

National, regional, and global burdens of disease from 2000 to 2016 attributable to alcohol use: a comparative risk assessment study



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Summary

Background Alcohol use has increased globally, with varying trends in different parts of the world. This study investigates gender, age, and geographical differences in the alcohol-attributable burden of disease from 2000 to 2016.

Methods This comparative risk assessment study estimated the alcohol-attributable burden of disease. Population-attributable fractions (PAFs) were estimated by combining alcohol exposure data obtained from production and taxation statistics and from national surveys with corresponding relative risks obtained from meta-analyses and cohort studies. Mortality and morbidity data were obtained from the WHO Global Health Estimates, population data were obtained from the UN Population Division, and human development index (HDI) data were obtained from the UN Development Programme. Uncertainty intervals (UIs) were estimated using a Monte Carlo-like approach.

Findings Globally, we estimated that there were 3.0 million (95% UI 2.6–3.6) alcohol-attributable deaths and 131.4 million (119.4–154.4) disability-adjusted life-years (DALYs) in 2016, corresponding to 5.3% (4.6–6.3) of all deaths and 5.0% (4.6–5.9) of all DALYs. Alcohol use was a major risk factor for communicable, maternal, perinatal, and nutritional diseases (PAF of 3.3% [1.9–5.6]), non-communicable diseases (4.3% [3.6–5.1]), and injury (17.7% [14.3–23.0]) deaths. The alcohol-attributable burden of disease was higher among men than among women, and the alcohol-attributable age-standardised burden of disease was highest in the eastern Europe and western, southern, and central sub-Saharan Africa regions, and in countries with low HDIs. 52.4% of all alcohol-attributable deaths occurred in people younger than 60 years.

Interpretation As a leading risk factor for the burden of disease, alcohol use disproportionately affects people in low HDI countries and young people. Given the variations in the alcohol-attributable burden of disease, cost-effective local and national policy measures that can reduce alcohol use and the resulting burden of disease are needed, especially in low-income and middle-income countries.

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Introduction

Alcohol use has been identified as one of the ten leading risk factors for the burden of disease in all global comparative risk assessments to date.^{1,2} There have been a series of global initiatives to reduce the harmful use of alcohol, including WHO's global strategy to reduce the harmful use of alcohol,³ the inclusion of the reduction of harmful alcohol use as one of the targets within the Noncommunicable Disease (NCD) Global Monitoring Framework, and alcohol use being addressed in the Sustainable Development Goals.⁴ Nevertheless, alcohol use globally has not decreased over the past three decades, and predictions forecast an increase in use until at least 2030.⁵

Even though the global trend in alcohol use shows an overall increase, trends have varied in different parts of the world.⁵ For example, alcohol use has declined in many European countries, a trend first observed in western European countries, and more recently also observed in eastern European countries, including Russia.⁶ By

contrast, alcohol use has increased in several Asian countries, most notably in India and Vietnam, albeit from substantially lower levels of use than in Europe.⁷ In China, there has been a substantial net increase in alcohol use since 1990, with periods of stagnation and decline for various reasons, such as alcohol policies.⁶ Another important region is sub-Saharan Africa, where alcohol use has increased and is now about equal to the global average.⁵

Such shifts in use have been accompanied by similar shifts in the burden of disease and rates of mortality.⁸ Furthermore, with the continued high ranking of alcohol use as a risk factor,² it is important to understand which regions and populations are disproportionately affected and to what degree in order to prioritise the implementation of evidence-based policies. Additionally, previously published estimates of the alcohol-attributable burden of disease have various methodological limitations which might have resulted in negative policy implications.⁹ Accordingly, we aimed to describe the alcohol-attributable

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Research in context

Evidence before this study

We manually searched WHO's Global Health Observatory and the Institute for Health Metrics and Evaluation's research articles database for publications on the burden of disease attributable to alcohol published between Jan 1, 2000, and Aug 1, 2019, in English. Alcohol is a leading contributor to the global burden of disease. Previous estimates of the alcohol-attributable burdens of disease enabled cross-country comparisons of alcohol use and its harms using data on alcohol sales, the prevalence of drinking and abstention, and self-reports of use, combined with corresponding relative risk functions. However, the alcohol-attributable burden of disease estimates from the 2017 Global Burden of Disease Study (GBD) have several limitations: estimates of liver cirrhosis are based on an aetiological model rather than a risk factor approach; HIV/AIDS is excluded from the estimations; the age-modification of the relative risk of ischaemic events is not considered; the effects of heavy episodic drinking are not taken into account; and the increased disease risk for former drinkers is not accounted for.

Added value of this study

This study improves estimates of the global alcohol-attributable burden of disease by addressing the limitations of GBD 2017.

Although the estimates of GBD 2017 and those of the present study are similar at the global level, our study suggests that the global alcohol-attributable burden of disease (when measured in disability-adjusted life-years) might be greater than previously thought. This study found that the alcohol-attributable burdens of disease in the sub-Saharan Africa and eastern Europe regions are considerably higher than were estimated by GBD 2017. Furthermore, the results of this study indicate that alcohol is a leading risk factor for communicable diseases in addition to non-communicable diseases and injuries.

Implications of all the available evidence

Variations in the estimates of the alcohol-attributable burdens of disease indicate that a large proportion of these burdens is preventable through the implementation of cost-effective policies. Although such policies have been implemented in some countries in the eastern Europe region (eg, Russia), resulting in large increases in life expectancies, alcohol policies remain underdeveloped in the sub-Saharan Africa region, where most countries have not done research on the effectiveness of alcohol policies, and where only 16 of 46 countries have national or subnational alcohol strategies.

burden of disease from 2000 to 2016 and to derive conclusions for effective alcohol policies, including treatment policies.

Methods

Study design

This comparative risk assessment study assessed the alcohol-attributable burden of disease for each of 2000, 2005, 2010, 2015, and 2016, which we modelled using a Levin-based population-attributable fraction (PAF) method¹⁰ based on the theoretical minimum risk exposure level being defined as lifetime abstention from alcohol.¹¹ In-depth details of these methods are in appendix 1 (p 7).

See Online for appendix 1

Alcohol exposure data

Alcohol exposure data were obtained from multiple sources. Drinking status data, namely the prevalence of past-year drinkers, former drinkers, and heavy episodic drinkers, specific to age (categories 15–19 years, 20–24 years, 25–34 years, 35–49 years, 50–64 years, and 65 years and older), sex, country, and year were obtained from a modelling study of population surveys.⁵ To correct for the undercoverage of alcohol use as measured by population surveys, average daily alcohol use among drinkers was modelled by combining data from surveys on alcohol use among current drinkers with data on alcohol per capita.¹² Details of the sources of alcohol per capita data, the applied model for describing the

distribution of alcohol use, and the model's assumptions are reported in appendix 1 (p 10).

Relative risk estimates

Relative risk (RR) estimates were obtained from multiple sources; the RR estimates used to estimate the alcohol-attributable burden of disease were selected by the WHO Technical Advisory Group on Alcohol and Drug Epidemiology. Selection criteria for RR estimates included whether the respective study's meta-analyses modelled the continuous dose–response risk relationship between alcohol and cancer using up-to-date data that controlled for confounding factors, used lifetime abstainers as the reference group (rather than non-drinkers), and matched WHO-reported disease and injury categories. For Belarus, Estonia, Latvia, Lithuania, Moldova, Russia, and Ukraine, RRs from the Russian cohort study by Zaridze and colleagues¹³ were used to account for the unique drinking patterns observed in these countries, differences in risk-taking disposition, and the contexts of alcohol consumption.^{14,15} The sources and formulas of the RR functions are in appendix 1 (p 15).

Mortality, morbidity, and population data

Data on mortality, years of life lost (YLL), and morbidity (years lived with disability [YLD] and disability-adjusted life-years [DALYs]) were obtained from WHO's Global Health Estimates; data were available by year, country, age, and sex, as well as by cause of mortality and morbidity.

