GLOBAL LIVER INSTITUTE

LIVER HEALTH IS PUBLIC HEALTH

GLOBAL STATE OF LIVER HEALTH

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A Note on Nomenclature

Following the publication of "A multisociety Delphi consensus statement on new fatty liver disease nomenclature" in 2023 by the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) in collaboration with the Asociación Latinoamericana para el Estudio del Hígado (ALEH), terminology has shifted in some regions to MASLD, while leading medical societies throughout the world continue to use both "NAFLD" and "MAFLD." Out of respect for the ongoing, global scientific discussion, this report defers to the terminology in use by the regional medical society at the time of publication. Additionally, interviews with experts have been conducted since 2022, and this report preserves terminology in use at the time of interview.

LETTER FROM LARRY R. HOLDEN

The liver plays a foundational role in the overall health of the body, far beyond what most people realize. Through its over 100 functions, the liver regulates metabolic health by processing nutrients, producing bile for fat digestion, and maintaining blood glucose levels. It detoxifies harmful substances and metabolizes drugs, supporting overall homeostasis. Unfortunately, the liver is poorly understood by the majority of the world and poorly protected by most healthcare systems. Global Liver Institute was founded out of personal experience and a goal that patients and their families be better supported when they face liver disease.

We connect people to the tools they need to take care of their livers, and we advocate for health systems and governments to step up and facilitate this for their people. Over the years, GLI has trained hundreds of patient advocates, convened leaders in liver health, and successfully urged equitable, sensible policies. These efforts help us realize our vision *for liver health awareness to be universal and for liver disease to take its proper place on the global public health agenda consistent with its prevalence and impact*.

The *Liver Health is Public Health* initiative is GLI's response to the world's failure to meaningfully prioritize liver health. Along with several of the most dedicated and respected organizations in hepatology and intersecting specialties, we are stimulating global conversations about liver health, *beyond* the circles that traditionally focus on liver disease, to draw the liver onto the health agenda for governments, NGOs, and the general public. Everyone who can make a difference in liver health must be spurred to action, from those who decide how to allocate research funds and run healthcare systems to the people who shop for food for their household each week.

Each year we work on this report, I become more resolute in my conviction that the current threats to liver health are dire, so the work of the liver health community is essential. As risk factors rise, so will the incidence of liver disease. At the current pace, the world is not ready to manage the approaching onslaught of liver disease. Formidable investment is necessary to reduce liver disease around the world. Still, I am confident that the world will come together to prevent chronic liver disease and diagnose and treat it early. It will save time, save money, and save lives.

I strongly believe that knowledge is power, and through this report, GLI strengthens global knowledge on liver diseases, ultimately serving our patients.

Thank you for taking the time to read this report. May it be a resource as you embark on a journey of advocacy for liver health within your circles of influence.

Larry R. Holden
President, & Chief Executive Officer
Global Liver Institute

INTRODUCTION

Despite meaningful advances in the diagnosis and treatment of liver disease in recent decades, many things remain nearly unchanged. Liver disease is still under-diagnosed, misrepresented and stigmatized. Advanced liver diseases, especially liver cancer, suffer from poor outcomes. There is also limited public knowledge about the danger that soaring rates of obesity pose to the health of our livers.

Far too many patients have been failed on a clinical level, as well. We hear of patients receiving liver transplants but unable to obtain the immunosuppressant medications that will keep them alive, while patients in other countries are charged unfeasibly high fees to receive the basic hepatitis tests that would prevent the spread of the virus.

Liver disease thus places a sizable personal and economic burden on communities across the world. This takes many forms: for instance, the many thousands of parents taking time off work to care for sick children, the loss of productivity caused by the millions living with fatty liver disease, or the developing countries that see significant portions of their working-age population succumb to liver cancer. Liver disease also increases the cost and outcomes of treating cardiovascular disease (CVD) and diabetes – for example, one recent study in India showed that diabetes was present in nearly 12% of all patients recently diagnosed with chronic liver disease.[1]

Nonetheless, several countries still have no policy on underage drinking, several have not operationalized the preventive and curative tools readily available for viral hepatitus B, and C, and too many governments have no public health policy on obesity and its link to nonalcoholic fatty liver disease (NAFLD). Liver disease, it appears, is simply not a public health priority today, tomorrow or in the foreseeable future.

This oversight has led the world directly to the public health catastrophe we now face:

- Today, **844 million people around the world are living with chronic liver disease,** which results in two million deaths per year[2] – including 700,000 from liver cancer[3] and 1.1 million from hepatitis B and C infection.[4]
- Globally 1 in 4 people are impacted by metabolic dysfunction-associated steatotic liver disease (MASLD), and of those, 1 in 5 will go on to develop the more advanced liver condition metabolic dysfunction-associated steatohepatitis (MASH).[5]

As this tide of liver disease swells in regions around the world, it, through varied etiologies, places similar burdens on patients and their healthcare systems.

A NOTE FROM THE LIVER HEALTH IS PUBLIC HEALTH PROGRAM DIRECTOR, GIACOMO DONNINI

While working on this report, I have been encouraged by speaking with so many competent, passionate leaders in research, clinical care, and advocacy. I am grateful to each expert who has shared their time and insights with us over the years. Now in its third edition, this report covers more than half of the global population through 29 distinct countries. We have found that even as global trends hold true in communities around the world, many communities still face unique challenges; cultural, historical, and political differences create vastly different landscapes. These local communities have rich resources to draw from as they invest creatively in liver health. One of GLI's strongest tools, this report helps to visualize the needs of the liver community and is being used to leverage change in health policy. I believe it will be an eye-opening resource.

AFRICA

Africa is home to 1.37 billion people – **around 18% of the world's population.**

HEALTH OVERVIEW

Africa is the second largest continent on Earth, spread over approximately thirty million square kilometers (twelve million square miles). Africa is home to 1.37 billion people, around 18% of the world's population. A developing region that spends amongst the least in the world on healthcare, relying heavily on public health initiatives and the involvement of NGOs along with aid from other countries.

Current public health challenges include high rates of neonatal deaths, diarrheal disease, HIV/AIDS, malaria, tuberculosis and viral hepatitis – which leads to cirrhosis. Additionally, the next few decades will bring the need to restructure existing health initiatives to cope with significant changes in demographics. In sub-Saharan Africa, for example, where more than 1 billion people live, 50% of the population are predicted to be under the age of 25 years old by 2050. Conversely, North Africa saw a 50% drop-in fertility rate between 1980 and 2017.

There are significant economic disparities between both countries and various economic indicators. Nigeria for example, has the highest GDP in Africa (US$441 billion and 27th in the world) yet ranks at 18th in Africa according to GDP per capita. Meanwhile, 18 of the 20 countries with the lowest GDP per capita, worldwide, are African.

Healthcare spending is, by and large, aligned to GDP per capita, demonstrating more extreme inequalities between countries. In 2019, for instance, the Seychelles (which has the highest GDP per capita in Africa) spent more than four times Morocco and forty times more than Madagascar on healthcare per person.

Sources: The World Bank, Statista

According to the WHO, cirrhosis of the liver is the tenth leading cause of death across the continent, with 195 deaths per 100,000 population.[1]

Though limited liver disease surveillance is conducted across Africa, it appears to be a growing issue: Cirrhosis rates in sub-Saharan Africa doubled between 1980 and 2010, driven mainly by viral hepatitis and alcohol-associated liver disease.[2] More than 50% of all liver patients in sub-Saharan Africa are admitted to hospitals with advanced stage liver disease due to a combination of poverty, geographic barriers and distrust of Western medicine.[2]

The WHO notes that 'Dying from viral hepatitis in Africa is becoming a bigger threat than dying from HIV/AIDS, malaria or tuberculosis.' [3] It estimates that chronic viral hepatitis affects over 70 million people in Africa, 60 million of whom are infected with HBV and ten million with HCC.[97] Despite these staggering figures, the disease is, in many African countries, neglected, with less than one in ten people able to access testing and treatment. As a result, each year, around 200,000 Africans die from advanced liver disease directly as a result of viral hepatitis.[3]

Although viral hepatitis and excessive use of alcohol account for 70% of cirrhosis,[4] the widespread use of traditional herbal medicines may also contribute to the rates of advanced liver disease in Africa.[2]

Estimates suggest that metabolic dysfunction-associated fatty liver disease (MAFLD) rates are generally lower in African countries around the world,[5] but these are based upon relatively small studies – typical of the dearth of up-to-date, high-quality data about liver disease available in the region.

As with the rest of the globe, however, Africa faces rising rates of obesity and type 2 diabetes (T2D), both of which are risk factors for MAFLD.[6]

In Africa, liver cancer is the

4th

most common cancer

> Dying from viral hepatitis in Africa is becoming a bigger threat **than dying from HIV/AIDS, malaria or tuberculosis.**

What is required as a priority from Africa, are well-designed epidemiology studies that screen for MAFLD in the general population as well as in high-risk groups such as patients with T2D or obesity.[6]

Liver cancer is the fourth most common cancer in Africa, and the second most common cancer for men.[9] In men, it is also the second most common cause of cancer death.[7]

As with cirrhosis, by far the major causes of liver cancer in Africa are hepatitis B and C, followed by alcohol misuse. However, this region has another unusual risk factor: aflatoxin, a substance secreted by a mushroom called *Aspergillus flavus* and a known carcinogen linked to HCC.[8] It is often found in several food items used across southern Africa such as cereal grains, spices and coffee and has been linked with hepatocellular cancer around the world. Around 30% of all HCC mortality is linked to aflatoxin, and 40% of those deaths are in Africa, these deaths would be easily preventable with education and awareness.[7]

Alcohol provides a risk factor of 18% of all cirrhosis in northern Africa and 10% in sub-Saharan Africa.[101] In many areas of Africa, the risk of alcohol consumption factor is heightened as a result of degraded, adulterated, or artificial quality alcohol.[7] Still, alcohol consumption across the region is low compared to many other parts of the world. In sub-Saharan Africa for example, per capita consumption is about half of that consumed in Europe.[9] However, these figures hide a wide variation between countries such as Sudan, where 0.5 liters are consumed and more developed countries such as Nigeria where the figures rise to 10.8 liters per person each year.[9]

Despite the challenges, there is much opportunity for improvement of liver health in the region. A combination of prevention programs - nearly all African countries now provide the hepatitis B vaccine for newborns and awareness campaigns to reduce obesity – and the increasing availability of better and cheaper drug therapies for viral hepatitis could turn around the state of liver disease in the future in Africa.

CAMEROON

Population: 27.22 million (2021)

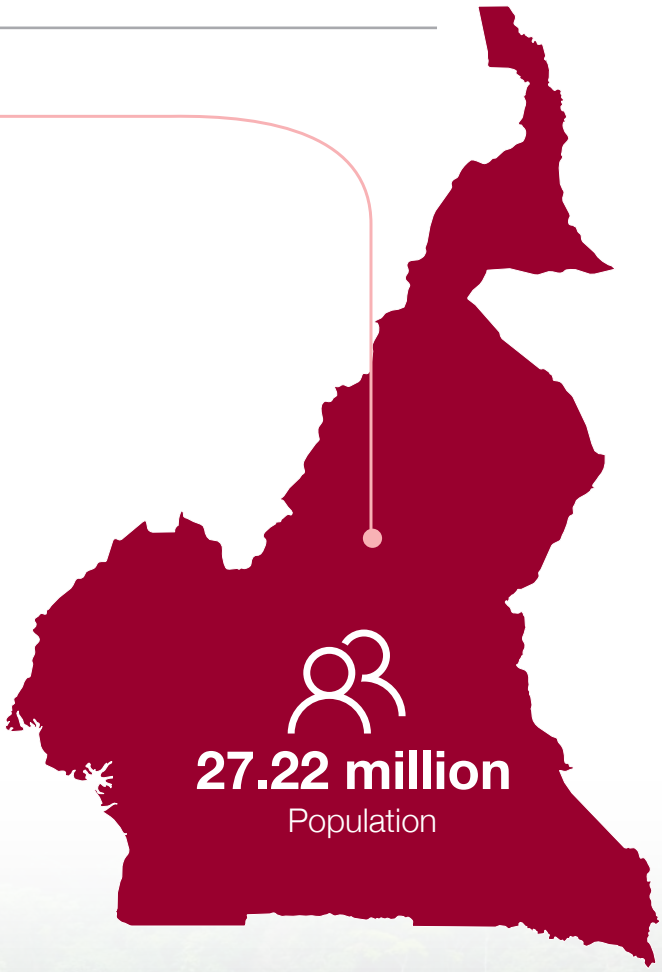
GDP per Capita: $1,674 USD

Life Expectancy: 59.4 years (men) and 62.6 years (women)

Healthcare Spending: 3.6% of GDP (2019)

Healthcare Funding: The main sources of funding for the health sector in Cameroon are: the state budget, households, external financing, local authorities, NGOs and private health insurance, which provide a marginal contribution. These sources do not contribute equally. In 2009, for example, out of a total funding estimated at $5,752,750,000, the contribution of households stood at 94.6% against 3.8% from the State and 1.6% for external partners. Healthcare hardly gets more than 5% of the country's budget – far below the 10% standard from the WHO.

Sources: WorldData.Info, Salary Explorer, Data. WorldBank, MacroTrends.net, International Anatolia Academic Online Journal



$1,674
GDP per capita

3.6%
of the GDP is spent on Healthcare

58.4 years (men)
and **60.9 years (women)**

There is a general lack of information on the prevalence and mortality of liver disease in Cameroon. To address this issue, a recent study gathered and analyzed data on liver disease in a group of patients admitted to Yaounde University Teaching Hospital. Among admitted patients, the prevalence of cirrhosis was 6.7%.[1] The three main causes of cirrhosis were HBV infection, HCV infection and alcohol intake, with a prevalence of 40.2%, 36.8% and 22.2% respectively. Mortality rate was also found to be high, with a rate of 20.5%.[1] These results demonstrate the high prevalence of liver disease within the country and, more worryingly, a pattern of late diagnosis that greatly increases the chances of mortality.

A similar study found that 47% of cirrhosis patients tested positive for HBsAg, so HBV infection has been a major risk factor for cirrhosis in Cameroon for decades.[2] Despite the introduction of the HBV universal vaccine in 2005, the overall prevalence of hepatitis B in Cameroon is high when compared to other countries, ranging between 6-16% within the general population.[3] Indeed, there were 12,000 new cases of the virus in 2019, up from 9,600 cases in the previous year.[4] Knowledge of effective HBV prevention and safe practice remains poor. Indeed, pregnant women across the country have been shown to adopt poor practices regarding HBV prevention.[3] Furthermore, as is the case for other universal vaccine programs, those born before the implementation of the HBV vaccine in Cameroon are at a high risk of developing chronic HBV infection.

To help combat the prevalence of hepatitis B infection, the Cameroon government has reduced the cost of treatment from $250 a month to $50, to encourage hospital attendance.[4] However, hospital attendance is still universally low in Cameroon, with only 35% of the population regularly using this healthcare service. The remainder of the population relies on more traditional healers or only attend hospitals once their conditions become critical.[4] An additional factor that must be considered when analyzing hepatitis B in Cameroon is the prevalence of hepatitis D co-infection, which is greater in severity than HBV infection alone.[5] In a recent study, of HBV-infected samples, 46.73% were positive for hepatitis D virus and 34.2% had an active co-infection.[5] This has major implications for viral hepatitis in Cameron, as those infected with hepatitis B are at a greatly increased risk of medical complications and death.

1 in 6

people in Cameroon has **chronic HBV infection.**

Hepatitis C is also a major healthcare issue in Cameroon, and the country has a prevalence rate of approximately 4.9% amongst adults–the highest prevalence rate in world for HCV.[6] However, in a study published in 2018, the prevalence of HCV in Cameroon was found to be half of previous estimates, with a much higher prevalence amongst the older cohorts.[6] This was due to ages 49-59 having a reduced access to quality medical care in late 1950s, greatly increasing this groups infection rates for HCV. Indeed, the HCV prevalence for the 15-49 age group and 15-19 age group were only 0.81% and 0.2% respectively.[6] Due to this improved quality of healthcare in Cameroon over the last decade, an HCV-free generation is fully achievable as long as the prevalence of intravenous drug use is controlled.

Liver cancer is the fourth most common cause of cancer mortality in Cameroon, with approximately 955 deaths and 1021 new cases in 2020.[7] Both hepatitis B and C infection are the most common causes of HCC and account for approximately 90% of cases.[8] In June 2020, the Ministry of Public Health constructed a national strategic plan for the prevention of cancer in Cameroon, with the aim of improving primary and secondary care cancer services, along with developing new therapies and stimulating research. By implementing this plan, they hope to halve the morbidity and mortality caused by cancer in Cameroon within the next decade.[9]

In terms of metabolic dysfunction-associated fatty liver disease (MAFLD) and its more advanced stage, metabolic dysfunction-associated steatohepatitis (MASH) prevalence in Cameroon, there is little to no data available. However, many related risk factors are increasing. Obesity rates are 11.4%, which places the country at number 135 in the world.[10] More notably, diabetes rates in Cameroon are rising, with prevalence increasing from 2% to 5.8% in 1999 and 2019 respectively.[10] These findings indicate a potential correlated increase in MAFLD and MASH rates in the Cameroonian population.

CAMEROON NEEDS INVESTMENT IN DATA, DISEASE TESTING & DIAGNOSIS

Dr. Mbianke Livancliff is a Senior Immunization Officer and founder of the Empowering Women Foundation in Cameroon.

In Cameroon, we have many barriers which prevent us from providing anything more than a basic healthcare system, with liver disease hardly registering as a health issue at the government level.

Firstly, similar to many sub-Saharan countries, we have huge issues with health funding. Our funding partly comes from the government and partly from international partners such as the WHO and UNICEF, who mainly concentrate on infectious diseases such as HIV, malaria and tuberculosis.

Further, government commitment to health funding– which is distributed by the Ministry of Health–is inconsistent, badly managed and open to corruption both at a local and national level. As a consequence, funding often does not reach the areas it was intended for.

A second barrier is that, although the government provides some free healthcare, the reality is that most is paid for 'out of pocket' as and when needed. However, with an average wage in Cameroon of just $10 a day, for most people, anything but the most basic healthcare is out of reach.

Additionally, many Cameroonians do not leave their local area, so unless they can reach a government or NGO clinic nearby, or a doctor travels to them, it is hard for them to receive consistent and ongoing healthcare. This is a problem for liver disease patients.

Many people in rural areas still believe in and rely on traditional medicine. Not only does this discourage patients from seeking proper medical help, but often traditional treatments themselves can cause significant harm, particularly to the liver, and we often see cases of liver failure from such treatments.

Corruption at local or national level is also a real issue. For example, we have one of the highest rates of hepatitis B and C in the world and the government and NGO are investing in this with testing and vaccinations. However in reality, even 'free' testing for viral hepatitis often requires a fee, paid by the patient. This is having devastating consequences on attempts to control the spread of viral hepatitis and other diseases.

> **5% of our population are thought to have T2D** which we know is prevalent in all metabolic disorders.
>
> - DR. MBIANKE LIVANCLIFF

Finally, and importantly, we are hampered by an acute shortage of good quality data around liver disease. Most research here is carried out by smaller private institutions and extrapolated out throughout the rest of the country which does not provide a true picture of health on the ground. The figures that are available likely misattribute the cause of death due to limited understanding of liver disease and folk beliefs, like witchcraft. All this prevents us from making meaningful assessments of how and where we need to focus our efforts.

Around 5% of our population are thought to have T2D, yet there has been no interest from the government about NAFLD or NASH, which we know is prevalent in all metabolic disorders.

We do know, however, that the rates of liver cancer are rising and now account for 5% of all cancer deaths with liver cancer the fourth largest cause of cancer mortality.

At the same time, over the last few years, even some of the bigger hospitals have had to close their radiology departments for lack of funding and there are still too few clinicians who are experts in treating cancer, let alone liver cancer. Virtually all liver cancers are detected at a very late stage, and liver cancer treatment is usually limited to palliative chemotherapy with liver surgery pretty much non-existent. We have no liver transplant centers in Cameroon.

All this is frustrating for us as medical professionals; many of my colleagues have left to work in other countries, and I sometimes feel like giving up. However, I strongly believe that if we can make some changes on overall health policy, we can make a huge difference on the ground.

I would like to see the government focus on breaking the infection chain of viral hepatitis by investing in diagnosis and testing – all of which must be free. Furthermore, we urgently need better public education on all aspects of liver disease, including hepatitis, obesity, NAFLD and NASH.

Finally, I would beg the government to invest in a system of providing good quality data on all aspects of liver health, including outcomes, so that we who are working in public health can start to develop a relevant and effective plan of action.'

OVERVIEW

EGYPT

Population: 111,247,248

GDP per capita: $17,000 (2023)

Life Expectancy: 73.8 years (men) and 76.2 years (women)

Healthcare Spending: 4.4% of GDP (2020)

Healthcare Funding: In Egypt, a large part of healthcare spending comes out of the people's pockets. Despite federal budget increases, the government only covers around one-third of the total cost of healthcare – leaving over 60% of the total healthcare costs to the people. To help reduce these expenses, the Universal Health Insurance law was passed in 2017. This law aims to provide everyone access to quality healthcare without financial strain. The system is funded by a combination of government money, premiums paid by citizens, and contributions from businesses. However, many Egyptians still face high out-of-pocket costs for medical care.

Sources: US CIA's The World Factbook, International Health Policies, Ahram Online, Ministry of Planning and Economic Development of Egypt

$17,000
GDP per capita

4.4%
of the GDP is spent on Healthcare

73.8 (men)
and **76.2 (women)**
Life Expectancy

In 2022, Egypt became the first country to achieve **"gold tier" status** for hepatitis C elimination

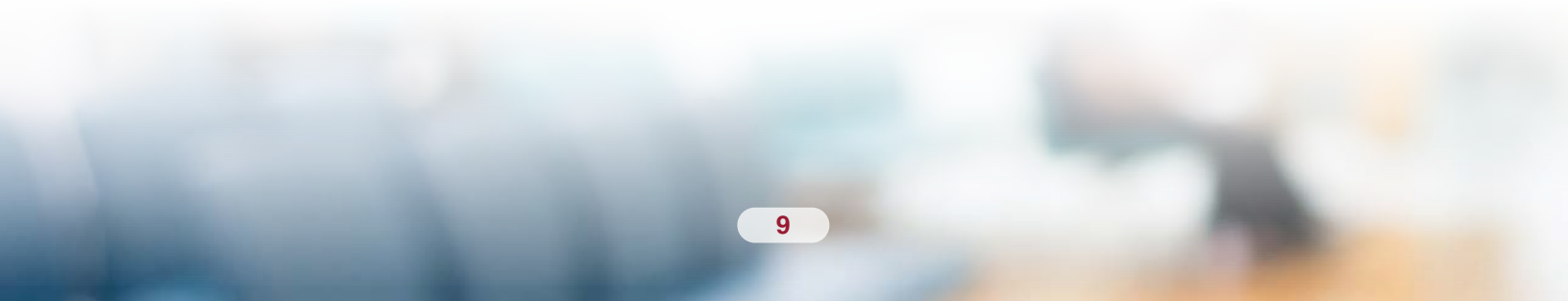
Liver health in Egypt has seen significant progress in recent years. While liver diseases such as viral hepatitis and metabolic dysfunction-associated fatty liver disease (MAFLD) have posed considerable challenges, Egypt has made impressive strides in combating these conditions. In 2022, Egypt became the first country to achieve "gold tier" status for hepatitis C elimination according to WHO criteria.[1] The following year, the World Bank Organization recognized this milestone as a significant achievement, marking the near eradication of an epidemic that had once been the third leading cause of death in the country.[2] By continuing to build on these achievements, Egypt is well-positioned to further enhance liver health outcomes and provide a model for other nations facing similar challenges.

Once known as a global epicenter for hepatitis C, Egypt's journey in improving liver health is a great example of combining accessibility and technology. In the mid-20th century, HCV infections swept through villages across the Nile Delta, a consequence of outdated medical practices like the use of parenteral antischistosomal therapy.[3] By 2015, Egypt's overall prevalence of HCV was the highest in world.

The country turned the tide through ambitious public health initiatives.[1,4] Over the past decade, Egypt has screened and treated millions to reduce hepatitis C prevalence by more than 95%. Globally, Egypt accounts for 3.6% of overall treatments provided.[1]

A cornerstone in Egypt's fight against hepatitis C was the "Miyat Milyon Sehha" or "100 Million Healthy Lives" campaign. This initiative sought to screen the entire adult population and ultimately reached over 60 million people and provided free treatment to more than 4 million patients.[5] Over three phases, the program targeted all Egyptians and residents 18 and above, with nearly 6,000 fixed testing sites and over 8,000 mobile units deployed to ensure even the most isolated communities were covered.[2,5] Additionally, a dedicated call center was established to handle follow-ups and answer questions from the public. Over 87% of people living with hepatitis C were diagnosed, and ultimately the prevalence of HCV dropped from 10% to just 0.38% within a decade.[1] This achievement earned Egypt "gold-tier" status with the World Health Organization.[1] This program not only provided life-saving treatment, but also raised awareness about liver health across the country, making it one of the most successful public health campaigns in Egypt's history.

Following the significant strides made in reducing hepatitis C prevalence, another challenge in Egypt's battle against liver disease is the small but persistent risk posed by schistosomiasis, commonly known as bilharzia. This parasitic disease, which has a long history in Egypt, is primarily transmitted through skin contact with contaminated water in the Nile River's canals, disproportionately affecting rural populations near the Nile.[6,7] As many as 50% of people with schistosomiasis in Egypt are co-infected with hepatitis C, which exacerbates liver disease.[7] Advanced cases of schistosomiasis often lead to liver enlargement, fluid accumulation in the peritoneal cavity, and hypertension of the abdominal blood vessels, all of which contribute to the development of liver fibrosis and increase the risk of bladder cancer.[8] Efforts including cementing the bottom of canals to eradicate snails, introducing natural predators, and mass treatment campaigns have helped eradication efforts significantly in Egypt. Still, schistosomiasis affects up to 4% of the population in certain areas.



In 2015, Egypt had the highest rate of hepatitis C **in the world.**

Additionally, Egypt is grappling with the ongoing burden of liver cancer, a condition closely tied to the country's past struggles with hepatitis C, making it a leading cause of cancer-related deaths.[9] It is especially prevalent among men, where it is responsible for 33.63% of all cancers, and among women it accounts for 13.54% of cancer cases.[9] The poor prognosis associated with HCC is often due to late-stage diagnosis, which limits the effectiveness of treatment options.[9] Immediately after the 100 Million Healthy Lives campaign, Egypt introduced a surveillance system for all patients presenting with liver steatotsis including free visits every four months to 58 surveillance centers and 93 imaging centers. At the regular visits, patients receive ultrasound screening and blood tests for HCC biomarkers. Although there are limited reports on HCC survival rates and relapse in Egypt, there is hope, as early detection and improved healthcare infrastructure offer new possibilities.[10]

Simultaneously, the country faces new challenges, such as the rising prevalence of MAFLD, driven by modern lifestyle changes. As of 2022, Egypt ranked as the 15th most obese country in the world.[11] This surge in obesity is significantly contributing to the increase in other metabolic disease, including cases of cancer, heart disease, and MAFLD cases. Despite this, awareness of MAFLD remains low, with only a third of the population aware that fat deposits in the liver can lead to serious health issues.[13] Alarmingly, MAFLD is not confined to adults; it also affects children and adolescents, with studies showing that 15.8% of Egyptian schoolchildren are impacted – higher than the global average of 13%.[14,15] In response, Egypt is making efforts to raise awareness about this condition, which remains poorly understood.

In response to the growing burden of liver disease, Egypt has expanded its liver transplantation services, offering a crucial lifeline to those with liver disease. As of 2022, Egypt has opened over 37 registered centers performing around 370 liver transplants annually across public and private hospitals.[16] However, a shortage of deceased donor organs due to cultural factors seriously limits the availability of liver transplants.[17] Many Egyptians do not subscribe to the concept of brain death; as a result, even after a 2010 law allowed deceased donor transplants in the country, Egypt's system still relies heavily on living donor transplantation.[17,18] Although it is lifesaving, living donor liver transplantation carries risks for donors and is not suitable for all patients, especially those with end-stage liver disease.[16] Despite these challenges, the growth of transplantation services marks a critical step forward in addressing liver health in Egypt.

