Alcoholic Liver Disease in Asia, Europe, and North America

Suthat Liangpunsakul, Paul Haber, and Geoff McCaughan
Division of Gastroenterology and Hepatology, Department of Medicine, Indiana University School of Medicine, Indiana, USA
#Roudebush Veterans Administration Medical Center, Indianapolis, Indiana, USA
$Drug Health Services, Royal Prince Alfred Hospital, Sydney Medical School, University of Sydney, Australia
^Centenary Research Institute, A.W Morrow GE/Liver Center Australian Liver Transplant Unit Royal Prince Alfred Hospital, University of Sydney, Sydney, Australia

Abstract

Alcoholic liver diseases (ALD) comprise a spectrum of clinical disorders and changes in liver tissue that can be detected by pathology analysis. These range from steatosis to more severe signs and symptoms of liver disease associated with inflammation, such as those observed in patients with alcoholic hepatitis or cirrhosis. Although the relationship between alcohol consumption and liver disease is well established, severe alcohol-related morbidities develop in only a minority of people who consume alcohol in excess. Inter-individual differences in susceptibility to the toxic effects of alcohol have been extensively studied—they include pattern of alcohol consumption, sex, environmental factors (such as diet), and genetic factors, which vary widely among different parts of the world. ALD is becoming more common in many parts of Asia but is decreasing in Western Europe. Treatment approaches, including availability of medications, models of care, and approach to transplantation, differ among regions.

Keywords
Clinical profiles; Alcoholic liver disease; Asia; Europe; North America

Alcohol is consumed worldwide and has been used in many cultures for centuries \(^1\). When consumed in excess, it can cause diseases that place social and economic burdens on societies. In 2012, about 3.3 million deaths, or 5.9% of all global deaths, were attributed to alcohol consumption \(^1\). Alcohol-related health disorders are generally determined by the volume and quality of alcohol consumed and the pattern of drinking \(^1\).

CORRESPONDENCE: Suthat Liangpunsakul, MD, MPH, Associate Professor of Medicine, Biochemistry and Molecular Biology, Division of Gastroenterology and Hepatology, 550 N. University Blvd, UH 4100, Indianapolis, IN 46202, Phone: (317) 278-1630, Fax: (317) 988-3180; Email: sliangpu@iupui.edu

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CONFLICT OF INTERESTS: NONE
Alcoholic liver disease (ALD) has been estimated to account for 48% of all deaths from cirrhosis. It comprises a spectrum of disorders and pathologic changes in individuals with acute and chronic alcohol consumption, ranging from alcoholic steatosis to alcoholic hepatitis (AH) and cirrhosis. Alcoholic steatosis, once considered benign, is now recognized as a condition that may lead to advanced liver disease or cirrhosis. Development of alcoholic steatosis depends on the dose and duration of alcohol intake. However, it is difficult to establish whether there is a threshold of alcohol intake required for development of fatty liver. Alcoholic steatosis can develop within 2–3 weeks in subjects who consume alcohol in the excessive range (120–150 g/day), but can be reversed with abstinence. If alcohol consumption continues, some patients develop AH—the most florid manifestation of ALD, associated with high mortality. Approximately 15% to 20% of patients who drink alcohol excessively develop cirrhosis in their lifetime.

Mortality from alcohol-associated cirrhosis in different countries correlates with per capita alcohol consumption. With recent changes in the economies and increases in average incomes in developing regions of the world, there has been a rapid rise in per capita alcohol consumption in countries such as China and India. In fact, alcohol consumption is increasing faster in China than other parts of the world. The per capita consumption of alcohol in India has increased by 55% over the past decade. Based on these statistics, it is expected that the prevalence of ALD will increase globally. We review the similarities and differences in epidemiologic factors, patterns of alcohol consumption, risk factors, and clinical features of patients with ALD in different geographic regions, comparing countries in Asia to those in Europe and the United States (US).