	Alcohol-attributable burden		Population-attributable fraction		Age-adjusted alcohol-attributable burden per 100 000 people		Percentage change in the age-adjusted alcohol-attributable burden per 100 000 people since 2000	
	Deaths (thousands)	DALYs (millions)	Deaths	DALYs	Deaths	DALYs	Deaths	DALYs
All causes	2967.8 (2606.4 to 3552.7)	131.4 (119.4 to 154.4)	5.3% (4.6 to 6.3)	5.0% (4.6 to 5.9)	38.6 (33.9 to 46.1)	1741.7 (1582.7 to 2045.8)	-17.9 (-27.3 to -12.1)	-14.5 (-22.5 to -9.4)
Communicable, maternal, perinatal and nutritional conditions	361.9 (205.6 to 615.8)	13.9 (7.5 to 23.5)	3.3% (1.9 to 5.6)	1.9% (1.0 to 3.2)	4.7 (2.7 to 8.0)	184.4 (99.7 to 311.5)	-15.5 (-36.4 to 5.4)	-15.2 (-36.9 to 6.1)
Tuberculosis	236.3 (74.6 to 456.6)	9.9 (3.2 to 18.6)	18.3% (5.8 to 35.3)	19.2% (6.2 to 36.1)	3.1 (1.0 to 6.0)	131.7 (42.7 to 247.4)	-14.1 (-40.3 to 9.4)	-11.8 (-37.8 to 10.5)
HIV/AIDS	30.4 (22.8 to 56.7)	1.7 (1.2 to 3.1)	3.0% (2.3 to 5.6)	2.8% (2.1 to 5.2)	0.4 (0.3 to 0.8)	22.4 (16.8 to 42.1)	-30.2 (-47.4 to 16.8)	-30.8 (-47.9 to 17.4)
Lower respiratory infections	95.2 (48.5 to 177.6)	2.3 (1.3 to 4.3)	3.2% (1.6 to 6.0)	1.8% (1.0 to 3.3)	1.2 (0.6 to 2.2)	30.4 (16.6 to 55.5)	-13.0 (-28.0 to 6.5)	-15.2 (-32.1 to 4.5)
Non-communicable diseases	1743.1 (1476.2 to 2080.5)	65.4 (59.7 to 73.2)	4.3% (3.6 to 5.1)	4.2% (3.8 to 4.7)	22.4 (19.1 to 26.7)	861.0 (787.4 to 962.9)	-19.3 (-30.1 to -13.9)	-14.6 (-24.8 to -10.1)
Malignant neoplasms	430.2 (329.6 to 451.5)	12.0 (9.0 to 12.4)	4.8% (3.7 to 5.0)	4.9% (3.7 to 5.1)	5.5 (4.2 to 5.8)	156.9 (117.3 to 162.0)	-5.5 (-31.2 to -9.9)	-5.9 (-33.9 to -11.2)
Lip and oral cavity cancer	52.2 (35.2 to 53.1)	1.7 (1.1 to 1.7)	31.3% (21.1 to 31.8)	31.3% (19.8 to 31.3)	0.7 (0.5 to 0.7)	21.7 (13.7 to 21.7)	16.1 (-30.2 to 8.6)	18.2 (-34.7 to 9.9)
Other pharynx cancers	38.6 (26.6 to 40.1)	1.2 (0.8 to 1.2)	34.9% (24.1 to 36.3)	35.4% (23.9 to 36.5)	0.5 (0.3 to 0.5)	15.6 (10.5 to 16.1)	12.2 (-29.9 to 7.0)	9.2 (-34.5 to 4.2)
Oesophagus cancer	82.9 (55.3 to 85.7)	2.2 (1.5 to 2.2)	19.3% (12.9 to 20.0)	20.0% (13.5 to 20.5)	1.1 (0.7 to 1.1)	28.2 (19.1 to 29.0)	-6.2 (-47.0 to -7.6)	-9.8 (-48.5 to -11.6)
Colon and rectum cancers	92.6 (73.7 to 109.1)	2.2 (1.8 to 2.6)	11.7% (9.3 to 13.7)	11.6% (9.2 to 13.6)	1.2 (0.9 to 1.4)	28.8 (22.8 to 33.6)	-14.2 (-25.0 to -14.0)	-13.5 (-25.3 to -14.0)
Liver cancer	101.4 (54.1 to 140.4)	2.8 (1.5 to 3.9)	12.2% (6.5 to 16.9)	11.9% (6.2 to 16.4)	1.3 (0.7 to 1.8)	36.9 (19.0 to 50.8)	1.8 (-29.4 to -0.7)	-0.7 (-33.3 to -2.6)
Breast cancer	42.0 (27.9 to 42.3)	1.4 (0.9 to 1.3)	7.2% (4.8 to 7.2)	7.3% (4.6 to 7.1)	0.5 (0.4 to 0.5)	18.2 (11.5 to 17.6)	-20.1 (-36.6 to -15.9)	-17.6 (-37.5 to -14.8)
Larynx cancer	20.5 (15.0 to 24.4)	0.6 (0.4 to 0.7)	22.3% (16.3 to 26.5)	22.6% (16.5 to 26.6)	0.3 (0.2 to 0.3)	7.5 (5.5 to 8.8)	-25.1 (-42.7 to -27.1)	-27.3 (-45.2 to -29.3)
Diabetes mellitus	-35.1 (-54.2 to 3.4)	-1.7 (-2.5 to 0.0)	-2.2% (-3.4 to 0.2)	-2.5% (-3.9 to 0.1)	-0.4 (-0.7 to 0.0)	-21.6 (-32.8 to 0.7)	-5.8 (-149.1 to 34.9)	5.0 (-93.4 to 60.4)
Alcohol use disorders	145.6 (145.6 to 145.6)	18.5 (18.5 to 18.5)	100.0% (100.0 to 100.0)	100.0% (100.0 to 100.0)	1.9 (1.9 to 1.9)	246.4 (246.4 to 246.4)	-30.8 (-30.8 to -30.8)	-17.3 (-17.3 to -17.3)
Epilepsy	16.4 (13.7 to 21.6)	1.4 (1.2 to 1.9)	12.0% (10.0 to 15.7)	9.8% (8.3 to 12.7)	0.2 (0.2 to 0.3)	19.2 (16.2 to 25.0)	1.5 (-17.4 to 19.8)	2.2 (-14.2 to 19.4)
Cardiovascular diseases	569.6 (328.4 to 874.9)	12.6 (8.5 to 18.7)	3.2% (1.8 to 4.9)	3.1% (2.1 to 4.5)	7.2 (4.2 to 11.0)	163.0 (110.7 to 241.6)	-37.5 (-53.3 to -21.5)	-36.3 (-52.6 to -19.4)
Hypertensive heart disease	66.5 (52.8 to 87.2)	1.5 (1.2 to 2.0)	7.4% (5.9 to 9.7)	8.0% (6.4 to 10.3)	0.8 (0.7 to 1.1)	19.6 (15.7 to 25.5)	15.2 (-12.5 to 42.7)	10.0 (-14.6 to 34.8)
Ischaemic heart disease	250.8 (13.6 to 467.5)	4.1 (0.0 to 7.8)	2.7% (0.1 to 5.0)	2.0% (0.0 to 3.8)	3.1 (0.1 to 5.7)	52.5 (-0.4 to 99.3)	-54.2 (-93.7 to -39.0)	-60.2 (-100.5 to -44.0)
Ischaemic stroke	-59.3 (-119.9 to 53.8)	-1.4 (-2.5 to 0.6)	-2.1% (-4.3 to 1.9)	-2.3% (-4.0 to 0.9)	-0.7 (-1.5 to 0.7)	-18.2 (-31.4 to 7.1)	39.0 (-783.4 to 992.3)	64.2 (-1002.2 to 1074.7)
Haemorrhagic stroke	287.0 (212.8 to 394.2)	7.5 (5.6 to 10.2)	9.7% (7.2 to 13.3)	9.9% (7.4 to 13.5)	3.7 (2.7 to 5.0)	97.8 (72.9 to 133.2)	-16.9 (-32.6 to 1.0)	-12.6 (-29.0 to 5.4)
Cardiomyopathy, myocarditis, endocarditis	24.7 (24.9 to 68.8)	0.9 (0.9 to 2.7)	6.6% (6.7 to 18.4)	7.3% (7.3 to 22.7)	0.3 (0.3 to 0.9)	11.3 (11.4 to 35.8)	111.5 (-69.9 to 238.2)	112.7 (-72.2 to 275.4)
Digestive diseases	616.4 (561.4 to 714.1)	22.5 (20.5 to 26.0)	24.4% (22.2 to 28.2)	25.3% (23.1 to 29.2)	8.1 (7.3 to 9.3)	297.1 (270.8 to 343.0)	1.1 (-9.7 to 12.2)	2.6 (-9.2 to 14.3)
Cirrhosis of the liver	588.1 (531.7 to 683.4)	21.5 (19.4 to 24.8)	46.9% (42.4 to 54.5)	47.4% (42.9 to 54.8)	7.7 (7.0 to 8.9)	283.4 (256.6 to 327.5)	1.5 (-9.8 to 12.7)	3.1 (-9.2 to 15.0)
Pancreatitis	28.2 (21.5 to 39.3)	1.0 (0.8 to 1.4)	24.4% (18.6 to 34.0)	26.5% (20.2 to 36.8)	0.4 (0.3 to 0.5)	13.6 (10.4 to 18.9)	-5.9 (-14.2 to 4.7)	-6.5 (-15.0 to 3.8)