In the ongoing fight to promote liver health and hope, Egypt is forging a path forward, addressing its challenges with determination and a clear vision for the future. The progress made so far is a testament to the power of concerted public health efforts and the resilience of a nation committed to improving the well-being of its people.

15.8%

of Egyptian schoolchildren has fatty liver disease, above the global average.

A TIMELINE OF PROGRESS FOR HEPATITIS ELIMINATION IN EGYPT

2006	Establishment of the National Committee for Control of Viral Hepatitis (NCCVH)
2008	Demographic health survey reveals 15% antibody prevalence and 10% virus prevalence between ages 13 to 59 NCCVH releases first National Control Strategy for Viral Hepatitis in collaboration with the Pasteur Institute
2014	DAAs developed, and Egypt negotiates 1% of global price – allows for scale up of treatment from 60,000 to more than 1 million annually; 100 Million Seha/ 100 Million Healthy Lives campaign launches Wait list for HCV treatment is cleared
2016	Egypt exclusively offering generic DAA treatment for HCV at the price of $ for the full course of treatment
2017	With 2 million people treated and 3 million still infected, nationwide rapid screening efforts launched and screening for those over 12 years completed within seven months
2018	First school screening program developed with confidential linkage to care
2023	Egypt becomes first country to receive “gold tier” status on the path to elimination of hepatitis C as per WHO criteria

OVERVIEW

GHANA

Population: 32.83 million (2021)

GDP per Capita: $2,238 USD (2023)

Life Expectancy: 61.8 (men) and 66.1 (women)

Healthcare Spending: 3.42% GDP

Healthcare Funding: About half of Ghana's health care is financed by taxes, through the national health insurance (NHI) levy. The other half is informally/privately funded through out-of-pocket payments and payroll deductions from health insurance.

Sources: The World Bank, World Life Expectancy, The Global Economy, International Journal for Equity in Health

$2,238
GDP per capita

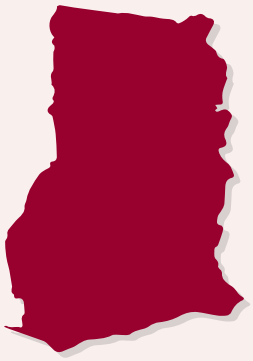
3.42%
of the GDP is spent on Healthcare

63.7 (men)
and **69.2 (women)**
Life Expectancy

Liver disease poses a significant health burden to the people of Ghana. In total, 8.8% of deaths in adults were due to liver-related causes – half due to HBV infection.[1] Liver cancer, overconsumption of alcohol, and viral hepatitis also contribute significantly to liver disease in the country, while metabolic dysfunction-associated fatty liver disease (MAFLD) and its risk factors are on the rise. With so many active paths to liver disease and damage, efforts both to raise awareness of the many risk factors and symptoms of liver disease and also to bolster the care pathways to prevent severe disease are necessary.

A change in lifestyle habits is increasing the prevalence of fatty liver disease and its risk factors in West Africa, including Ghana, following the global rise of fatty liver disease in developing countries, behind developed countries.[2] One study in the Ashanti region of Ghana found that more than half of the people with T2D had MAFLD, of whom more than 1 in 10 had significant liver fibrosis – though less than the global proportion of MAFLD in those with T2D, still a sizeable portion.[3] A prospective study on surgical patients found that 56% of patients had MAFLD – and those patients had a 5x likelihood to have an extended length of hospital stay.[4] While this is not representative of the general population – it is more than double the global prevalence of MAFLD, which is nonetheless alarming.

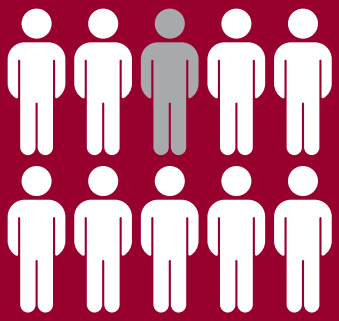
Although broader population prevalence data on fatty liver disease is unavailable in Ghana, there is a lack of reliable, safe, and cost-effective screening for MAFLD; referral is not standardized, biopsy is risky, while safe, low-cost diagnostic techniques like transient elastography are inaccessible.[2] Meanwhile, obesity and overweight are on the rise, with an overall prevalence found to be 15.6% overweight and 5.5% obese, with rates higher in women than in men.[5] While these rates are low on a global scale, lack of physical activity, drinking, and unbalanced diets appear to be heavily contributing and could snowball into increased numbers of liver disease as well, since obesity is a major risk factor for fatty liver disease. Screening and treatment should be standardized and accessible in order to mitigate this rising crisis early.



Deaths due to liver disease have **risen 80% in Ghana** over the last 3 decades.

Though a large proportion of Ghana's population abstains from alcohol consumption, it still poses a major obstacle to liver health in Ghana, driven predominantly by men. Yearly consumption on average is 2.7 liters per person, though this is 4.6 liters for men and 0.7 for women.[6] Among drinkers, these averages are much higher. Though nearly 3 in 4 Ghanaians has abstained from alcohol in the past year, 9.4% can be considered Heavy Episodic drinkers – and 7.3% of men can be considered to have alcohol use disorder.[6] Over time, this consumption leads to cirrhosis, alcohol-associated liver disease, and alcohol-associated hepatitis that account for 77.5 deaths per 100,000 each year.[6] Over the last three decades, mortality from cirrhosis and other chronic liver diseases has risen in Ghana by 80%.[6] Further, alcohol consumption was the main etiology for 38% of those hospitalized for cirrhosis in a district hospital in Ghana.[7]

Nearly 1 in 10 people in Ghana has viral hepatitis.



There is a relatively high prevalence of viral hepatitis in Ghana, especially hepatitis B, which is considered to have a high endemicity with a prevalence of approximately 8% in the population.[8] Higher prevalence was noted in northern regions of the country.[8] While surveillance data is unavailable on hepatitis A in the country, prevalence of HCV is estimated to be 3% in the population, while HDV prevalence has been measured at 8% of people with liver disease (much lower in the population overall).[9,10] HEV, particularly in pig farmers, has been found to have a seroprevalence greater than 10%.[11]

Ghana does not have a viral hepatitis (B or C) elimination plan in place.[9] HBV testing in Ghana is currently risk-based.[8] Population testing and appropriate linkage to care are necessary to overcome the heavy burden of HBV in the country. In good news, Ghana has 99% coverage with its infant vaccine program and all newborns are supposed to receive the hepatitis B vaccine, while a testing and treatment program is being developed.[12]

Unsurprisingly, the high rates of HBV lead to end-stage liver disease (about half of HCC liver cancer cases are attributable to the viral infection).[8] Deaths due to liver cancer in Ghana have been on the rise for the past two decades.[13] One study of hospital deaths found that nearly 2% were related to HCC.[1] Notably, liver cancer cases present at a young age and advanced stage in Ghana compared to non-African populations.[14] Double the amount of men than women present with liver cancer, and the mean age is 45.[15] This may be due to workplace or other risk factors for exposure as well as the greater alcohol consumption in men.

DID YOU KNOW?

Liver cancer patients are **diagnosed younger and at more advanced stages** in Ghana than in non-African populations.

Very little is known about pediatric and rare liver diseases in Ghana, which suggests that stronger screening measures should be implemented.

A locally based team in Ghana conducted the country's first liver transplant in 2021.[16] In a study of patients with HCC at the Komfo Anokye Teaching Hospital in Ghana, less than 8% of patients were eligible for transplantation – which is largely inaccessible in the country anyway.[17] Before it can grow as a curative treatment for end-stage liver disease, screening must catch these conditions when they are early enough to be treated.

Ghana does not have a **viral hepatitis plan** in place.

PUBLIC HEALTH AND PRIMARY CARE APPROACH NEEDED TO IMPROVE LIVER HEALTH IN GHANA

Dr. Josiah Nang-Bayi is an entrepreneur, researcher, and physician in Sunyani, Bono Region, Ghana with experience in internal medicine.

CHALLENGES

1. **Lack of Awareness:** A good percentage of those who are formally educated still don't know much about liver health beyond viral hepatitis, after government initiatives on hepatitis B vaccination. The rest of the population, without formal education, is almost completely ignorant of liver health. Even so, most people forget about non-infectious liver disease and mistake symptoms for malaria or other gastrointestinal infections.
2. **Over-Reliance on Traditional Medicine:** Traditional medicine is a very common practice in Ghana. People rely on herbal preparations – especially when they are advertised on the radio and TV as treatments for diabetes, hypertension, general chronic and even infectious diseases. These things have side effects on the kidneys and the liver that are not usually communicated, since these organs process and filter most of the medications – worsening any existing liver conditions.
3. **Late Diagnosis and Treatment:** Primary care facilities don't have doctors present most of the time – only a nurse or physician assistant or a community health worker. These health workers tend to not think about chronic liver conditions. Even when an individual's liver levels are elevated, they only check for viral hepatitis and just manage for common infections. People often are not referred for secondary care for the liver until they present with end-stage liver disease, usually in severe pain and too late for a positive outcome.

OPPORTUNITIES

1. **Government-Led Awareness Campaigns:** The people here tend to pay more attention to a message if they heard it in the media – TV ads or the radio. The government could go out on a massive sensitization program about chronic liver disease. The First Lady of Ghana currently has a campaign on TV telling women, especially pregnant wome about the need to take HIV antiviral medication, so we could do the same for liver health. We could combine this with dedicated health personnel in each district or health facility trained to constantly educate on liver health.
2. **Fortified Primary Healthcare:** People tend to access healthcare first through primary health facilities. When people present with nonspecific liver symptoms, they check for salmonella, malaria, or *h. pylori* bacteria as well as viral hepatitis – but if these are negative, they are sent away with minimal follow-up. At secondary facilities, we are beginning to run liver function tests, and we are picking up chronic liver disease in young people. Primary healthcare workers should be educated to provide these referrals and follow-ups.
3. **Expand Viral Hepatitis Programs:** Ghana has an immunization protocol in which all newborns are supposed to be vaccinated against hepatitis B. However, we still have a lot of children, especially in rural communities, who do not receive these vaccines, whether the vaccine ran out of stock or the mother delivered with a traditional birth attendant. We ran a project on university campuses and found over half of students were not vaccinated. We have to go back to a public health orientation to address viral hepatitis.

PERSPECTIVES AS BOTH A PATIENT AND A NONPROFIT ADVOCATE

William J. Ocran co-founded The Empowerment for Sustainable Livelihood, a charity that promotes disease awareness, prevention, education, advocacy, and research in 2007. He has over 25 years of experience in NGO activities throughout the war-torn and impoverished communities of Ghana.

I had very little awareness of liver health until I developed abdominal pain, went to the hospital, and was asked to do a scan. I learned that I had liver disease, which led me to do a lot of research into it. Later, I found Global Liver Institute, which has helped us to educate many people, especially in vulnerable regions, on the liver and its challenges. We have been able to run a sensitization program to raise awareness in the general public on the liver and challenges to the liver. We've met with industry associations, the church – even health workers!

> Later, I found Global Liver Institute, **which has helped us to educate many people**, especially in vulnerable regions, on the liver and its challenges.
>
> - WILLIAM J. OCRAN

One of the challenges that we have is the lifestyle. We don't have any good medicine to prescribe to solve liver disease – you have to check your lifestyle, you have to check your weight, and you have to make sure your cholesterol level is low. This is a major part of our education program.

KENYA

Population: 54 million (2021)

GDP per Capita: $1,950 USD

Life Expectancy: 59.6 (men) and 64.7 (women)

Healthcare Spending: 4.59% of GDP (2019)

Healthcare Funding: Kenya's health sector relies on different sources of funding, namely public (government), private firms, households and donors, as well as health insurance schemes.

Public healthcare service delivery is divided into four levels, starting with community services on the ground, followed by primary care health services, and secondary and national hospitals. Primary healthcare and maternity services are free in public health centers and dispensaries. However, public hospitals continue to charge user fees.

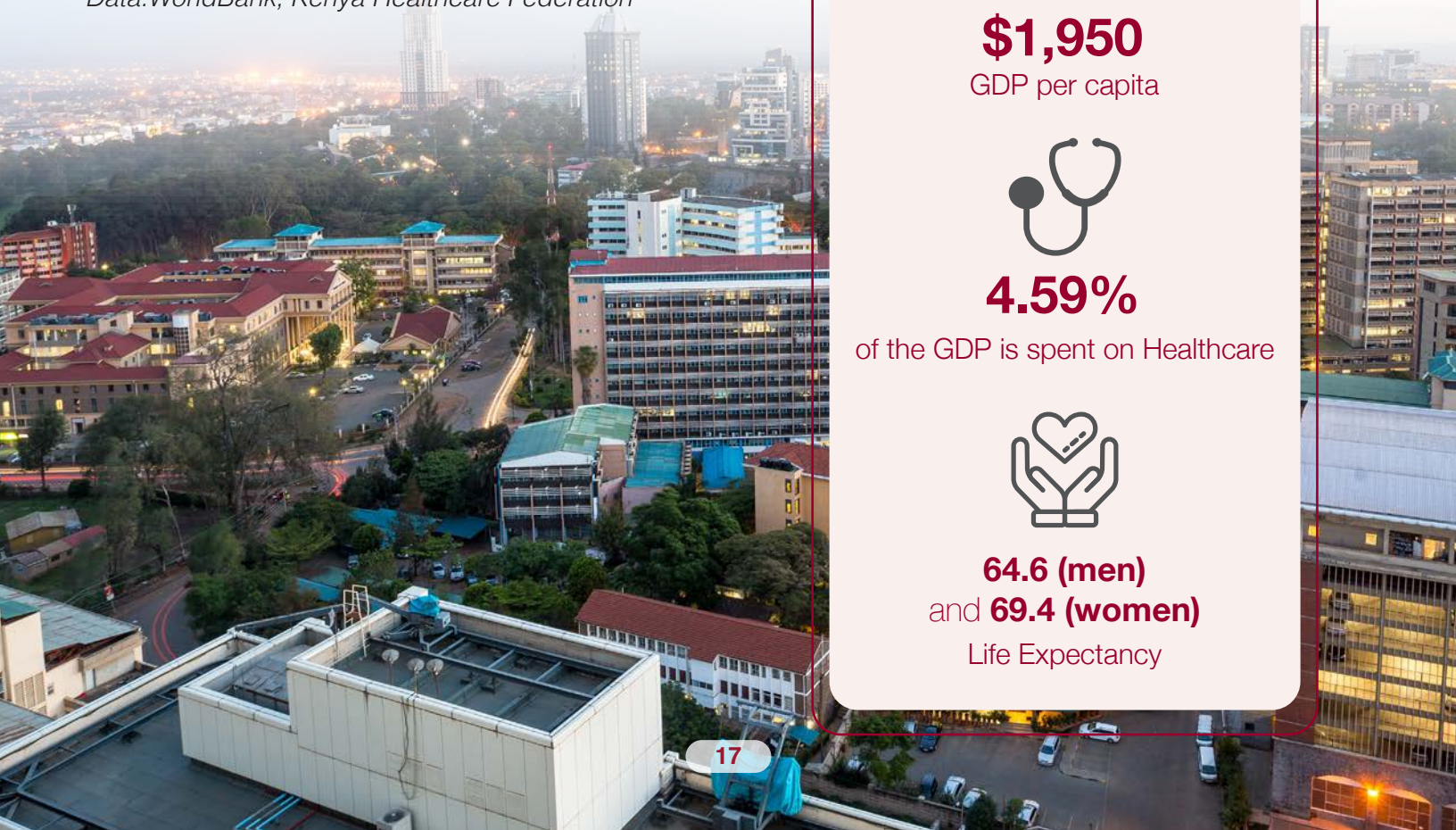
Due to the devolutionary shift within Kenya's healthcare financing structure, there is a significant inter-country variation in financing arrangements for healthcare facilities and services.

Sources: WorldData.Info, World Population Review, Data.WorldBank, Kenya Healthcare Federation

$1,950
GDP per capita

4.59%
of the GDP is spent on Healthcare

64.6 (men)
and **69.4 (women)**
Life Expectancy



Similar to other countries in sub-Saharan Africa, there is a significant lack of available data on the prevalence, incidence, and mortality of liver disease in Kenya. Between 1980 and 2010, cirrhosis-related mortality doubled in sub-Saharan Africa, making liver disease a major healthcare burden for this group of countries.[1] Significant investment in liver disease treatment, diagnosis and prevention, as well in the collection and analysis of data is required to address this growing healthcare issue.

HCC is the 11th most prevalent form of cancer and the 9th highest cause of cancer-related death in Kenya.[2,3] A major risk factor for liver cancer in Kenya is hepatitis B infection, with the virus having a prevalence of approximately 5-8% within the Kenyan population and attributing to over 60% and 90% of chronic liver disease and HCC cases, respectively.[4,5] The western area of Kenya, specifically the region of North Rift, has a particularly high prevalence of hepatitis B. It is hypothesized that this is due to a high concentration of mycotoxin grain contamination, since this region has extensive cereal production.[2]

To address the high prevalence of liver cancer in the region, the country's first liver cancer surgeries, funded by The French Ministry of Foreign Affairs, will be available in West Kenya.[3] Clinicians at the Moi Referral and Teaching Hospital (MTRH) will be trained to identify early risk factors, make diagnoses, and operate on living cancer patients with specialized equipment in both Peru and Paris.[3] If successful, this could be a flagship center to be replicated and established in other high-risk countries.

5 MILLION

people in Kenya are living with chronic HBV infection.

9 OUT OF 10 CHILDREN develop immunity to hepatitis A once they reach the age of 10

The hepatitis B vaccine was introduced in early 1980s, with the Kenyan Expanded Program of Immunization (KEPI) incorporating it into their initiative in 2002 by vaccinating newborns at six, 10 and 14 weeks.[5] Despite this program, a large proportion of the Kenyan population remain unvaccinated, especially those born prior to 2002 who missed out on the vaccine and are consequently at much higher risk of developing chronic hepatitis.

Although not as prevalent as hepatitis B, hepatitis A, C, D and E infection must also be considered when analyzing liver disease etiology in Kenya. In a 2017 report across four Kenyan hospitals, the most common cause of jaundice was chronic hepatitis B infection, with over half of the study participants testing positive for this virus.[6] Acute hepatitis A was the second most common cause of the symptom.[6] This was a relatively unexpected result, as previous studies carried out in Kenya have shown that 9 out of 10 children develop immunity to hepatitis A once they reach the age of 10. This indicates a re-evaluation of the need for an adult hepatitis A immunization program in Kenya.[7] Recent infection of hepatitis C, D or E was not found in the study.

Given the relatively limited data on the prevalence of metabolic dysfunction-associated fatty liver disease (MAFLD) in sub-Saharan Africa, the two main studies investigating this disease prevalence in Kenya have fairly small sample sizes.[8,9] A recent study involving 783 individuals in Kenya found that 15.9% had MAFLD, with a three-fold higher risk in urban populations when compared to rural population groups.[10] A surprising female-to-male prevalence ratio of 2.8 to 1 was also identified in this study, calling for further investigation on the potential high-risk level for black African women in developing MAFLD compared to their male counterparts.[10]

WE NEED A COHERENT STRATEGY FOR VIRAL HEPATITIS

Michael Nyawino is Executive Director Financial Awareness Foundation Ambassador of the Christian Community Healthcare Foundation in Kenya.

Liver disease accounts for 5% of deaths in Kenya, making it a serious public health issue. Yet despite this high figure, it has largely been ignored by our government. As a result, liver disease, whether from alcohol abuse, hepatitis or NASH is usually only detected when it is at an advanced stage. This is partly due to lack of awareness but also lack of funding for healthcare in general - most people must pay a certain amount towards hospital treatment including testing - so generally the poorer populations will wait until the last minute until they absolutely cannot carry on without medical help.

Unfortunately, by the time they have reached that stage, it is usually far too late to carry out any effective treatment and in any case, there is usually a wait for beds in most public hospitals. It is a desperate situation for them. Sometimes, if a transplant or other complex treatments are needed, the family in many cases raise funds so they can send the patient to India. Alternatively, the private hospitals have good facilities including diagnostic equipment, but this has to be funded upfront, and this is out of reach for most people in Kenya.

One of the key causes of liver disease in Kenya is the relatively high rate of hepatitis B, particularly in the coastal regions, which are the least developed part of our country. Although we have free vaccinations for infants, there is no coherent testing program for adults, and generally people are only diagnosed when they are being treated for something else. A lot of government - and external - funding has been put into raising public awareness of HIV, malaria and tuberculosis. I would very much like to see the same being done for viral hepatitis including highlighting its impact on liver disease.

IT'S A VERY SAD SITUATION

Liver disease is not only widespread but it is often fatal. We urgently need a program of education around obesity and alcohol abuse, starting from an early age in the schools.

- MICHAEL NYAWINO

We have no specific data on liver cancer in Kenya, although what we do have seems to indicate that liver is the third most common cancer amongst Kenyan males. It is almost certainly underdiagnosed. We hear regularly of people only going to the hospital at the very last minute or not even receiving treatment at all with their death not being correctly recorded as cancer. Currently viral hepatitis is believed to be the main cause of liver cancer here, but there is also concern about the rising rates of alcohol abuse.

In line with the rest of the world, obesity rates are rising, particularly in the urban areas where fast food consumption increases, moving away from the traditionally vegetarian diet of the past. We have no idea how people have NAFLD or NASH, as it is simply not recorded, partly due to government inaction, but also because we simply don't have the scanning equipment to carry out a proper testing program.

T2D is also becoming common, but it needs regular medication. Many people can't afford that, thus they resort to traditional remedies, which can often make things worse.

It's a very sad situation. Liver disease is not only widespread but it is often fatal. We urgently need a program of education around obesity and alcohol abuse, starting from an early age in the schools. Hospitals desperately need more diagnostic resources so that we can begin a proper screening program for those at risk of liver disease.

If we carry on as we are, especially with the new challenges presented by NAFLD and NASH, we will be looking at a very serious crisis in liver disease in the next decade. The government needs to take action – and soon.

OVERVIEW

NIGERIA

Population: 236 million (2024)

GDP per capita: $5,000 USD

Life Expectancy: 60.4 years (men) and 64.2 years (women)

Healthcare Spending: 3.4% of GDP

Healthcare Funding: Nigeria's healthcare system includes public and private providers and modern and traditional systems in a three-tier system. The primary healthcare system consists of community-based and primary care, mostly run by local government areas. Secondary care facilities include general clinics and hospitals, many run by the state government. Tertiary centers provide specialized care at federal government centers and research institutes. In response to the growing healthcare needs, Nigeria is actively working towards implementing its Universal Health Coverage Plan through a series of initiatives and investments to bring health security by 2030. However, due to a lack of funding through this complex transition, over 90% of Nigerians still do not have personal health insurance, and 77.2% rely on out-of-pocket healthcare spending.

Sources: U.S.'s CIA The World Factbook, Severe Malaria, Nigeria Solidarity Fund

$5,000
GDP per capita

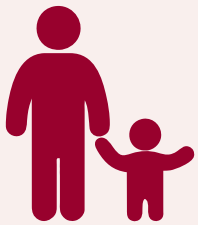
3.4%
of the GDP is spent on Healthcare

60.4 (men)
and **64.2 (women)**
Life Expectancy

Nigeria, a lower-middle-income country in West Africa, faces significant chronic liver disease due to widespread hepatitis B infection and excess consumption of alcohol. The healthcare system, facing financial inaccessibility and structural limitations, further contributes to high rates of treatable diseases among residents.

Metabolic dysfunction-associated fatty liver disease (MAFLD) is becoming increasingly prevalent in Nigeria, driven by rising rates of overweight, obesity, and diabetes. However, the incidence is not as high as in studies from Western and European countries.[1] The rise in obesity in Nigeria is linked to increased consumption of high-calorie foods and sedentary lifestyles, with higher rates among the upper and middle classes due to higher access to fast food restaurants.[1,2] Despite policies promoting healthy physical and nutritional habits, the focus remains more on undernutrition than obesity in Nigeria.[1,2] With the country's industrialization and the proliferation of nutrient-poor processed foods, this condition will pose an increasing challenge for Nigeria if it is not proactively addressed.

At the same time, 2 million children in Nigeria are currently suffering from severe acute malnutrition and only two out of 10 children receive treatment.[3] This introduces another pathway to fatty liver disease. With high rates of undertreated malnutrition, many children experience wasting and/or stunting, which can lead to metabolic syndrome and increase the likelihood of developing conditions like obesity, high blood pressure, and insulin resistance later in life.[4,5] Metabolic disease can lead to fatty liver disease due to the body's increased fat mobilization and insufficient nutrients for proper liver function. This is speculated to be further exacerbated by increasing urbanization that has introduced processed food and fast food chains in Nigeria while lifestyles become more sedentary.[4] Thus, malnutrition in childhood increases the risk of fatty liver disease for many Nigerians, and that risk may come to fruition if they gain access to high-calorie, low-nutrient foods in adulthood.



Malnutrition in childhood increases the risk of fatty liver disease in adulthood

In Nigeria, viral infections are the primary causes of chronic liver disease and liver cancer.[6] It is estimated that 35 million people are infected with hepatitis B and C virus, with higher prevalence in rural areas.[6] Those who suffer from HBV infection have a 15-25% chance of dying early in adulthood from cirrhosis and liver cancer, and a small number of people with acute infections might also die from sudden liver failure.[6] The rate of HBV infection is high among frontline health workers/surgeons as well as among people who have had certain health procedures, including traditional circumcision, a dental procedure outside of a health facility, a vasectomy, and wanzami – a traditional, surgical removal of the uvula.[6,7] Nigeria also has the second-highest rate of HIV infection in the world, so people with viral hepatitis are often co-infected with HIV.[8,9]

Although HBV is preventable through a free, three-part infant vaccination series as part of Nigeria's routine childhood immunization programs, only 51% of children are vaccinated.[10] This is due to a fractured medical system and inconsistent funding, promotion, and availability.[10] Even with annual screenings for HBV and HCV during National Hepatitis Day, much of the population is left vulnerable to these infections – and this situation has resulted in HBV causing nearly 80% of cases of liver cancer in Nigeria.[10,11]

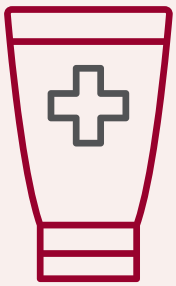
35 million
people are infected with
hepatitis B and C virus

In 2016, hepatocellular cancer (HCC), accounted for 4.4% of cancer cases and 7.3% of cancer deaths, making it the fourth deadliest cancer in Nigeria.[12] Those who receive an HCC diagnosis have an average of 2.5 to 3 months to live – less when the patient also has HIV; this is a poor prognosis compared to global averages.[11] Further, aflatoxin, a cancer-causing poison naturally found in fungus, has been found at levels higher than is considered safe in major food sources like rice, maize, legumes, ground nuts, and more.[13] With over 90%of households consuming these products, it poses a major liver health risk to the population.[13]

Because many Nigerians pay out-of-pocket for healthcare, many seek affordable options for self-medication from places like roadside chemists, unauthorized shops, and stalls.[14] Therefore, the lack of standard screening for risk factors means that many patients with liver cancer do not see a physician until they have symptoms, have thus already developed advanced disease, and therefore have limited effective treatment options.[11]

Alcohol consumption contributes to chronic liver disease in Nigeria, especially for men. The country leads Africa at 13 liters per capita alcohol consumption per year.[15] In a 2022 self-report survey of Southeast Nigeria, 79% of participants indicated that men in their area drink daily, and 57% agreed that most men depend on alcohol.[16] This growing problem has increasingly begun to affect the younger populations, prompting the government to ban the sale of alcohol in small sachets, which are more accessible and popular among the youth.[17] Although the legal drinking age is 18, many begin drinking years earlier – especially boys.

Only
51%
of children are
vaccinated for HBV



The country leads Africa at **13 liters per capita alcohol** consumption per year.

This pattern of alcohol consumption leads to liver disease. Alcohol consumption follows viral hepatitis as the second leading cause of liver cancer.[18] A nationwide study also found that 80% of cases of cirrhosis were caused by alcohol consumption.[19] Enforcement of laws and stronger public health measures to reduce excess consumption of alcohol are necessary to address this growing problem and prevent cirrhosis and liver cancer.

