liver cirrhosis due to insidious replacement of hepatocytes with connective tissue, and subsequent liver failure.

Diagnosis of ALD is based on various clinical and laboratory findings and confirmation of alcohol as the etiological factor [10,11]. Clinical symptoms of ALD vary from asymptomatic hepatic steatosis to malaise, anorexia, weight loss, abdominal discomfort, tender hepatomegaly, jaundice, and remote sequelae of liver dysfunction characteristic of more advanced forms of disease. Differentiation between ALD and liver disease not due to alcohol consumption is often made by a history of regular alcohol consumption above the threshold of 20 grams of pure ethanol per day for women and 30 grams of pure alcohol per day for men [9,12]; however, the risk curve between the level of alcohol consumption and liver disease is exponential, so ALD is more often associated with much higher levels of consumption [5,13,14]. Laboratory findings can be used to describe the severity of ALD and might be indicative of recent alcohol consumption. Differentiation between the forms of ALD is based on specific imaging or histological findings [15,16]; for a more detailed description see [9].

In addition, consumption of alcohol can also cause liver cancer through similar biological pathways [6]. This condition will be discussed later in our review.

### Organization of the paper

We start with an overview of available data at the global level, and with the methodology used to estimate the proportion of the health burden caused by alcohol-attributable liver cirrhosis and liver cancer. After presenting the results of our estimations, we discuss potential interventions to reduce the burden of ALDs, and the implications of these interventions.

## Materials and methods

### Global data availability

While alcoholic liver cirrhosis and other ALDs constitute a large portion of all liver disease (e.g., more than 75% of all liver cirrhosis in the European Union in 2004 was estimated to be caused by alcohol [17]; for earlier estimates of global figures see [18]), the incidence of ALDs cannot be reliably estimated for all regions of the world as causes of death are often based on verbal autopsies, which remain the main method underlying global mortality statistics [19,20]. In fact, ALDs cannot be reliably estimated in the small number of countries with vital registries, as the assessment of whether a liver disease is due to alcohol consumption or otherwise is highly impacted by socio-cultural factors. For instance, in their seminal study in 12 cities in 10 countries, Puffer and Griffith [21] found that after triangulating data on death certificates with data from hospital records and interviews

(attending physicians, family members), the number of deaths assigned to alcoholic liver cirrhosis more than doubled, with the majority of new cases being re-coded from categories of cirrhosis which do not mention alcohol. This under-reporting has persisted in later studies [22], and seems to be the case for all alcohol-attributable disease categories [23] which are impacted by stigma, including, but not limited to, the disclosure of heavy alcohol consumption and alcohol use disorders [24]. As one consequence, alcohol use disorders are currently the least treated mental disorder [25,26].

The 2010 GBD study attempted estimates of liver cirrhosis and cancer “secondary to alcohol use” [1,2,27]. While the methods used to calculate these estimates were not part of the publications, the limitations specified above apply, and should be kept in mind when interpreting the data. For the specific secondary causes of liver cirrhosis and liver cancer, liver cirrhosis secondary to alcohol use for 2010 was estimated to be 282,800 deaths and 8,575,000 DALYs (representing 19.8% and 19.8% of all liver cirrhosis deaths and DALYs in 2010, respectively). The mortality and DALYs from liver cancer secondary to alcohol for 2010 was estimated to be 149,000 deaths and 3,782,000 DALYs (representing 27.4% and 27.6% of all liver cirrhosis deaths and DALYs in 2010, respectively). The full burden of liver cirrhosis and liver cancer attributable to alcohol is not reflected in the deaths or DALYs secondary to alcohol use, as specified. Not only is there a stigma attached to the labelling of heavy alcohol use or abuse as a cause of disease or mortality, but such alcohol consumption often interacts with other secondary causes of death, such as hepatitis B. Thus, a person, who develops liver disease secondary to hepatitis B and who consumes alcohol while living with the disease, has a markedly increased risk of mortality compared to a person who develops liver disease secondary to hepatitis B but abstains from alcohol consumption. As a result, some of the burden of liver disease secondary to hepatitis B, hepatitis C, or other causes is attributable to alcohol (i.e., outcomes, that would not have occurred if alcohol had not been consumed [28,29]).

Given the lack of reliable direct estimates of mortality and the burden of disease due to ALD, we estimated the burden of alcohol-attributable liver cirrhosis indirectly using standard epidemiological methodology. We used the respective GBD study category for liver cirrhosis, which comprises all of the K70 codes, and estimated the proportion of alcohol-attributable liver cirrhosis based on the prevalence of alcohol consumption and the risk relations between levels of consumption and the disease outcomes (for details see the next section).