(Table continues on next page)

	Alcohol-attributable burden		Population-attributable fraction		Age-adjusted alcohol-attributable burden per 100 000 people		Percentage change in the age-adjusted alcohol-attributable burden per 100 000 people since 2000	
	Deaths (thousands)	DALYs (millions)	Deaths	DALYs	Deaths	DALYs	Deaths	DALYs
(Continued from previous page)								
Injuries	862.8 (697.2 to 1125.2)	52.1 (42.3 to 67.5)	17.7% (14.3 to 23.0)	17.5% (14.2 to 22.7)	11.4 (9.2 to 14.9)	696.3 (563.9 to 902.8)	-16.3 (-20.3 to -11.7)	-14.1 (-17.9 to -9.9)
Unintentional injuries	629.0 (504.8 to 854.6)	39.7 (32.0 to 53.1)	18.3% (14.7 to 24.9)	18.4% (14.9 to 24.7)	8.3 (6.7 to 11.3)	528.9 (426.8 to 708.4)	-9.7 (-14.1 to -4.7)	-8.7 (-12.5 to -4.6)
Road injury	370.8 (270.3 to 553.3)	22.2 (16.2 to 33.1)	26.4% (19.3 to 39.5)	26.9% (19.6 to 40.1)	4.9 (3.6 to 7.4)	297.9 (217.1 to 443.5)	2.9 (-1.2 to 8.3)	1.6 (-2.1 to 6.5)
Poisonings	12.7 (8.7 to 18.1)	0.6 (0.4 to 0.9)	11.9% (8.1 to 17.0)	10.2% (7.0 to 14.5)	0.2 (0.1 to 0.2)	8.6 (5.8 to 12.1)	-39.6 (-44.6 to -35.3)	-39.3 (-43.6 to -35.4)
Falls	79.4 (51.6 to 116.5)	6.0 (4.2 to 8.3)	12.0% (7.8 to 17.6)	15.8% (10.9 to 21.8)	1.0 (0.7 to 1.5)	79.1 (54.6 to 109.5)	4.5 (-5.7 to 13.1)	-4.2 (-10.8 to 0.9)
Fire, heat, and hot substances	17.2 (12.9 to 23.3)	1.2 (0.9 to 1.6)	11.2% (8.5 to 15.3)	11.0% (8.0 to 14.9)	0.2 (0.2 to 0.3)	15.6 (11.4 to 21.1)	-43.0 (-48.2 to -38.2)	-33.4 (-38.6 to -29.2)
Drowning	38.1 (25.0 to 54.2)	1.9 (1.2 to 2.7)	11.8% (7.8 to 16.8)	9.4% (6.1 to 13.4)	0.5 (0.3 to 0.7)	25.4 (16.6 to 36.3)	-29.8 (-38.2 to -23.9)	-31.6 (-39.7 to -26.1)
Exposure to mechanical forces	21.5 (13.4 to 31.0)	2.0 (1.3 to 2.8)	14.3% (8.9 to 20.7)	15.0% (9.5 to 21.1)	0.3 (0.2 to 0.4)	26.4 (16.8 to 37.1)	-21.4 (-29.0 to -16.6)	-14.6 (-20.4 to -10.8)
Other unintentional injuries	89.3 (60.4 to 125.9)	5.7 (3.8 to 8.0)	14.1% (9.5 to 19.9)	13.0% (8.7 to 18.3)	1.2 (0.8 to 1.6)	76.0 (50.8 to 107.0)	-30.0 (-36.5 to -25.4)	-22.7 (-28.8 to -18.4)
Intentional injuries	233.9 (114.8 to 360.9)	12.5 (6.0 to 19.4)	16.1% (7.9 to 24.8)	15.2% (7.2 to 23.6)	3.1 (1.5 to 4.8)	167.4 (79.7 to 261.0)	-29.9 (-43.6 to -23.8)	-27.6 (-41.5 to -21.9)
Self-harm	147.0 (79.6 to 220.5)	7.0 (3.8 to 10.5)	18.5% (10.0 to 27.8)	18.7% (10.0 to 27.9)	1.9 (1.1 to 2.9)	93.9 (50.3 to 140.5)	-28.6 (-40.3 to -22.9)	-27.9 (-40.0 to -22.5)
Interpersonal violence	86.8 (34.0 to 140.1)	5.5 (2.1 to 8.8)	18.2% (7.1 to 29.4)	17.5% (6.7 to 28.3)	1.2 (0.5 to 1.9)	73.5 (28.3 to 119.2)	-32.1 (-50.9 to -25.1)	-27.3 (-45.6 to -21.0)

Numbers in parentheses are 95% uncertainty intervals. DALYs=disability-adjusted life-years.

Table: Global alcohol-attributable burden of disease in 2016, by cause, and the change in this burden since 2000

Mortality and morbidity due to alcoholic cardiomyopathy have not been estimated by WHO and are contained in the larger category of cardiomyopathy, myocarditis, and endocarditis mortality and morbidity. Accordingly, alcoholic cardiomyopathy mortality and morbidity were estimated using the methods of Manthey and colleagues¹⁶ (appendix 1 p 8). Estimates of motor vehicle deaths due to alcohol use were stratified into those involving the driver and those involving others (ie, deaths of drivers and deaths of people other than the driver) based on the fractions of motor vehicle deaths that involved drivers and those that involved people other than the driver as obtained from the WHO road traffic deaths database.

Population data by country, age, sex, and year were obtained from the UN Population Division (2017 revisions).¹⁷ Age-standardised rates were estimated on the basis of the WHO standard population.¹⁸ To match age-standardisation data, deaths, YLLs, YLDs, and DALYs were aggregated into 5-year age groups starting at 0 years up to 84 years, and a final category of 85 years and older. Consequently, the alcohol PAFs were applied to mortality and morbidity age groupings, which were encompassed within the alcohol PAFs' age groupings. Data were aggregated by the GBD regions¹⁹ to assess

regional differences. GBD regions were chosen rather than the WHO regional groupings because the GBD regions were constructed for public health purposes and not for administrative purposes.¹⁹ Furthermore, data were aggregated by the 2016 human development index (HDI) categories as obtained from the UN Development Programme human development data tool.

Estimates of uncertainty

Estimates of uncertainty (95% uncertainty intervals [UIs]) were constructed using 1000 simulated estimates using a Monte Carlo-like approach (appendix 1 p 76). From these simulated estimates, the 2.5th and 97.5th percentiles were used to construct the 95% UIs.

Results

In 2016, an estimated 3.0 million (95% UI 2.6–3.6) deaths and 131.4 million (119.4–154.4) DALYs were attributable to alcohol globally, representing 5.3% (4.6–6.3) of all deaths and 5.0% (4.6–5.9) of all DALYs (table).