Unfortunately, treatment options for this type of end-stage liver disease are limited. Although renal transplantation has been available in Nigeria since 2000 from living donors, the skill and infrastructure to support liver transplantation is still under development.[20] Surgeons in Nigeria have held symposiums to establish a liver transplant center in the country and promote liver health.[21] This has led to an announcement from government-run Aminu Kano Teaching Hospital that it has acquired the equipment and technical expertise to conduct liver transplants soon.[21] However, liver transplantation services require substantial financial investment, advanced infrastructure, and highly specialized human resources, and the current health system in Nigeria is not built to sustainably meet this need.[22]

Liver health in Nigeria faces significant challenges due to high rates of viral infections like hepatitis B and C, compounded by inaccessible healthcare infrastructure and economic barriers that hinder early detection and treatment. Additionally, high alcohol consumption, particularly among men, exacerbates liver health issues, leading to increased cases of liver cancer and hepatitis. To improve liver health outcomes, Nigeria should expand its infrastructure to increase vaccinations and screenings, enhance public health education, and enforce regulations that curb harmful practices.

SOUTH AFRICA

Population: 60 million (2021)

GDP per Capita: $6,253 USD

Life Expectancy: 61 years (men) and 67.9 years (women)

Healthcare Spending: 9.11% of GDP (2019)

Healthcare Funding: Around 71% of the population is cared for by public sector healthcare, which is largely underfunded. The private sector is primarily funded by individual contributions to health insurance or medical aid schemes and serves ~27% of the population. To help mitigate this inequality, the South African government has introduced the National Health Insurance Scheme, which buys healthcare services for patients, which are then delivered at either public or private facilities.

Sources: WorldData.Info, Time Doctor, GlobalData, Data.WorldBank

$6,253
GDP per capita

9.11%
of the GDP is spent on Healthcare

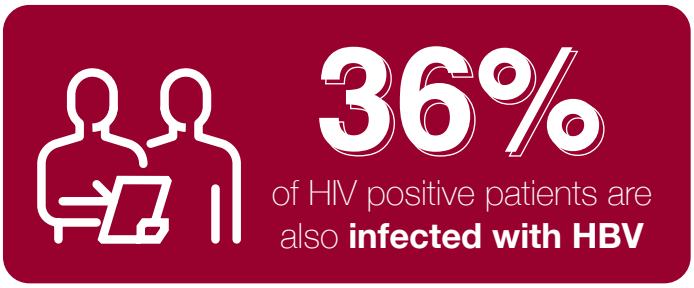
61 years (men)
and **67.9 years (women)**
Life Expectancy

South Africa has experienced great political and economic upheaval in the last few decades, which has inevitably impacted on the provision of healthcare. The additional burden of HIV and then COVID-19 have unsurprisingly contributed to significant gaps in the structure of the healthcare system, resulting in lack of progress in many key areas of health including liver disease. Overall, liver disease appears to take low priority: There are only three health professional councils registered as hepatologists in South Africa, all of whom are based in Groote Schuur Hospital in Cape Town.

There is also a dearth of epidemiological data on liver disease. Compared for example, to the widely accessible data on HIV, the quantification and management of viral hepatitis is greatly under-resourced.[1]

Much like most of southern sub-Saharan Africa, data shows an increasing prevalence of obesity in South Africa, with 13.5% of men and 42% of women obese.[1] However, despite having a greater prevalence of the associated risk factors, studies indicate that Black ethnic groups may have a lower risk of developing metabolic dysfunction-associated fatty liver disease (MAFLD) when compared to white or Hispanic ethnic groups.[2] It is hypothesized that this may be due to predominantly subcutaneous rather than visceral fat distribution; visceral fat is correlated with buildup of hepatic fat, which causes MAFLD.[2] This notion has been corroborated by, a study in South Africa that found that despite having a higher level of total body fat, African women had a lower level of hepatic fat when compared to the Caucasian and Asian Indian study participants.[3] This suggests that, all else equal, the African region would bear a lessened burden of MAFLD.

When examining the prevalence of viral hepatitis in South Africa, it is impossible to ignore the impact of HIV co-infection. South Africa has the highest prevalence of HIV in the world – 7.7 million people.[4] Due to the shared modes of transmission, HIV/HBV and HIV/HCV co-infections are common.[4] Figures from West and Southern sub-Saharan Africa show that approximately 36% of HIV positive patients are also infected with HBV.[5] Co-infection with HBV, however, has been shown to be more fatal than co-infection with HCV.[1]



Attempts to tackle the burden of viral hepatitis have had varying results. In April 1995, the South African government introduced a universal HBV vaccine program for newborns and infants, but has not yet begun to screen for the hepatitis B surface antigen (HBsAg), which indicates current or recent infection, during pregnancy.[6]

Still, the HBsAg prevalence in infants under the age of one, is high: 65.7%.[7] Meanwhile, the national prevalence will continue to grow, as it recently jumped ~20% over a period of 5 years.[7]

Alcohol consumption in South Africa varies between two extremes, with the population having a high prevalence of both binge drinkers and those who abstain from alcohol altogether.[8] Per 100,000 of compensated cirrhosis cases in South Africa, approximately 90,513 were due to alcohol-associated liver disease.[9] To counteract the alcohol-related harm that occurs within the population, political leaders in South Africa have taken drastic action, which included a nationwide prohibition of alcohol that was put in place during the COVID-19 lockdown.

Based on GLOBOCAN data, there were an estimated 37,353 deaths in South Africa due to liver cancer in 2012, with this figure expected to nearly double to 64,525 by 2030.[10] In addition, in recent years liver cancer rates have had a significant decrease among younger Black African men but increased in older Black African men and women.[10] The increased mortality in these age groups may be the consequence of improved overall life expectancy and the rising prevalence of risk factors related to lifestyle behaviors, though further investigation is merited.

For end-stage liver disease, approximately 40-50 liver transplants are carried out per year in South Africa, and outcomes are comparable to international transplant centers. However, transplant services are only available at three transplant centers in the country – one in Johannesburg and two in Cape Town.[11,12] Transplant facilities are in great need of expansion to address the increasing prevalence of liver disease in South Africa.

STIGMA AROUND LIVER DISEASE HOLDING BACK PROGRESS

Professor Wendy Spearman is Head of the Division of Hepatology, Department of Medicine, Faculty of Health Sciences at the University of Cape Town and Head of the Liver and Liver Transplant clinics at Groote Schuur Hospital. She is the Local Chair of the Conference on Liver Disease in Africa (COLDA) and was the WHO Africa appointed lead clinician for the development of the National Guidelines for the Management of Viral Hepatitis in South Africa.

Liver disease is generally not seen as a major health problem in South Africa, especially when compared to infectious diseases such as HIV and TB or respiratory and cardiovascular disease. Policymakers and the general public have struggled to get beyond the idea that liver disease must somehow be related to alcohol abuse, and this has allowed it to be relegated as a public health issue.

This lack of focus has a number of implications. Firstly, there is a lack of awareness about the causes of liver diseases within the general public and even amongst many clinicians. Secondly, there is an ongoing lack of investment into research and collating real world data so there is difficulty in accessing reliable information across all the etiologies of liver disease. Of course, without reliable data it is difficult to ask for, and obtain, appropriate funding for testing, diagnostics and treatment therapies.

For example, hepatitis B is endemic and underestimated. It is probably running at around 4% prevalence in the general population.These "HBV-infected individuals often present with complications of advanced liver disease such as inoperable liver cancer in their early 20s." Although in theory, viral hepatitis is a notifiable disease, the majority of these infections are not notified and in reality many of the deaths due to cirrhosis or liver cancer- particularly if they take place in rural areas which are serviced by overwhelmed primary care clinics - are not correctly recorded.

HBV-infected individuals often present with complications of advanced liver disease such as **inoperable liver cancer in their early 20s.**

Likewise, the majority of liver cancer patients present at the late or end stage of disease, usually after becoming jaundiced or suffering weight loss. Although there are screening and diagnostic facilities in secondary care across all the provinces, for MRI scans, chemotherapy and the latest interventional radiology, the patient must be referred to tertiary care. Unfortunately, tertiary care cannot deal with everyone who needs us, so we have to select depending on whether we can provide them with an appropriate treatment. Even in tertiary care, the reality is that lack of funding is a barrier. For example, we do not have access to the latest first-line combination systemic therapy for liver cancer.

Alcohol-associated liver disease is a big issue in South Africa, although we have no specific data on this. Alcohol plays a big part of life in South Africa, across all socioeconomic strata, and although there are high numbers of the population who don't drink at all, many South Africans are heavy drinkers.

> Of course, without reliable data it is difficult to ask for, and obtain, **appropriate funding for testing, diagnostics and treatment therapies.**
>
> - PROFESSOR WENDY SPEARMAN

STIGMA AROUND LIVER DISEASE HOLDING BACK PROGRESS
continued

There is little data on NAFLD or NASH in South Africa, nor is NAFLD currently incorporated into any non-communicable disease guidelines on diabetes, dyslipidemia and hypertension, even though obesity and diabetes rates are rising fast across the country. Obesity awareness campaigns do not mention fatty liver disease nor is there any education within schools. Even some clinicians are unaware of the link. This lack of awareness is also apparent within the health system - currently if a test shows abnormal liver enzymes, an obese patient will be referred straight to the hepatology department - whereas the correct management should probably be one of weight and metabolic control. Indeed, as the numbers of patients with NAFLD continue to increase, we are going to have to break down the barriers that see different specialists working in isolation and aim for a multi-disciplinary team approach.

We also must understand that social economic factors present real challenges to improving health care. Many South Africans live in rural areas and often have difficulty accessing tertiary healthcare. As a result, people will often only seek help when they become very ill. This is particularly relevant to liver disease which is mostly a silent disease with complications arise.

> **Obesity awareness campaigns do not mention fatty liver disease** nor is there any education within schools. Even some clinicians are unaware of the link.
>
> - PROFESSOR WENDY SPEARMAN

Recently there have been some positive developments in liver disease. For example, palliative care is now available even at primary care level with access to opiates and other forms of palliative support. In 2019, the first National Guidelines for the Management of Viral Hepatitis were published, providing clear pathways for testing and treatment – although many of these recommendations will take some time to implement.

How can we improve? We really do need to get on top of hepatitis B by screening pregnant women for HBsAg, identifying highly viraemic women for third trimester tenofovir prophylaxis and implementing the HBV birth dose vaccines. We also need simplified treatment algorithms with access to molecular diagnostics and imaging to identify those individuals with hepatitis B and C who need upscaling through the health system from those who can be managed in primary or secondary care.

Finally, we urgently need more data across all liver diseases so that we can properly assess the resources needed to tackle the ever-increasing burden of liver disease in South Africa.

ASIA

HEALTH OVERVIEW

Asia, the largest continent in the world, makes up one third of the Earth's surface. It is also the most populous continent but, due to extreme geographical features, many of its 4.7 billion people live in some of the most densely populated cities in the world including Dhaka, Bangladesh, and Manila and Pateros in the Philippines.

Although Asia is generally classified as a developing region and has three of the poorest countries in the world (Afghanistan, Cambodia and Nepal) within its boundaries, it is also home to Japan and Singapore, two of the most economically advanced countries in the world. As well as wide economic disparities and resultant inequalities, Asia has a vastly diverging range of cultural, political and social models including around health.

Asia has a **diverse range** of cultural, political and social models, **including health models.**

Liver disease has long extracted a heavy toll of illness and mortality across Asia with the region experiencing some of the highest global rates of liver cancer and chronic liver disease.[1] In 2019 for example, estimates put the number of deaths from cirrhosis in southeast Asia alone at 442,000 – the highest in the world – and the WHO notes that 72.7% of global deaths due to HCC occur within the Asia Pacific region.[2]

Much of this disease burden has traditionally been ascribed to relatively high rates of viral hepatitis – which is still not fully controlled across many regions of the continent. Though richer countries have introduced successful vaccination and testing programs, many of the poorer countries – often with populations living in densely urbanized cities with poor sanitation and healthcare, or in very remote areas – have failed to reach similar targets. Indeed, between 1990- 2019, Asia had the largest burden of acute viral hepatitis of the continents.[3]

While struggling to control viral hepatitis at pace with the rest of the world, Asia still faces the globalized pattern of growing rates of obesity and an epidemic of T2D, particularly amongst the aging population. Further, research has indicated that Asians may be genetically predisposed to the negative effects of metabolic disorders on liver health.[4]

Studies predict that the prevalence of metabolic dysfunction-associated fatty liver disease (MAFLD) cases across the Asia Pacific region will increase between 2019-2030 by 6% to 20%, and NASH cases will increase by 20% to 35%.[5] Concurrently, cases of decompensated liver cirrhosis are expected to as much as double, and cases of hepatocellular carcinoma are also projected to rise by 65% to 85%.[5] Nonetheless, there have been some positive initiatives over the last few years. Asia was one of the first regions to put together a work group to establish guidelines on metabolic dysfunction-associated fatty liver disease (MAFLD, then known as NAFLD) in 2017, and in 2020 the Asian Pacific Association for the Study of the Liver released clinical practice guidelines for the diagnosis and management of metabolic–associated fatty liver disease.[6]

442,000

estimated deaths in 2019 from cirrhosis in Southeast Asia – the highest in the world

OVERVIEW

CHINA

Population: 1.42 billion

GDP per capita: $12,614 USD (2023)

Life Expectancy: 76 years (men) 81.7 years (women)

Healthcare Spending: 5.38% GDP

Healthcare Funding: China's overarching health reform goal is to establish a universal basic health care system that provides safe, effective, convenient, and affordable services to all citizens. To achieve this, health financing policies have been implemented to ensure that financial resources are effectively allocated, allowing different population groups — especially the most vulnerable and high-risk — to access affordable care. Since the reforms began in 2009, government health expenditure has more than tripled from approximately 71 billion USD in 2009 to approximately 248 billion USD in 2018. As a result, the basic health insurance system now covers over 95% of the population. In 2018, the National Healthcare Security Administration was established to manage all basic health insurance schemes nationwide. These efforts have led to a significant reduction in out-of-pocket expenses for individuals; the percentage of out-of-pocket expenditure as a portion of total health expenditure dropped from 37% in 2009 to 29% in 2018, the lowest point in 20 years.

Sources: US CIA's The World Factbook, World Health Organization, World Bank Group

$12,614
GDP per capita

5.38%
of the GDP is spent on Healthcare

76 (men)
and **81.7 (women)**
Life Expectancy

Liver disease has emerged as a significant public health challenge in China, affecting an estimated 300 million people.[1] As the country has undergone rapid economic transformation, it has also witnessed a rise in liver-related health problems. Conditions such as viral hepatitis, metabolic dysfunction-associated fatty liver disease (MAFLD), and alcohol-associated liver disease (ALD) have surged in recent decades, driven by changing lifestyles, environmental factors, and the prevalence of infectious diseases. Today, China faces one of the largest liver disease burdens in the world, both per capita and in raw numbers.

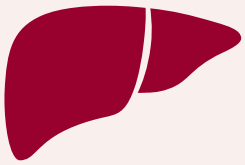
Viral hepatitis remains a dominant health concern in China, particularly hepatitis B virus (HBV) and hepatitis C virus (HCV). An estimated 90 million people live with chronic HBV, contributing to about 300,000 deaths annually.[2] Chronic carriers of HBV in China account for nearly one-third of the global burden.[3] From 2002 to 2021, HBV was responsible for nearly 80% of hepatitis cases in China.[3] The incidence rate has begun to decline thanks to proactive public health initiatives.

China has made substantial progress in combating viral hepatitis through financing HBV treatment and the hepatitis B vaccination program for newborns, which began in 2002.[4,5] These efforts have dramatically reduced HBV transmission among infants and young children.[5] By 2015, nearly 90% of children in China had received the full three-shot HBV vaccination series.[6] As a result of these widespread vaccination efforts, the HBV incidence rate of new cases, which had peaked at 89 per 100,000 people in 2007, declined to 69.25 per 100,000 by 2021.[3] However, the fight is far from over. Many adult populations, especially in rural and economically disadvantaged regions, remain vulnerable to HBV.[3]

For HCV infection, challenges persist. HCV incidence climbed from 1.24 new cases per 100,000 people in 2002 to 15 in 2013.[3] The WHO has that stated roughly 7.6 million people are living with chronic HCV in China.[3,4] In response, China has made strides in controlling and preventing hepatitis C. In 2018, the country launched the Hepatitis C Elimination Action by 2030 in accordance with WHO's HCV elimination campaign and later introduced the National Action Plan for Eliminating Hepatitis C (2021–2030).[7] This plan outlines a main objective and 15 specific targets that cover areas like health education, prevention, free testing, free treatment, and capacity building.[7,8] It emphasizes strategies such as enhancing health education and expanding testing – particularly universal screening for people aged 3-80 years, which has proven to be cost-effective and capable of reducing excess mortality by 62%.[9] The Chinese Medical Association has also developed guidelines to increase awareness among medical professionals and standardize the screening, diagnosis, treatment, and management of hepatitis C, contributing to reduced infection rates through the focus on at-risk groups.[8] Yet, infection rates are higher in certain regions due to socioeconomic and environmental factors.[10]

In recent decades, MAFLD has emerged as a major liver health crisis in China, fueled by the country's rapid economic development and changing lifestyles.[1,11] As industrialization has spread, sedentary lifestyles, extended working hours, lack of physical exercise and sleep, and the adoption of Western diets have increased the prevalence of obesity, which has increased MAFLD.[11] In just one decade, MAFLD nearly doubled from 17% in 2003 to almost 30% of the population in 2022.[1,11] MAFLD has become the leading contributor to chronic liver disease in China. As a result, MAFLD is expected to account for 34% of liver-related deaths by 2030.[11]

The prevalence of **MAFLD nearly doubled** from 17% to 33% in the last decade



MAFLD is not limited to obese individuals. Recent data reveal that 30.5% of the non-obese population in China suffers from this condition, with a notable presence of 21.4% even in lean individuals.[11] The co-existence of MAFLD with metabolic disorders such as type 2 diabetes and hypertension has further complicated the issue. If not controlled, the rise in MAFLD could have far-reaching implications for public health in China, particularly due to its progression to liver cirrhosis and cancer.[12]

China has initiated various policies, campaigns, recommendations, and guidelines to fight obesity in both children and adults over the past decade.[13] In 2022, the Obesity Prevention and Control Section of the Chinese Nutrition Society published "The Expert Consensus on Obesity Prevention and Treatment in China."[14] This consensus aims to guide national efforts in obesity prevention and control, promote widespread societal participation, and contribute to the "Healthy China 2030" development goals which aim to curb obesity by 2030.[13,14]

Also, studies in China have linked exposure to air pollutants like PM1, PM2.5, PM10, and NO_2 to an increased risk of MAFLD, particularly among males, alcohol drinkers, smokers, those with high-fat diets, and individuals with central obesity.[15] 70% of cities fail to meet national air quality standards, so this environmental risk is widespread in China.[16] Recognizing many pollution-related health risks, China pledged at the 2015 Paris Climate Conference to reduce carbon intensity by 60–65% relative to 2005 levels and to peak carbon emissions by 2030 or earlier, emphasizing a shift to clean and low-carbon energy sources that should also benefit liver health.[16]

Alcohol-associated liver disease (ALD) is another growing concern in China, driven by increasingly accessible alcohol leading to rising alcohol consumption in recent decades. This, in turn, has fueled the increase in ALD, which now affects about 4.5% of the population.[1]

The Chinese Society of Hepatology established the Fatty Liver and ALD Study Group in 2001, which has since published several Clinical Practice Guidelines for the Diagnosis and Management of ALD, starting in 2003.[17] Despite these efforts, ALD prevention in China remains challenging when the annual per capita alcohol consumption is expected to reach 8.1L – more than 2L above the global average – by 2025 for people aged 15 and above.[18] The low cost of hard liquor, easy access to alcohol, and widespread alcohol advertising contribute to the difficulty in curbing alcohol consumption and reducing the prevalence of ALD across the country.[17] However, the rate of alcohol consumption in China is rising fast, with 56% of men and 15% of women identified as current drinkers.[1] ALD is a significant contributor to liver cancer and other chronic liver conditions.[19] In fact, in 2005, ALD accounted for nearly a quarter of liver cancer deaths in men.[19]

Alcohol-associated liver disease (ALD) is a growing concern in China driven by rising alcohol consumption in recent decades.

Liver cancer remains a significant concern, with China accounting for over half of the world's liver cancer deaths and approximately 383,203 fatalities annually.[17] 3 in 4 reported cases are men, making it the third most common cancer among males.[12] As of 2024, the survival rate for liver cancer in China remains significantly low, with a five-year survival rate of approximately 12%.[12,20] The survival rates have not seen substantial improvement over the years due to late-stage diagnoses and the high prevalence of risk factors that include chronic HBV and HCV infections, exposure to aflatoxins from contaminated food, cirrhosis, diabetes, and metabolic disorders.[20]

In response, China has worked to extensively expand and develop its liver transplant system.[21] According to the China Liver Transplant Registry (CTLR), China now performs over a third of all liver transplants worldwide.[21] Efforts to increase transparency and efficiency in organ donation have led to the establishment of the China Organ Transplant Response System.[21] From 2015 to 2020, 24,423 adult patients underwent liver transplantation in China.[22] After more than 20 years of progress, liver transplants in China now have a 90% survival rate one year after the procedure and a 70% survival rate after three years.[17]

Living donor liver transplantation has also expanded, offering an alternative to address the donor shortage. Yet, traditional beliefs about maintaining an intact body after death impact the availability of living donors.[21] While deceased donors account for a large proportion of donations, options to increase the donor pool are limited due to extremely narrow criteria for brain death.[21,22]

Liver health is a growing concern in China because of diseases like hepatitis and fatty liver disease. Education, vaccinations, and promoting healthy lifestyles are key to fighting these illnesses. The government has shown commitment by adding hepatitis prevention to national health plans and covering treatments with health insurance since 2020. Ongoing efforts in public education, awareness campaigns, and affordable treatments are essential to improve liver health outcomes in China.

More than half of the world's deaths due to liver cancer occur in China.

OVERVIEW

INDIA

India is the 7th largest country in the world by geographic size. Split between 29 states and seven union territories, India is second only to China as one of the most populous countries in the world.

Population: 1.37 billion (2020)

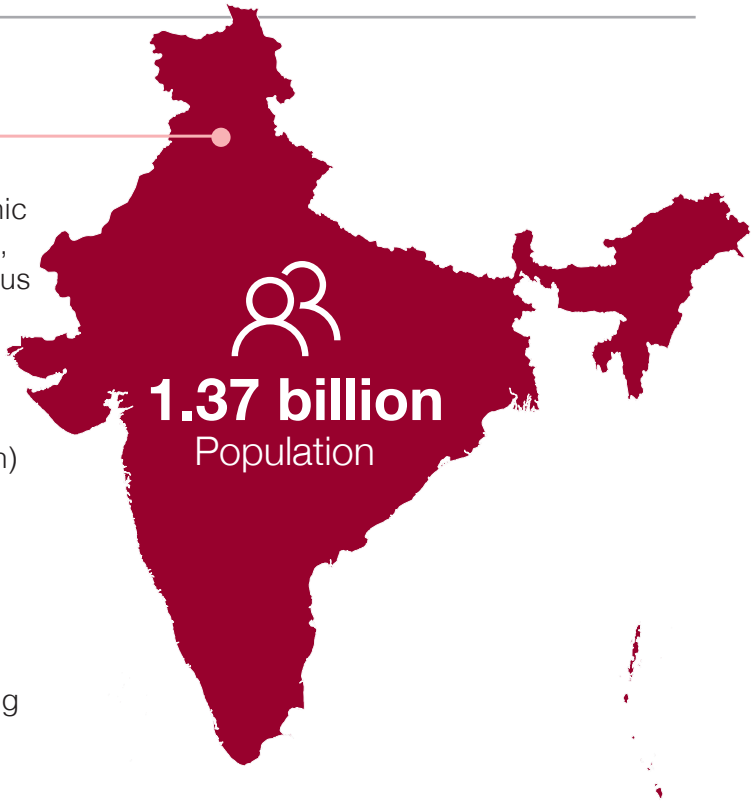
GDP per Capita: $2,485 USD

Life Expectancy: 66.3 years (men), 69.4 years (women)

Healthcare Spending: As of 2019, India has a GDP of $2.83 trillion USD, and government spending on healthcare is approximately 1.23% of GDP (2019). Including out-of-pocket costs paid by patients, the country's total healthcare GDP equates to 3.6%

Healthcare Funding: About 20% of healthcare spending in India falls under the category of public funding, with the remainder being privately based. Due to the rapid rise of urbanization and a cultural lifestyle shift, almost 50 percent of this healthcare spending is now directed at in-patient beds to cope with the rising prevalence of lifestyle diseases. Unlike most other countries, demand for private healthcare in India is primarily driven by poorer patients, who are forced to pay out-of-pocket due to the shortcomings of public healthcare facilities.
To mitigate this, in 2018 the Indian government introduced Ayushman Bharat, a national health protection plan, which allocates $7,200 in annual coverage per patient for the most vulnerable and created Health and Wellness Centers to increase primary care access.

Sources: World Bank, Understanding India's Healthcare System



$2,485.40
GDP per capita

3.6%
of the GDP is spent on Healthcare

70.19 years
Life Expectancy

Out of the 2 million global liver disease deaths in 2015, liver disease mortality in India made up approximately 18.3%.[1] Indeed, mortality due to chronic liver disease has been steadily increasing in India since 1980, while with other large Asian countries, such as China, liver disease mortality has either remained stationary or been on downward trajectory.[1] Liver disease is rapidly being recognised as a major public health issue for India.

As is the case with most developing nations, there is a limited body of epidemiological data available on liver disease in India. This can mainly be attributed to a lack of electronic healthcare databases, poor uniformity of reporting and low levels of diagnostic precision and phenotyping.[1] Still, the increasing impact of liver disease on India's economy and healthcare system is evident.

A cultural, lifestyle shift is a driving factor in this increasing burden of liver disease. Western diets and sedentary habits are becoming the norm in India, and once-prominent taboos about alcohol consumption have begun to ease.[2] As these lifestyle patterns shift, NAFLD/NASH and alcohol-associated liver disease are now among the main contributors to cirrhosis and liver-cancer related mortality in India, in addition to hepatitis B and C.[3]

As is the case worldwide, the increasing prevalence of obesity, hypertension and T2D has resulted in a significant increase in the prevalence of NAFLD in India. Current estimates state that approximately 16-32% of the country's population have NAFLD, with around 31% of these patients being diagnosed with NASH.[4] Data also suggests that this condition is highly prevalent within younger population, with one study estimating that over one in three children have NAFLD in India – much higher than the global estimates.[5]

DID YOU KNOW?

In 2015, there were 2 million global liver disease deaths. **India made up 18.3%.**

Interestingly, an anomaly has been identified within Asian populations when analyzing the prevalence of NAFLD, referred to as the 'Asian Paradox.' NAFLD patients with Asian ethnicity, including in South Asia specifically, appear to have lower BMI and obesity rates when compared to patients from the west, making them more susceptible to developing NAFLD and other BMI related chronic conditions.[4]

In June 2022 as part of International NASH day, the Indian National Association for the Study of the Liver (INASL) and Indian Consortium on NAFLD (ICON-D) announced the creation of an action plan for the prevention and control of NAFLD, in partnership with Global Liver Institute. Although the Action Plan is not yet complete, the first survey was launched in August 2022 to gather data for the second national action plan in the world.

Viral hepatitis is a major healthcare threat for India; it can be compared, in terms of risk level, to the "big three" communicable diseases – tuberculosis, malaria and HIV/AIDS. According to the WHO, there are over 40 million carriers of HBV in India, with over 115,000 deaths per year associated with the virus.[6] Despite the fact that hepatitis B vaccinations have been part of India's Universal Immunization Program for over a decade, only half of children are effectively immunized against the virus.[7]

Hepatitis B vaccinations have been part of India's Universal Immunization Program.

Only half of the children are effectively immunized against the virus.