**Patterns of Alcohol Consumption**

In comparing similarities and differences of ALD among different regions of the world, it is important to understand current and evolving patterns of global alcohol consumption. The World Health Organization (WHO) reported that in 2010, total alcohol per capita consumption was highest in the developed world—mostly in the Northern Hemisphere. Eastern Europe had the highest per capita consumption per year, with 15.7 liters per person (8.1 liters per woman and 24.9 liters per man). The US had per capita consumption with 9.2 liters per person (4.9 liters per woman and 13.6 liters per man). By comparison, per capita consumption values for China, India, Republic of Korea, and Japan were 6.7 liters per person (2.2 liters per woman and 10.9 liters per man), 4.3 liters per person (0.5 liters per woman and 8 liters per man), 12.3 per person (3.9 in woman and 21 in man) and 7.2 liters per person (4.2 liters per woman and 10.4 liters per man), respectively. The total adult per capita consumption in 2010, in liters of pure alcohol, is shown in Fig. 1.

In general, men that consume up to 2 drinks/day (1 drink/day for women) are defined as moderate drinkers. Drinking at this level does not increase risk of organ injury. Daily consumption beyond these limits is considered to be heavy drinking, which can have adverse health and social outcomes. This definition of chronic drinkers does not include the pattern of binge drinking—the definition varies among different geographic regions. The US National Institute on Alcohol Abuse and Alcoholism proposed a definition of binge drinking as the consumption of 5 or more drinks for men (4 or more drinks for women) within 2
In the United Kingdom (UK), binge drinking is defined as consuming 8 units or more for men (6 units or more for women; ~5 or 4 American standard drinks, respectively)\(^\text{17}\).

The WHO uses the patterns of drinking score (a composite measure of drinking patterns) to determine how people drink, instead of how much they drink, on a scale of 1 (least risky pattern of drinking) to 5 (most risky pattern of drinking)\(^\text{18}\). Parameters used to create this indicator include quantity of alcohol consumed per occasion, festive drinking, proportion of drinking events that result in becoming drunk, proportion of drinkers who drink daily, drinking with meals, and drinking in public places. Eastern Europe had the highest pattern of drinking score (4.9)\(^\text{17}\), whereas the score for the US was 2—similar to countries in Asia such as China, Japan, and Singapore\(^\text{18}\). India and Republic of Korea each had a score of 3.

In the US in 2013, 86.8% of people 18 years or older reported that they drank alcohol at some point in their lifetime. Of these people, 24.6% stated that they engaged in binge drinking and 6.8% reported that they engaged in heavy drinking in the past month\(^\text{19}\). The percentage of men who had at least 1 heavy drinking day in the past year decreased from 31.6% in 1997 to 27.8% in 2006, then increased to 32.4% in 2009. Since the time period of 2009 to 2014, there has been no decrease or increase\(^\text{20}\). In the UK, the Health Survey for England reported that 57% of young men were binge drinkers\(^\text{21}\). Most European countries have had the same trend toward an increase in binge drinking, even in southern countries\(^\text{14}\).

In Asia, alcohol consumption in China is increasing faster than other parts of the world\(^\text{11}\). A recent national survey found 56% of men and 15% of women to be current drinkers. Among them, heavy drinking was reported in 63% of men and 51% of women, whereas binge drinking occurred for 57% of men and 27% of women\(^\text{11}\). Alcohol use disorders (AUDs), defined as harmful patterns of drinking such as alcohol dependence and abuse, have become a frequent problem linked to disturbances in mental and physical health and in social functioning in China\(^\text{11}\). There was a dramatic increase in the proportion of individuals with AUDs, from 0.45% in mid-1980s to 3.4% in mid-1990s,\(^\text{11}\) with the life-time prevalence of 9% during the years of 2001 to 2005\(^\text{22}\). India has also increased alcohol use, from 3.6 to 4.3 liters/person/year\(^\text{13}\).