### Data sources and statistical model

To estimate the number of deaths, potential years of life lost (PYLL), years lived with disability (YLD), and DALYs from liver cirrhosis and liver cancer that are attributable to alcohol consumption, we combined the risks of each of liver cirrhosis and liver cancer with the prevalence of alcohol exposure using alcohol-attributable fractions (AAF) calculated using the 2010 GBD study methodology [30,31]. AAFs represent the proportion of each outcome that would not have occurred in a counterfactual scenario where no one consumes alcohol (see [29,32] for more information on attributable fractions). The method to calculate the number of deaths, PYLL, YLD, and DALYs attributable to alcohol consumption has two main steps: (1) calculation of the race-, age-, sex-, and consumption-specific AAFs, and then (2) application of these AAFs to the corresponding mortality, PYLL, YLD, and DALYs data (see [1,2,27] for an overview of GBD study procedures to calculate these outcome indicators). For details on the model please see the section on statistical models below.

All data were available by age and sex at the regional level. Regions were defined in accordance with the 2010 GBD study [30]. Grouping of countries into regions was determined by geographical location and epidemiological profile (child and adult mortality levels and major causes of death). Neither income nor population of the countries in a region had an impact on the grouping structure. The countries included within each GBD region are described in Supplementary data 1.

### Alcohol consumption data

Data on alcohol consumption and drinking patterns were obtained for 2005 and estimated for 2010 (see [33] for country- and region-specific data on alcohol consumption and patterns). Data for recorded, unrecorded and tourist *per capita* consumption of pure alcohol (ethanol) were obtained from the Global Information System on Alcohol and Health [34] based on surveys conducted by the WHO and regularly published in the Global Status Reports on Alcohol and Health (for the most recent report see: [7]). The prevalence of lifetime abstainers (people who have never consumed one standard drink of alcohol), former drinkers (people who have consumed alcohol but have not done so within the past year), and current drinkers were obtained from large, nationally representative surveys in the respective countries [33].

## Review

Alcohol consumption was modeled using data on *per capita* consumption triangulated with data on the prevalence of current drinkers and using methods described elsewhere [35,36].

### Mortality data

Data on the number of deaths, PYLL, YLD, and DALYs for all causes, malignant neoplasms (ICD-10 codes: C00–C97), liver cirrhosis (K70 and K74), and liver cancer (C22) were obtained from the 2010 GBD study [1,2,27].

### Risks of liver cancer and liver cirrhosis

Relative risk (RR) estimates for liver cirrhosis were obtained from a meta-analysis performed by Rehm and colleagues [5] and the RR estimates for liver cancer were obtained from a meta-analysis performed by Corrao and colleagues [37] (see Supplementary data 2 for graphs of the RR functions differentiated by sex for liver cirrhosis and liver cancer).

### Statistical modeling

The following formula was used to derive the AAF:

$$AAF = \frac{P_{abstainers} + P_{former\_drinkers} RR_{former\_drinkers} + \int_{>0}^{150} P_{current\_drinkers}(x) RR_{current\_drinkers}(x) - 1}{P_{abstainers} + P_{former\_drinkers} RR_{former\_drinkers} + \int_{>0}^{150} P_{current\_drinkers}(x) RR_{current\_drinkers}(x)}$$

where  $P_{abstainers}$ ,  $P_{former\_drinkers}$  and  $P_{current\_drinkers}(x)$  represent the prevalence of abstainers, former drinkers and current drinkers (given an average daily alcohol consumption of  $x$ ), respectively.  $RR_{former\_drinkers}$  and  $RR_{current\_drinkers}(x)$  represent the risk of liver cirrhosis or liver cancer for former drinkers and current drinkers (given an average daily alcohol consumption of  $x$ ) relative to the risk of liver cirrhosis or liver cancer for lifetime abstainers. For more information on how AAFs are calculated see [38].

Age- and sex-specific population data for 2010 were obtained from the 2010 GBD study based on UN Population Division estimates. Standardized mortality rates were calculated based on the global population structure.

### Association between alcohol-attributable harms and gross domestic product

A linear regression was employed (weighted for population size) to investigate the association between the number of alcohol-attributable liver cirrhosis and liver cancer deaths and DALYs per 100,000 people per litre of alcohol consumed *per capita*, and gross domestic product adjusted for purchase power parity (GDP (PPP)). Data on GDP (PPP) for 2010 (measured in current US dollars) was obtained from The World Bank [39].