Hepatitis C is also common in India, with many of the major risk factors for the virus being highly prevalent throughout the country, including hazardous medical practices, such as unsafe injections, and intravenous drug use. Consequently, 12-18 million people are infected with the virus, with an estimated prevalence of 0.1-1.5%.[8] A high concentration of HCV has also been observed specifically in the state of Punjab, known as the 'hepatitis C belt.'[8] An initiative has been launched by the Punjabi state government to combat this prevalence; however, similar efforts must also come from HCV stakeholders, such as healthcare professionals, drug companies and non-government organizations, if HCV is to be effectively controlled in this region.

Hepatitis E is still the most common cause of acute liver failure in India.[3] Indeed, a study in north western India found that 49.7% of acute sporadic hepatitis cases were associated with HEV infection.[9] Unique to India, acute liver failure due to HEV infection is associated with a very high mortality in pregnant women, 20-30% in contrast to 0.2-1% in the general population.[9]

In response to the high prevalence of viral hepatitis, the Indian government launched an initiative in 2018 called the National Viral Hepatitis Control Program (NVHCP).[10] The NVHCP aims to strengthen diagnostics and management services, and develop treatment protocols for the management of viral hepatitis, with the aim of eliminating viral hepatitis in India by 2030.

According to the WHO organization there are

40 MILLION

carriers of HBV in India.

As is the case globally, alcohol consumption is the most important and common cause of liver mortality in India, accounting for 34.3% of all cirrhosis cases and 20% of liver disease patients.[10] Alcohol-associated liver disease has severely increased in prevalence over the recent years in India, mainly due to the increased availability and consumption of alcohol from younger ages.[11]

Estimated incidence rates for liver cancer range from 0.7 to 7.5 per 100,000 and 0.2 to 2.2 per 100,000 for men and women, respectively.[12] The readily available guidelines on liver disease management from Europe, Asia and the USA are often inapplicable for the Indian population due to the expense of the proposed treatments. To address this, a task force set up by INASL was developed. They presented a consensus guide for diagnosis and management of liver cancer in 2014, tailored to the issues and resources of India.

India has also made some great strides in the last decade with its liver transplantation program. The Indian Liver Transplant Registry was recently formed, with the aim of providing more transparent and prospective data on liver transplantation. It is, however, still worth noting that less than 2000 liver transplants are carried out each year in India, in a country of 1.3 billion people.[3]

AN URGENT CALL TO ACTION FOR GOVERNMENT AND CLINICIANS
continued

Retired hepatologist Dr. Shivaram. P. Singh is President of the South Asian Association for Study of the Liver and of the Indian National Association for Study of the Liver.

The data tell the story of liver diseases in India today. While the incidence of alcohol-associated liver disease is rising exponentially, obesity rates and the numbers of people with T2D are climbing steadily and, with them, the rates of NAFLD and NASH. Meanwhile, millions of people in India are still infected with hepatitis B, with only around half of babies currently receiving the infant vaccination. I have been fighting to get the government to prioritize liver health for the last 20 years but, if nothing changes soon, liver diseases have the potential to become a real threat to public health across the country within the next decade.

Across India, public awareness of liver disease is patchy at best and non-existent at worst. For example, despite all the data we have on HBV and the resources given to treating it, around two in three Indians still have no idea what hepatitis B is. We need a widespread public awareness campaign so that people can understand how to protect themselves together with an effective testing program.

When it comes to alcohol, it could be argued that the government is more interested in raising taxes rather than reducing rates of alcohol consumption. To date, there have been no national government campaigns warning of the risk of alcohol abuse, and, although alcohol is banned in some states, there is little attempt to prevent the manufacture and sale of illicit and highly dangerous non-regulated alcohol.

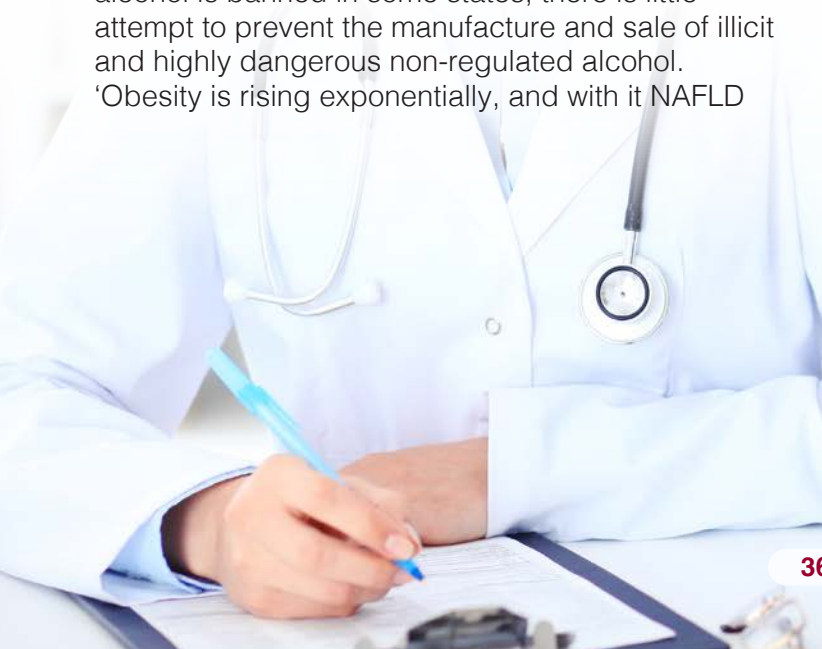
‘Obesity is rising exponentially, and with it NAFLD and NASH. This is of great concern to us all, given that south Asians are predisposed towards NAFLD, either genetically or through some other factor such as a unique gut microbiome. It is heartening that the government appears to have recognized this risk and have included NAFLD in a national action prevention program, although we are yet to see what this will mean in practice.

> **Liver disease is almost always preventable** and awareness is key.
>
> - PROFESSOR DR. SHIVARAM. P. SINGH

Meanwhile, together with my colleagues at the INASL, we are in the process of setting up an educational program on NAFLD for schools and colleges to raise awareness in young people. To do that, we have joined forces with The Rotary Club who are providing us with financial and other support.

Health inequality is a real challenge to receiving good quality healthcare. Although all states provide free medicines, whether you receive free diagnostic or other treatment depends on the state in which you live. This inequality especially affects liver diseases, which in the later stages will often require complex surgery or other treatments such as liver transplant. If you live in a state which requires you to pay for these treatments, and you are unable to do so, you either travel to another state and hope you can get admitted to a hospital there or, sadly, you die.

Liver disease is almost always preventable, and awareness is the key to this. We really need a concerted and joined-up effort by our government and professional medical bodies to ensure that the population is properly educated about how they can protect themselves and their families against viral hepatitis, alcoholic liver disease, NAFLD and other liver conditions. We need to do it now.



OVERVIEW

JAPAN

Population: 124.3 Million (2023)

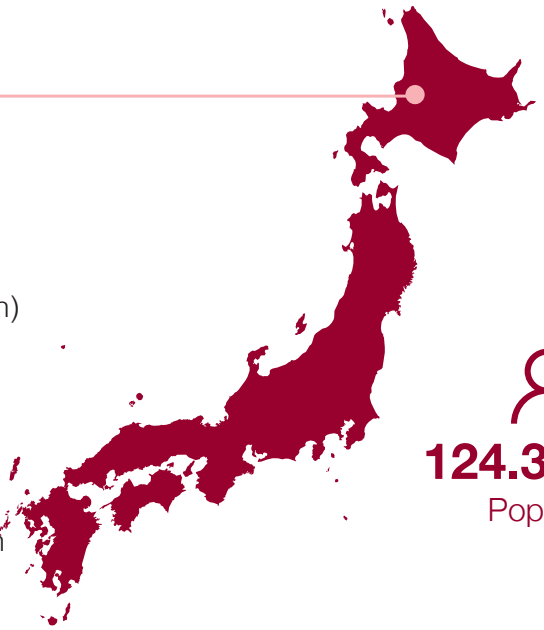
GDP per capita: $33,834 (2023)

Life Expectancy: 82.3 years (men) and 88.2 years (women)

Healthcare Spending: 10.9% of GDP

Healthcare Funding: Japan's healthcare system is predominantly funded by public sources, with over 85% of health spending coming from public funds. Private out-of-pocket spending accounts for approximately 12% of health spending.

Sources: World Bank Open Data, OECD, Worldometer, Trading Economics, The Commonwealth Fund



124.3 million
Population

$33,834
GDP per capita

10.9%
of the GDP is spent on Healthcare

82.3 (men) and **88.2 (women)**
Life Expectancy

Liver disease has become a prevalent health issue in Japan. Some of the main causes of liver disease include hepatitis B, hepatitis C, alcohol misuse, and metabolic dysfunction-associated fatty liver disease (MAFLD), which affects over 10 million people in Japan, with men at greater risk than women.[1] Viral hepatitis constitutes the leading cause of liver cancer in Japan, including hepatitis C virus (HCV) infection (more than half of cases) followed by hepatitis B virus (HBV).[2] However, the etiology of liver disease in Japan is undergoing a significant transition. Proactive prevention, screening, and treatment efforts have led to a decline in viral hepatitis, while alcohol-related liver disease (ALD) and metabolic liver diseases such as MAFLD are increasing.[3] This shift reflects broader changes in liver health in Japan in recent years, highlighting the need for continued public health focus on these emerging concerns.

Alcohol consumption in Japan is a significant public health concern. In Japan, there is a cultural tradition of social drinking integral to work and social life, often facilitated by the custom of *nomikai*, parties specifically meant for drinking. There is often social pressure that pushes many to attend and drink heavily.[4] As a result, heavy alcohol consumption is the second leading cause of liver diseases such as ALD and cirrhosis in Japan.[5] The Japanese government has recognized this issue and thus implemented public health campaigns to reduce excessive drinking and promoting liver health awareness.[5] Currently, the *nomikai* culture is gradually shifting from mandatory to optional outings to socialize with friends and colleagues.[4] The COVID-19 pandemic further complicated the situation, with a 21% rise in hospital admissions for alcohol-associated liver disease and alcohol-associated cirrhosis in the first year of the pandemic.[6] Though the precise etiology of this change is unclear, liver health nonetheless declined during that period. These trends highlight the lasting impact of the pandemic on public health, beyond the direct effects of the virus.

The rising prevalence of MAFLD in Japan is a public health issue that demands attention. This condition affects 15.2% of non-obese individuals and an alarming 68.5% of obese individuals.[7] Those who have a poor diet or high alcohol consumption, frequently smoke, and have low levels of physical activity, especially in urban areas, are at a higher risk. 20% of those with fatty liver disease were considered lean – and those with lean fatty liver disease were older on average and faced a higher mortality rate.[8] This is highly concerning, since Japan has a rapidly aging population of which the elderly comprise 1 out of 4 people.[9] With these factors at play, half of Japan's population is expected to have fatty liver disease by 2040.[8] Although Japan has a lower obesity rate than most Western countries, MAFLD is steadily increasing and measures need to be put into place to combat the growing issue.

The Japanese population, like many other Asian populations, is at risk of these conditions at lower BMI levels compared to Europeans. This heightened risk is due to greater amounts of visceral and subcutaneous fat and an earlier onset of insulin resistance.[2] These complexities showcase the need for targeted public health strategies to address fatty liver disease and associated health conditions separate from interventions and discussions solely about weight.

Heavy alcohol consumption is the **second leading cause of liver diseases** such as ALD and cirrhosis in Japan

20%

of those with fatty liver disease were **considered lean**

Japan has the tenth highest tobacco use in the world.[10] Liver disease has directly claimed at least 1.7% of the many lives lost by smoking, including secondhand smoke.[11] Researchers have found a strong link between smoking and increased relative risk of liver disease, in addition to well-known links to lung and heart disease.[1] Therefore, the government has enacted several laws to decrease the amount of smoking, such as higher taxes on tobacco and banning indoor smoking.[10] As a result, the amount of smokers in Japan has decreased by nearly half over the last decade.[1,12]

While the link between smoking and liver disease underscores the importance of public health interventions, Japan also faces challenges with rare liver conditions that require specialized attention and care. For example, rare and varied symptoms for conditions present in Japan like Alagille syndrome – a rare, congenital disease that affects the heart and liver– can make the diseases challenging to diagnose.[13] Thus, genetic testing is needed for proper identification and management of the disease and others like it.

Japan has the **tenth highest** tobacco use in the world.

Since the 1980s, Japan has consistently sought prevention methods to address viral hepatitis, the main upstream risk factor for liver cancer. First, gamma shot programs were introduced to prevent mothers with hepatitis B from transmitting it to their children.[14] This was followed by an intense effort to screen blood and educate the people, which worked to reduce the infections from blood, razors, and tattoos.[14] To further reduce rates, Japan started testing people over 40 for hepatitis B and C between 2002 and 2006.[15] Because of these efforts, the number of people with hepatitis in Japan decreased by 2.20 million people from 2000 to 2011.[15] This led to enacting the Basic Act of Hepatitis Control which set a nationwide guideline on how to prevent, control, and promote hepatitis safety.[15]

Two years later, Japan enacted the Basic Guidelines for Promotion of Control Measures, which further emphasized the need to spread awareness and accurate information on viral hepatitis.[15,16] This policy framework focused on promoting research and information, ensuring equal access to testing and treatment despite location, and safeguarding the rights of hepatitis patients.[16] As a result, Japan's efforts to raise awareness included designating July 28 as Hepatitis Day and launching a national campaign to improve understanding of hepatitis, promote prevention and treatment, and encourage screenings in partnership with governments, medical organizations, and employers.[16] The Ministry of Health, Labour and Welfare launched the "Shitte kan-en" ("Let's Learn About Hepatitis") subsidy program in 2011, using popular celebrities to raise awareness. By 2013, it had become a national campaign promoting accurate hepatitis information and testing through celebrity visits, events, and workplace initiatives.[16] Awareness efforts shifted after the COVID-19 pandemic to focus on youth engagement, and this content has garnered millions of views.[16] The program's impact is reviewed every five years, and Japan remains committed to eradicating hepatitis through ongoing prevention and treatment initiatives.[16]

While smoking, drinking, overeating, and lack of exercise are the most important risk factors for the development of cancer of all types, HCV is the leading cause of liver cancer in Japan, followed by HBV.[1,14] To catch liver cancer early, Japan has set up nationwide screening programs that regularly check high-risk individuals with advanced imaging tools and special blood tests.[17] Treatment is then executed through a mix of approaches – including surgery to remove tumors (radiofrequency ablation), local treatments that destroy cancer cells (transarterial chemoembolization), procedures that block the tumor's blood supply, and new medicines like lenvatinib, sorafenib, that help the immune system fight cancer or target cancer cells directly.[17] The combination of surveillance programs and advanced treatment options have significantly improved survival rates for liver cancer patients at all stages, with a five-year survival rate of 58% – the highest in the world.[17]

Japan has become proficient in liver transplantation, particularly with living donor liver transplants (LDLT). Acute liver failure patients who undergo LDLT show high survival rates.[18] The country has successfully implemented a system for LDLT with over 7,837 transplants since 2014, projected to increase each year.[19,20]

The combination of surveillance programs and advanced treatment options have significantly improved survival rates for liver cancer patients at all stages, with a

five-year survival rate of 58%

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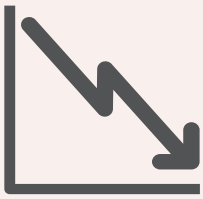


The number of people with hepatitis in Japan **decreased** by

2.20 million

people from 2000 to 2011

However, many patients who suffered from liver cirrhosis or alcoholic liver diseases and received transplants have experienced substance relapse after receiving surgery.[1,20] Compared to those who received mental health care, those who did not address their mental health were more than likely to relapse.[1,20] Therefore, additional mental health services are needed to address mental health discrepancies that could lead to further liver damage.

Japan has made significant progress in liver health through advances in transplantation, effective surveillance, early detection, and proactive disease management. While there are successes, there is also a need for more information and focus on alcohol consumption and specific prevention programs to continue improving liver health outcomes.

SUCCESS IN JAPANESE LIVER CANCER CARE THROUGH COOPERATION AND COMPREHENSIVE SURVEILLANCE

Masatoshi Kudo, MD, PhD, is a professor and chairman of the Department of Gastroenterology and Hepatology at Kindai University in Osaka, Japan. A research leader on the diagnosis and treatment of HCC, Dr. Kudo has published prolifically, contributed to clinical guidelines in Japan for HCC, and has served on leadership teams for several medical societies including the Liver Cancer Study Group of Japan, the Japan Society of Hepatology, the International Liver Cancer Association, and more.

The current topic in Japan's hepatology is liver cancer – and nationally, that still is the biggest problem. Japan has the highest five-year survival rate for liver cancer in the world. Surveillance and early detection are very key. For this success, the Japan Society of Hepatology (JSH) patient advocacy groups, and the government (especially the Ministry of Health, Labour and Welfare) work well together to eliminate hepatitis and liver cancer.

Hepatitis testing is available free of charge at any clinic, hospital, or health center. JSH asked for this widespread access, and the government responded. The national health insurance covers everything for DAA treatment for patients with HCV as well as nucleoside analogs to treat HBV. Additionally, HBV infection is on the decline because of universal infant vaccination.

Japan has had nationwide surveillance for liver cancer since the 1980s. In 1999, JSH released a white paper that discussed "How to Eliminate Viral Hepatitis and Liver Cancer," which has been our guide. From then on, we launched a nationwide campaign to eradicate HCC, and each year, JSH appoints at least one person for each of the 47 prefectures to give a lecture or hold a meeting to educate ordinary people who are at high risk or super high risk for liver cancer.

After years of public lectures about liver health, awareness of the liver is very high. The public will voluntarily ask their doctors for a referral to the hepatologist for ultrasound, because the people think that liver disease is very important.

Japan regularly screens for
3 highly effective liver cancer biomarkers
unavailable elsewhere:

Globally, only AFP is measured, but the other markers, PIVKA-II and AFL-L3 are also important.

Similarly, almost all physicians, especially those in internal medicine, acknowledge the risk of liver cancer. If they find a patient with viral hepatitis, they know to refer to a hepatologist or perform an ultrasound and check for tumor markers themselves. In the past ten years, not only the private practitioners but also ordinary people have known about liver cancer. Patients can sue if a tumor is found more than 10 cm, unresectable, without any surveillance. The doctor should have known to check for liver cancer.

We recommend checking patients with HBV, HCV, or cirrhosis at least every six months with ultrasound and the measurement of three tumor markers. Globally, only AFP is measured, but the other markers, PIVKA-II and AFL-L3 are also important. Japan developed these two markers 20 years ago, and they have been very effective in screening for liver cancer. Other countries have not developed the process to measure these routinely, and these tests are not covered by insurance elsewhere. I have written several papers that PIVKA-II and AFP-L3 should be measured globally.

In 2009, JSH released clinical practice guidelines defining high-risk and super high-risk patients. Every six months, high-risk patients should be surveyed with ultrasound, and super high-risk patients should receive CT or MRI scans once or twice a year. For this group, cirrhotic or viral hepatitis patients, sometimes the ultrasound cannot detect a small tumor. MRI, especially the EOB-MRI technology, can detect less than 1cm HCC.

The Japanese government is generous and wants to help viral hepatitis patients, and listens to the medical societies and patient groups, so we can maintain this very thorough surveillance system.

OVERVIEW

PHILIPPINES

Population: 111 million (2021)

GDP per Capita: $3,726 USD

Life Expectancy: 67.4 (men) and 75.6 (women)

Healthcare Spending: 4.08% of GDP (2019)

Healthcare Funding: In general, there are four main sources of financing:
(1) national and local government,
(2) insurance (government and private),
(3) user fees/out of pocket and (4) donors.

As of 2007, 57% is paid out-of-pocket, 12% is paid for by the national government, 11% is paid for by the local government, 9% is paid for by social health insurance and 11% is paid for by other sources.

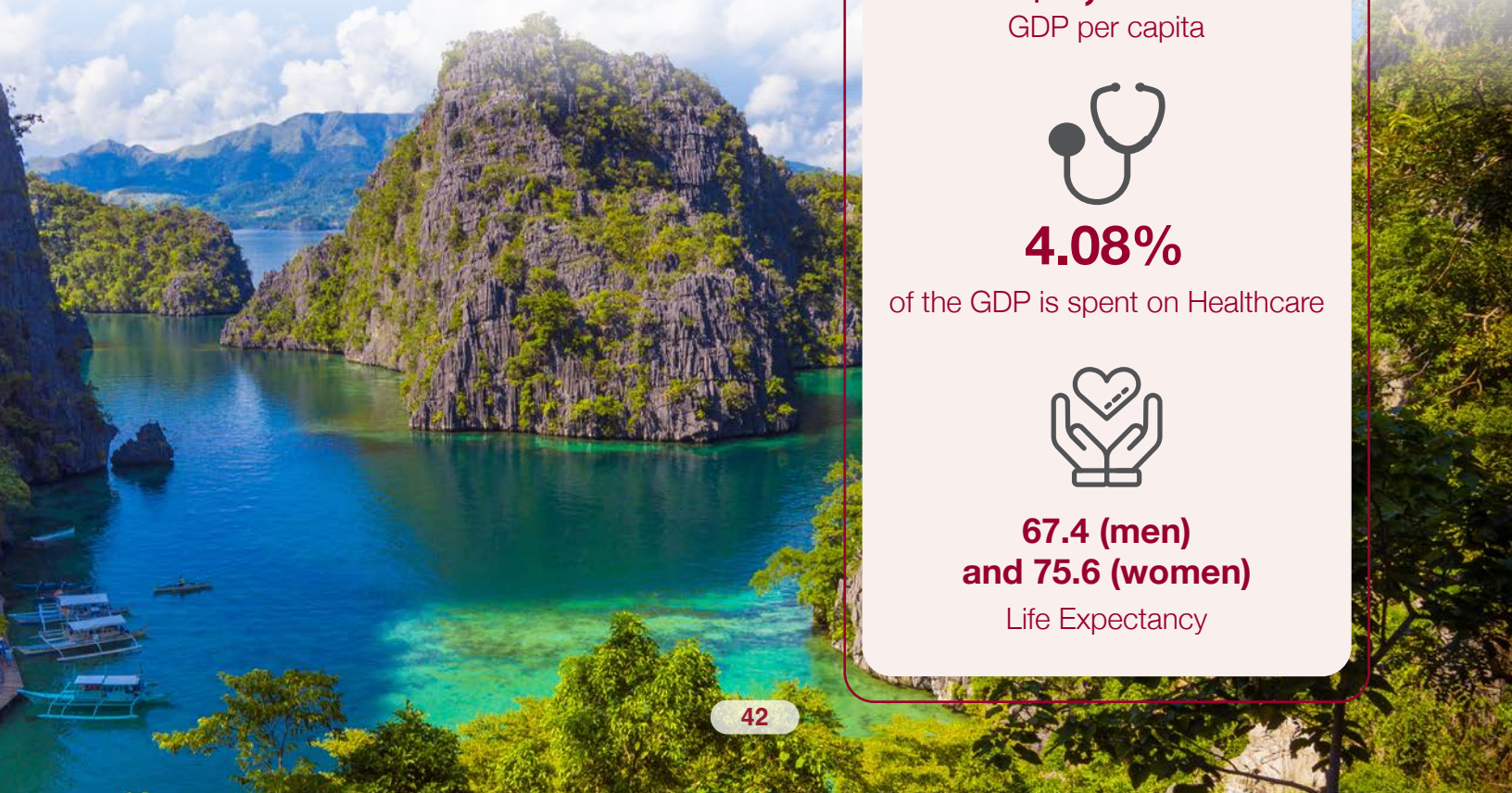
The 'Sin Tax' introduced in 2012, raised the State income from duty on alcohol and tobacco directly to fund healthcare, tripling the Department of Health budget within a year. Since then, two further tax bills have cemented this as part of the national health funding program.

Sources: WorldData.Info, Statista, Data.WorldBank, Republic of the Philippines – Department of Health

$3,726
GDP per capita

4.08%
of the GDP is spent on Healthcare

67.4 (men) and 75.6 (women)
Life Expectancy



Liver disease is a significant healthcare burden in the Philippines, with approximately 16,500 deaths per year due to liver disease complications, accounting for 2.65% of the country's total deaths in 2017.[1] Chronic hepatitis infection, metabolic dysfunction-associated fatty liver disease (MAFLD) and alcohol-associated liver disease are the country's most common causes of liver disease.[1] Furthermore, liver cancer is the fourth most common cause of cancer in the Philippines, leading to approximately 9,950 deaths in 2020.[2]

Hepatitis B is a major concern, with the WHO considering the Philippines to be hyperendemic for the virus. It is the country's leading cause of hepatocellular carcinoma (HCC) and has a prevalence of approximately 16.7% within the general population, equating to 7.3 million persons infected.[3] Whereas with other countries in the Asia Pacific region in which the prevalence rate for hepatitis B has steadily decreased in the last few decades, mainly due to effective vaccination programs, the hyperendemic status of the Philippines has persisted.[3] As is the case in other countries, studies have also found that a lower annual income is a significant determinant of HBV infection in the Philippines, reducing the patients access to quality healthcare and increasing the risk of missed vaccinations.[3] The limitations in healthcare resources available for treatment underscore the necessity for prevention to limit infection. Although a universal immunization program was introduced for infants for hepatitis B in 1992, it wasn't fully implemented until 2007 due to significant lack of funding. This greatly delayed its preventative effect, which may be a key reason for why the Philippines is so far behind many other nations in relation to hepatitis B eradication.[3]

Chronic hepatitis infection, NAFLD and alcohol are **common causes of liver disease.**

Since 1988

59
Liver Transplants

56%
Overall Survival Rate

Following global trends, obesity is a growing healthcare issue in the Philippines. The number of Filipinos that are overweight or obese is approximately 27 million, with these numbers nearly doubling in the past two decades for both adults and adolescents.[4] Consequently, MAFLD risk is also increasing, though specific prevalence data is scarce. In one study published in 2008, patients admitted to a Philippine general hospital were tested for MAFLD and analyzed for common characteristics. Out of 12% of admitted patients in the study had MAFLD, with 29% being male and 71% being female and a mean age of 42.2 – a lower age when compared to previous studies.[5] A more recent study investigating Filipino MAFLD patients found that 11.9% of them were classed with "lean MAFLD," providing an insight into this sub-condition found more frequently in Asian populations.[6,7]

Excessive alcohol use is common in the Philippines: A 2018 WHO study noted that around 60% of adult Filipinos were binge drinking regularly.[8] In that year, 6 deaths per 100,000 were caused by alcohol-associated cirrhosis.[9]

Since 1988, there have only been 59 liver transplants carried out in the Philippines, with an overall survival rate of 56%; this is below the standard rate for transplant centers worldwide.[10] Liver transplantation is expensive in the Philippines – at least three times more than in India, meaning many patients require travel abroad for the life-saving procedures.[11] To address this issue, a new center has been funded by the Filipino government – the NKTI Liver Center. This facility will be equipped to carry out surveillance on liver disease patients, as well as provide treatments, preventative measures, and a state-of-the-art liver transplant service.[12]

AN URGENT NEED FOR DATA, CLINICAL STUDIES AND AWARENESS OF LIVER HEALTH CHALLENGES

Dr. Diana Payawal is a professor at Fatima University Medical Center. She is the former President of the Asian Pacific Association for the Study of Liver and the current President of the Philippines College of Physicians.

Similar to many other countries in southeast Asia, we are facing an epidemic of obesity which will almost inevitably result in an increase in the rates of NAFLD and NASH and eventually a burden of end stage liver disease.