The global alcohol-attributable burden of disease was due primarily to premature mortality (106.6 million [95% UI 95.3–127.7] YLLs; 5.7% [5.1–6.8] of all YLLs) rather than

For the human development data tool see <http://hdr.undp.org/en/data>

For the WHO road traffic deaths database see https://www.who.int/gbd/road_safety/mortality/en/

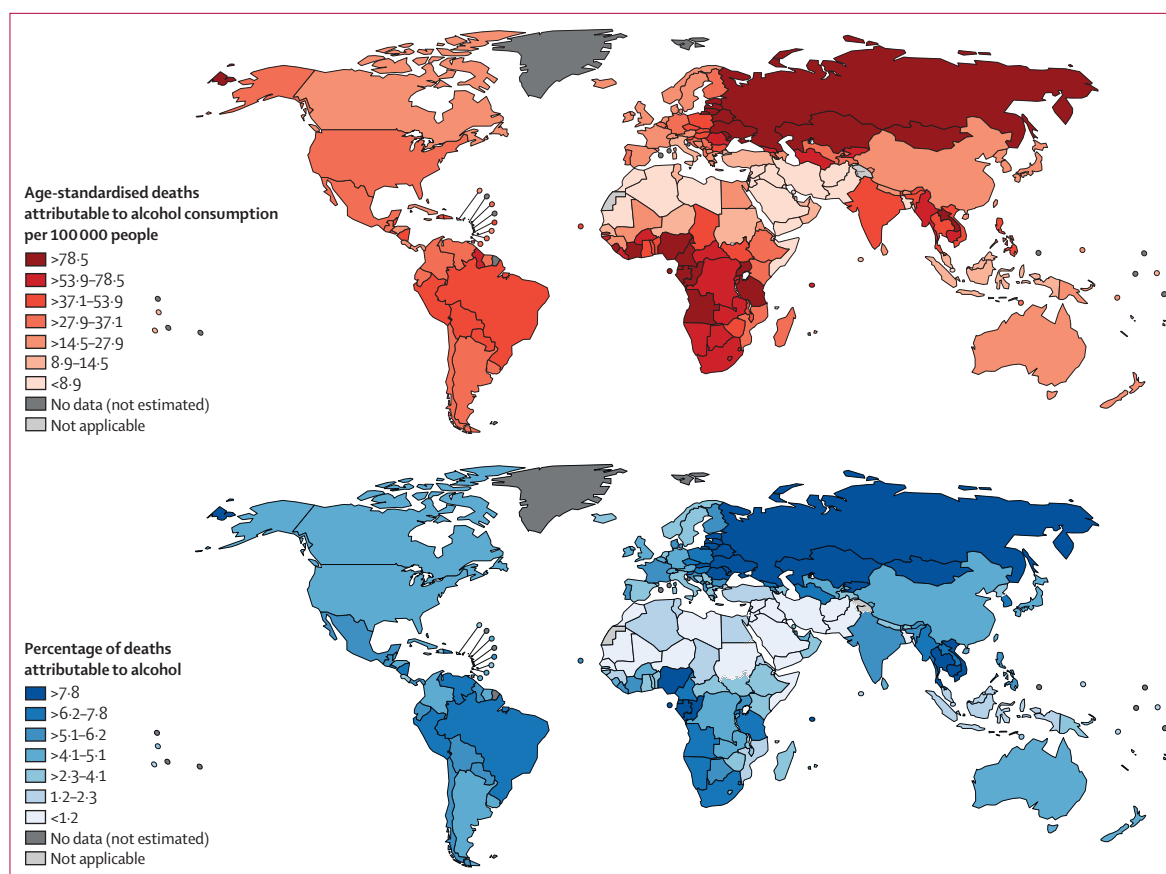


Figure 1: Burden of alcohol-attributable deaths globally in 2016, by country

morbidity (24.8 million [22.8–28.3] YLDs; 3.4% [3.1–3.8] of all YLDs; appendix 1 p 98).

Alcohol was a large contributor to the burden of communicable, maternal, perinatal, and nutritional conditions, with 0.4 million (95% UI 0.2–0.6) alcohol-attributable deaths (3.3% [95% UI 1.9–5.6] of total) and 13.9 million (7.5–23.5) alcohol-attributable DALYs, (1.9% [1.0–3.2] of total); to the burden of NCDs, alcohol contributed 1.7 million (1.5–2.1) deaths (4.3% [3.6–5.1] of total) and 65.4 million (59.7–73.2) DALYs (4.2% [3.8–4.7] of total); and to the burden of injuries, alcohol contributed 0.9 million (0.7–1.1) deaths (17.7% [14.3–23.0] of total) and 52.1 million (42.3–67.5) DALYs (17.5% [14.2–22.7] of total). Furthermore, 0.19 million (95% UI 0.14–0.30) deaths and 11.6 million (8.7–18.7) DALYs were attributable to the drinking of others (ie, alcohol-attributable motor vehicle accident injuries inflicted on people other than the drunk driver).

At the regional level, the alcohol-attributable age-standardised death rates were highest in the eastern Europe and western and southern sub-Saharan Africa regions, and lowest in the north Africa and Middle East region (figure 1). Similar to the alcohol-attributable death rates, the alcohol-attributable age-standardised rates for DALYs were highest in the eastern Europe, western, central, and southern sub-

Saharan Africa, and central Asia regions, and lowest in the north Africa and Middle East region (figure 2). At the country level, the alcohol-attributable age-standardised death rates were highest in Moldova (224.1 per 100 000), Belarus (174.5 per 100 000), Russia (171.3 per 100 000), Lithuania (163.7 per 100 000), and Nigeria (164.6 per 100 000). Similarly, the age-standardised rates of alcohol-attributable DALYs were highest in Russia (7224.7 per 100 000), Moldova (7072.9 per 100 000), Belarus (6410.2 per 100 000), Lithuania (6183.7 per 100 000), and Nigeria (6157.1 per 100 000; appendix 2).

The largest contributors to the alcohol-attributable burden of disease varied by geographical region. In the eastern Europe region (the region with the highest alcohol-attributable burden), ischaemic heart disease was the largest contributor, with 47.1% of all alcohol-attributable deaths and 25.7% of all alcohol-attributable DALYs. In western sub-Saharan Africa (the region with the second highest alcohol-attributable burden of disease), liver cirrhosis was the largest contributor to the alcohol-attributable burden of disease, contributing to 26.7% of all alcohol-attributable deaths and 22.3% of all alcohol-attributable DALYs (figure 3).

In 2016, countries with a low HDI had the largest age-standardised rates of alcohol-attributable deaths (67.5