## Results

### Global alcohol consumption

Fig. 1 outlines the adult *per capita* consumption of alcohol by country for 2010. Eastern Europe had the highest *per capita* consumption, with 15.7 L per person (8.1 L per woman and 24.9 L per man), while the GBD region of North Africa/Middle East had the lowest adult *per capita* consumption of alcohol, with 1.0 L per person (0.2 L per woman and 1.7 L per man). Southern Sub-Saharan Africa had the highest per drinker consumption of alcohol, with 30.3 L of alcohol consumed per drinker in 2010 (37.8 L per man and 23.0 L per woman). Eastern Europe had the highest pattern of drinking score at 4.9, indicating that people in that region consumed large quantities of alcohol frequently, often drank to intoxication, engaged in prolonged binges, and consumed alcohol mainly outside of meals [40,41]; for a definition of patterns of drinking score, see Rehm *et al.* [42].

### Global burden of liver cirrhosis

As indicated above, in 2010 liver cirrhosis was responsible for 1,030,800 deaths and for 31,027,000 DALYs lost. Of all deaths caused by liver cirrhosis, 493,300 deaths were alcohol-attributable (47.9% of all liver cirrhosis deaths), representing 0.9% of all

deaths due to any cause (0.7% of all deaths of women and 1.2% of all deaths of men). Of the net burden of disease of mortality attributable to alcohol consumption in 2010, alcohol-attributable liver cirrhosis was responsible for 10.4% of this burden (9.3% for women and 11.0% for men). Table 1 outlines the number of deaths from liver cirrhosis that are attributable to alcohol consumption, the percentage of all deaths that were due to alcohol-attributable liver cirrhosis, and the percentage of all alcohol-attributable deaths that were due to liver cirrhosis.

Globally, in 2010 7.2 deaths per 100,000 people (4.6 deaths per 100,000 females and 9.7 deaths per 100,000 males) were caused by liver cirrhosis attributable to alcohol consumption. Fig. 2 displays the number of liver cirrhosis deaths per 100,000 people, attributable to alcohol consumption differentiated by sex and region. Central Asia experienced the greatest number of alcohol-attributable liver cirrhosis deaths per 100,000 people, with 17.5 deaths per 100,000 people (14.6 deaths per 100,000 women, and 20.4 deaths per 100,000 men). Central Latin America had the second highest rate of alcohol-attributable deaths due to liver cirrhosis, with 15.8 deaths per 100,000 people (7.8 deaths per 100,000 women, and 23.6 deaths per 100,000 men).

The number of deaths from liver cirrhosis (corrected for population size) attributable to alcohol consumption was much greater among people 65 years of age and older (31.1 deaths per 100,000 people) when compared to people 15–34 years of age (1.0 deaths per 100,000 people) and people 35–64 years of age (13.1 deaths per 100,000 people). This relationship between alcohol-attributable deaths from liver cirrhosis and age was observed for both men and women. In terms of relative contributions, the impact of alcoholic liver cirrhosis is the greatest in the middle age group: 4.9%, 62.1%, and 33.0% of all deaths from alcohol-attributable liver cirrhosis occurred in people aged 15–34, 35–64, and 65 years and older, respectively.

Of all DALYs due to liver cirrhosis 14,544,000 DALYs were attributable to alcohol consumption. This represents 0.6% of all DALYs (0.4% of all DALYs for women and 0.8% of all DALYs for men) and 10.9% (12.3% for women and 10.5% for men) of all DALYs attributable to alcohol consumption. See Table 2 for the number of DALYs from liver cirrhosis that are attributable to alcohol consumption, the percentage of all DALYs that were due to alcohol-attributable liver cirrhosis, and the percentage of all alcohol-attributable DALYs due to liver cirrhosis.

Globally, in 2010 there were 211.1 DALYs per 100,000 people (120.4 DALYs per 100,000 women and 300.3 DALYs per 100,000 men) caused by liver cirrhosis attributable to alcohol consumption. Fig. 3 shows the number of liver cirrhosis DALYs per 100,000 people attributable to alcohol consumption by sex and region. Central Asia experienced the greatest number of alcohol-attributable liver cirrhosis DALYs per 100,000 people for both men and women, with 546.0 DALYs per 100,000 people (435.1 DALYs per 100,000 women, and 655.0 DALYs per 100,000 men). Eastern Europe had the second highest rate of liver cirrhosis DALYs due to alcohol consumption, with 456.1 DALYs per 100,000 people.