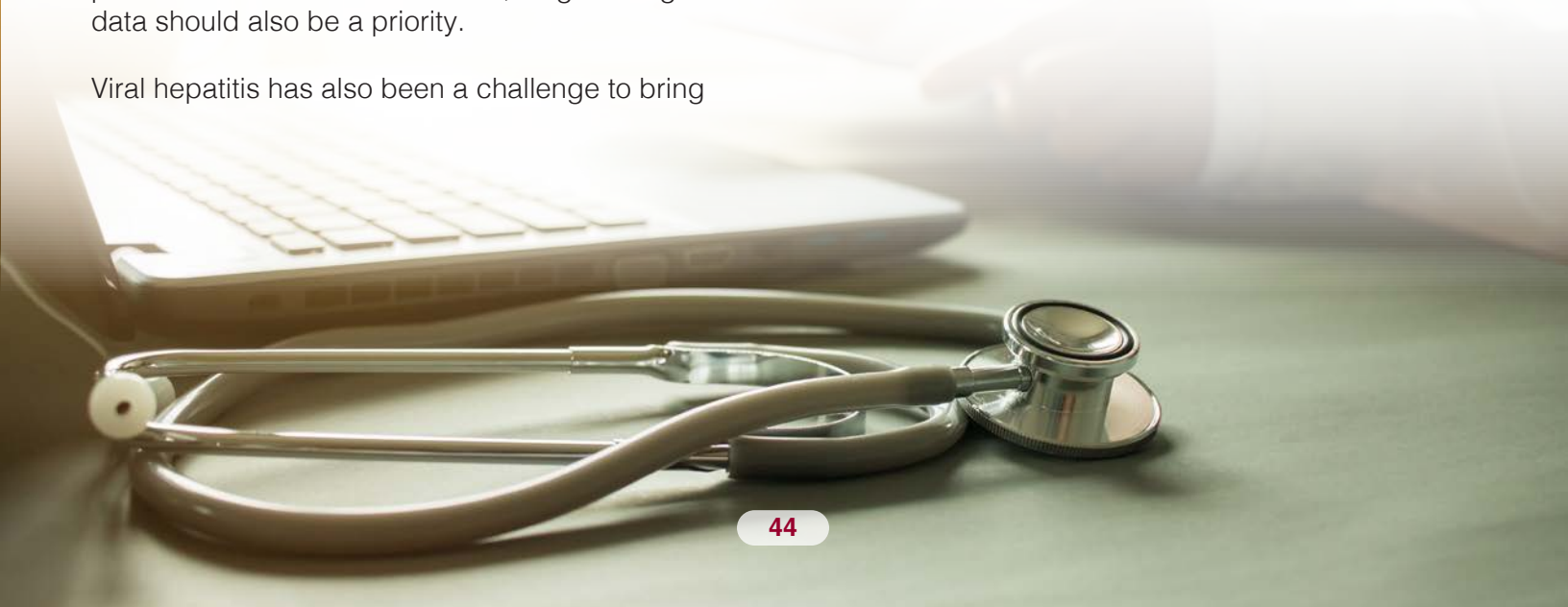
So far, the government has run awareness campaigns on healthy eating, and there are many weight-loss programs available, particularly on the internet. **However, the link between obesity and liver health has not been highlighted and most of the public have no awareness that it is a health issue.** Even some doctors will concentrate more on diabetes and cardiovascular disease rather than focus on the risk to the liver when they see an obese patient.

We need both national and clinical strategies to deal with obesity, NAFLD and NASH including awareness campaigns along with clinical treatment guidelines. A multi-disciplinary approach within hospitals and clinics would also help, for example, endocrinologists working alongside gastroenterologists and dieticians. This is not something that hepatologists can manage on their own. Finally, in common with many developing countries, we have very little information on the prevalence of NASH and NAFLD, so gathering this data should also be a priority.

Viral hepatitis has also been a challenge to bring under control, and this, along with our high rate of alcohol consumption, is one reason why we have relatively high rates of liver cancer. However, over the last few years, the government has made efforts to focus on reducing the rates of viral hepatitis with the Department of Health recently producing comprehensive guidelines on the management of hepatitis B, C and hepatocellular cancer.

> **We are facing an epidemic of obesity** which will almost inevitably result in an increase in the rates of NAFLD and NASH and eventually a burden of end stage liver disease.
>
> - DR. DIANA PAYAWAL

Although the introduction of the ‘Sin Tax’ in 2012 made some impact on the sales of alcohol and tobacco, our rates of alcohol– induced liver cirrhosis are still far too high. As well as focussing on increasing taxes, we need an effective and sustained awareness campaign to try to reduce our national dependence on alcohol.



SINGAPORE

Population: 5.45 million (2021)

GDP per Capita: $84,734 USD

Life Expectancy: 80.7 (men) and 85.2 (women)

Healthcare Spending: 5.9% GDP

Healthcare Funding: Singapore has achieved universal health coverage through a combination of financing sources, including the public statutory insurance system, MediShield Life, which covers large bills from hospital care and certain outpatient treatments, private health insurance and insurance through employers, government subsidies, and a compulsory medical savings account called MediSave, which can help with inpatient care and certain outpatient services. Patients pay premiums, deductibles, co-insurance, and any costs above the claim limit. A safety net called MediFund helps those who cannot cover their out-of-pocket expenses.

Sources: The World Bank, World Health Rankings, International Trade Administration, The Commonwealth Fund

$84,734
GDP per capita

5.9%
of the GDP is spent on Healthcare

81.5 (men) and **83.2 (women)**
Life Expectancy

Liver disease accounts for approximately 4% of deaths each year in Singapore, and liver cancer is the 5th most common cancer in men in the country.[1, 2] While hepatitis B continues to cause a significant portion of end-stage liver disease, rising rates of obesity and fatty liver disease are beginning to change the etiology landscape. Coherent efforts for screening for liver disease are necessary in Singapore to prevent large, ongoing challenges to liver health in the country.

Like many neighboring countries in southeast Asia, Singapore's population faces endemic viral hepatitis. About 1 in 25 people in Singapore has chronic hepatitis B infection.[3] This is considered an intermediate prevalence.[4] Hepatitis A, C, and E are also endemic, though reported in small numbers in the country (single digit cases, for instance, of HCV).[5] Treatment is available for hepatitis B and C in the country, while its prevention efforts for HBV are also effective for HDV.[5] Chronic hepatitis B is the leading cause of liver cirrhosis in Singapore – with approximately 20-40% of patients developing the condition if it is not treated.[6]

As part of the Singapore National Childhood Immunisation Schedule, all children should complete the hepatitis B vaccination series beginning at birth and finishing at around 6 months of age.[7] Singapore is one of the first countries to implement such a program. Adults who were not previously vaccinated are also recommended to receive the full series.[7] This immunization scheme began in 1985.

DID YOU KNOW?

About **1 in 25 people** in Singapore has chronic hepatitis B infection.

Liver disease accounts for approximately

4% OF DEATHS

each year in Singapore

The obesity rate has risen over the past several decades and is now 8.9% for working-age adult Singaporeans, with a rate of 6.9% for older adults (above 60); this is driving increasing rates of fatty liver disease in the country.[8, 9] Based on trends in diabetes and obesity, cases of metabolic dysfunction-associated fatty liver disease (MAFLD) are expected to increase by 20% in the nation by 2030 to affect 28.7% of the population – placing a sizeable potential burden on the nation's healthcare system.[9] This also affects liver disease later in the progression: NASH cases are expected to increase by 35% during that same time, and fatty liver disease-cases of compensated cirrhosis are expected to double.[9]

A significant portion of MAFLD in the Singaporean population includes non-obese individuals.[10] At the same time, cost analysis in Singapore has found that transient elastography and FIB-4 have been identified as cost-effective MAFLD screening strategies in the diabetic population, so long as the annual cost of treatment remains under control.[11] An estimated 9.8% of liver transplants in Singapore are related to MAFLD.[9] Given all this information about the current state and trends in fatty liver disease, increased public awareness and education about the disease is becoming necessary.

Liver cancer is the fourth most common cancer in men in Singapore and **the third most deadly.**

Alcohol also poses a small but nontrivial challenge to liver health in Singapore. An average of two liters of pure alcohol per person are consumed each year in Singapore (though this number is about three times higher in men than in women) – among the lowest in Asia, in part due to heavy taxation.[12] However, health officials have noted a rise in unhealthy drinking habits in the younger population – especially with the rise of buffet-style drinking.[12] Though available data is limited on the liver impact, one study found that 11.2% cases of cirrhosis at Singapore's largest tertiary hospital were mainly due to alcohol.[13]

Though studies are limited, rare liver diseases appear to be particularly uncommon in Singapore, though whether this is due to prevalence or gaps in diagnosis is unclear.[14,15,16]

Liver cancer is the fourth most common cancer in men in Singapore and the third most likely to be deadly; it is also the fourth most common cause of cancer death in women.[17] The most prominent etiology for liver cancer in Singapore has historically been the hepatitis B virus – which makes carriers about a hundred times more likely to develop liver cancer than those without the virus.[17] The overall survival rate of liver cancer in Singapore is greater than 20% – one of the best in the world.[18]

Chronic hepatitis B is the **leading cause of liver cirrhosis** in Singapore.

Liver transplantation is a treatment option available for those with end-stage liver disease in Singapore. The first liver transplant in the nation took place in 1990 – and more than 500 transplants have been performed since then.[19] Both living donor and deceased donor transplants are available in Singapore, and there are two public and two private liver transplant centers.[19] Unfortunately, Singapore has low deceased donation rates (about 6 per million each year), potentially linked to discrepancies in donor referral and conflicting cultural and religious beliefs, especially when there are concerns of family objection. Meaningful effort to increase participation in organ donation upon death will be helpful in increasing the supply of transplantable livers for patients in Singapore.

More than **500 liver transplants** have been performed in Singapore.

OVERVIEW

SOUTH KOREA

Population: 52.08 million (2023)

GDP per capita: $33,121 USD (2023)

Life Expectancy: 80.3 years (men) and 86.6 years (women)

Healthcare Spending: 8.4% of GDP (2020)

Healthcare Funding: Korea has adopted a unique health security system that includes social health insurance and medical aid. This universal healthcare system, known as the National Health Insurance Service (NHIS), is mandatory for all Korean nationals and residents to participate in at a fee. The fee is dependent on each person's work income but starts at a base of 150,000 won ($112 USD) each month. Compared to other OECD countries, Korean nationals and residents pay less for healthcare out-of-pocket since the NHIS covers 50-80% of most medical costs. Despite this, many opt for additional private health insurance to cover fees incurred with the NHIS plan.

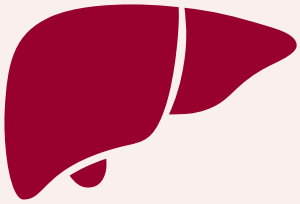
Korea has also adopted a fee-for-service model, which requires patients to pay for their care prior to rendered services. The Health Insurance Review and Assessment Service has stated that this has widened the variety of services a doctor gives to patients. Korean emergency room wait times tend to be 10 minutes or less.

Sources: US CIA's The World Factbook, World Bank Group, Health Insurance, Review and Assessment Service

$33,121
GDP per capita

8.4%
of the GDP is spent on Healthcare

80.3 (men)
and **86.6 (women)**
Life Expectancy



The country has achieved one of the **highest five-year liver cancer survival** rates in the world.

Liver health in South Korea is influenced by a mix of factors like viral infection, alcohol use, lifestyle diseases, and socioeconomic conditions. The country has made significant progress in tackling these issues through its strong healthcare system, but challenges remain. For instance, despite the establishment of the National Liver Cancer Surveillance Program in 2003, the screening rate for hepatocellular carcinoma (HCC) among high-risk groups remains low; the country has nonetheless achieved one of the highest five-year liver cancer survival rates in the world.[1] At the same time, South Korea has made significant progress in liver transplants, achieving the highest rate of living donor liver transplantation (LDLT) globally. [2] Liver health in South Korea is characterized by both achievements and ongoing challenges that emphasize the need for more efforts to improve early detection, access to care, and management of long-term outcomes for those affected.

The fight against viral hepatitis faces persistent challenges despite well-directed efforts. Hepatitis B (HBV) has long cast a shadow over the nation, being the leading cause of chronic liver disease and responsible for 60–70% of chronic liver disease.[3] The government's response to this challenge began in the 1980s, in the lead-up to the 1988 Seoul Olympics.[3] The establishment of the "Hepatitis B Eradication 5-Year Plan" marked a turning point that led to widespread vaccination efforts for infants and toddlers to protect the next generation from this pervasive threat.[3] Yet, even with these measures, hepatitis B still accounts for a significant amount of chronic liver disease cases.

Hepatitis C (HCV), though less prevalent, poses its own challenges. With no vaccine available, the focus remains on treatment, where highly effective antiviral therapies have offered hope.[3] Despite these advances, many patients with HCV have not received the care they need, with treatment rates falling below global targets set by the WHO.[4] As a result, the Korean Association for the Study of the Liver has set a goal to eliminate HBV and HCV by raising awareness from 30% to 90%, increasing testing rates from less than 10% to 90%, and boosting treatment rates from 60% to 90% by 2030.[5] This plan would also include establishing a dedicated division for viral hepatitis within the Korea Disease Control Agency, increasing funding for hepatitis C research, and evaluating the cost-effectiveness of introducing HCV antibody testing into the National Health Screening program.[5]

In addition to the challenges posed by viral hepatitis, South Korea faces increasing rates of alcohol consumption. The average Korean consumes 10.2 liters of alcohol annually, significantly higher than the global average of 6.4 L.[6] Therefore, alcohol accounts for more than 13% of liver disease cases.[7] High-risk drinkers face a much greater likelihood of developing liver cirrhosis or HCC than social drinkers.[7]

This is exacerbated by hoe-siks, after-work company outings, that are often seen as mandatory and necessary depending on the company's culture.[8] These events often involve high-calorie foods and excessive drinking.[8] One study found that more than 30% of office workers in metropolitan areas reported binge drinking more than four times in one month.[9] This is concerning when 82.1% of the Korean population live in metropolitan cities. Such practices are amplifying the rise in liver diseases linked to alcohol.

13%

of cases of liver disease in South Korea are **caused by alcohol consumption.**

Liver cancer is the **second leading cause of cancer-related deaths** in South Korea.

As South Korea has become more globalized and rapidly expanded into the 14th largest economy worldwide, the prevalence of lifestyle-related diseases has also risen.[11] Metabolic dysfunction-associated fatty liver disease (MAFLD) has emerged as a significant public health concern, driven by increasing rates of obesity and diabetes, with the prevalence of metabolic disorders in Korea rising from 24.9% in 1998 to 30.3% in 2020, further contributing to the issue.[12] Korean food has undergone "Westernization," with an increased consumption of refined grains, processed meats, and fried foods.[13] Recent studies have shown that the traditional Korean diet, high in carbohydrate intake, is associated with an increased risk of MAFLD.[14] Other lifestyle changes, such as sedentary behaviors, have exacerbated the effects of this diet on liver health.[14] In contrast, a "simple meal" pattern, characterized by lower carbohydrate intake, has been associated with a decreased risk of MAFLD in the Korean population.[14] MAFLD is not a benign condition; it can progress to scarring, liver cirrhosis, and even liver cancer.[15] As the prevalence of metabolic disorders continues to rise, so too does the burden of MAFLD.

Beyond the well-known risk factors, Korea faces unique challenges that further complicate liver health. One of the most troubling aspects is an increased risk of suicide among patients with liver cirrhosis, particularly in the early stages of diagnosis.[16] The psychological toll of living with a chronic, often irreversible disease is immense, and for many, the burden becomes too great to bear.[16] This is exacerbated by the socioeconomic inequalities that pervade the healthcare system. Despite the universal coverage provided by NHIS, out-of-pocket expenses remain high, particularly for low-income individuals.[17] This financial strain can limit access to necessary care, further exacerbating health disparities.[17]

In South Korea, liver cancer is the second leading cause of cancer-related deaths, accounting for 13% of the nation's cancer fatalities.[18,19] The primary factor behind this epidemic is chronic HBV infection, which significantly increases the risk of developing hepatocellular carcinoma (HCC).[20] As a result, the National Liver Cancer Surveillance Program (NLCSP) in 2003, aimed at reducing the socioeconomic burden of liver cancer, many challenges remain.[1] During this time, the 5-year relative survival rate for liver cancer significantly improved, rising from 10.7% for those diagnosed between 1993 and 1995 to 32.8% for those diagnosed between 2010 and 2014.[21] However, screening rate among high-risk groups is only 23%, and the incidence of liver cancer continues to rise.[19] Liver cancer in Korea challenges the healthcare system to keep pace with the rapidly growing public health crisis.

For those with end-stage liver disease, liver transplantation offers a lifeline. Annually, South Korea performs more than 10x the number of living donor liver transplants per million than neighboring Japan and Hong Kong.[2] Since its first liver transplant in 1988, the number of procedures has skyrocketed in South Korea, given the country's commitment to meet the increased demands for donors.[22] The five-year survival rate for LDLT is 81% post-transplant.[22] However, the reliance on living donors illustrates a critical shortage of deceased donors, with only 8.7 per million people in South Korea, far lower than countries like Spain, with 49.6 per million, and the USA, with 36.1 per million.[23] This has prompted the creation of laws like the National Transplant Act, and organizations like the Korean Network for Organ Sharing and the Korea Organ Donation Agency to regulate and manage organ donations from deceased and brain-dead patients.[1,24] Yet, despite efforts, stigma continues to be a major barrier, with 58% of families refusing organ donation, even when the donor had expressed their consent to donate.[25] The future of liver transplantation in Korea hinges on addressing the persistent shortage of deceased donors.

Despite challenges like high rates of viral hepatitis, alcohol use, and MAFLD, South Korea is making progress. It leads globally in living donor liver transplants and continues to improve public health initiatives and healthcare access, working to reduce the overall burden of liver disease and its effects.

OVERVIEW

VIETNAM

97.47 million
Population

Population: 97.47 million (2021)

GDP per Capita: $4,347 USD

Life Expectancy: 71 years (men) and 80 years (women)

Healthcare Spending: 5.25% GDP

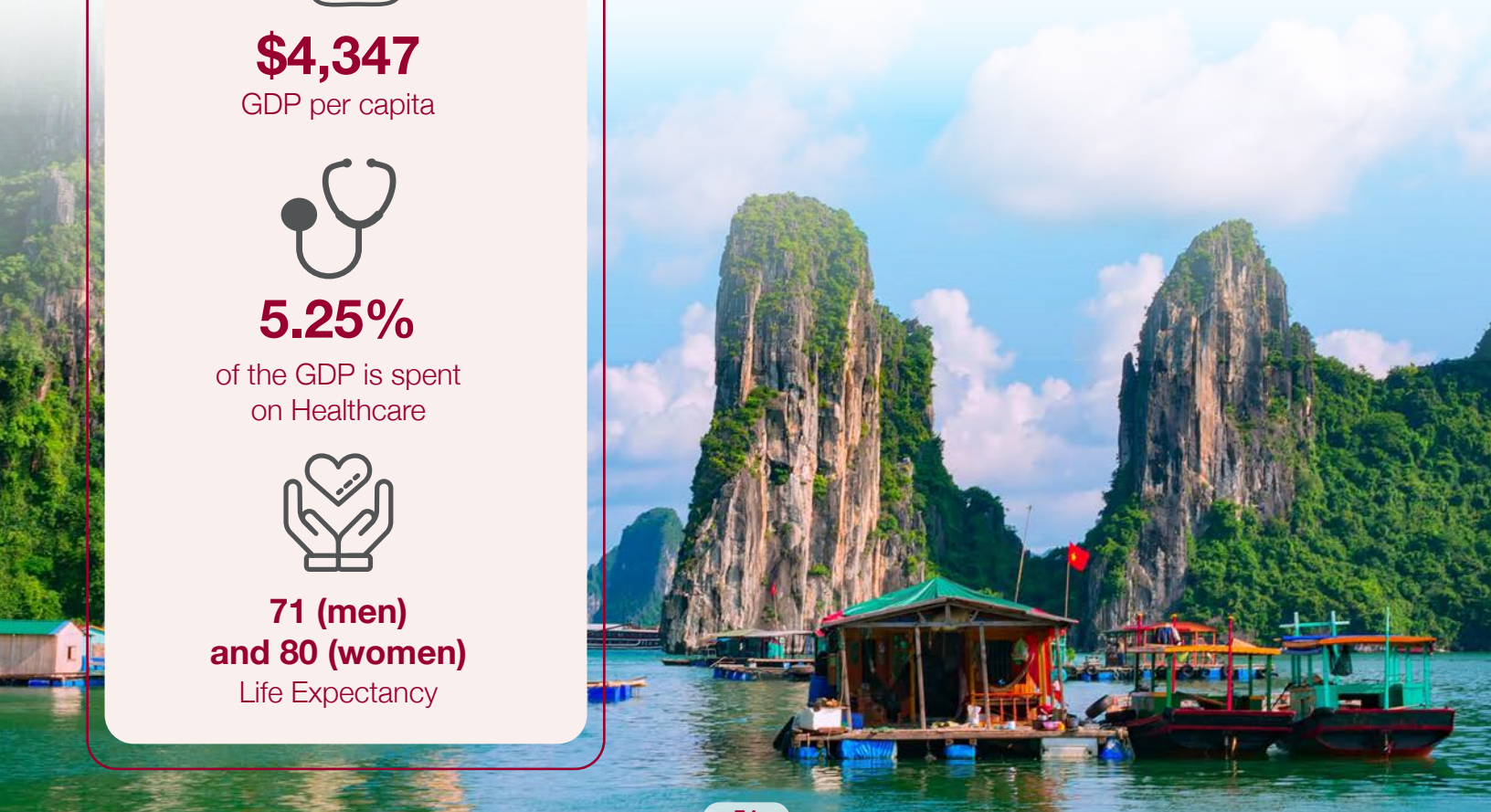
Healthcare Funding: About 87% of the population in Vietnam is covered by health insurance. Public spending on health care, which accounts for about half of healthcare spending, comes from the social health insurance program as well as additional tax-funded supplements for vulnerable populations. Still, 41% of total expenditure on healthcare in the country is out-of-pocket.

Sources: World Health Organization, The World Bank, Macrotrends

$4,347
GDP per capita

5.25%
of the GDP is spent on Healthcare

71 (men) and 80 (women)
Life Expectancy



A unique combination of risk factors, including smoking, alcohol consumption, high BMI and HBV prevalence lead to devastating consequences for liver health in Vietnam.[1] As a result, unlike in most other countries, the leading cause of cancer death in Vietnam is liver cancer.[2] Further, Vietnam has an alarming rate of cirrhosis, it is estimated that by 2025 related to HBV alone, there will be 60,000 cirrhosis patients, 25,000 liver cancer patients, and 40,000 deaths in Vietnam due to cirrhosis.[3]

Vietnam currently has low rates of obesity compared to the rest of Asia and the Western world at large, with the most recent available rate of 2.1% in 2016.[4] However, the rate has nearly doubled since 2010.[4] This suggests that rather than being a nonissue, obesity in Vietnam is in fact lagging behind other nations but will rise to become a dominant health concern in coming years. Furthermore, using the WHO BMI cut-off for Asian populations, this rate goes up to nearly 15% as of 2015.[5]

As obesity and diabetes continue to rise in the nation, metabolic dysfunction-associated fatty liver disease (MAFLD) become more prevalent as well. In one study of patients with T2D in Vietnam, the prevalence of MAFLD was more than 70%, on par with the highest estimates worldwide.[6] With these changing lifestyle patterns, experts in Vietnam should continue to keep an eye on MAFLD and take guidance from best practices developing elsewhere in the world.

Liver health risk factors: high smoking, alcohol consumption, high BMI, and HBV prevalence.

Alcohol consumption remains a major concern for liver health in Vietnam. Per capita, adults in Vietnam consume 8.3 liters of pure alcohol annually, the equivalent of 170 liters of beer.[7] This number has more than doubled in two decades, signaling changing cultural patterns and driven primarily by men.[7] This increases risks of alcohol-associated liver disease, and also increases the risk of cirrhosis for those infected with viral hepatitis.[8] To fully address the issues in liver health in Vietnam, efforts to reduce alcohol consumption, whether public education campaigns or policy measures, are absolutely necessary.

Vietnam has one of the highest prevalence rates of viral hepatitis in the world. In the general population, chronic HBV infection has an estimated prevalence of 12% and chronic HCV has at least 1% prevalence.[9] Unfortunately, rates have not been reported at the national level and rely on regional or community-based reports. Still, these rates are even higher amongst at-risk groups, including health care workers, blood donors, and intravenous drug users.[10] In part due to the lack of a laboratory test, a national prevalence of HDV and its complications has not been reported.

In 2003, universal infant HBV vaccination was introduced in Vietnam, after which the peak number of infections occured in about 2012.[11] The prevalence of infection was estimated to decline in subsequent birth cohorts by as much as 90%.[11] HBV control, however, relies heavily on this program, which leaves all non-infant age groups to bear the burden of HBV infection. The general population lacks knowledge on HBV transmission, progress, and risk factors – and few are able to receive treatment due to financial constraints and lack of awareness.[12]

Calls for a systematic screening program in the country for high-risk populations were made by experts as recently as 2010 and 2017.[12, 13] Further, for the millions in Vietnam who are infected with HBV, therapeutic intervention is absolutely necessary but may be financially out-of-reach, and the government as well as international agencies must increase investment in infrastructure and subsidies for HBV and HCV treatment for the Vietnamese people.[11] A collaborative center from Johns Hopkins called the Center of Excellence for Liver Disease in Vietnam and its initiatives provide promise for advancement on this front.[14]

HCV, which is less prevalent but still relatively high (1-4%) amongst the Vietnamese population compared to neighboring countries, is a particular issue amongst high-risk populations and the more populous northern and southern provinces.[13] A pilot HCV program supported by the Clinton Health Access Initiative has been successfully implemented in Vietnam using pricing negotiations, policy development, fast-track registrations of generic treatments, financing advocacy, and strengthened service delivery.[15]

Vietnam has the fifth highest rate of liver cancer incidence in the world.[16] Distressingly, as reported by a nationwide study that covered nearly 95% of the health service stations in the country, liver cancer is both the most common cancer among both men and women and causes one in four cancer deaths in the nation – the leading cause of cancer death.[17, 2] The incidence of liver cancer has also been observed to be rising in recent years.[18]

Vietnam has one of the highest prevalence of viral hepatitis **in the world.**

Vietnam has the

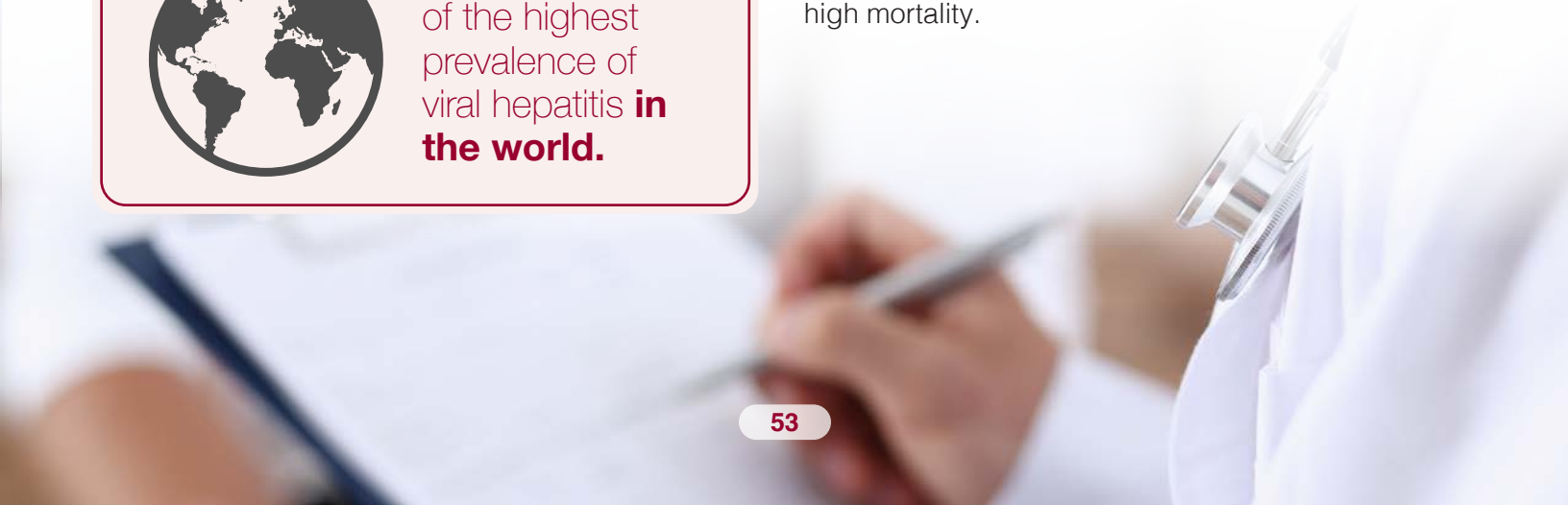
5TH HIGHEST RATE

of **liver cancer** incidence in the world

While it is the leading cause among both genders, prevalence has been nearly three times higher among men.[17] This is understood to be primarily the downstream effect of high prevalence of HBV and followed by HCV and alcohol.[19] This is similar to many other developing countries, in which the dominant causes of cancer are related to infectious factors.[17] Aflatoxin exposure is also thought to be an upstream risk factor for the development of HCC.[20]

Though the state of liver cancer is dire in Vietnam, there is much hope in the fact that its etiology in the nation is overwhelmingly preventable via available technologies, and the universal HBV infant vaccination is an important first step. Clear education about the relationship between HBV and liver cancer is important to turn the tide, and long-term surveillance for liver cancer are of the utmost importance.