See Online for appendix 2

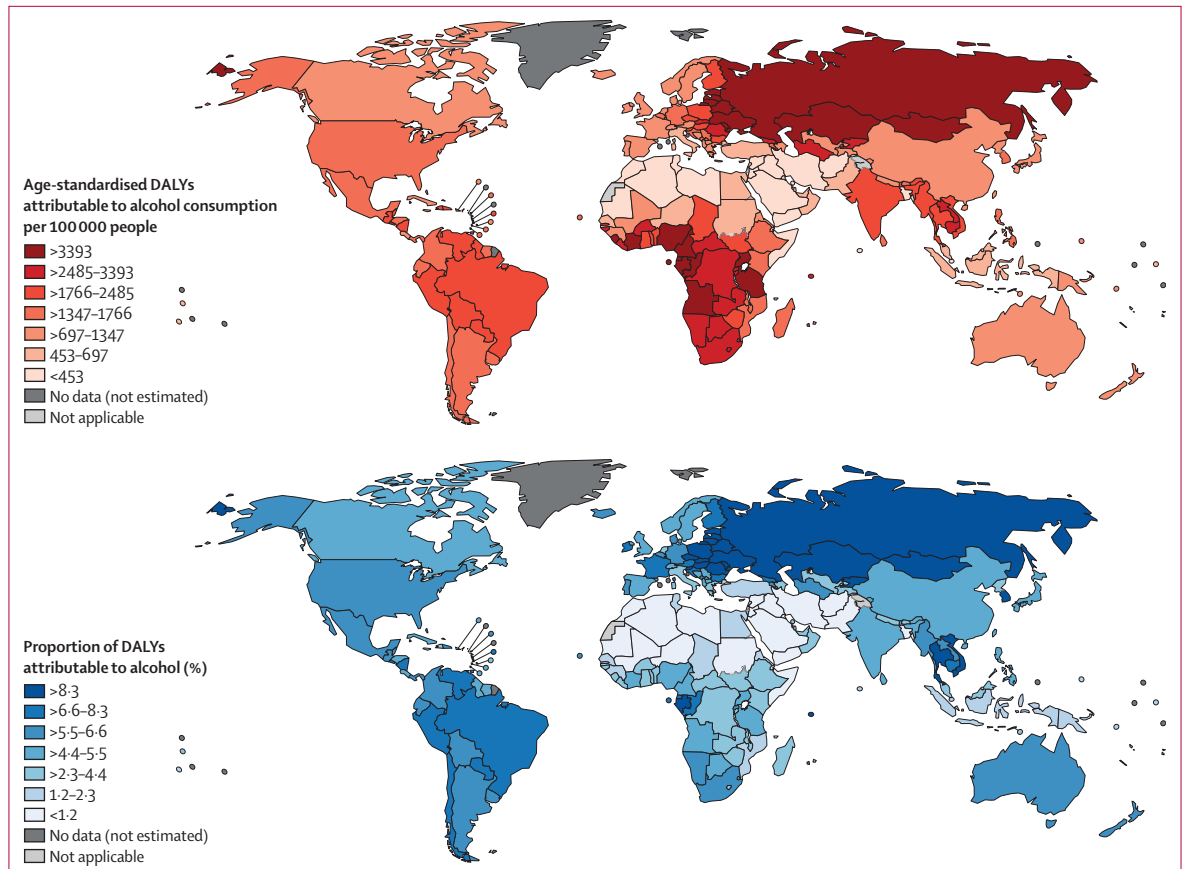


Figure 2: Burden of alcohol-attributable DALYs globally in 2016, by country
DALYs=disability-adjusted life-years.

per 100 000) and alcohol-attributable DALYs (2872.6 per 100 000), followed by countries with a very high HDI (41.8 per 100 000 for alcohol-attributable deaths and 2017.9 per 100 000 for DALYs), countries with a medium HDI (35.8 per 100 000 for alcohol-attributable deaths and 1582.9 per 100 000 for DALYs), and countries with a high HDI (32.7 per 100 000 for alcohol-attributable deaths and 1448.2 per 100 000 for DALYs; figure 4). The largest contributing causes to the alcohol-attributable absolute burden of disease varied by HDI grouping. In low HDI countries, the leading cause of alcohol-attributable deaths was liver cirrhosis (22.2% of alcohol-attributable deaths) and the leading cause of alcohol-attributable DALYs was road injuries (21.3% of alcohol-attributable DALYs lost). In very high HDI countries, ischaemic heart disease was the leading cause of alcohol-attributable deaths (18.8% of alcohol-attributable deaths) and alcohol use disorders were the leading cause of alcohol-attributable DALYs (16.4% of all alcohol-attributable DALYs lost).

Alcohol-attributable deaths mostly occurred at young ages, with 52.4% of all alcohol-attributable deaths occurring in people younger than 60 years. Stratified by sex, 57.4% of alcohol-attributable deaths in men and 39.3% in women occurred at ages younger than 60 years.

The alcohol-attributable PAF for deaths was the highest among the age group 30–34 years, with 13.7% (95% UI 12.0–16.6) of deaths attributable to alcohol within this age group (figure 5). Among men, the alcohol-attributable PAF was highest for ages 25–29 years, with 18.4% of all deaths in this age group attributable to alcohol; whereas for women, the alcohol-attributable PAF was highest for ages 40–44 years, with 6.6% of deaths attributable to alcohol among this group. The alcohol-attributable causes of death varied by age; among people 0–39 years of age, unintentional injuries (42.4% of all alcohol-attributable deaths) and self-harm (10.0%) were the leading causes of alcohol-attributable deaths, among people aged 40–59 years, liver cirrhosis (25.6%) and unintentional injuries (18.8%) were the leading causes of alcohol-attributable deaths, and among people aged 60 years and older, ischaemic heart disease (20.9%) and malignant neoplasms (17.7%) were the leading causes of alcohol-attributable deaths (appendix 1 p 78).

In 2000, 2.5 million (95% UI 2.3–3.1) deaths and 114.5 million (105.3–137.1) DALYs globally were attributable to alcohol, representing 4.9% (4.4–5.9) of all deaths and 4.2% (3.9–5.0) of DALYs globally. According to WHO's Global Health Estimates, from 2000 to 2016,

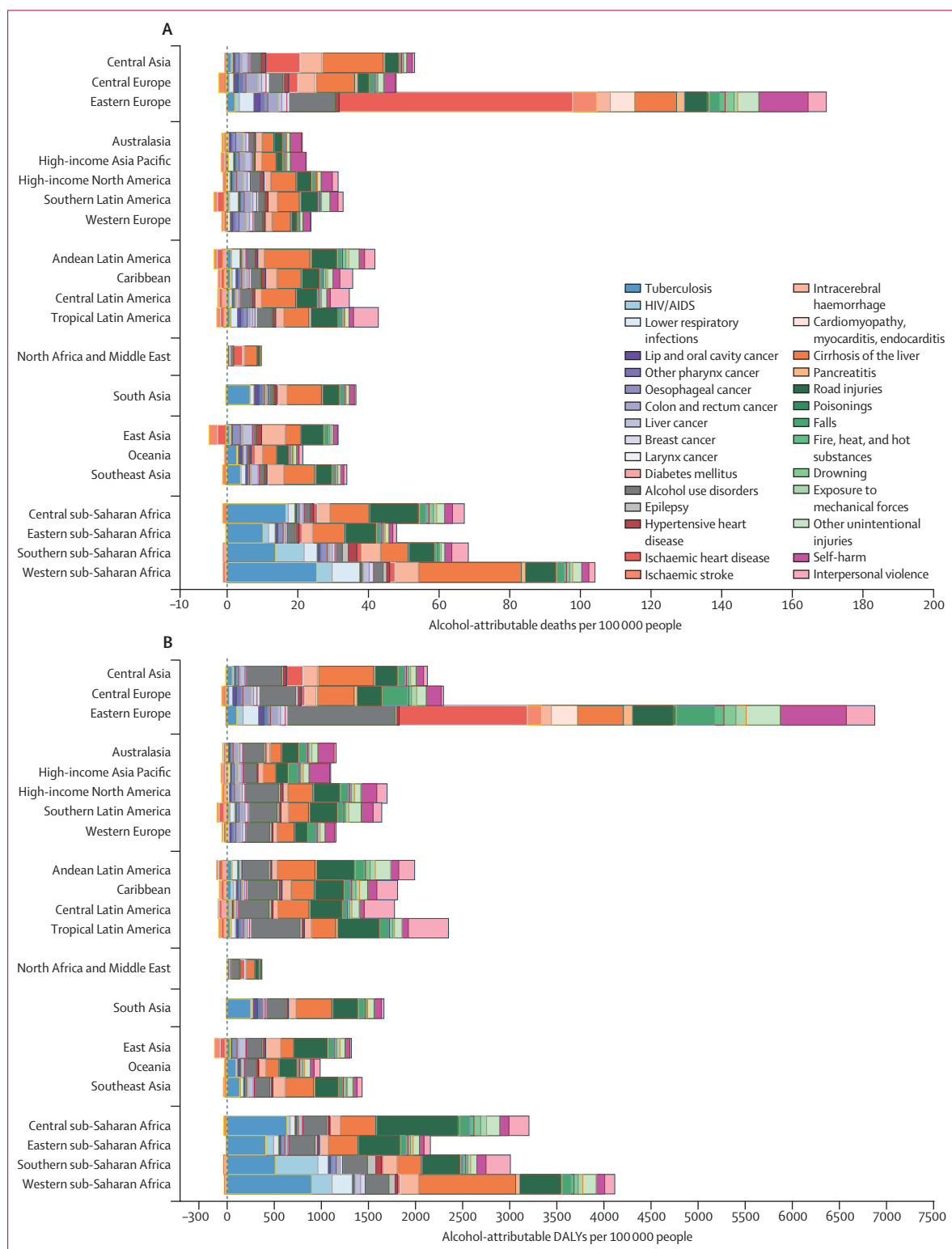


Figure 3: Age-standardised rates of alcohol-attributable deaths and DALYs, by cause and region
 DALYs=disability-adjusted life-years.