Unlike deaths, the number of DALYs from liver cirrhosis (corrected for population size) attributable to alcohol consumption was greater among people 35–64 years of age (459.4 DALYs per 100,000 people) when compared to people 15–34 years of age (59.7 DALYs per 100,000 people) and people 65 years of age and older (448.5 DALYs per 100,000 people). The relationship between alcohol-attributable DALYs from liver cirrhosis and age was observed for both men and women. Of all DALYs from liver

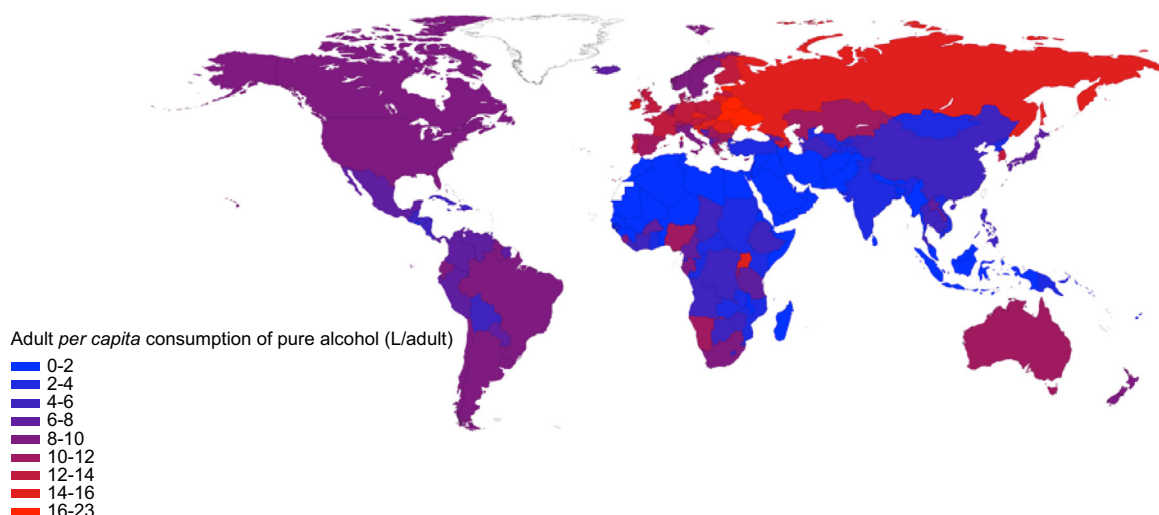


Fig. 1. Total adult per capita consumption, in litres of pure alcohol, 2010.

Table 1. Alcohol-attributable deaths caused by liver cirrhosis in 2010.

Global burden of disease region	Women			Men			Total		
	Deaths	% of all deaths	% of alcohol-attributable deaths	Deaths	% of all deaths	% of alcohol-attributable deaths	Deaths	% of all deaths	% of alcohol-attributable deaths
Asia, Pacific [high income]	7300	1.0	15.3	13,900	1.7	14.3	21,200	1.3	14.6
Asia, Central	5400	2.1	11.7	6800	2.0	9.8	12,200	2.0	10.5
Asia, East	17,100	0.5	8.1	53,300	1.0	9.0	70,500	0.8	8.8
Asia, South	22,700	0.4	16.7	64,900	0.9	14.6	87,500	0.7	15.0
Asia, Southeast	6500	0.4	12.6	27,900	1.3	16.2	34,500	0.9	15.4
Australasia	400	0.5	4.5	800	0.8	5.8	1200	0.7	5.2
Caribbean	900	0.4	8.7	1600	0.6	8.3	2500	0.5	8.4
Europe, Central	6600	1.1	6.9	16,600	2.5	10.3	23,200	1.8	9.0
Europe, Eastern	17,000	1.1	3.7	16,100	1.1	4.1	33,100	1.1	3.9
Europe, Western	19,900	1.0	9.0	32,100	1.6	10.5	52,000	1.3	9.9
Latin America, Andean	1700	1.5	21.1	2200	1.7	15.4	3900	1.6	17.5
Latin America, Central	7600	1.5	20.9	23,900	3.6	20.0	31,500	2.7	20.2
Latin America, Southern	2300	1.1	12.7	4800	2.1	14.8	7100	1.6	14.0
Latin America, Tropical	4500	0.8	11.1	13,600	1.9	12.2	18,100	1.5	11.9
North Africa/Middle East	4500	0.5	18.3	3800	0.3	5.8	8300	0.4	9.2
North America [high income]	13,400	0.9	8.2	19,700	1.4	9.3	33,100	1.1	8.8
Oceania	400	1.0	23.7	500	1.0	18.3	900	1.0	20.4
Sub-Saharan Africa, Central	1700	0.4	16.8	3200	0.5	14.3	5000	0.5	15.0
Sub-Saharan Africa, East	8500	0.6	21.8	12,300	0.8	14.4	20,800	0.7	16.7
Sub-Saharan Africa, Southern	1000	0.3	10.9	2400	0.6	6.1	3400	0.5	7.0
Sub-Saharan Africa, Western	7400	0.5	15.2	15,900	0.9	17.0	23,200	0.7	16.4
World	156,900	0.7	9.3	336,400	1.2	11.0	493,300	0.9	10.4