Chemicals and parasitic infections also pose distinct threats to certain communities. Agricultural pesticides, industrial chemicals, and herbicides have been linked to increased rates of hepatitis among agricultural workers in south Vietnam.[20] In part due to the tropical nature of the country, liver abscesses are common in Vietnam.[20] Prompt identification and surgical treatment of these conditions is an important feature of the healthcare system in order to avoid high mortality.



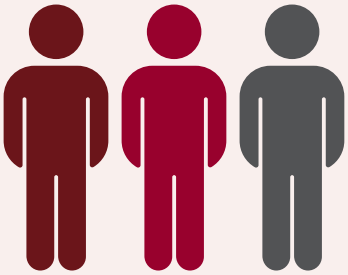
Vietnam performed their first **liver transplant** in

2004

For autoimmune, pediatric, and other rare liver diseases, little epidemiologic or investigative research is available. Alpha 1 antitrypsin (A1AT) deficiency has been identified in Vietnam – which was previously considered a disease of Caucasians.[21] Biliary atresia is the leading indication for liver transplantation and main cause of end-stage liver disease for children.[22] Otherwise, data that has not been updated in nearly two decades points to the fact that unsurprisingly, viral hepatitis was the primary diagnosis, followed by congenital bile duct dilation, liver/biliary tract infections, cholestasis syndrome, cirrhosis, autoimmune and drug-induced hepatitis, liver tumors, metabolic disorders, and biliary atresia.[23] There is much to be learned about the incidence and etiology of rare and pediatric liver diseases in Vietnam.

The first liver transplant in Vietnam occurred in 2004, and several hospitals have since launched liver transplant centers.[24, 25] Still, between 1992 and 2018, only about 2,400 total organ transplantation procedures had been conducted in Vietnam (including the liver, kidney, and heart). This falls far short of the nearly 8,000 patients each year who require a transplant in the nation – many of whom need a new liver due to end-stage liver disease. The primary barriers to transplantation were financial costs, distance from home, lack of ability to commit to lifelong follow-up and treatment, and shortage of organ donors.[24] As a middle-income country, Vietnam has developed an impressive technical capacity for liver transplantation, and has even incorporated living donor transplantation as an effective, safe treatment for HCC – but there is still room for improvement in accessibility, affordability, and organ donation.[26]

Liver cancer prevalence is



3X

higher among **men than women.**

STRENGTHS, CHALLENGES, AND NEXT STEPS FOR LIVER CARE IN VIETNAM

Dr. Dao Viet Hang is the Vice General Secretariat of the Vietnam Association of Gastroenterology (VNAGE) and an experienced gastroenterologist and hepatologist, a clinical researcher and a lecturer at the Hanoi Medical University. She focuses on viral hepatitis, liver cancer treatment, and the application of IT in the medical field.

CHALLENGES

1. Patients struggle to become connected to the healthcare system, especially in HBV and HCV. Though there is a lack of data available on the process, we would find that there are many lacking points where the system fails to monitor at-risk patients.
2. In most cases, especially rural areas, the care a liver patient receives depends on which specialty they go to first, which means a lot of nonstandard care. The several overlapping specialties who treat the liver – including surgery, transplantation, infectious disease, internal disease, hepatology, oncology, and even radiology – becomes challenging, because everyone wants to keep the patient in their specialty.

STRENGTHS

1. In recent years, there has been a more active and impactful involvement of academic associations around liver health. This has helped educate doctors across different fields about viral hepatitis, liver cancer, and other liver diseases.
2. Digital health technologies have strengthened liver care and will continue to in the future:
   - **a**. The ecosystem of smartphone apps has been building. In other fields of gastroenterology, there are many good products available for patients. In the next few years, smartphone apps will be used more and more to help monitor chronic viral hepatitis patients.
   - **b.** Online and hybrid webinars have become more popular, which has allowed greater access for doctors to have CME, especially in the rural areas.
   - **c.** The awareness of liver disease has been strengthened immensely by social media. If you go on Facebook in Vietnam, there is a huge community to educate and raise concern for chronic hepatitis and liver cancer. It helps because most people in Vietnam have basic knowledge of hepatitis B – which is important when it affects about 8% of the population.
3. Rapid tests used during the COVID-19 crisis have made the general population much more comfortable with rapid tests for hepatitis – so they can take what they are learning on social media and apply it to screen their families in real time. Sometimes they even post it on social media!

CALL TO ACTION

1. We absolutely need a national screening program for viral hepatitis. Even after the introduction of a universal screening program, the greatest risk factor for liver cancer in Vietnam is still HBV.
2. We need to use the tools we have to prevent the spread and progression of liver disease: checking pregnant women for HBV and follow-up for liver cirrhosis patients so they don't develop liver cancer.
3. There are many efforts and resources invested in Vietnam now, which is great – but many of these efforts overlap. It is critical that the many NGOs develop a strong, comprehensive network to inform each other about what we are doing and save resources.

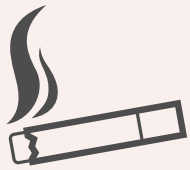
DIGGING INTO EPIDEMIOLOGY TO UNDERSTAND FACTORS DRIVING LIVER HEALTH

Dr. Tung Pham is a lecturer, researcher, and curriculum fellow in cancer epidemiology at the Harvard T.H. Chan School of Public Health. His research focuses on topics including developing a cancer prevention strategy system in low resource settings, mental health, and medical education.

"My research focus is on epidemiology – and it's important to take a look at the risk factors that drive the key issues in liver health here in Vietnam. Regarding obesity in Vietnam, for instance, the rate of obesity is not very low once you consider abdominal obesity and the BMI cut-off for Asian populations. In a study we just published in the Lancet Regional Health, using the WHO BMI cut-off for Asian populations, the prevalence of obesity among women in 2009 was almost 10%, and by 2015 it had increased to 16%. If you use the waist-to-hip ratio in women, that number goes up to 40% in 2015.

The interesting thing is that when we use BMI, the rates of obesity are much lower among men. That is partly due to the fact that about half of the men in Vietnam are smokers. When you smoke, you tend to have a lower BMI, even if your abdominal obesity is high. When we only screen with BMI, we miss all the male smokers.

Smoking, as well as alcohol consumption, actually account for a substantial proportion of liver disease in Vietnam. About 22% of liver cancer cases in the country are attributable to smoking. We also have very high alcohol consumption here, and although the government has tried to put some limits on it, such as taxes or rules about driving, they face strong pushback from the alcohol industry about job loss and economic impact. And there is also a lot of homemade alcohol production, which cannot be regulated or taxed – especially in the rural areas. Alcohol accounts for about 6% of all cases of liver cancer. Even high BMI is attributed to 10% of cases of liver cancer. So even though HBV drives the high rate, there are many other factors at play.



22%

of liver cancer cases in the country are **attributable to smoking**

I think we will begin to see the impacts of the universal HBV vaccine program in the coming years, since it takes a few decades to see that decrease – although a growing anti-vaccine movement does put all that work at risk. Now, we don't have many tools currently to control tobacco smoking, alcohol consumption, and to control unhealthy diets in Vietnam. These are the second and third leading factors, so a tightening of standards, maybe raising taxes and implementing other promotional programs, will be essential.

From an economic perspective, taxing these things will decrease the consumption and then the chronic disease that results. That would eventually save money for the government in the long run, since most people draw funds from the social insurance program. So not only would these policies save lives, they would also save money."

EUROPE

750 MILLION
people

HEALTH OVERVIEW

Covering 10.53 million km, Europe is the second most densely populated continent after Asia.

The many countries of Europe straddle a widely varying range of economic indicators. The top four economies, Germany, UK, France and Italy, between them hold more than 50% of the share of the European GDP, and annual GDP per capita ranges from US$143,000 dollars (Liechtenstein) to $14,150 (Ukraine).

Across Europe, healthcare is the responsibility of, and administered by, individual countries and virtually all provide some form of universal healthcare. Funding is either wholly or partly by taxes, sometimes supplemented with varying forms of point of care payments.

Health spending per head varies widely across the continent, with Norway and Germany coming out top at around €4,500 per capita. Italy, despite being the fourth largest economy in Europe, spends nearly 45% less at €2,470.

Sources: International Monetary Fund: World Economic Outlook Database

According to a recent commission report published in the Lancet, chronic liver disease led to 287,000 deaths in Europe in 2019, of which 63,500 were due to primary liver cancer.[1]

Liver-related deaths accounted for 3% of all deaths in Europe in 2019, which is an increase from the 204,000 deaths in 1990 (2%-3% of all deaths).[1] These changes equate to a 25% increase in deaths due to chronic liver disease and a 70% increase in deaths to primary liver cancer.[5] After ischaemic heart disease, liver disease is now the second biggest cause of deaths of people of working age in Europe.[1]

Obesity rates across the continent are, in line with the rest of the world, rising quickly. According to a World Health Organization Report released in May 2022, Europe has the second highest rates of obesity globally, after America.[2] Across Europe as a whole, 21.8% of men and 24.5% of women are deemed obese, with the UK leading the way (26.9% of men and 28.6% of women).[2]

Obesity is currently responsible for around 1.2 million fatalities in the region each year – around 13% of all deaths – and predicted by the WHO to overtake cancer as the leading cause of death in the next decades.[2]

The WHO notes that the European Region has the highest proportion in the world of total ill health and premature death due to alcohol. One-fifth of the European population aged 15 and above report heavy episodic drinking (five or more drinks on one occasion) at least once a week. Binge drinking is widespread across all ages and across all the countries of Europe, not just those in the North.[3] More than 50% of all end-stage liver disease across Europe is due to unhealthy alcohol consumption.[4]

Chronic liver disease led to

287,000 Deaths

63,500 Due to Liver Cancer

Obesity is responsible for

1.2 MILLION

fatalities in the region each year

There have, however, been some success stories across Europe, most notably in the vaccine and treatment programs introduced to combat viral hepatitis, including childhood vaccination against the hepatitis B virus (HBV) and antiviral drugs to combat the hepatitis C virus (HCV). So, although it is currently estimated by the European Centre for Disease Control (ECDC) that more than 10 million Europeans may be living with chronic HBV or HCV, the prevalence of chronic HCV is estimated to have declined, perhaps by as much as a third, in many western European countries during the past five years.[5]

Liver disease is now a major threat to public health in every country across Europe. Yet the three main causes of liver disease – viral hepatitis, obesity and alcohol abuse - are all preventable. A concerted commitment to address the need for education around obesity and alcohol, intervention programs, early detection, readily available and free vaccinations and treatments could save the lives of almost 300,000 people across Europe each year.[1]

Liver disease is a **major threat to public health** across Europe

BULGARIA

Population: 6,916,548 (2021)

GDP per Capita: $15,798 USD
Almost half of Bulgarian households say they find it difficult to cover healthcare costs.

Life Expectancy: 70.8 years (men) and 78.1 years (women)

Healthcare Spending: 8.1% of GDP

Healthcare Funding: A mix of a compulsory social health insurance (SHI) scheme with additional 'out-of-pocket costs' (mainly for medicines and medical devices) borne by the individual. There are a small number of voluntary health insurance schemes. An estimated one million Bulgarians have no health insurance, and out of pocket spending is 2.5 times the EU average.[10]

Sources: EC Commission Report: The State of Health in the EU, Bulgaria: Country Health Profile 2021

$11,635
Average Income Per Household

8.1%
of the GDP is spent on Healthcare Spending

71.1 years (men)
and **78.2 years (women)**
Life Expectancy

Collating data on the causes, epidemiology, treatment pathways and outcomes around liver disease in Bulgaria has proven to be a challenge. Bulgaria's first National Cancer Plan for example, published in May 2022, made no specific mention of liver cancer even though Bulgaria ranks eighth in the WHO European Region for alcohol consumption, which is closely tied to liver cancer.

A search for figures on autoimmune liver disease proved to be fruitless. Likewise, it has proven impossible to establish the economic burden of liver disease to the Bulgarian people.

The Global Nutrition Report estimates that 26.3% of adult women and 28.3% of adult men in Bulgaria live with obesity. This is higher than the regional average of 25.3% for women and 24.9% for men (an average of 25.1%). At the same time, diabetes is estimated to affect 7.6% of adult women and 9.7% of adult men (an average of 8.65%).[1]

Assuming that the prevalence rate for metabolic dysfunction-associated steatotic liver disease (MASLD) is around 60% in high-risk populations including the obese and those with diabetes, it could be estimated that around 2.1 million Bulgarians are living with the condition.[2]

According to the Organization for Economic Co-operation and Development (OECD), Bulgaria has one of the highest levels of alcohol consumption – 12.7 liters of pure alcohol per capita per year.[3] The WHO International Agency for Research on Cancer cites 640 cases of liver cancer in 2020.[4]

The National Program for the Prevention and Control of Hepatitis was finally implemented in 2021, after a nine-year campaign by the HepActive Patient Association Bulgaria and other patient and clinical groups. The current plan (running from 2021-2025) aims to test all adults between the ages of 40-65 for HBV and HCV every five years.

In 2021 there were

13 Liver Transplants

26.3%
OF ADULT WOMEN

28.3%
OF ADULT MEN

in Bulgaria **live with obesity**

There have been compulsory vaccinations for all newborn children against HBV since 1992. However, these rates are dropping. In 2011, 96% of newborns completed the course of vaccinations but, in 2018, that number had fallen to 85.1%.

There is currently no national or regional register for chronic viral hepatitis, but there were 2,249 cases of acute viral hepatitis registered in 2019, over 50% of which were specified as caused by hepatitis A.

According to data from the Polaris Observatory, in 2020 1% of the population of Bulgaria (around 86,000) people were living with HCV, and 3% (around 227,000) with HBV (2016 figures). They estimate that 19% of HCV are diagnosed and there are 412 deaths each year from the disease. Only 13% of HBV infections are diagnosed, 3% are treated, and there are 93 deaths each year.[5]

In 2021 around 540 people were being actively treated for HCV and 2,300 for HBV. This represents a drop in numbers from 2019, which has been directly attributed to a cessation of the screening program during COVID-19.[5]

Liver transplants are extremely rare in Bulgaria. The register of the Executive Agency Medical Supervision records that, between 2016-2019, only 41 liver transplants took place in Bulgaria. There were 13 liver transplants in 2021.[6]

LIFE ON THE FRONT LINE OF LIVER DISEASE IN BULGARIA

Silvana Lesidrenska has been the President of the HepActive Patient's Association, Bulgaria since 2012. She lives with chronic hepatitis B and campaigns for improved treatment for hepatitis and liver disease patients.

In Bulgaria, nearly all medicine is clinic-based, doctors and hospitals are paid by the government according to the numbers of procedures and tests they carry out. The downside of this is that, sadly, the patient often undergoes needless hospital-based tests which could easily be carried out on an outpatient basis or, sometimes, are not needed to begin with. For example, patients may have to be admitted twice a year for three days just to undergo a simple blood test, missing out on work and family life. I am relatively lucky because my doctor only admits me for a few hours for my blood tests. Others are not so fortunate.

FEW STATISTICS BUT MANY CHALLENGES TO LIVER HEALTH

LACK OF DATA:

There is currently no national register for the number of patients living with viral hepatitis, liver cancer or autoimmune liver disease, NAFLD or NASH. There is no data on long term patient outcomes in liver disease either by disease or region. Hospitals and clinics are not required to keep data on their patient outcomes.

HEALTH SPENDING IS CONCENTRATED ON HOSPITAL/IN PATIENT CARE:

Because of a system that rewards state and private hospitals and doctors for inpatient care, inpatient spending took up 40% of the health budget in 2019, almost double that of other European countries, with outpatient care only accounting for 18.3%.[7]

In order to receive a hepatitis blood test check, a healthy patient will have to spend up to three days in the hospital twice a year. After a five-year court battle, which was contested by the hospitals, patients with well-managed HCV are no longer required to have a mandatory liver biopsy, although this is still required for HBV.

HIGH BURDEN OF 'POINT OF CARE' PAYMENTS:

State spending accounts for around 60% of all health spending. This leaves nearly 40% to be covered by the individual at point of care – one of the highest rates of out-of-pocket payments in Europe. The majority of this spending is on medicines. Many patients, particularly those who are uninsured, may struggle to pay for vital treatments. This is particularly relevant for liver disease which tends to be a chronic condition often requiring lifelong medication.

HIGH NUMBER OF UNINSURED AND VULNERABLE PATIENTS:

The Ministry of Finance estimates that around 10% of the population are not paying into the social health insurance (SHI) scheme and are therefore uninsured. These include the long-term unemployed and those unable to obtain a national identity card. These populations are more likely to experience lifestyle and living conditions that are implicated in liver disease, including poor nutrition and sanitation, alcohol and drug abuse.

REFERRAL QUOTAS:

GP and clinic referrals to specialist centers for tests and diagnostic procedures are subject to a quota system that often results in patients paying for the procedures themselves, or if they are unable to pay, going without. Effective ongoing management of liver disease relies heavily on lifelong liver function and other crucial tests. Without these, patient outcomes will most likely be greatly reduced.

LACK OF PALLIATIVE CARE:

Palliative care in a hospital setting is rationed to 22 days within the SHI scheme. End-stage liver disease requires specialist palliative care to include treatments for many potentially distressing complicationss.

POSITIVE CHANGES:

The Bulgarian government is planning a €310 million investment to modernize state hospitals and to upgrade diagnostic and other equipment.

OVERVIEW

DENMARK

Population: 5.9 million

GDP per capita: $76,687 USD (2023)

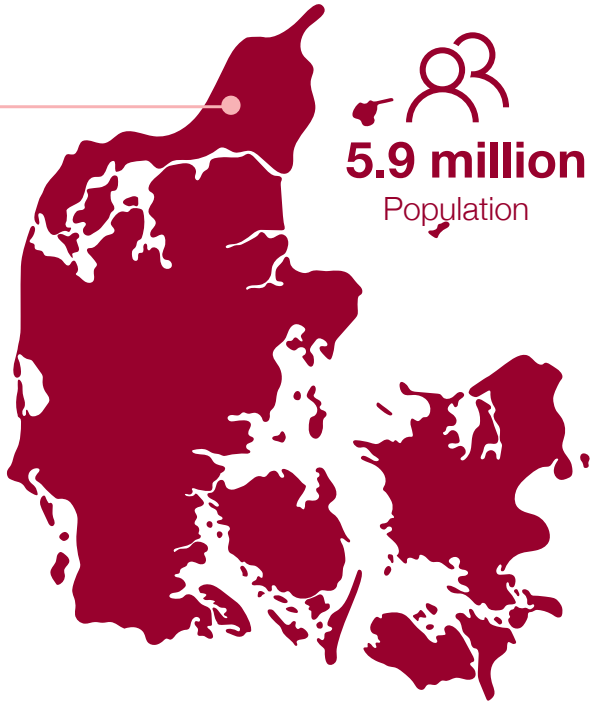
Life Expectancy: 80.2 years (men) and 84.1 years (women)

Healthcare Spending: 10.5% GDP (2020)

Healthcare Funding: Denmark's healthcare system provides universal access through a decentralized structure that offers publicly financed medical care to all registered Danish residents — including citizens, immigrants, and asylum-seekers. Undocumented immigrants have access to acute-care services through a voluntary, privately funded initiative supported by the Danish Medical Association, the Danish Red Cross, and the Danish Refugee Council.

Regions and municipalities receive tax-funded, block grants from the federal government to deliver health services. While services are largely available without a fee at the point of service, out-of-pocket payments still account for about 13% of current health expenditures (as of 2021), mainly for outpatient prescription medicines and dental care. As a result, approximately 40% of Danes hold voluntary private health insurance, often an employee benefit, to cover services not fully included in the public system, secure quicker access to elective surgeries, or utilize private hospitals and clinics.

Sources: US CIA's The World Factbook, World Bank Group, Euro Health Observatory, The Common Wealth Fund

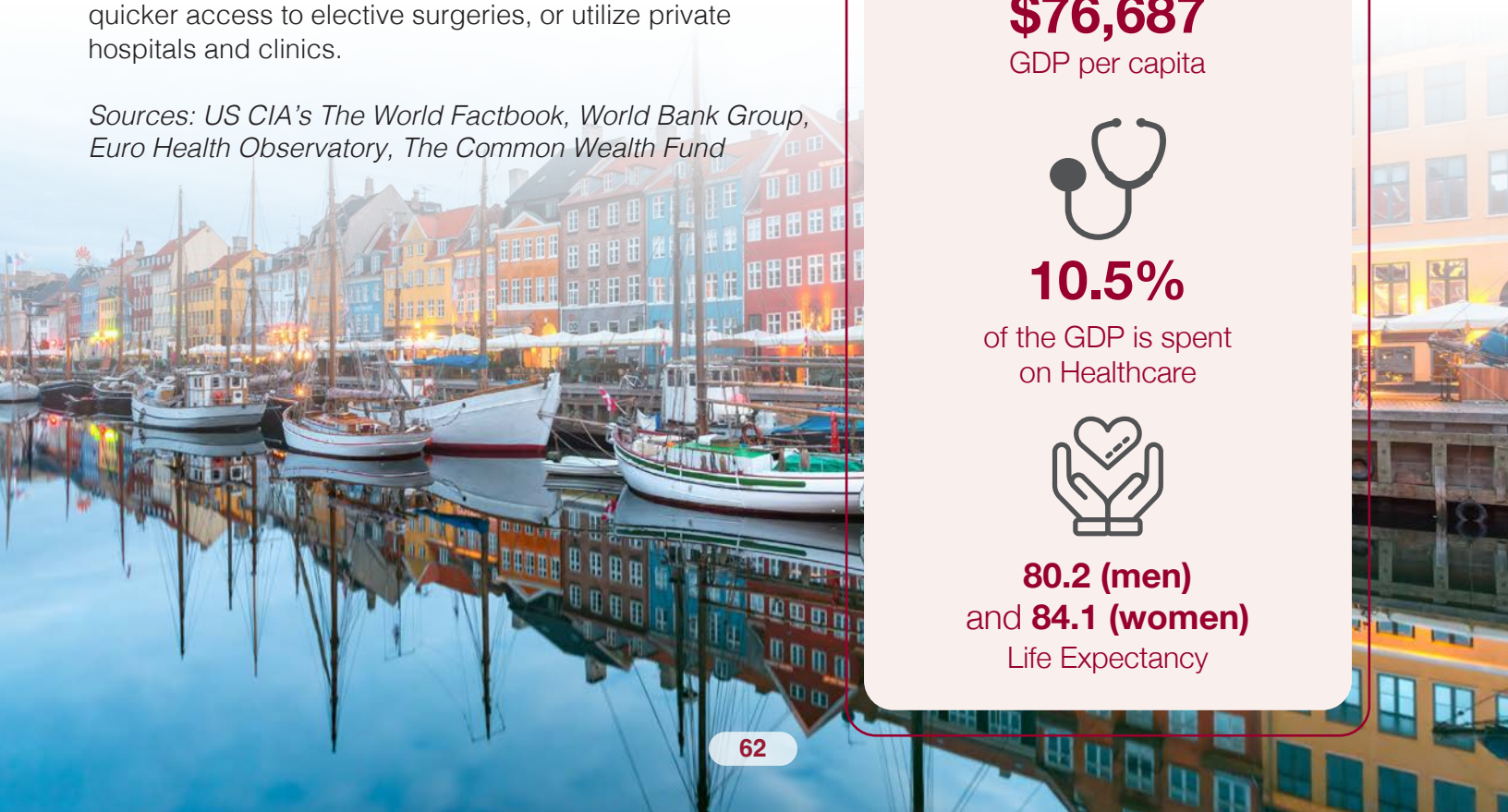


5.9 million
Population

$76,687
GDP per capita

10.5%
of the GDP is spent on Healthcare

80.2 (men)
and **84.1 (women)**
Life Expectancy



Denmark's healthcare system is committed to public well-being, with universal access and health interventions across all areas of medicine, including liver health. Central to this effort is the Danish Liver Association, a key player in raising awareness and reducing the stigma around liver diseases.[1] Although Denmark has relatively low rates of liver disease compared to many other countries, challenges persist, particularly in the final push to eliminate viral hepatitis, an emerging concern about fatty liver disease, and alcohol-related liver damage.

As Denmark faces rising rates of obesity, like many other nations, metabolic dysfunction-associated steatotic liver disease (MASLD) is a growing problem. Roughly 20% of the general population has MASLD, and those with metabolic conditions like type 2 diabetes and obesity have even higher rates. A 2023 survey has found that 52.6% of Danes have a BMI greater than 25 (considered overweight) and 18.5% have a BMI greater than 30 (considered obese). [3] As these numbers rise, MASLD is expected to become more widespread as well. Denmark has taken active steps to curb obesity and metabolic health disease. In 2001, Denmark launched a pioneering health policy banning trans fats, one of the first of its kind worldwide.[4] The policy directly reduced cardiovascular mortality and halted a rise in adolescent obesity.[4] Although adult obesity rates have been rising, Denmark's proactive public health measures showcase the country's commitment to long-term solutions for liver and public health.

More than
52%
of Danes have an **overweight BMI,** and more than **18% have an obese BMI.**

Alcohol has a significant impact on liver health in Denmark. Approximately one in five Danes can be considered heavy drinkers, while 14% have what is considered to be harmful alcohol consumption.[5] For years, alcohol consumption in Denmark has damaged liver health by causing cirrhosis and the majority of cases of liver cancer.[6] However, recent trends show a decline.[6] In 2023, for instance, the average Dane consumed around 9.3 liters of pure alcohol—down from previous years.[7] This is mirrored by liver health outcomes: The incidence of new cases of alcohol-associated liver disease (ALD) in Denmark each year dropped by about 33% between 2009 and 2018.[8] Mortality rates also declined during this period.[8] Despite this decline, Denmark still leads Nordic countries in alcohol consumption – especially in binge drinking among the youth.[9] Fifteen-year-olds in Denmark lead Europe in binge drinking, consuming five or more alcoholic drinks in one sitting.[10] The strong influence of the alcohol industry makes it difficult to implement impactful, proven policies, while enforcement of the legal drinking age is often lax.

Those most at risk for ALD tend to come from lower socioeconomic backgrounds, and age, low educational level, and lack of employment are each correlated with heightened risk.[11] Still, there is some legislative momentum to reduce excessive drinking, especially among younger people. A recent law increased the minimum age for purchasing high-alcohol-content beverages from 16 to 18, but beer, wine, and other low-alcohol-percentage beverages are available for purchase at 16.[7] Unfortunately, metabolic factors interact with alcohol consumption to the detriment of liver health in Denmark, as the two risk factors act synergistically to damage the liver.

Denmark has managed to maintain one of the lowest prevalence rates of viral hepatitis in Europe, particularly for hepatitis B and C. Hepatitis B (HBV) affects around 0.3% of the population, with approximately 14,500 individuals living with the infection.[12] 93% of HBV cases have been diagnosed.[12] Despite – or perhaps because of – this success, Denmark does not have a national strategy to reach full disease elimination of viral hepatitis.[12,13]

Still, Denmark has committed to the World Health Organization's ambitious goal of eliminating hepatitis C virus (HCV) infection by 2030.[13] Regions like Southern Denmark have implemented local action plans for early diagnosis and treatment.[13] The plan targets key populations, such as individuals who inject drugs, and sets a goal to diagnose 90% of those infected by 2025.[13] Shifts in drug consumption patterns as well as broadly implemented harm reduction programs like opioid substitution treatments and needle exchange programs are thought to have lessened the spread of the infection in Denmark.[14] Alongside a low prevalence of 0.21%, about three in four people with HCV infection are estimated to be diagnosed in Denmark.[15] Proactive community outreach to identify and treat these final undiagnosed cases will be needed to reach elimination.