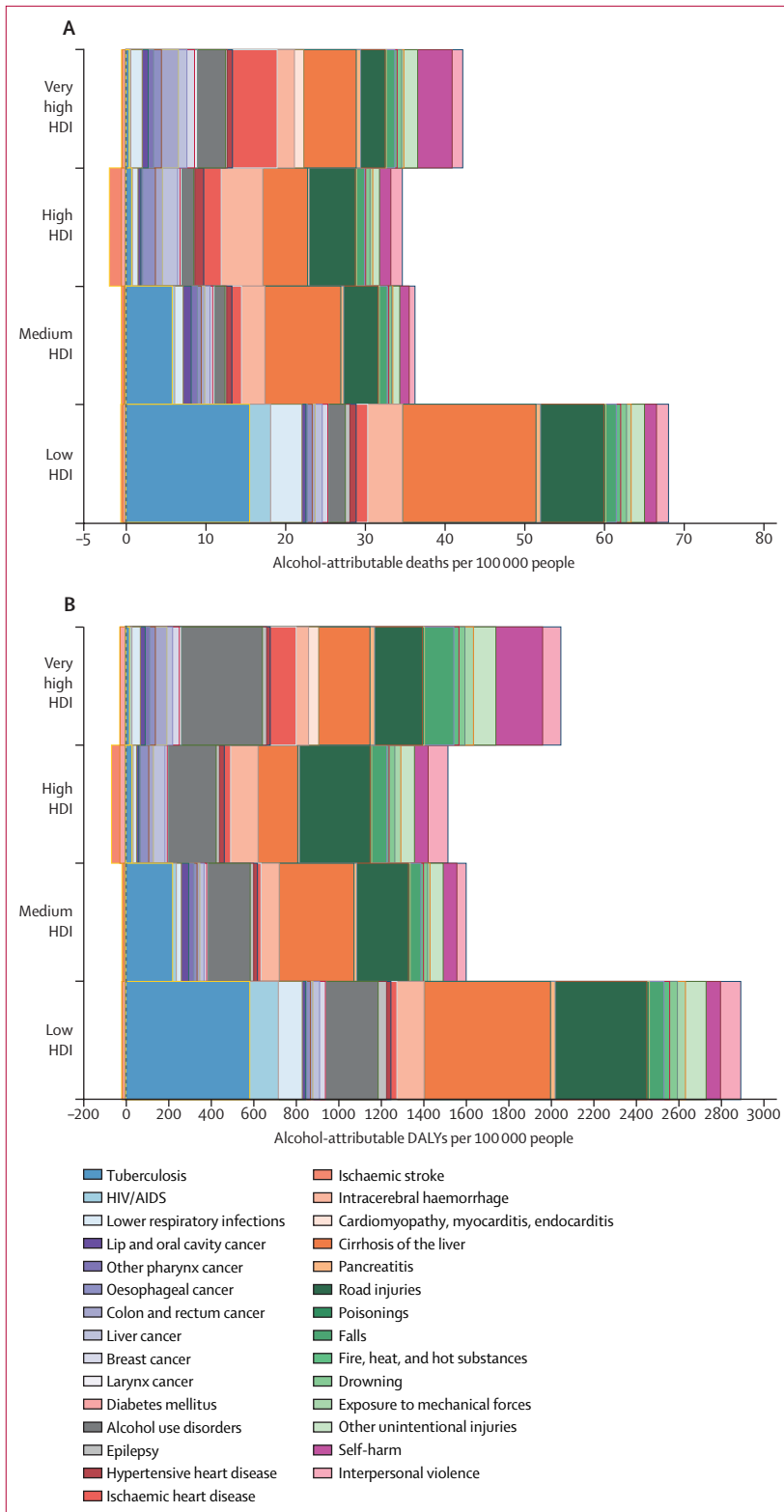


Figure 4: Age-standardised rates of alcohol-attributable deaths and DALYs, by cause and HDI group
DALYs=disability-adjusted life-years. HDI=human development index.

the alcohol-attributable age-standardised rates decreased by 17·9% for deaths and 14·5% for DALYs, less than the relative decreases in the age-standardised rates of all deaths of 23·7% and all DALYs lost of 25·2%. Stratified by sex, the alcohol-attributable age-standardised rates for deaths and DALYs decreased less among men (by 14·5% for deaths and 13·1% for DALYs) than in women (decreases of 26·0% for deaths and 18·8% for DALYs; appendix 1 p 98; appendix 2. According to WHO's Global Health Estimates, alcohol-attributable age-standardised rates for deaths and DALYs declined less than the respective rates for all deaths and DALYs (among men, decreases of 23·4% for deaths and 24·6% for DALYs, and among women, decreases of 24·8% for deaths and 26·1% for DALYs [age-standardised rates]).

These estimates differ from the latest GBD estimates of the alcohol-attributable burden of disease for the same year.² To understand these differences, we examined differences in the underlying mortality and DALY estimates, and in the PAFs (appendix 1 p 101).

Discussion

Alcohol use continues to be a major risk factor for the global burden of mortality and disease, and is a leading risk factor for communicable diseases, NCDs, and injuries. Although the alcohol-attributable age-standardised rates for mortality have decreased since 2000, these decreases were lower in magnitude than the respective decreases in non-alcohol-attributable mortality. Furthermore, substantial gender, age, and geographical temporal differences exist in the alcohol-attributable burden of disease, with the alcohol-attributable burden of disease being higher in countries with low HDI than in countries with high HDI. These differences in the alcohol-attributable burden of disease should have implications for the prioritisation of alcohol control policies.

Our study's findings are limited by various factors. The methods assumed no lag time between exposure and outcome, except for the assumption of a 10-year lag between exposure and cancer outcomes. As such, the exposure data ranged from 1990 to 2016, and outcome data ranged from 2000 to 2016. This introduces errors due to changes in the measurement of exposure, mortality, and morbidity. If these changes led to measurement improvements, then older data might be less reliable than more recent data.

This study did not include the alcohol-attributable burden resulting from major depressive disorders or dementia despite these outcomes being causally related to alcohol,²⁰ because the causal effect of alcohol on these diseases is difficult to quantify through epidemiological studies. Furthermore, this study did not include alcohol poisonings related to alcohol, except direct alcohol poisonings. For example, one in five opioid overdose deaths and one in four benzodiazepine-related overdose deaths in the USA involved alcohol;²¹ however, despite alcohol being a contributory cause, by coding