cirrhosis, 9.7%, 74.1%, and 16.2% occurred in people aged 15–34, 35–64, and 65 years and older, respectively.

The DALYs due to liver cirrhosis were mainly caused from years of life due to premature mortality rather than due to YLD. Of the burden of DALYs due to alcohol-attributable mortality, 98.5% of

the burden was from PYLL and 1.5% of the burden was from YLD. The proportion of PYLL to all DALYs ranged from 97.1% (2.9% from YLD) for the GBD region of East Asia to 99.1% (0.9% from YLD) in the Southeast Asia region. Women had a greater proportion of the alcohol-attributable burden of liver cirrhosis due to YLD (2.4% of

## Review

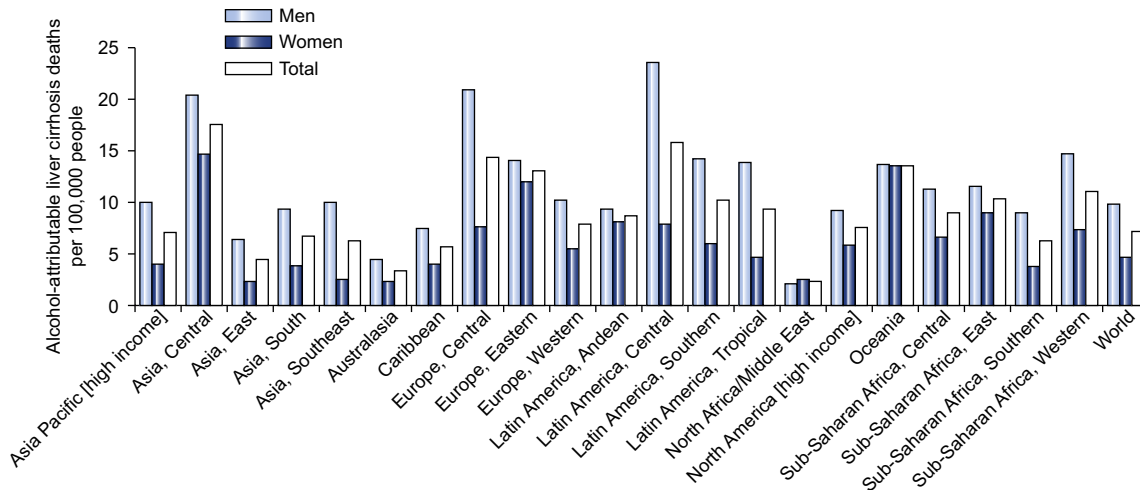


Fig. 2. Alcohol-attributable liver cirrhosis deaths per 100,000 people in 2010 by sex and region.

Table 2. Alcohol-attributable disability adjusted life years (DALYs) caused by liver cirrhosis in 2010.