Although liver cancer is on the rise in Denmark, survival rates are also increasing.[16] Unfortunately, Denmark still has the lowest five-year survival for liver cancer among Nordic countries and poor survival among high-income countries.[17,18] Alcohol-associated cirrhosis accounted for nearly 62% of liver cancer cases in Denmark, and underlying conditions like cirrhosis and chronic viral hepatitis are also closely linked.[6] As alcohol consumption and viral hepatitis decline, this cause of liver cancer is expected to decline as well. However, a growing proportion of liver cancer is attributable to overweight, obesity, and MASLD.[19] Cohort studies have also linked cases of liver cancer to occupational exposure and air pollution.[19,20] The risk of developing liver cancer is four times greater for those over 70 than younger people in Denmark.[21] Also, though liver cancer tumors are extremely rare in the pediatric population, they have many times greater survival than adult cases.[22] Prevention remains a key focus, with early detection of all-cause cirrhosis and viral hepatitis playing a crucial role in reducing the incidence of liver cancer.[16] Monitoring at-risk patients has become a central strategy in managing and mitigating cancer risks.

For patients who reach end-stage liver disease, Denmark's liver transplantation program is integrated into the broader Scandinavian transplant network called Scandiatransplant.[23] This collaboration allows Denmark to share organs with neighboring countries like Finland, Iceland, Norway, Sweden, and Estonia.[23] In 2023, Denmark completed 63 deceased donor liver transplants and no living donor transplants.[24] While short-term survival rates post-transplant have improved dramatically, long-term outcomes remain more challenging, with cardiovascular complications posing a significant risk for liver transplant recipients.[25]

Denmark has made strides in improving liver health through proactive public health policies, effective treatment programs, and continued research. While challenges remain—such as undiagnosed viral hepatitis cases, rising obesity, and the ongoing risks of alcohol-related liver disease—the country's efforts in prevention, awareness, and medical intervention provide a strong foundation for tackling liver health issues.

OVERLAPPING, MODIFIABLE RISK FACTORS THREATEN LIVER HEALTH IN DENMARK

Aleksander Krag, MD, PhD, MBA is Professor and Department Chair, Department of Gastroenterology and Hepatology Odense University Hospital, Director of Centre for Liver Research (FLASH) Odense University Hospital and DIAS Chair of Health Sciences, University of Southern Denmark. He also serves as Secretary General of the European Association for the Study of Liver (EASL) 2023-2025. His research interest focuses on clinical aspects of steatotic liver diseases (alcohol and non-alcohol related).

The main problem of liver health going into the future is steatotic liver disease – overweight, obesity, and alcohol. We are a country with very high alcohol consumption and a high level of cardiometabolic risk factors. 18% of the population has a BMI over 30. Around 10% have a harmful level of alcohol consumption.

Unfortunately, even in a well-educated, wealthy country like Denmark, we have low health literacy and low awareness regarding the liver. We have some of the highest rates of young people consuming alcohol. Our society and our government need to do a better job to protect these kids, because they don't know.

Alcohol has been a taboo. Socially, it is very common, but as soon as it is related to health, it is stigmatized, even among doctors. We have not taken it seriously enough: alcohol is the number one driver of severe liver disease. But that also means we can work on several layers.

1. Policy can make the most impact, but that is also where the resistance is the biggest, with a very strong lobbying alcohol industry. **Minimum unit pricing** is shown to reduce consumption and reduce the burden of cirrhosis and liver cancer – one study reduced the burden by between five and seven percent in the population. **Increasing the age limit** for purchasing alcohol is important. **Advertising laws** can be adjusted, as well as accessibility – the hours that alcohol is available for sale.

2. At the doctor level, we can also do a lot. Most people drink alcohol, yet we are not good enough at asking, and considering how we ask, about our patients' alcohol consumption. Do we actually use the unit that they would recognize? Otherwise, we will miss an important risk factor.

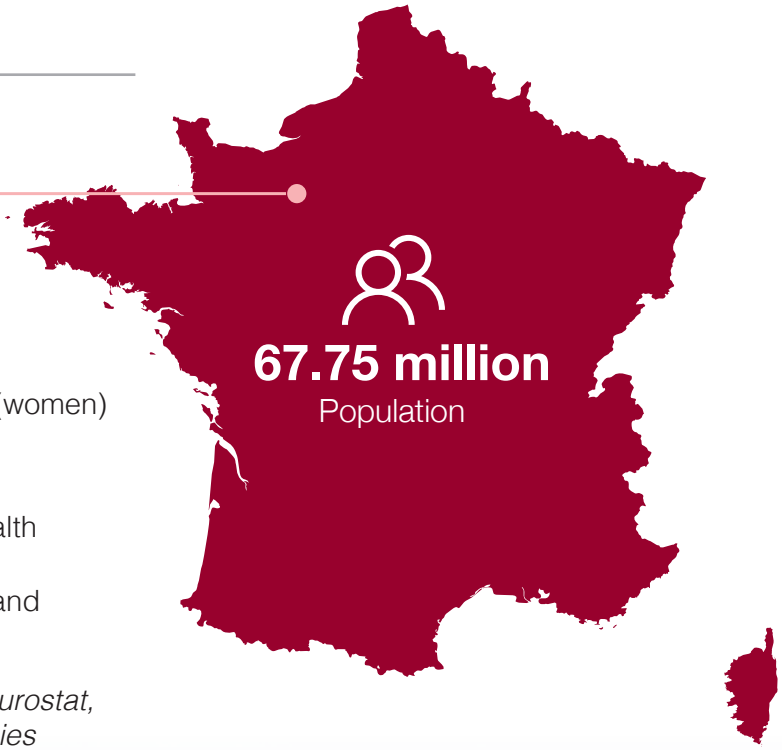
3. Then there's the patients themselves. They know alcohol is a taboo topic, and they also know it is unhealthy, so there is a massive underreporting of consumption. New biomarkers to detect alcohol consumption will be a helpful point of departure for a conversation.

We also need to begin to talk about alcohol consumption in conjunction with unhealthy food and obesity, because the synergy of these risk factors puts people at much, much higher risk. Reduction of alcohol consumption must be linked to healthy eating behaviors. Why is it so difficult to make unhealthy food expensive? Why is it so difficult to alleviate some of the tax for healthy food? So unfortunately there is a big overrepresentation of socioeconomically deprived people, with lower education and less money, with liver disease.

However, we are at the brink of being able to do something about liver disease in the next five to ten years. One, I think we will have less stigma, and easier to talk about for both doctors and patients. Then, I think the success of treatments for obesity and type 2 diabetes that are now showing promise in testing for steatotic liver disease, will lead to more options. Historically, when we have breakthroughs in the drugs, we have a push for more diagnostics, and greater awareness, because suddenly we have something to offer patients. So that would mean a declining burden of liver disease.

OVERVIEW

FRANCE



Population: 67.75 million (2021)

GDP per Capita: $44,461 USD (2021)

Life Expectancy: 79.4 years (men) and 85.2 years (women)

Healthcare Spending: 12.2% GDP

Healthcare Funding: France provides universal health coverage to its residents through a statutory health insurance (SHI) system that is funded by employer and employee contributions and various taxes.

Sources: The World Bank, World Life Expectancy, Eurostat, European Observatory on Health Systems and Policies

$44,461
GDP per capita

12.2%
of the GDP is spent on Healthcare

79.8 (men)
and **85.1 (women)**
Life Expectancy

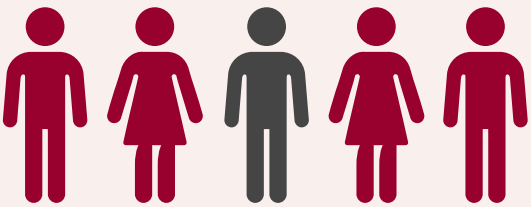
France ranks in **the best quartile** for liver health.

Relative to the rest of the world, liver health in France is in a good position. French culture keeps the liver in high regard, with longstanding myths of "liver attacks" understood as common ailments.[1] With approximately 1.5% of deaths each year due to liver disease, France ranks in the best quartile for liver health.[2] While historically more than two-thirds of primary liver cancer cases have been caused by excess alcohol consumption, the deaths due to chronic liver disease has declined by more than half in the past fifty years.[3, 4] Still, attention to emerging patterns in nutrition and physical activity will be important to keep up this high standard of liver health in the nation.

Excessive consumption of alcohol is the leading cause of liver-related death and severe liver disease in France.[5] The country has seen about a threefold decrease in liver deaths since the 1970s, while other countries in Europe saw opposite patterns. Total alcohol consumption has fallen by 12 liters per capita since the 1950s, perhaps because wine consumption was closely linked to the rural lifestyle, which became less prevalent over the decades.[4] Per capita consumption annually now sits at 10.82 liters.[6] At the same time, a consumer focus on quality rather than quantity of wine in France (which has led to increased profits for the wine industry) has driven consumption forward – which suggests that the alcohol industry in France and other countries can maintain profitability by embracing this trend.[4]

A recent population-level study in France estimates that one-fifth of French adults (without excess alcohol consumption or viral hepatitis) are affected by metabolic dysfunction-associated steatotic liver disease (MASLD).[7] While this is notably below the global average, it is still tied to known risk factors. Prevalence was higher among the following groups: men (with double the rate), increasing age, and metabolic disorders. Advanced fibrosis was 3 times higher for those with type 2 diabetes.[7] Unfortunately the rates of MAFLD and and the more advanced metabolic dysfunction-associated steatohepatitis (MASH) are at risk, as almost half of the French population can be considered overweight, with 17% considered obese.[8] Rates of people either overweight or obese have held steady for about a decade, but the proportion of obesity within that group has continued to increase.[8] Meanwhile, diabetes, another close risk factor for MASH, is estimated to be 6% of people, the highest prevalence among chronic conditions covered 100% by French SHI.[9] If these trends persist, MAFLD and MASH rates will also increase.

Viral hepatitis remains endemic in France, though available epidemiological data is suspect. Excluding a spike in 2017, when almost 3400 cases were reported, each year a low number of hepatitis A cases are reported: between several hundred and about 1,500.[10] France is classified as a low-endemic country with HBsAg prevalence below 2%, but it remains the most frequently detected virus in blood donors.[11] In EU epidemiological reports, France is estimated to underreport nearly 3 in 4 hepatitis B cases, having only reported 82 acute cases between 2014 and 2018.[12] Approximately 0.3% of the adult population in France is chronically infected with HCV;[13] France is on the road to elimination of HCV but still far from WHO's 2030 target.[14] Though France does not have consistent data estimating HDV prevalence in the population, it appears that prevalence has increased primarily due to migration from endemic countries.[15] Further, a bolstered HBV prevention campaign will reduce new incidence of HDV. Finally, though data is limited, HEV appears to be highly endemic in southwestern France in particular, perhaps tied to local dietary practices such as eating uncooked pork and game products.[16]



1 in 5

French adults

is affected by NAFLD.

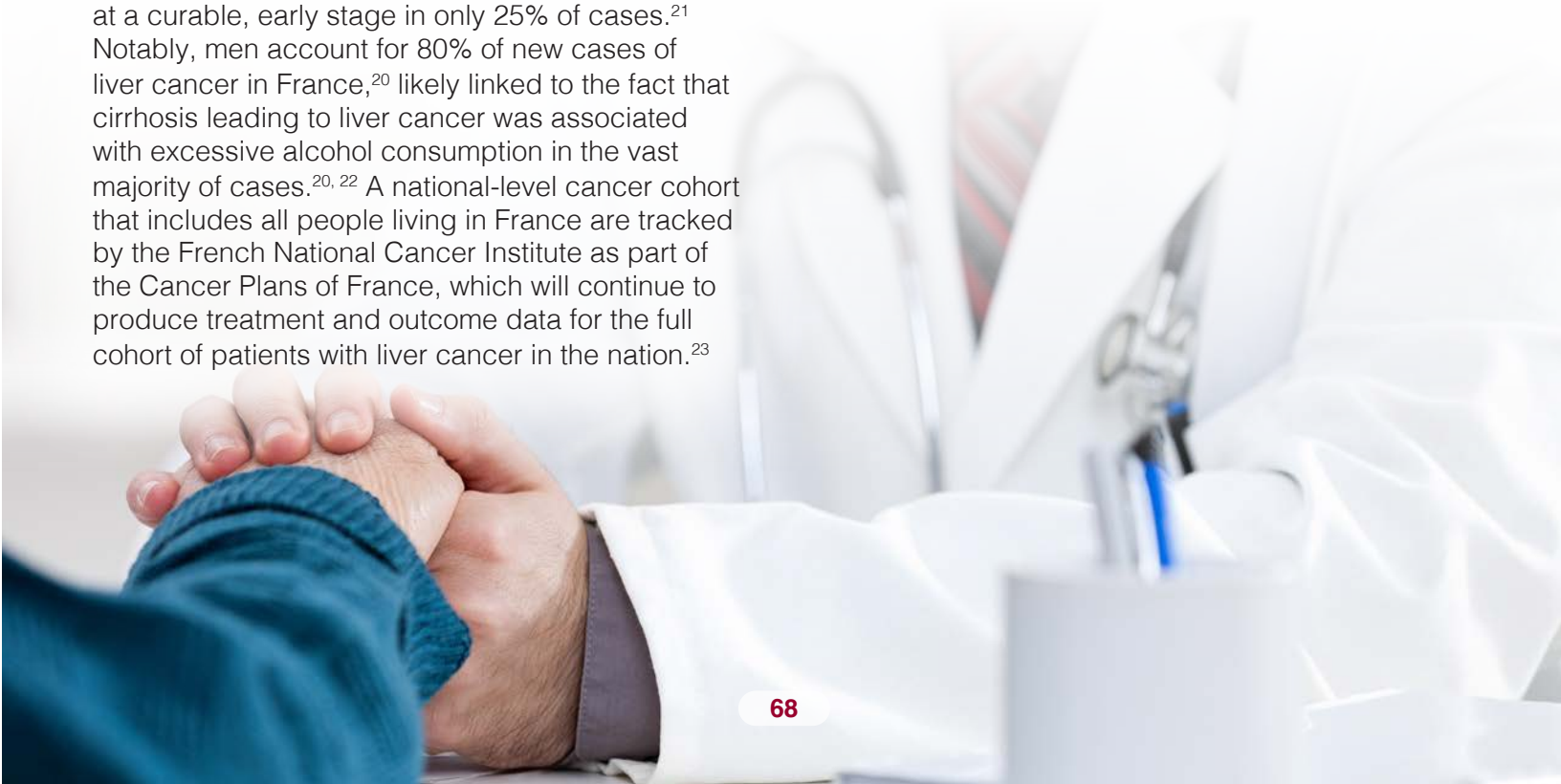
Men account for
80%
of new cases of liver cancer in France.

Targeted vaccination programs against hepatitis B began in France in 1982, with the vaccination included in the infant immunization schedule in 1995.[17] Since then, controversy tied to misinformation about risks from the vaccine sharply decreased the rate of vaccination in France, which remains low among older cohorts.[18] Today, the vaccination for hepatitis B is a mandatory part of the vaccine schedule for residents of France and covered by the SHI system; vaccines are provided at birth, 2, 4, and 6 months as well as two doses from 11 to 15 years.[19]

Approximately 8,500 to 9,000 cases of HCC occur each year in France, with between 6,700 and 8,000 deaths each year due to liver cancer.[20] With a meager 5-year survival rate of only about 10%, this places it in one of the lowest survival rates of all cancers.[21] Since it is "silent" and symptoms often do not present until late stages, it is diagnosed at a curable, early stage in only 25% of cases.[21] Notably, men account for 80% of new cases of liver cancer in France,[20] likely linked to the fact that cirrhosis leading to liver cancer was associated with excessive alcohol consumption in the vast majority of cases.[20, 22] A national-level cancer cohort that includes all people living in France are tracked by the French National Cancer Institute as part of the Cancer Plans of France, which will continue to produce treatment and outcome data for the full cohort of patients with liver cancer in the nation.[23]

Though epidemiologic data about rare liver diseases is limited, an estimated 12,000 people in France are affected by rare liver diseases. In children, almost half of cases are life-threatening and lead to an approximately 35% mortality rate in the first year of life.[24] Notably, the French Network for Rare Liver Diseases (FILFOIE), a network created by the second French National Plan for Rare Diseases, helps track patient prevalence and outcomes in addition to bringing together all stakeholders to guide patients and healthcare providers through the care pathway and encourage exchanges in research and best practices.[25] Some research into treatment options and disease pathophysiology of rare liver diseases in France, for instance for PBC and PSC.[26, 27, 28]

The primary indications for liver transplantation in France are HCC and alcohol-associated cirrhosis. Since direct-acting antiviral agents were introduced, hepatitis C has been a much smaller contributor to transplantation. Compared with other developed countries, NASH contributes to a lower proportion of liver transplants. Donation is almost exclusively from deceased donors, with very limited living donor transplantation, and campaigns are underway to increase the number of people willing to donate their organs upon death.[29] Approximately 18.7 liver transplants are carried out in France per million people in 2021, more than the previous year and comparable to peer countries in Europe.[30]

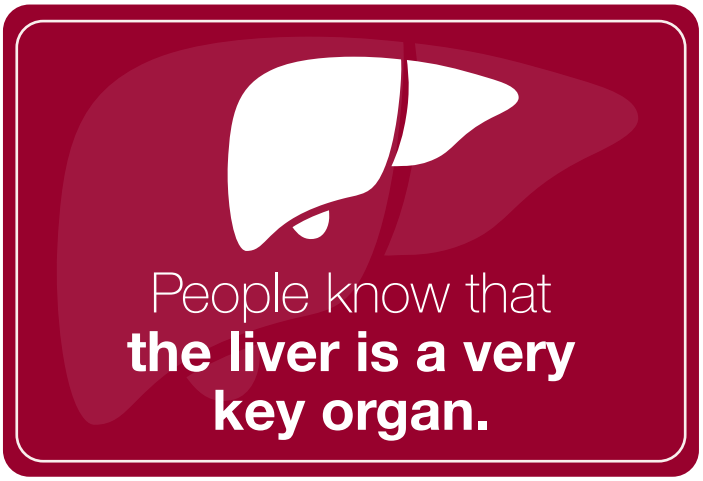


Cyrielle Caussy, MD, PhD is a Professor of Nutrition and an Endocrinologist/Diabetologist at Lyon 1 University and Lyon South Hospital in France. While her research interests include insulin resistance, obesity, and NAFLD, she now has a special interest in non-invasive biomarkers and pathophysiology of NAFLD, especially in high-risk populations such as type 2 diabetes and obese patients.

As both a physician and researcher, I have the opportunity to involve research in my practice. A recent study we undertook studied patients at high risk (with diabetes or obesity) and screened them with a fibroscan for liver stiffness assessment, as well as blood-based biomarkers. Our major finding was that among all T2D or obese patients over 40 years old, we found 38% above the threshold required for referral. About 7% had advanced fibrosis, in the end. This gives a good idea for how screening could be implemented in the existing patient journey. My department is equipped with transient elastography, so we integrated the liver stiffness assessment directly when our patients come in for their yearly check-up.

This research is part of the work driven by a special interest group that I am leading with Prof. Laurent Castera which includes the French Society for the Study of Liver Disease (AFEF) and the French Diabetes Association (SFD). We have a group of diabetologists and hepatologists working together to design studies and write reviews as well as making recommendations for the treatment of patients with cirrhosis and diabetes.

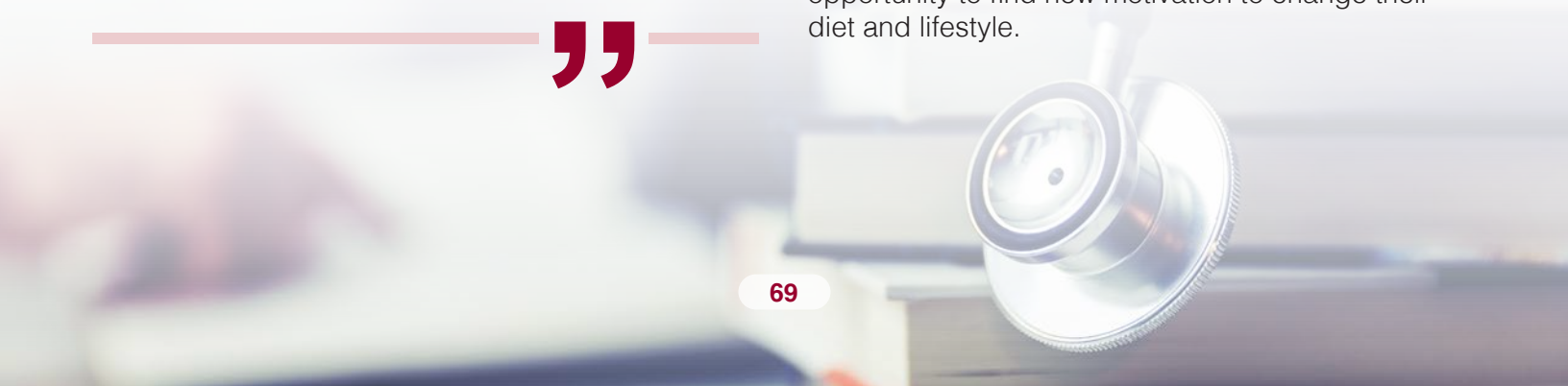
> For some patients, a new diagnosis of liver disease has provided new motivation to change their lifestyle.
>
> - CYRIELLE CAUSSY, MD



We recognize the importance of not just advancing the science of fatty liver disease but also how critical it is to mentor future researchers, so both senior and junior participants are encouraged to participate in the collaboration.

Unfortunately, this collaboration is less frequent in the field. Specialists are busy and often practice out of different centers – which is a huge barrier to working together. So far, the scientific program that joins diabetology and hepatology is mostly academic.

In France, people know that the liver is a very key organ – if it fails, it can really ruin your health. A few celebrities have discussed NASH and other liver diseases in the past, which has elevated public awareness. It is still confusing in the minds of the people because it's an asymptomatic disease in early stages. People have in mind the representation of very bad, severe cirrhosis, but at the spectrum in between scarring or fibrosis, people do not feel that they need an intervention. At the same time, there is a notion that the liver is very important compared to diabetes or obesity. For some of our patients, a new diagnosis of liver disease has provided them the opportunity to find new motivation to change their diet and lifestyle.



OVERVIEW

GERMANY

Population: 84.5 million (2023)

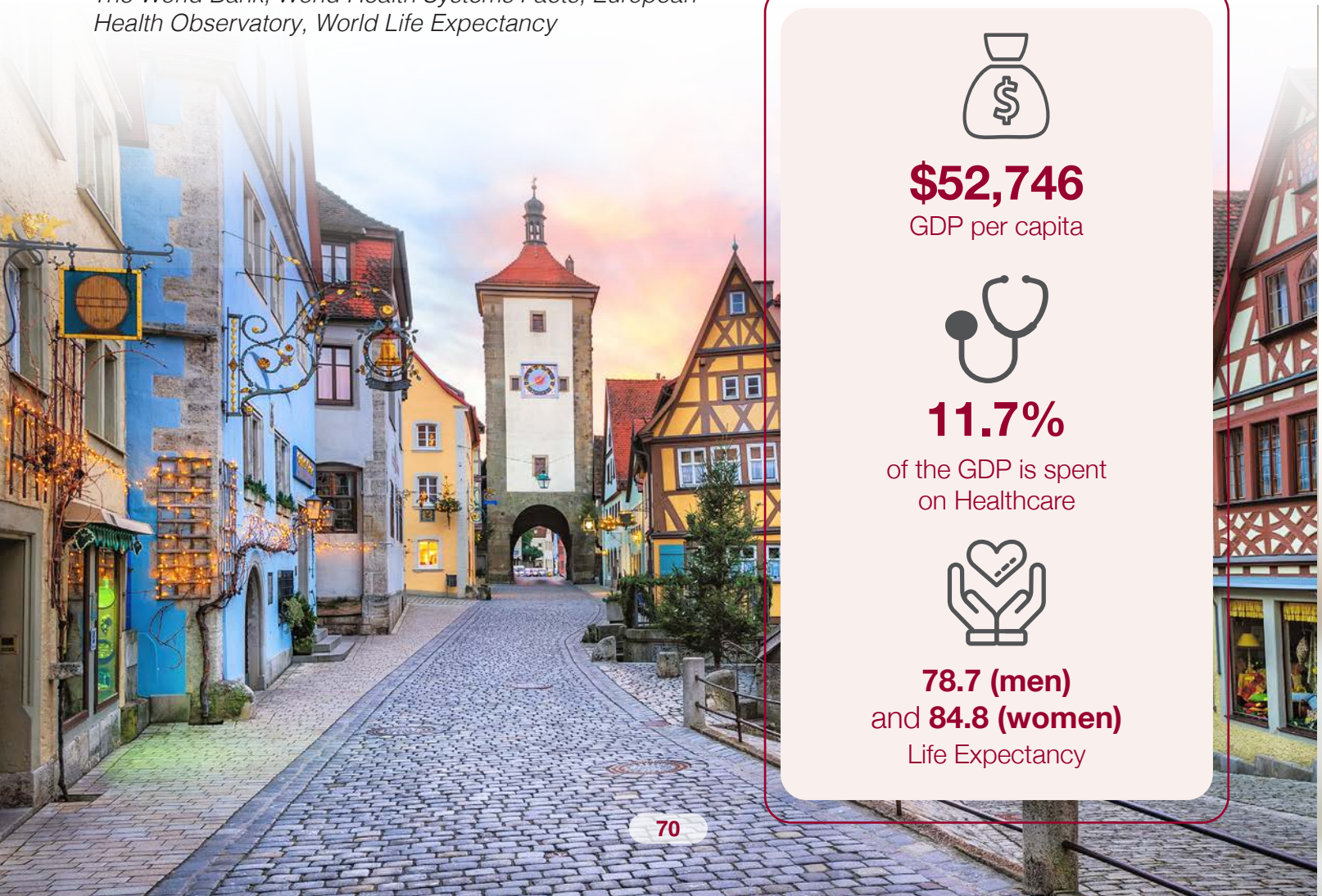
GDP per Capita: $52,746 USD

Life Expectancy: 78.3 years (men) and 83.2 years (women)

Healthcare Spending: 11.7% GDP

Healthcare Funding: Health insurance is mandatory in Germany – and it spends the highest proportion of its GDP on healthcare amongst the European Union. This is mostly managed by nongovernmental agencies called sickness funds, which are funded by general wage contributions as well as dedicated contributions from both employees and employers. All employed citizens and their dependents are covered under this statutory health insurance (SHI) system, which covers around 88% of the population. Above a specific income threshold, Germans can opt out of SHI in favor of private insurance.

Sources: The Commonwealth Fund, Worldometer, The World Bank, World Health Systems Facts, European Health Observatory, World Life Expectancy



$52,746
GDP per capita

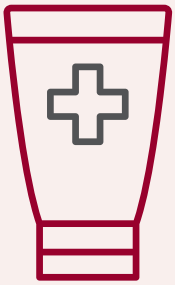
11.7%
of the GDP is spent on Healthcare

78.7 (men)
and **84.8 (women)**
Life Expectancy

Liver disease is prevalent in Germany as a source of both morbidity and mortality in the population. In many cases, lifestyle factors are linked to the greatest proportion of liver disease, with metabolic dysfunction-associated steatotic liver disease (MASLD) being the most common form of liver disease and misuse of alcohol linked to most cirrhosis cases.[1] Troublingly, liver cirrhosis has the highest rate of mortality of any condition that requires hospital admission in Germany – and when it is a diagnosed comorbidity with other diseases, the mortality rate doubles.[1] Per the WHO, liver disease accounted for 2.17% of total deaths in Germany in 2020, or the 15th leading cause of death.[2] Liver cancer itself ranks as the 25th leading cause of death in the country.[2] Between 2005 and 2018, nearly 1% of all hospital admissions in the country involved a liver cirrhosis diagnosis.[3] Liver disease clearly poses a significant burden to Germany.