Unrecorded alcohol use varies greatly between countries, from below 10% in wealthy and highly regulated nations to above 50% in less well-developed nations\(^\text{23}\). Official statistics are typically based on taxation records of recorded consumption—these substantially underestimate total consumption, particularly in the developing world\(^\text{24}\). The chief concern regarding home brew is access to beverages with high alcohol content at relatively low cost. As a secondary concern, they may be contaminated with methanol, leading to life-threatening poisonings or consumption of other hepatotoxins, such as polyhexamethyleneguanidine, which has been linked to an outbreak of acute cholestatic liver injury in Russia\(^\text{23}\).

**Prevalence and Burden of ALD**

Mortality from ALD, regardless of country, correlates with per capita of alcohol consumption\(^\text{7 8}\). Overall consumption or average volume of alcohol consumed has been the usual measure of exposure, and that there is a dose-response relationship between the
volume of alcohol consumed and risk of ALD. A meta-analysis found that consumption of more than 25 g/day increased the relative risk of cirrhosis. This threshold is in accordance with that from a study showing a significant increase in risk of cirrhosis with alcohol consumption of more than 30 g/day. A separate study showed that recent drinking, rather than earlier in life consumption, was associated with the risk of alcohol-associated cirrhosis.

Although studies correlate average volume of alcohol consumption with ALD, several studies have associated risk with drinking patterns. Binge drinking (too much too fast) and chronic excessive drinking (too much too often) are significant risk factors for ALD. In addition to the quantity of alcohol consumption, there is controversy over whether risk of ALD depends on the type and pattern of alcohol intake, independent of absolute levels of consumption. Some studies have found red wine drinkers to have a lower risk of ALD than consumers of other beverages. However, other studies produced contradicting results.

AH

The precise incidence and prevalence of AH are unknown, partly because AH may be completely asymptomatic and thus remain undiagnosed. The available data on the burden of AH from each geographic region are difficult to compare, primarily because of the disparity in the studied population. In a population-based cohort study of all patients with a hospital discharge diagnosis of AH in Denmark from 1999 to 2008, the overall incidence rate for AH was 36.6 per million/year. The incidence was higher in men compared to women (46.4 vs 26.9 per million/year, respectively). The incidence increased for men and women during the decade of study. A study in France analyzed liver biopsies from 1604 subjects with chronic heavy alcohol use. Of these, 119 subjects (7.4%) had acute AH and 179 subjects (11%) had AH with cirrhosis. In the US, total cases of AH-related hospitalization increased from 249,884 (0.66% of total admissions) in 2002 to 326,403 (0.83% of total admissions) in 2010, based on analysis of National Inpatient Sample data. AH was found in ~29% of hospitalized patients with ALD in India.

Alcohol-associated cirrhosis

The global burden of ALD, measured by deaths and disability-adjusted life years (DALYs), has been recently reported. DALYs are an indicator of overall disease burden, providing the number of years lost due to poor health, disability, or early death. Globally, alcohol contributed 4.5% of all DALYs in 2004, making it the third leading risk factor for disease (after childhood underweight and unsafe sex), ahead of tobacco and other established risk factors. Alcohol-attributable liver cirrhosis was responsible for 493,300 deaths (156,900 deaths in women and 336,400 deaths in men) and 14,544,000 DALYs (4,112,000 DALYs for women and 10,432,000 DALYs for men) in 2010. It accounts for 0.9% of all global deaths (0.7% for women and 1.2% for men), 0.6% of all global DALYs (0.4% for women and 0.8% for men), 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). There were 211.1 DALYs per 100,000 people caused by liver cirrhosis attributable to alcohol consumption in 2010. Central Asia experienced the greatest number of alcohol attributable
liver cirrhosis DALYs per 100,000 people for 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 \(^2\). Alcohol-attributable DALYS caused by liver cirrhosis in each geographic region is shown in Table 1.