Global burden of disease region	Women			Men			Total		
	DALYs	% of all DALYs	% of all alcohol-attributable DALYs	DALYs	% of all DALYs	% of all alcohol-attributable DALYs	DALYs	% of all DALYs	% of all alcohol-attributable DALYs
Asia, Pacific [high income]	106,000	0.5	16.6	359,000	1.5	14.4	465,000	1.1	14.8
Asia, Central	167,000	1.3	17.9	231,000	1.4	10.3	398,000	1.4	12.6
Asia, East	424,000	0.3	9.4	1,625,000	0.8	9.1	2,049,000	0.6	9.2
Asia, South	657,000	0.2	15.2	2,142,000	0.6	13.3	2,799,000	0.4	13.7
Asia, Southeast	174,000	0.2	13.5	923,000	0.9	14.9	1,097,000	0.6	14.6
Australasia	8000	0.3	6.8	19,000	0.6	6.5	28,000	0.5	6.6
Caribbean	21,000	0.2	11.0	46,000	0.3	8.1	68,000	0.3	8.9
Europe, Central	173,000	1.0	11.9	473,000	2.2	11.6	646,000	1.7	11.7
Europe, Eastern	531,000	1.3	7.0	554,000	1.1	4.0	1,085,000	1.2	5.0
Europe, Western	383,000	0.7	13.3	793,000	1.3	11.5	1,176,000	1.0	12.0
Latin America, Andean	42,000	0.6	20.3	70,000	0.9	11.5	113,000	0.8	13.7
Latin America, Central	185,000	0.7	21.3	734,000	2.2	16.8	918,000	1.6	17.6
Latin America, Southern	48,000	0.7	15.1	126,000	1.5	13.5	174,000	1.1	13.9
Latin America, Tropical	120,000	0.5	11.6	462,000	1.4	10.0	582,000	1.0	10.3
North Africa/Middle East	137,000	0.2	20.5	126,000	0.2	5.6	263,000	0.2	9.0
North America [high income]	314,000	0.7	13.3	551,000	1.2	10.1	865,000	1.0	11.0
Oceania	13,000	0.6	23.4	17,000	0.7	14.5	30,000	0.6	17.3
Sub-Saharan Africa, Central	61,000	0.2	16.6	119,000	0.3	12.1	179,000	0.2	13.3
Sub-Saharan Africa, East	254,000	0.3	18.8	407,000	0.4	11.6	661,000	0.3	13.6
Sub-Saharan Africa, Southern	35,000	0.2	9.1	84,000	0.4	4.2	120,000	0.3	5.0
Sub-Saharan Africa, Western	258,000	0.2	14.2	570,000	0.4	14.0	827,000	0.3	14.1
World	4,112,000	0.4	12.3	10,432,000	0.8	10.5	14,544,000	0.6	10.9

DALYs lost) when compared to men (1.1% of DALYs lost). This difference by sex was observed for all regions (see [Supplementary data 3](#) for the percentage of DALYs that were attributable to PYLL and to YLD differentiated by sex and region).

Of the total burden of liver cirrhosis, 47.9% of liver cirrhosis deaths (46.5% for women and 48.5% for men) and 46.9% of DALYs (44.5% for women and 47.9% for men) were attributable to alcohol consumption. Central Europe had the highest proportion of liver cirrhosis deaths and DALYs attributable to alcohol consumption, with 72.3% of all liver cirrhosis deaths (62.6% for women and 77.1% for men) being attributable to alcohol consumption and 74.6% of all liver cirrhosis DALYs (67.8% for women and 77.4% for men) being attributable to alcohol consumption. North Africa/Middle East had the lowest proportion of liver cirrhosis deaths and DALYs attributable to alcohol consumption, with 14.0% of all liver cirrhosis deaths and 15.9% of all liver cirrhosis DALYs attributable to alcohol consumption.

The alcohol-attributable liver cirrhosis deaths and DALYs per 100,000 people per litre of alcohol consumed *per capita* were significantly associated with GDP (PPP). As GDP (PPP) increased by 1,000 USD, the number of alcohol-attributable liver cirrhosis deaths per 100,000 people per litre of alcohol consumed *per capita* decreased by 0.05 (95% confidence interval (CI): 0.01–0.08) and the number of alcohol-attributable liver cirrhosis DALYs per 100,000 people per litre of alcohol consumed *per capita* decreased by 1.44 (95% CI: 0.39–2.49). For comparison, in 2010 the world average alcohol-attributable liver cirrhosis deaths per 100,000 people per litre of alcohol consumed *per capita* was 1.31 and the number of alcohol-attributable liver cirrhosis DALYs per 100,000 people per litre of alcohol consumed *per capita* was 38.48.

#### Global burden of liver cancer

In 2010, 337,400 deaths (91,500 female deaths and 245,900 male deaths) and 8,670,000 DALYs (2,252,000 DALYs for women and 6,418,000 DALYs for men) from malignant neoplasms were attributable to alcohol consumption. Of these alcohol-attributable malignant neoplasm deaths, 80,600 deaths (14,800 deaths of women and 65,900 deaths of men) were caused by liver cancer and were attributable to alcohol consumption. Liver cancer deaths attributable to alcohol consumption were responsible for 0.2% of all deaths (0.1% of all deaths of women and 0.2% of all deaths of men), 10.7% (6.4% for women and 12.7% for men) of the deaths from liver cancer, 1.7% (0.9% for women and 2.1% for men) of the net number of alcohol-attributable deaths and 23.9% (16.2% for women and 26.8% for men) of all alcohol-attributable cancer deaths. Of the DALYs due to malignant neoplasms attributable to alcohol consumption, 2,142,000 (335,000 DALYs for women and 1,807,000 DALYs for men) were caused by liver cancers attributable to alcohol consumption. This represents 0.1% of all DALYs (0.03% of all DALYs for women and 0.1% of all DALYs for men), 11.2% (6.4% for women and 13.0% for men) of the DALYs from liver cancer, 1.6% (1.0% for women and 1.8% for men) of the net number of alcohol-attributable DALYs lost, and 24.7% (14.9% for women and 28.2% for men) of the DALYs from alcohol-attributable cancers; (see [Supplementary data 4](#) for information on the burden of alcohol-attributable liver cancer).