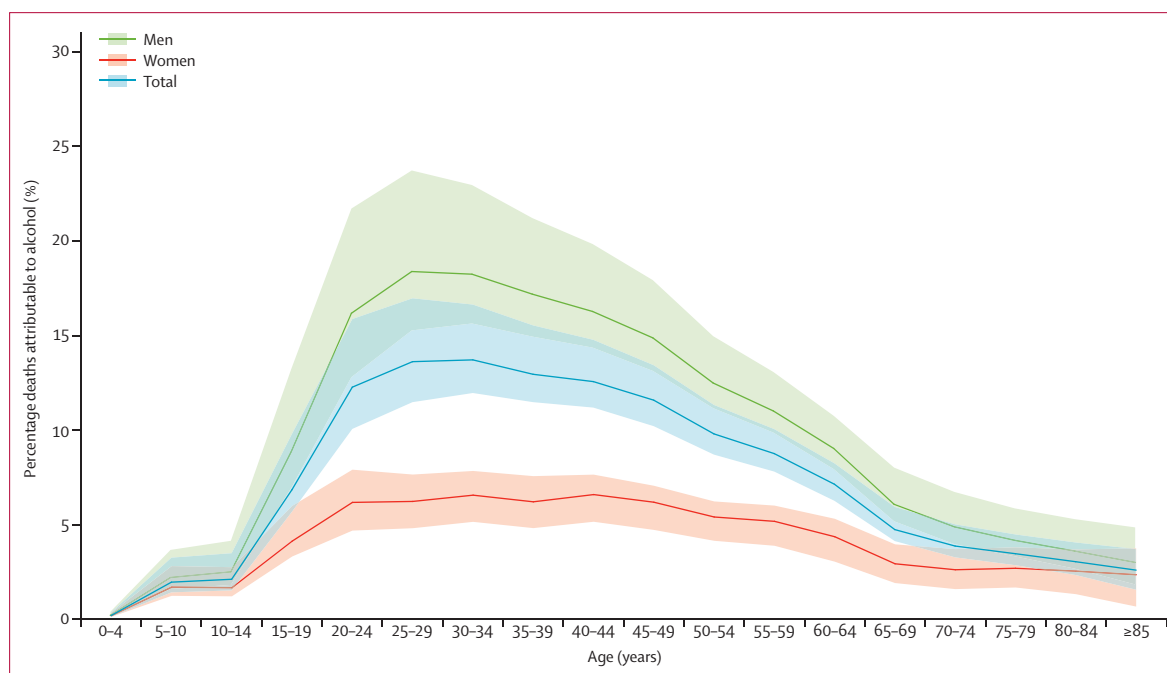


Figure 5: Percentage of deaths attributable to alcohol use in 2016, by age and sex

convention these deaths are not considered alcohol attributable.

The results of different meta-analyses vary greatly, demonstrating that the assumptions of a meta-analysis markedly affect the resulting RRs. This study assumed that the RRs used in the estimates were applicable globally, an assumption underlying all meta-analyses (with the exception of countries in the eastern Europe region where Russia-specific RRs were used).¹⁵ The assumption of globally applicable RRs is questionable. Alcohol RRs for injuries are dependent upon differences in risk-taking disposition.¹⁴ Different genetic dispositions also might affect the RRs. For example, variants of those genes that lead to a slower metabolism of the carcinogen acetaldehyde are more prevalent in Asian populations.²² As a result, global alcohol RRs for developing oesophageal cancer underestimate the risk for Japan by a factor of 2 and China by a factor of 1.5.²³ Furthermore, the RRs might depend on synergistic effects between alcohol and other risk factors; alcohol has a synergistic effect with hepatitis B virus and hepatitis C virus infection for the development of liver cirrhosis and liver cancer,²⁴ with tobacco for head and neck cancers,²⁵ with other drug use for injuries,²⁶ and with socioeconomic status for numerous causes of mortality.²⁷ Indeed, the co-occurrence of these risk factors with alcohol use depends, in part, on the per capita economic wealth of a nation.²⁷

The presented UIs probably underestimate the true error. This is because of the unavailability of error estimates for the global health estimates of mortality and morbidity. Furthermore, the presented estimates do

not account for the contribution of systematic errors (eg, errors introduced by the assumption that there are globally applicable RRs) to the overall measurement uncertainty.²⁸

The large burden of disease caused by alcohol and the observation that global health gains due to decreases in alcohol-attributable deaths lag behind total mortality gains indicate the need for the implementation and strengthening of alcohol policies. In particular, despite having an overall low volume of alcohol consumption,⁵ the alcohol-attributable burden of disease was highest in countries with a low HDI, and in particular in countries in the sub-Saharan Africa region. The high alcohol-attributable burden of disease in the sub-Saharan Africa region was driven by infectious diseases, liver cirrhosis, and injuries. Cirrhosis-related deaths doubled in the sub-Saharan Africa region between 1980 and 2010, with most incident cases (about 70%) attributable to hepatitis B virus, hepatitis C virus, and alcohol use.²⁹ However, independent of the cause, alcohol use can worsen the course of any liver condition. For example, in a large French hospital study, most liver complications in patients with hepatitis C virus infection were attributable to alcohol.³⁰ Treatment of liver cirrhosis is unavailable in most parts of sub-Saharan Africa, because of a shortage of hepatologists and gastroenterologists, interventional radiologists, hepatobiliary surgeons, and pathologists.³¹ The costs related to liver transplants preclude the use of this form of treatment in most sub-Saharan Africa countries, except South Africa.

Despite the overall high level of alcohol-attributable burden of disease, alcohol policy development in the sub-

Saharan Africa region seems to have been overlooked; only 30 of the 46 countries in the region where alcohol use is not banned have national or subnational alcohol policies, 17 countries have no regulations covering the use of media to advertise or promote alcohol use, and eight countries have no minimum legal purchasing age for on-premises beer sales.³² Furthermore, seven countries in this region do not have blood alcohol content limits while driving, and just over a half of the countries in the region (24 countries) perform random breath testing.³² The implementation of alcohol policies in this region is complicated by the scarcity of empirical evidence on the effectiveness of both alcohol control measures and interventions in low-income and middle-income countries. This scarcity of policy research hinders the successful adoption of evidence-based practices as research conducted in high-income countries might not be transferable to low-income and middle-income country contexts.³³

Increases in adult per capita consumption of alcohol and heavy episodic drinking have been observed in east Asia, south Asia, and southeast Asia (eg, China, India, and Vietnam), and such increases have been linked to economic development.⁵ Correspondingly, this study observed increases in the alcohol-attributable age-standardised rates of deaths for these regions. These increases are problematic because any health gains in these regions are being offset, in part, by increases in the alcohol-attributable burden of disease.³⁴ Furthermore, alcohol consumption is projected to increase in these regions, which might lead to additional increases in the alcohol-attributable burden of disease. Thus, alcohol use in these regions, as well as globally, presents a barrier to sustainable development.^{35,36}

The eastern Europe region, which has a high overall volume of alcohol consumption⁵ and a high prevalence of heavy episodic drinking, had the highest alcohol-attributable burden of disease, with the main contributors being alcohol use disorders, cardiovascular diseases, and injuries. However, alcohol control policy measures have been implemented in the eastern Europe region and have resulted in marked downward shifts in mortality and the burden of disease.³⁷ In particular, restrictions on and regulations addressing alcohol marketing and availability, increases in alcohol excise taxes, the establishment of and increases in minimum unit prices, and regulations to decrease unrecorded consumption in Russia since 2004 led to increases in life expectancy of 9 years for men and 6 years for women between 2003 and 2018.³⁸ The WHO SAFER alcohol control initiative and best buys report³⁹ provide further information on alcohol policies.

The successful formulation and implementation of alcohol policies is complex and dependent upon numerous factors. However, changes in alcohol consumption and harms have also occurred because of non-policy factors. For example, in Europe, changes in advertising media, increased popularity of non-alcoholic beverages, economic

factors, homogenisation of behaviours across Europe, and changes in public opinion from alcohol being a healthy drink to a drink that causes health harms have affected the levels and patterns of consumption.⁴⁰

Despite an increase in alcohol use globally, this study observed that the global alcohol-attributable burden of disease decreased between 2000 and 2016.⁵ However, globally, health gains attained through improvements in the alcohol-attributable burden of disease have proportionally not kept pace with total health gains. Accordingly, alcohol remains a leading risk factor for the global burden of disease with increasing relative importance. Given the high global alcohol-attributable burden of disease, and, in particular, in the sub-Saharan Africa region, this study supports the development and implementation of country-specific alcohol control policies in order to further reduce the alcohol-attributable burden of disease in the near future.

Contributors

KS and JR conceptualised the study. KS, JM, MR, CP, CDHP, and JR were responsible for the methodology. KS wrote the software. KS, JM, and JR did the data validation. KS did the formal analysis. KS, JM, MR, CP, AW, and JR did the investigation. KS, MR, AW, and JR curated the data. KS, CP, CDHP, JM, and JR wrote the original draft. KS, JM, MR, CP, CDHP, AW, and JR reviewed and edited the manuscript. KS was responsible for visualisation. JR and KS supervised the study. KS and JR were responsible for project administration.