The overall alcohol-attributable deaths from cirrhosis among different geographic regions is shown in Fig 2 (ref \(^2\)). Among western countries, time trends in mortality over the past 3 decades have varied. Countries such as Austria, France, Germany, and Hungary have had a decrease in mortality, whereas Finland, Ireland, and the UK have had increases in mortality \(^39\). In the UK and Scotland, there was a 5-fold increase in cirrhosis mortality among men and 4-fold increase among women from 1950 through 2000 \(^40\), \(^41\). In the past 40 years, the UK has seen substantial reductions in the mortality of most common diseases whereas cirrhosis mortality has risen 5-fold—a striking exception \(^42\).

**Factors Associated With ALD**

In most of the studies from the US and Europe, the mean age of patients at the time of diagnosis with ALD has been 45–55 years old \(^36\), \(^35\), \(^43\), \(^44\). Data from the US using the National Hospital Discharge Survey 2010 and National Inpatient Sample showed that most patients with a diagnosis of ALD were 45–64 years old, with the average age of 53 years \(^36\). The age of diagnosis of patients with ALD in the US is similar to that from several countries in Europe \(^35\), \(^43\), \(^44\). The mean age at which ALD is detected in the western countries is older than that from a population-based study in China, which found most subjects with ALD to be 36–48 years old \(^46\). In a separate population-based study from China, Wang et al observed a trend of an increase in incidence of ALD as the population increased in age, until 50 years old. The highest prevalence rate of ALD was found in people 40–49 years old \(^47\). The age differences between each demographic region are likely due to the care setting from which data were collected (population vs hospital-based), age structure of the population itself, and patterns of alcohol consumption. In fact, there were no differences in the mean age of hospitalized ALD patients in each geographic location \(^48\), \(^50\).

The greater vulnerability of women and lower safe limits for consumption have long been recognized \(^25\). However, cases reported from each geographic region have indicated a higher prevalence of ALD and mortality in men \(^2\), \(^35\), \(^36\), \(^46\), \(^49\). This could be because men typically drink more than women, have a greater proportion of heavy drinkers and alcoholics, regardless of geographic locations \(^51\). The longstanding sex difference in alcohol consumption has decreased in Western countries. In the UK, mortality from ALD has increased more in women than in men with a 7-fold increase in women younger than 30 years \(^41\).

**Socioeconomic status**

Rising income among people in the developing world increases their access to alcohol and in turn, associated morbidities, including ALD \(^52\), \(^53\). However, the link between socioeconomic status and ALD is complex. Multiple factors are involved, such as market liberalization, increased advertising, and growing affluence; these have made alcohol more available in
and to people of low socioeconomic status, in particular. Alcohol-related problems have increased rapidly in this group. One study found significant increases in risks of cirrhosis-associated mortality among patients who are not married or are urban residents, unemployed, or with lower levels of education and family income. An analysis of the US National Inpatient Sample showed that patients hospitalized for AH come primarily from low-income households. In China, the production and consumption of alcoholic beverage have increased with the country’s rapid economic growth. A study from North-Eastern China showed that that people with a low level of education or income, or people who are unmarried, have a high risk of ALD. The findings which are similar to those reported from the US.

Race and ethnicity

There are few data on the effects of race and ethnicity on alcohol-associated disease from Asian countries, primarily because of their homogenous populations. In the US, age-adjusted rates of alcohol-associated cirrhosis are higher for Blacks than for Whites, and mortality is highest in Hispanic groups. However, these findings cannot be attributed to higher alcohol consumption among Hispanics and Blacks than Whites—alcohol consumption among Blacks has been less than or comparable with that of Whites. The reasons for the differences in cirrhosis and mortality are not clear, but could involve the limited access of Blacks and Hispanics to alcohol rehabilitation, or hepatitis C virus infection, which is more common in Hispanics.

Body mass index (BMI) and obesity

In an epidemiologic study from the US, overweight and obesity were found to increase risk for alcohol-related abnormalities in aminotransferase activity. A large study from France identified excess body weight for at least 10 years as a risk factor for AH and alcohol-associated cirrhosis. A study from Scotland found that high BMI and excessive alcohol intake increased mortalities from liver disease. Similar observations have been made in studies in Asia. In a large prospective study of 1270 subjects from China, 16% had BMI ≥ 25 kg/m². Though the average daily alcohol intake in this group was lower than those with BMI<25, ALD morbidity in this group was 11.5%, compared to ~5% in those with normal BMIs. The presence of obesity was an independent predictor for ALD.