The alcohol-attributable liver cancer deaths and DALYs per 100,000 people per litre of alcohol consumed *per capita* were not significantly associated with GDP (PPP).

#### Key Points

- The burden of alcoholic liver diseases is large and resulted in 493,300 deaths and 14,544,000 disability adjusted life years (DALYs) in 2010. This burden represents 0.9% of all deaths and 0.6% of all DALYs in 2010
- Alcohol is strongly associated with overall liver cirrhosis rates, with 47.9% of liver cirrhosis deaths (46.5% of women and 48.5% of men) and 46.9% of DALYs lost from liver cirrhosis (44.5% for women and 47.9% for men) attributable to alcohol consumption
- Alcohol-attributable liver cancer was responsible for 80,600 deaths and 2,142,000 DALYs in 2010, representing 0.15% of all deaths and 0.09% of all DALYs lost globally
- To reduce the burden of alcoholic liver diseases and alcoholic liver cancer, interventions are required to reduce alcohol consumption, including taxation increases and increases in treatment rates for alcohol use disorders
- In addition, clinical interventions for alcoholic liver disease should focus on timely treatment of its initial, reversible, stages, via screening and early detection of alcohol use disorders

#### Discussion

Before discussing the implications of our results, the potential limitations of our research should be addressed. When reading our numbers it should be kept in mind that for both diseases the estimation of alcohol-attributable fractions was made indirectly, by combining distribution of exposure and risk relations. Thus, we avoid the subjectivity of a direct diagnosis for alcoholic liver cirrhosis, but we introduce potential other biases. Each review or summary analysis is only as reliable as the underlying data and since our analyses are dependent on three main sources of data, namely, exposure to alcohol, estimates of the mortality and disease burden, and the risk relations between exposure and outcome, the validity and reliability of these components must be considered. Alcohol consumption consists of recorded and unrecorded consumption data [42,43], which, in comparison to other risk exposures, is fairly reliable at the country level [7,31,44], even though the unrecorded consumption data contain more measurement error.

With respect to risk relations, the analyses contained in this paper are often limited by the use of one-time measurements of exposure when calculating the alcohol-attributable burden of liver cirrhosis and liver cancer. The exclusion of past patterns of drinking is problematic when studying the role of alcohol in the development of long-developing diseases, such as malignant neoplasms, where the time between exposure(s) to a carcinogen and exhibiting symptoms of cancer can range from between 15 and 30 years [45]. Liver cirrhosis at the individual level is also

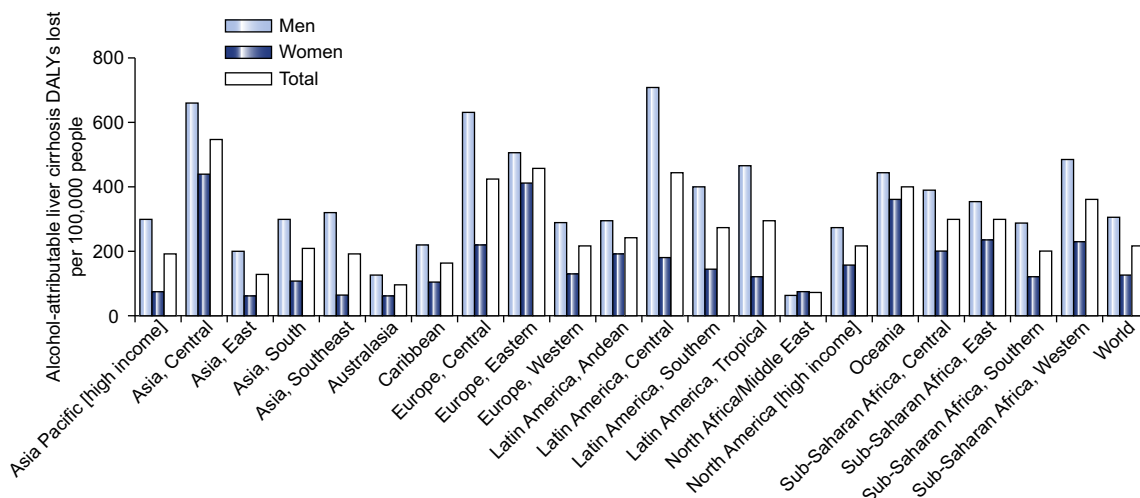


Fig. 3. Alcohol-attributable liver cirrhosis disability adjusted life years (DALYs) per 100,000 people in 2010 by sex and region.