Declaration of interests

We declare no competing interests.

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References

- 1 Rehm J, Imtiaz S. A narrative review of alcohol consumption as a risk factor for global burden of disease. *Subst Abuse Treat Prev Policy* 2016; **11**: 37.
- 2 GBD 2017 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; **392**: 1923-94.
- 3 WHO. Global strategy to reduce harmful use of alcohol. Geneva: World Health Organization, 2010. https://www.who.int/substance_abuse/activities/gsrhua/en/ (accessed Dec 12, 2019).
- 4 WHO. WHO Global Coordination Mechanism on the Prevention and Control of NCDs. Geneva: World Health Organization, 2004. <http://www.who.int/global-coordination-mechanism/ncd-themes/sustainable-development-goals/en/> (accessed Aug 1, 2019).
- 5 Manthey J, Shield KD, Rylett M, Hasan OSM, Probst C, Rehm J. Global alcohol exposure between 1990 and 2017 and forecasts until 2030: a modelling study. *Lancet* 2019; **393**: 2493-502.
- 6 WHO. Global status report on alcohol and health 2018. Geneva: World Health Organization, 2018. https://www.who.int/substance_abuse/publications/global_alcohol_report/en/ (accessed July 1, 2019).
- 7 Rehm J, Room R, Monteiro M, et al. Alcohol use. In: Ezzati M, Lopez AD, Rodgers A, Murray CJL, eds. *Comparative quantification of health risks. Global and regional burden of disease attributable to selected major risk factors*. Geneva: World Health Organization, 2004: 959-1108.

- 8 GBD 2017 Mortality Collaborators. Global, regional, and national age-sex-specific mortality and life expectancy, 1950-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; **392**: 1684-735.
- 9 GBD 2016 Alcohol 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.
- 10 Levin ML. The occurrence of lung cancer in man. *Acta Unio Int Contra Cancrum* 1953; **9**: 531-41.
- 11 Rehm J, Irving H, Ye Y, Kerr WC, Bond J, Greenfield TK. Are lifetime abstainers the best control group in alcohol epidemiology? On the stability and validity of reported lifetime abstinence. *Am J Epidemiol* 2008; **168**: 866-71.
- 12 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**: 2245-49.
- 13 Zaridze D, Brennan P, Boreham J, et al. Alcohol and cause-specific mortality in Russia: a retrospective case-control study of 48,557 adult deaths. *Lancet* 2009; **373**: 2201-14.
- 14 Sorock GS, Chen L-H, Gonzalgo SR, Baker SP. Alcohol-drinking history and fatal injury in older adults. *Alcohol* 2006; **40**: 193-99.
- 15 Shield KD, Rehm J. Russia-specific relative risks and their effects on the estimated alcohol-attributable burden of disease. *BMC Public Health* 2015; **15**: 482.
- 16 Manthey J, Probst C, Rylett M, Rehm J. National, regional and global mortality due to alcoholic cardiomyopathy in 2015. *Heart* 2018; **104**: 1663-69.
- 17 United Nations. World population prospects: the 2017 revision. New York, USA: United Nations, June 21, 2017.
- 18 Ahmad O, Boschi-Pinto C, Lopez A, Murray CJ, Lozano R, Inoue M. Age standardization of rates: a new WHO standard. Geneva, Switzerland: World Health Organization, 2001. <https://www.who.int/healthinfo/paper31.pdf> (accessed Aug 1, 2019).
- 19 Institute for Health Metrics and Evaluation. Protocol for the global burden of diseases, injuries, and risk factors study. Seattle, 2018. http://www.healthdata.org/sites/default/files/files/Projects/GBD/GBD_Protocol.pdf (accessed Aug 1, 2019).
- 20 Rehm J, Gmel GE Sr, Gmel G, et al. The relationship between different dimensions of alcohol use and the burden of disease-an update. *Addiction* 2017; **112**: 968-1001.
- 21 Jones CM, Paulozzi LJ, Mack KA. Alcohol involvement in opioid pain reliever and benzodiazepine drug abuse-related emergency department visits and drug-related deaths - United States, 2010. *MMWR Morb Mortal Wkly Rep* 2014; **63**: 881-85.
- 22 Boffetta P, Hashibe M. Alcohol and cancer. *Lancet Oncol* 2006; **7**: 149-56.
- 23 Roerecke M, Shield KD, Higuchi S, et al. Estimates of alcohol-related oesophageal cancer burden in Japan: systematic review and meta-analyses. *Bull World Health Organ* 2015; **93**: 329-38C.
- 24 Joshi K, Kohli A, Manch R, Gish R. Alcoholic liver disease: high risk or low risk for developing hepatocellular carcinoma? *Clin Liver Dis* 2016; **20**: 563-80.
- 25 Hashibe M, Brennan P, Chuang SC, et al. Interaction between tobacco and alcohol use and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *Cancer Epidemiol Biomark Prev* 2009; **18**: 541-50.
- 26 Drummer OH. Drugs in drivers killed in Australian road traffic accidents: the use of responsibility analysis to investigate the contribution of drugs to fatal accidents. Melbourne, Australia: Victorian Institute of Forensic Pathology, 1994.
- 27 Katikireddi SV, Whitley E, Lewsey J, Gray L, Leyland AH. Socioeconomic status as an effect modifier of alcohol consumption and harm: analysis of linked cohort data. *Lancet Public Health* 2017; **2**: e267-76.
- 28 Attivissimo F, Cataldo A, Fabbiano L, Giaquinto N. Systematic errors and measurement uncertainty: An experimental approach. *Measurement* 2011; **44**: 1781-89.
- 29 Mokdad AA, Lopez AD, Shahrz S, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. *BMC Med* 2014; **12**: 145.
- 30 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. *J Hepatol* 2017; **67**: 454-61.
- 31 Vento S, Dzudzor B, Cainelli F, Tachi K. Liver cirrhosis in sub-Saharan Africa: neglected, yet important. *Lancet Glob Health* 2018; **6**: e1060-61.
- 32 Ferreira-Borges C, Esser MB, Dias S, Babor T, Parry CD. Alcohol control policies in 46 African countries: opportunities for improvement. *Alcohol Alcohol* 2015; **50**: 470-76.
- 33 Head BW. Reconsidering evidence-based policy: Key issues and challenges. *Policy Soc* 2010; **29**: 77-94.
- 34 GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; **392**: 1736-88.
- 35 Collin J, Casswell S. Alcohol and the Sustainable Development Goals. *Lancet* 2016; **387**: 2582-83.
- 36 WHO Regional Office for South-East Asia. Alcohol policy in the WHO South-East Asia region: a report. New Delhi: World Health Organization, 2018. <https://apps.who.int/iris/handle/10665/259828> (accessed Aug 1, 2019).
- 37 NCD Countdown 2030 collaborators. NCD Countdown 2030: worldwide trends in non-communicable disease mortality and progress towards Sustainable Development Goal target 3.4. *Lancet* 2018; **392**: 1072-88.
- 38 WHO Regional Office for Europe. Alcohol policy impact case study: the effects of alcohol control measures on mortality and life expectancy in the Russian Federation. Copenhagen: World Health Organization, 2019. <https://apps.who.int/iris/bitstream/handle/10665/328167/9789289054379-eng.pdf?sequence=1&isAllowed=y> (accessed Nov 1, 2019).
- 39 WHO. Tackling NCDs: best buys and other recommended interventions for the prevention and control of non-communicable diseases. Geneva: World Health Organization, 2017. <https://apps.who.int/iris/bitstream/handle/10665/259232/WHO-NMH-NVI-17-9-eng.jsessionid=57D3AD327ACE304AD5BB739F256B844B?sequence=1> (accessed Aug 1, 2019).
- 40 Kraus L, Seitz N-N, Piontek D, et al. 'Are the times a-changin'? Trends in adolescent substance use in Europe. *Addiction* 2018; **113**: 1317-32.