Genetic factors

Variants in genes encoding members of the alcohol dehydrogenase (ADH) family affect their ability to metabolize alcohol. Levels of ADH enzymatic activity determine risk for alcohol dependence and susceptibility to alcohol-induced liver injury. Individuals carrying variants that encode enzymes with high levels of activity (ADH1B*2 and ADH1C*1 alleles) are believed to be at increased risk for ALD, due to higher levels of acetaldehyde exposure. In a Japanese cohort of alcoholic men, the ADH1B*2 allele was associated with greater risk of cirrhosis compared with the ADH1B*1 allele. However, a large study of 876 Caucasian individuals (from Spain, France, Germany, Sweden, and Poland) did not detect a significant association between ADH1C variants and alcohol-associated cirrhosis, although it did find that ADH1B*2 reduced risk for excessive alcohol intake. A recent meta-analysis confirmed this association in Asian populations but found no association in Western
populations. This could be because ADH1B*2 is a rare allele in Caucasians; some smaller studies found no patients to carry this allele. Approximately 40%–50% of Chinese people are homozygous or heterozygous for the ALDH2*2 allele and have low ALDH2 activity. These individuals have high blood concentrations of acetaldehyde after alcohol consumption and may be more susceptible to liver injury.

Alcohol can be metabolized, to a lesser extent, by cytochrome P450 family 2 subfamily E member 1 (CYP2E1). CYP2E1 is an inducible enzyme; its activity can increase up to 20-fold following continuous alcohol consumption. The c1 and c2 alleles of CYP2E1 affect activity of the gene product. The product of the CYP2E1*5 (c2) allele has higher activity than that of c1 allele, and could lead to a higher exposure of the liver to acetaldehyde and reactive oxygen species. In a study of a Caucasian population in the West, the c2 allele was associated with increased risk of ALD in subjects with higher cumulative levels of alcohol consumption. However, the risk was only in subjects who also had the ADH1C*2 allele. Interestingly, another polymorphism in CYP2E1, Taq I, is associated with reduced susceptibility to ALD, although this allele does not directly affect alcohol metabolism.

Several studies from Japan and Korea have searched for associations between the polymorphisms in CYP2E1 and ALD without positive results. A study of Chinese of Han, Mongol, and Chaoxian nationalities found a positive association between the c2 genotype and ALD.

Altered activities of cytokines and proteins that respond to endotoxin are involved in the pathogenesis of ALD, so variants in their genes could affect susceptibility to ALD. CD14 is a coreceptor for the toll-like receptor 4, which interacts with bacterial lipopolysaccharide in the portal bloodstream. A C/T polymorphism at position −159 in the promoter region of the CD14 gene, producing a TT genotype, is associated with increased expression of CD14. In a study of autopsy results from 442 men in Finland, with valid alcohol consumption data, the TT genotype increased risk for advanced ALD by almost 2.5-fold and cirrhosis by almost 3.5-fold, compared to men without the TT genotype. Individuals with the TT polymorphism at position −159 in the promoter region of the CD14 are therefore at high for cirrhosis. Interestingly, a study from Taiwan did not associate this polymorphism with ALD.