affected mainly by long-term heavy drinking; however, an immediate decrease in the incidence of liver cirrhosis is seen at the country level, a short time after decreases in alcohol consumption [46,47]. For example, the Gorbachev reforms involving a substantial decrease of alcohol resulted in a marked immediate decrease of liver cirrhosis mortality [48]. Similar observations were made in France during the World War II occupation, when alcohol was confiscated [46]. Thus, estimates presented in this paper for 2010 should be accurate as most cases of mortality are triggered by the recent heavy use of alcohol [47].

Another potential limitation of the methodology used to calculate the alcohol-attributable burden of liver cancer and of liver cirrhosis is the use of adjusted RR functions. The AAF formulas used in our analysis rely on the assumption that the RR functions are unadjusted, and therefore the use of RR functions from meta-analyses (where adjusted RR estimates were used) in our analysis may have introduced an error into our results [49]. However, this error should have no noticeable effect on the results, since most analyses show no marked differences after adjustment for the usual risk factors tested (see [4] for an overview of relevant meta-analyses). In addition, if unadjusted RR functions had been used in our analysis, our results would have been more limited. This is because only a small proportion of older studies could have been included if we had used unadjusted RR functions, which would have led to inaccurate estimates of the number of alcohol-attributable deaths. It should be noted that in risk analyses, such as the Comparative Risk Assessment for the GBD studies [44], almost all of the underlying studies for the different risk factors only report adjusted RR estimates. The need for adjustment to the RR functions may change when other dimensions of alcohol consumption, such as frequency of heavy drinking occasions, are considered.

The burden of ALDs is huge on a global level. The most direct clinical approach to minimizing the burden of ALD would be timely treatment of its initial, reversible, stages of disease. Given that in early stages ALD is often asymptomatic and can only be identified by laboratory findings [9], a focus on screening for alcohol use disorders and their treatment [50,51] seems to be the most feasible approach for prevention of ALD. At the same time,

given that alcohol use disorders are very likely to be accompanied by at least a mild form of ALD, clinicians should approach treatment of alcohol use disorders with the prevention and potential treatment of ALD in mind. Thus, treatment should include psychosocial and pharmacotherapies – treatment of alcohol use disorders, treatment of alcohol liver disease, correction of nutritional status, etc. Prescription of the most widely used pharmacotherapies for alcohol use disorders, i.e., disulfiram, naltrexone and acamprostate, should be considered after assessment of ALD, and in cases of advanced ALD preference should be given to medications that are not hepatotoxic [9].

In principle, all burden associated with ALD is avoidable [28], but prevention is difficult as it attempts to change culturally engrained habits such as heavy alcohol consumption. To combat this burden, the World Health Organization has recently launched a global strategy to reduce the harmful use of alcohol [52], building on earlier recommendations [53,54]. This global strategy focuses on ten key areas of policy options and interventions at the national level and four priority areas for global action. The ten areas for national action include health services' response and community action, but focus on preventive public health actions such as drink-driving policies and countermeasures; reductions of availability of alcohol; ban of marketing of alcoholic beverages; and increase of prices (i.e., via taxation). It also includes harm reduction measures to reduce the negative consequences of drinking and alcohol intoxication of those who drink. Other foci refer to a reduction of unrecorded illicit and informally produced alcohol, and the establishment of a monitoring and surveillance system [52].

Most of these measures are not only effective but also cost-effective, with taxation increases to increase the price of alcoholic beverages, reductions of availability of alcohol, and bans of its marketing being identified as “best buys” for the reduction of alcohol-attributable harm [54–56].

The global burden of ALDs strongly reinforces the necessity of implementing such public health strategies to prevent alcohol-attributable harm, even though to do so may not always be the most popular with politicians who tend to focus on education or individual-based responses [50,57].

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**Conflict of interest**

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

**Supplementary data**

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.jhep.2013.03.007>.

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