A C/A polymorphism at position −627 in the promoter of the interleukin-10 (IL10) gene has been associated with decreased expression, resulting in an increase inflammatory response. Researchers investigated the prevalence of this polymorphism among 287 heavy drinkers with biopsy-proven advanced ALD, 107 heavy drinkers with no evidence of liver disease or steatosis from biopsy analyses, and 227 individuals without liver disease (controls). At this position in IL10, 50% of patients with advanced ALD had at least 1 allele with the A C/A polymorphism, compared with 33% of controls and 34% of drinkers with no or mild disease. These findings indicate an association between genetic variants that reduce expression or activity of IL10 and ALD. However, subsequent studies of polymorphisms in IL10 in other European populations produced contradictory results. A study from the Bengali population of Eastern India associated a genetic variant of IL10 with alcoholic cirrhosis as did smaller study from Taiwan.
The patatin-like phospholipase domain-containing protein 3 (PNPLA3) gene is located on the long arm of chromosome 22 and encodes adiponutrin. This protein has triglyceride lipase and acylglycerol transacylase activities, and is expressed in response to energy mobilization and storage of lipid droplets. A genome-wide screen for non-synonymous single nucleotide polymorphisms in Hispanic, African, and European Americans participating in the Dallas Heart Study associated a variant in PNPLA3 (rs738409 [M148I]) with hepatic fat content, measured by proton magnetic resonance spectroscopy. PNPLA3 rs738409 increased risk for alcoholic cirrhosis 2.25-fold. The association between PNPLA3 variants and ALD was confirmed in a German cohort and patients with alcohol-associated cirrhosis of European descent. In this study, carriers of PNPLA3 rs738409 (G/G) were found to be at high risk for progression of clinically silent to overt ALD. In total, 26.6% of the population-attributable risk for the progression of early to advanced ALD were found to be conferred by this risk allele. A recent meta-analysis clearly associated the rs738409 variant with alcoholic liver cirrhosis. A number of studies have associated variants in PNPLA3 with non-alcoholic fatty liver disease in different regions of Asia, but there are few data on ALD. A small study from India (of 60 patients with alcohol-associated cirrhosis) found that the rs738409 polymorphism increased risk for ALD 2.1-fold. However, further studies are needed to determine the association between PNPLA3 and ALD in Asian populations.

Clinical Presentation

We have no evidence to support significant differences in the clinical presentation of ALD among patients in Asia, Europe, or North America. Most patients present with signs and symptoms related to portal hypertension or cirrhosis. Jaundice, as expected, is common among patients presenting with AH.

Treatment of AUD

The most powerful determinants of alcohol use are price, availability, and promotion. Public policies that address these factors can influence population level use of alcohol and in turn rates of cirrhosis and other health disorders. The WHO has endorsed a global strategy to reduce harmful use of alcohol that includes 10 priority actions for nations (see Fig 3) and 4 international priority actions. However, the strength of public policy varies strikingly among nations and over time.

Internationally, there is evidence that strength of public policy correlates with levels of consumption. For example, during the alcohol prohibition era in the USA, cirrhosis mortality was reduced by approximately half. In Russia, alcohol-attributable mortality varied by year as national controls were imposed and relaxed; in several recent years, alcohol caused more than half of all deaths among Russians 15–54 years old. Current policies in China and India promote increased use—alcohol is cheap and there is widespread access to high-strength alcoholic beverages. As prosperity has increased, the global alcohol industry has increased its focus on sales in these regions, but this may have adverse effects on health. Many believe that the alcohol industry is currently focusing on women and young people, who are most vulnerable to alcohol-related disorders, including ALD.
China has implemented several changes in alcohol taxes, for general economic reasons, and these have been linked to changes in both consumption and alcohol-associated harm. These policy approaches could reduce the burden of ALD, but a recent review reported a dearth of alcohol policy research in China. An increase in alcohol tax in Taiwan in 2002 reduced hospital expenditures on ALD.

There has been a recent significant review of the effects of ALD and liver disease in general in the UK. The review recommended a minimum price on alcoholic beverages—particularly for cheap wine—health warnings on packages (similar to tobacco), a volume-based tax, reduction in the number of liquor outlets, restrictions on advertising, and improved screening and access to treatment for alcohol problems. Such policies have been introduced in some European countries. However, there seems to be resistance in the UK to their implementation—it has been proposed that this is related to pressure on government from the alcohol industry. Similar recommendations have been made elsewhere, and there has been comparable reluctance to introduce alcohol control policies in India, China, and the US.

Alcohol use can be detected by clinical and laboratory tests, but screening instruments for alcohol disorders have been developed; these are more sensitive than routine care and are cheap and readily available. The AUD Identification Test (AUDIT) developed by the WHO in the 1990s is the most widely used but was validated in the English language. AUDIT has been translated and validated into a number of languages including Tamil, Konkani (the language of Goa), Chinese, and Korean. Other screening measures have not been disseminated into many languages other than English.

The most widely available treatment involves provision of brief advice to reduce or stop drinking. Many patients with ALD may have little evidence of a severe AUD and may not require formal treatment. Structured brief interventions have been shown to be effective in a range of clinical settings, including for patients with liver disease, and may be repeated during long-term follow up. Brief intervention does not require specialist skills and can be provided by any credible health care provider. An Indian study is exploring use of lay counsellors and if successful, will allow widespread dissemination of this intervention at lower cost. Many alcohol brief interventions have been made available online in recent years but are largely in the English language to date.

**Treatment of ALD**

Pharmacologic treatments for ALD are limited in efficacy, apart from corticosteroids for life-threatening AH. The use and indications for corticosteroids in different geographic regions do not seem to differ. However, there is much interest in India in the use of granulocyte colony stimulating factor (GCSF) in treatment of patients with acute on-chronic liver failure of which ALD is the predominant cause. Surprisingly, GCSF increased survival times, by a small amount, in patients with AH. A larger randomized trial is underway in India to determine the efficacy of GCSF in the management of steroid non-responsive severe AH.
Medicines to reduce relapse to heavy drinking are less widely used in the Asia than in Europe and the US. In China, treatment approaches differ from the West, because some drugs are not available, and involve use of traditional Chinese medicines and acupuncture. Challenges to treatment in the West include limited access to treatment, stigma, and limited training of health care professionals.

Liver transplantation for patients with ALD is accepted internationally; ALD has been a leading indication in Europe and the US and has been increasing in China. Currently, 7.5% of all liver transplants go to patients with ALD. Most liver transplants in the East come from living related donors. In general, assessment principles are similar to those of Western countries. Survival times following transplantation seem to be similar in the East vs West. However, a report from 38 Japanese centers found that mortality associated with recidivism was particularly high compared to reports from the West.

Ethical concerns about liver transplantation in China have been raised and are progressively being addressed. The overall system to provide adequate access to evidence-based care that integrates health problems is still evolving in many parts of the world. An integrated approach that combines medical care with psychosocial treatment for AUD is more effective at maintaining abstinence. A study from Korea highlighted the difficulty in establishing this system of care for patients with AUD. This may also be a challenge to implement broadly in Western nations.

**Future Directions**

There are worldwide differences in the prevalence of ALD, as well as in mortality, treatment, and the factors that contribute to development of ALD. It is undeniable that the ALD will continue to be a major cause of morbidity and mortality throughout the world. Global strategy and public policy to reduce harmful use of alcohol use and effective therapies for ALD are needed.

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**Biographies**

Suthat Liangpunsakul
LIST OF ABBREVIATION

- **ADH**: Alcohol dehydrogenase
- **ALD**: Alcoholic liver disease
- **ALDH**: Aldehyde dehydrogenase
- **AH**: Alcoholic hepatitis
- **AUD**: Alcohol use disorder
- **AUDIT**: Alcohol Use Disorders Identification Test
- **BMI**: Body mass index
- **DALYs**: Disability-adjusted life years
- **GCSF**: Granulocyte colony-stimulating factor
- **WHO**: World Health Organization

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Figure 1.
Total adult per-capita consumption of pure alcohol in Asia, Europe, and North America
(modified from ref 13)
Figure 2.
Overall alcohol-attributable deaths caused by cirrhosis in different geographic regions (modified from ref 2)
Figure 3.
WHO Global Strategy to Reduce Harmful use of alcohol (modified from ref 94)
Table 1

Alcohol-attributable DALYs Attributed to Cirrhosis in 2010

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Note: modified from ref 2