MAFLD has rapidly become the most common form of liver disease in Germany following the trends of rising obesity and diabetes in the nation. Between 2005 and 2018, for instance, MAFLD prevalence among hospital admissions increased four times.[3] 18 million Germans have MAFLD, and 3 million of those people have the more advanced metabolic dysfunction-associated steatohepatitis, MASH.[4] These patients place an estimated burden of $4.3 billion in direct medical costs on the nation, though the figure increases tenfold when the total societal costs are considered.[5]

The epidemic of obesity in Germany is tied very closely to rising rates of fatty liver disease in the country. Among adults, 53.5% are overweight, and 19% are obese.[6] The prevalence of overweight and obesity is higher with greater age, in lower education groups, and in men compared with women.[6] Disease Management Programs are being developed for obesity to better prevent and treat the disease,



Hospitalizations due to alcohol-related liver disease are on the rise in Germany among younger patients.

Costs associated with NASH and NAFLD in Germany account for

$4.3 BILLION

in health spending

which should provide promise to those at risk of developing obesity as well as fatty liver disease in the future.[6]

Even though the impact of fatty liver disease is rising in Germany, alcohol consumption still plays a large role in the etiology of liver disease throughout the nation. Germans consume 13.4 liters of pure alcohol each year per capita, higher than the European region average and more than double the global average.[7] In light of this high volume of consumption, it is unsurprising that alcohol-related cirrhosis accounts for more than half of hospital admissions with cirrhosis – and this rate has been rising.[3] Notably, these patients are markedly younger than patients with other etiologies for their cirrhosis.[3] Population-level alcohol consumption measures are necessary to prevent a significant proportion of severe cases of liver disease and resulting hospitalization.

As a high-income country, Germany has been able to successfully deploy the prevention and treatment measures for viral hepatitis such that it is well-controlled throughout the nation. Prevalence of HBV is only 0.3% in the population, though this prevalence is greater in specific groups such as travelers, the immunocompromised, and those with occupational risk.[8] HAV has low rates on the global scale,[9] and for HCV infection, for instance, infection is more prevalent among those not of German descent.[10] Notably, 17% of the German population is estimated to have been infected with HEV, but the disease is severely underreported because

many cases are asymptomatic and resolve without becoming chronic.[11]

There is still ongoing work in Germany to prevent, treat, and control viral hepatitis. Twenty-five years after inclusion in the national immunization schedule, vaccine coverage for HBV is still well below the WHO target of 95%.[8] The HBV vaccine is still recommended for everyone under the age of 60, covered in entirety by SHI and most private plans, and many programs target increased vaccination among the following groups: pediatric/adolescent patients, immunocompromised people, and those with occupational exposures to viral hepatitis.[8] A drug to treat HDV is also currently under research and development.[12]

There is evidence that PBC, AIH, and PSC are all increasing by about 30% in the German population in recent years.[13, 14] Unfortunately, especially among older patients, under-treatment is common, treatment can be inaccessible, and increased understanding among providers and support in general for these patients is necessary.

End-stage liver disease, especially liver cancer, burdens the German people and healthcare system. In 2022, over 10,000 cases were estimated to have occurred, leading to more than 8,000 deaths.[15] Even though it is relatively rare, with only a 14% five-year survival rate for women and 18% for men, a diagnosis of liver cancer remains a severe diagnosis. At the same time, both noninvasive cancer treatment and surgical resection can cost thousands of euros, which is out of reach for many.[16] Ongoing research is being conducted in Germany to reduce the economic impact on both patients and the broader system of cancer, including liver cancers, in the region.[17]

Transplantation remains the most effective solution for liver failure and end-stage liver disease. Selection criteria to receive a liver transplant is based on urgency, following the Model for End-Stage Liver Disease (MELD). In 2015, there were 1500 patients on the waiting list for liver transplantation, with the leading causes being fibrosis, cirrhosis, and alcohol-associated liver disease; that same year, however, less than 900 transplants were carried out at the 23 centers due to a shortage of organs.[18] This imbalance between need and availability of donor livers underscores a need for increased organ donation, whether through a public campaign or changes in policy that might expand the number of suitable donors.

This imbalance between **need and availability of donor livers** underscores a needfor increased organ donation.

MISSED OPPORTUNITIES AND NEW CHANCES FOR LIVER HEALTH

Dr. Jörn Schattenberg is a renowned professor of medicine, Director of the Metabolic Liver Research Program at the University Medical Center Mainz, Germany. In addition to his research on acute and chronic liver injury with a focus on metabolic liver disease and NASH, he is part of the scientific steering committee of the United European Gastroenterologist (UEG) and the public health, policy, and advocacy committee of the European Association for the Study of the Liver (EASL).

Liver health is crucial to the well-being of a person, and liver disease moves slowly. This means that there are many opportunities we have to intervene: to identify disease, and use established, proven techniques to improve liver health, and through liver health, global health and overall well-being.

Unfortunately, in Germany as well as globally, we often miss those opportunities. So even though liver disease is usually slowly progressive, in my clinic I'll see a patient come in with liver cancer – or decompensation – and their quality of life is miserable. The whole family suffers. We could have done something over the course of 10 years leading up to that.

There are multiple layers to why this is the case.

1. **AWARENESS:** Patients, physicians, payers, and even regulators don't always give appropriate consideration to the impact liver health has on total well-being.

2. **FUNDING:** For clinicians to incorporate a liver exam into regular checkups, payers need to provide reimbursement – which means that we need to define which inexpensive tests are effective for which at-risk populations. I think those tests already do exist.

3. **STIGMA:** We need to move away from the blame game and the lie that liver disease is self-inflicted. It's no one's fault and no one's choice. One's environment, financial situation, genetic predisposition, or even geography can play a defining role – and if we focus on individual choices, we miss key opportunities for improvement.

In Germany, a standard clinical care pathway has been established for T2D and is currently being developed for obesity. Neither of these realize liver disease as significant morbidity leading to a loss in quality of life or years lived. The lack of a health research agenda around liver disease needs to be addressed in the face of a growing burden.

I think, when we talk about liver health, we should link it to environmental health and healthy living. If our planet becomes burdened and we see an environmental crisis, we will see a parallel healthcare crisis.

- For example, if you have a little bit less meat per week, you're cutting down on CO2 emission from livestock while balancing your diet.

- We have found in a recent study that if you have a park next to your apartment, you are more likely to go out and exercise versus when you are growing up next to a subway or a highway where there's no greenspace. You might not feel safe on the streets and never exercise.

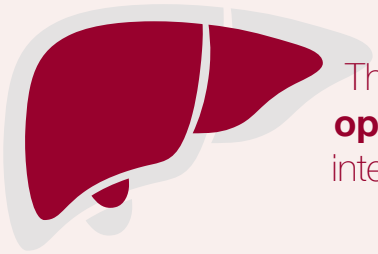
These are things that could even be implemented at a small scale, first. The mayor of a town could decide, "we want to provide a healthier living space to our people." They might close down a high-traffic street by a school, add trees and some public transportation there and soon people are playing and walking and shopping outside in their neighborhoods. The environmental crisis and the liver crisis are interrelated, but there are so many levels of well-being that stand to benefit.

BEST PRACTICES: PARTNERING WITH PRIMARY CARE AND ENDOCRINOLOGISTS

From Dr. Jörn Schattenberg

We have run small experiments with partners in primary care and endocrinology to develop best practices. The whole project relied on research funding, since there was no reimbursement for our efforts. However, we were able to provide our partners with a study nurse and equipment, and once we did that, people were intrigued. They would volunteer to be scanned using an ultrasound elastography device or have a blood test or filling out a questionnaire about the risk factors of liver disease. And we did find patients with early liver disease. I'm hopeful that through this intervention we will help them avoid deterioration and cirrhosis that otherwise might not have been detected.

> When we talk about liver health, **we should link it to environmental health and healthy living.** If our planet becomes burdened and we see an environmental crisis, we will see a parallel healthcare crisis.
>
> - DR. JÖRN SCHATTENBERG



There are **many opportunities** to intervene with liver disease.

Of course, it could be a burden to know their result early, which is the downside of screening. This is why it's essential to have the voice of the patients and make sure they have a choice. I think the right to choose is important.

For this model to work outside a study, we need reimbursement of liver testing for the payers. We are in the process of generating evidence to convince physicians and payers that these liver exams will save money in the long run and be medically useful.

OVERVIEW

ITALY

60 million
Population

Population: 60 million (2019)

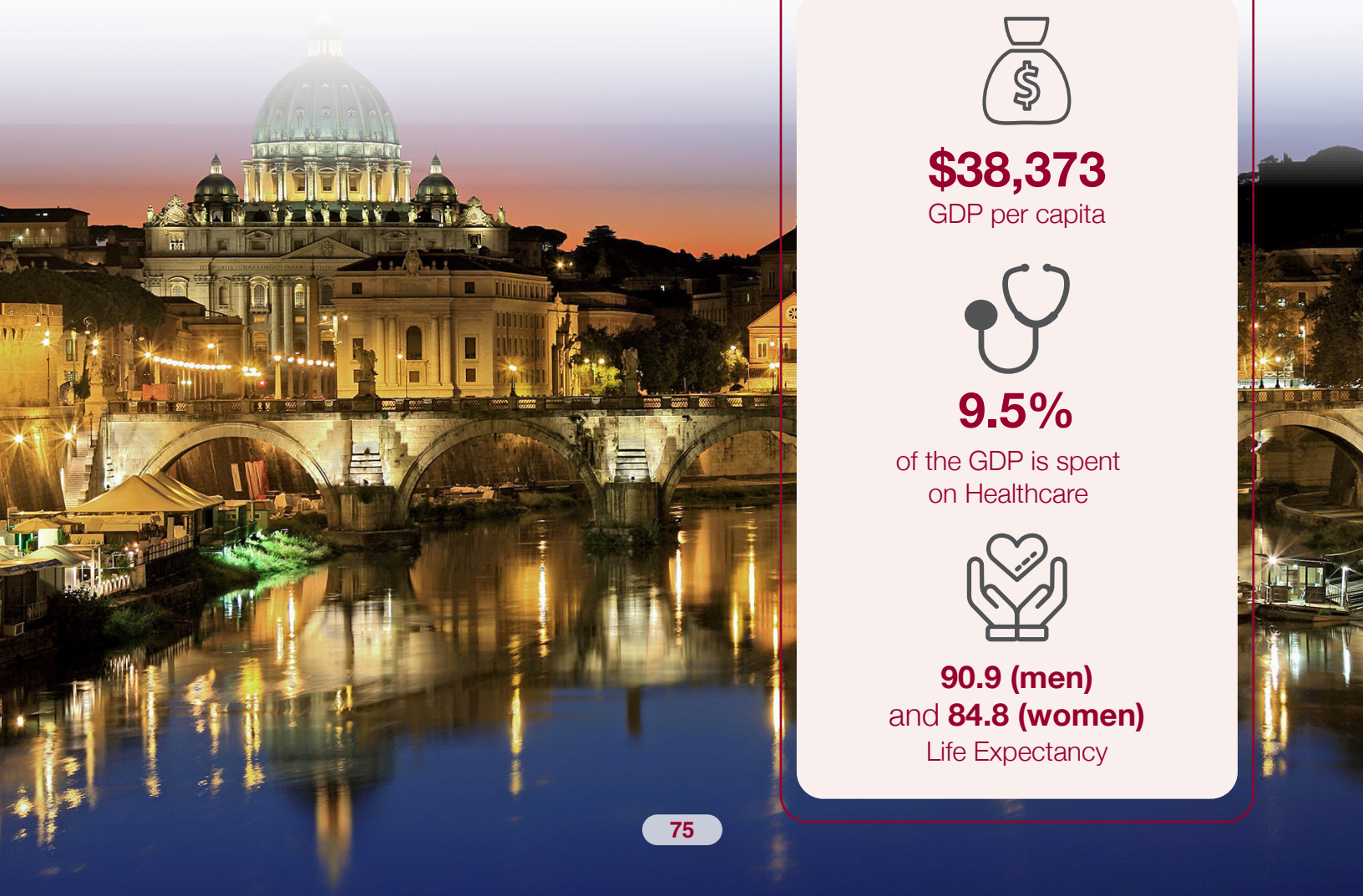
GDP per Capita: $38,373 USD

Life Expectancy: 80.9 years (men) and 85.0 years (women)

Healthcare Spending: 9.5% GDP

Healthcare Funding: Italy has a decentralized National Health Service (Sistema Sanitario Nazionale or SSN), in which each region organizes and delivers its own health services, funded through the central government's national benefits package and financial allocation. The SSN automatically covers all citizens and legal foreign residents. This leads to comprehensive care throughout the nation, though regional differences are apparent. About three-quarters of health expenditure in Italy is funded by public sources, while the remaining expenses come from household, out-of-pocket expenses.

Sources: Worldometers, World Bank, Statista, European Health Observatory



$38,373
GDP per capita

9.5%
of the GDP is spent on Healthcare

90.9 (men)
and **84.8 (women)**
Life Expectancy

The SSN automatically covers all citizens and legal foreign residents. This leads to comprehensive care throughout the nation, though regional differences are apparent.

As reflected by long life expectancies and other strong outcomes, Italy has a relatively robust and comprehensive healthcare system – and this is also true in liver health. Liver diseases in Italy claim about 2.77% of total deaths each year – which is better than more than 90% of countries, for liver disease.[1,2] Still, lifestyle factors in the country have adverse effects on livers and affect quality-of-life as well as place financial burdens on the broader system.

Studies in Italy show a prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) between 22.5 - 27%, or approximately the same as the global prevalence.[3] As in many other countries, obesity, metabolic syndrome, and especially diabetes have strong associations with MAFLD.[3] Italian studies have also linked MAFLD to an increased chance of dementia and cognitive decline – which will continue to be a problem as Italy's population ages.[4] The total direct cost for MAFLD to progress to advanced stage, including liver transplant and HCC, is an estimated € 65.000/ year.[3] As more and more Italians develop MAFLD, this cost will continue to rise.

Currently, 1 in 10 people is obese in Italy – less than the global average. However, more than 50% of men, and more than 33% of women and children are overweight.[5] Overweight rates are projected to continue to increase by at least 5% within ten years, and the rates are higher amongst those who are less educated.[5] As the prevalence of overweight and obesity continues to grow in Italy, so will the issue (and related expenses) of fatty liver disease.

Clinical practice guidelines for NAFLD in adults were released in Italy in 2021 as a joint project by the Italian Association for the Study of the Liver (AISF), the Italian Society of Diabetology (SID) and the Italian Society of Obesity (SIO).[3] This suggests that meaningful collaboration between related specialties is ongoing in Italy to stem the rising tide of metabolic conditions, including fatty liver disease.

Alcohol consumption also plays a leading role in liver disease in Italy. Men consume on average 12.5 liters of pure alcohol per person, per year, while women consume 3.5 liters.[6] A study done in 2016 of people ages 11 and older found that 65% had consumed at least one alcoholic drink in the year.[7] Approximately 1 in 5 individuals with chronic liver disease in Italy reports a risky level of alcohol intake – and of these, more than 40% have alcohol consumption as their only causal factor for liver disease.[8] Alcohol-associated liver disease is unsurprisingly more common in men, with a shift towards older age in both sexes as well as more advanced disease state.[8] In good news, the proportion of risky alcohol consumers has decreased in recent decades, a promising trend.

Italy has a relatively robust and comprehensive healthcare system – and this is **reflected in liver health.**

Italy has the **highest prevalence of HCV** in Europe

Despite its relatively high GDP, hepatitis remains an ongoing issue in Italy: It has, for instance, the highest prevalence of HCV in Europe (between 3 and 4.4%).[9] Rates as high as 26% have been reported in Southern regions and major islands.[9] HCV screening remains minimal on a national scale.

For HBV, a gradual reduction of both acute and chronic disease has occurred over the last 50 years.[10] In 1991, universal, compulsory vaccination of newborns and adolescents was implemented to stem the large number of carriers and resulting deaths due to the virus.[10] Unfortunately, one-third of healthcare resources for chronic HBV patients, especially those in the countryside, have devolved due to the COVID-19 pandemic, which threatens to disrupt the favorable trends thus far.[10]

Much of the existing and ongoing hepatitis prevalence in Italy is due to continuous migration from eastern Europe and sub-Saharan Africa, which means that even as the country works towards eradication, ongoing surveillance and vaccination efforts will remain vital to keep the virus contained.[10] This is reflected in the relative disappearance of HDV infections, with most new cases only from migrants in HDV-endemic areas.[11]

The features of rare, autoimmune liver diseases in Italy are not notable. AIH, PBC, and PSC are all incident, and the first two primarily affect women, while more men develop PSC in Italy.[12, 13, 14] Patients with these diseases will benefit as advances in treatment techniques and technologies become available.

In many cases, other liver disease progresses to end-stage liver disease in Italy, including HCC and other liver cancer. Italy has one of the highest incidences of liver cancer outside of Asia, although its survival figures are relatively strong, having reached a 30% five-year survival rate.[15] In recent years, the total incidence of HCC has decreased for both sexes, which reflects a trend in prevention; an opposite trend is shown through increasing intrahepatic cholangiocarcinoma (ICC) incidence rates.[15]

The major risk factors for HCC (approximately 80% of liver cancer cases) are HBV and HCV, which are both on the decline in Italy; other factors include aflatoxins, alcohol misuse, diabetes, obesity, and MAFLD.[15] Still, liver cancer due to HCV infection is as high as 50-60%, much higher than the global average of 19%.[16] Due to universal vaccination as well as a historical understanding of HCV spread and its correlation to downstream peaks in liver cancer incidence (first when syringes were reused and blood transfusions were common, and then again during a period of IV drug use in people born after WWII), this trend is expected to taper off.

The downtrend in HCC reflects decreasing prevalence of exposure to viral infections as well as improved surveillance and treatment of HBV and HCV patients. New chemotherapy, as well as multiple embolisation, ablation surgery, and liver transplantation have expanded the treatment options for Italians who develop liver cancer.[15]

Liver transplantation, both from living and deceased donors, is available in Italy for those with end-stage liver disease. Over the past 15 years, more than 1000 liver transplants have been conducted each year in Italy, with steady growth and more than 1400 transplants conducted in 2022.[17] The vast majority of these procedures are conducted from a deceased donor. Over the last decades, following disease patterns, patients on the liver transplant waitlist for cirrhosis decreased from over 60% to less than half, while those due to HCC increased from less than a third to nearly half.[18] Still, a substantial number of skilled transplant centers provide promise for those in Italy with end-stage liver disease.

Dr. Alessio Aghemo is the Hepatology Unit Director in Humanitas Research Hospital in Milan, Italy. In addition to clinical practice in liver disease, Dr. Aghemo conducts research in viral hepatitis and its natural history and treatment, metabolic hepatitis, and liver cirrhosis. He is a member of the AISF (Italian Association for the Study of the Liver) commission for antiviral drugs directed against HCV, a member of the scientific committee of the European Association of Gastroenterology (UEG) and a former scientific member of the governing board of the European Association for the Study of the Liver (EASL).

An Undefined Field with an Undefined Path

Hepatology is not a clinical specialty for physicians in Italy, so the people that cure liver diseases might be infectious disease specialists, gastroenterologists, internal medicine specialists, and sometimes diabetologists for NAFLD/NASH. It is a bit of a mess, which could translate into confusion and possibly negative effects for patients. They do not know where to go for liver problems. Even the general practitioner is sometimes confused on where to send the patient.

This means there is no standard diagnostic-therapeutic path for liver disease. There is no dedicated space for liver treatment, no dedicated agenda for surveillance of liver cancer in regular screenings, and no indication of who should be the first referral for someone with liver disease. A patient's pathway and care vary widely depending on who they visit first – and where in the country they seek care.

DID YOU KNOW?

Over the past 15 years more than **1,000 Liver Transplants** have been conducted **each year in Italy**

> **There is no dedicated space for liver treatment,** no dedicated agenda for surveillance of liver cancer in regular screenings, and no indication of who should be the first referral for someone with liver disease.
>
> - DR. ALESSIO AGHEMO

Prevention Is Key

This makes prevention and education key. A lot of this work begins with diet education in schools. All food provided at schools is centralized and follows strict rules in terms of calories, fat, and quality. The students receive training on nutrition, water consumption, recycling, and meat consumption. Of course, there is less training about alcohol, maybe at a high school level, but this is more challenging since alcohol (red wine) has powerful interests in Italy.

Generally, wine is perceived to be a healthy drink, and "moderate" quantities of wine, say one to two glasses at lunch and one to two glasses at dinner (which is not really moderate) is not even considered to be drinking. So that is a barrier to liver health in the country.

Trends In Liver Health

We have seen a huge change in etiology of liver diseases throughout my career. Italy was a country mainly affected by viral hepatitis C until the introduction of directly-acting antivirals. Now it is a country which is more affected by metabolic liver diseases – NAFLD, NASH. This is supported by data in the scientific literature, but it is also reflected in our practice as well.

This shift has also had a huge impact on liver cancer. Where we previously had huge numbers of patients with viral hepatitis who would go for regular screening every six months, we had early diagnosis of HCC. Now, when patients present with HCC, they more often have large masses and are symptomatic – and unlike hepatitis patients, they are less adherent to follow-up. So the type of liver cancer patients has changed, too.

POLAND

Population: 37,747,124 (2021)

GDP per Capita: $22,113 USD

Life Expectancy: 73.5 years (men) 81.3 years (women)

Healthcare Spending: 6.6% of GDP

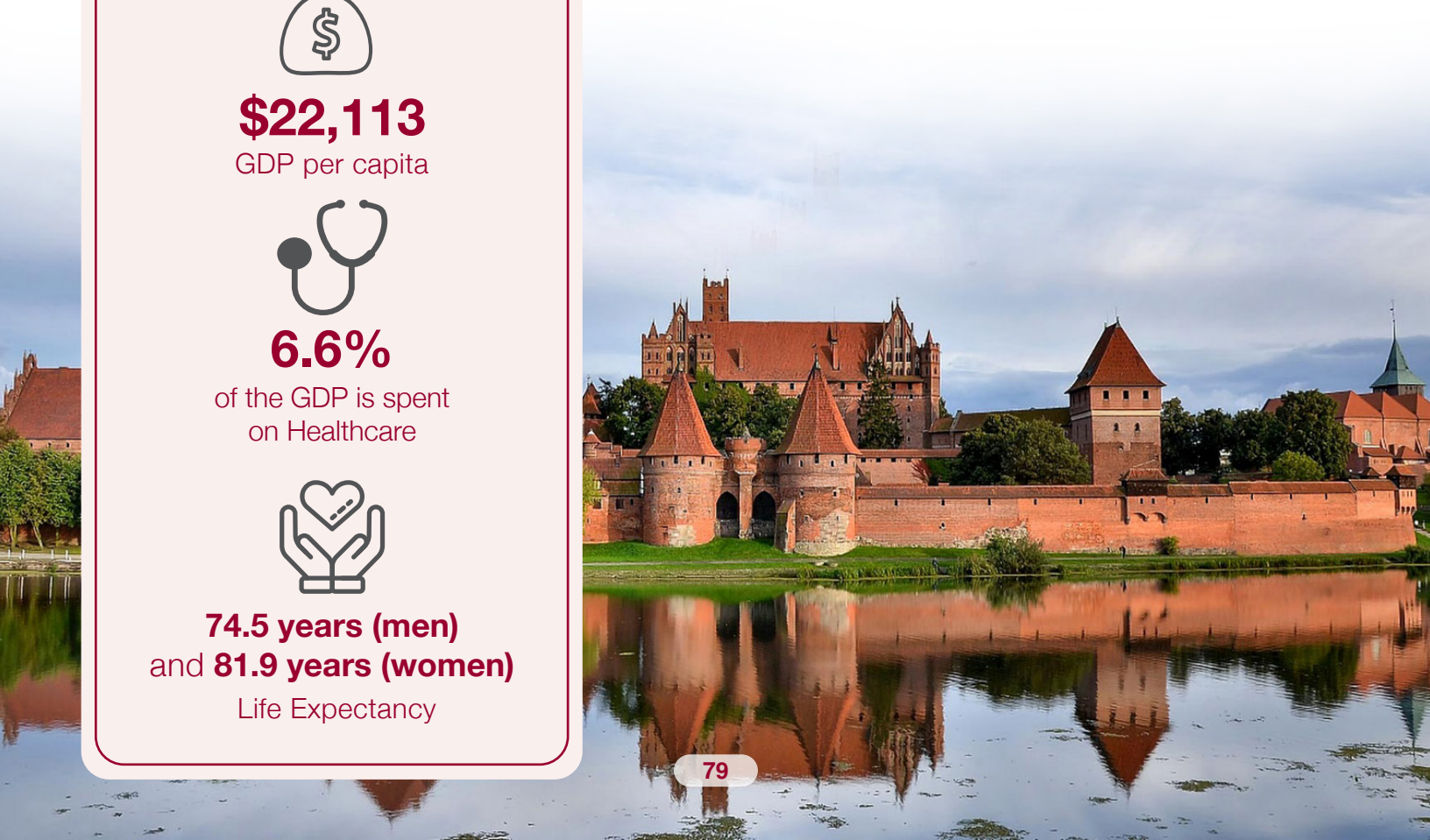
Healthcare Funding: Poland's healthcare system is decentralized and partially privatized. 72% of funding comes from tax revenue, with the other 28% from the private sector. Only 2.7% of healthcare spending focuses on public health and disease prevention, while cancer, cardiac disease, and mental health receive the bulk of the budget.

Sources: The World Bank, World Health Rankings, Macrotrends, World Health Organization, European Observatory on Health Systems and Policies

$22,113
GDP per capita

6.6%
of the GDP is spent on Healthcare

74.5 years (men)
and **81.9 years (women)**
Life Expectancy



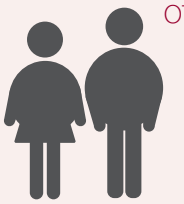
Like in many other European countries, liver disease is on the rise in Poland. Each year, about 8,000 deaths are attributed to liver disease in Poland, which accounts for 2.22% of total deaths – or, in other words, the ninth leading cause of death in the country.[1] While issues related to HIV, life expectancy, and infant mortality improve in the nation, there is adequate evidence that similar, appropriate prioritization is now necessary to address liver health. While the majority of its healthcare funding goes to cancer and cardiac diseases, liver disease is just as prevalent and can lead to cancer and other expensive complications.[2]

Each year, about **8,000** deaths are attributed to liver disease in Poland, which accounts for **2.22%** of total deaths – or, in other words

THE 9th LEADING CAUSE OF DEATH IN POLAND

The most prevalent form of liver disease in Poland is metabolic dysfunction-associated steatotic liver disease (MASLD), which comprises an estimated 59.7% of liver disease.[3] 68% of men and 53% of women are considered overweight, and a quarter of Poland's total population is considered obese. The outlook for future generations is not better: Child obesity is sharply increasing in Poland at one of the highest rates in all of Europe.[4] Though a lower proportion of women are obese, the rates vary widely depending on occupational status and parental status for women only, suggesting that further research is necessary to understand and address this variation.[5] Still, average BMI is on the rise in Poland, and rates of MAFLD and more advanced metabolic dysfunction-associated steatohepatitis (MASH) are expected to follow this pattern.

68% of men and **53% of women** are considered overweight, and a quarter of Poland's total population is



CONSIDERED OBESE

As alcohol consumption also increases, deaths due to related liver disease are drastically increasing. Alcohol consumption increased by nearly half, from 6.5 liters per capita each year to more than 10 liters.[6] From 2002-2017, the prevalence of liver disease from alcohol consumption increased from sevenfold in women.[6] For men, the rate tripled.[6] In the same manner, the absolute number of deaths from the effects of alcohol-related liver disease for those ages 20-64 have increased sevenfold for women and more than threefold for men since the turn of the century.[7] Changes in alcohol consumption are likely to have an immediate impact on decreasing mortality rates, which means that it is not too late for immediate, impactful action.

Between 2003 and 2017, **ALCOHOL CONSUMPTION** increased by nearly half.

Of the forms of viral hepatitis, hepatitis B is the most common form of viral hepatitis with almost 3,000 yearly cases in Poland – though the vast majority of cases are not active carriers.[7] Vaccines are available to protect against hepatitis A and B and are recommended for all travelers to Poland as well as residents of the country.[8] Hepatitis B vaccines are free of charge for infants and those at high risk of the disease, but should be offered free of charge to everyone in order to decrease liver disease and death incidence in Poland.[9] Polish public health

officials have set a vaccine schedule for HBV that includes immediate vaccination and two boosters in the first year of life.[10] Failure to adhere to vaccination requirements may jeopardize a child's ability to attend school, daycare, and other populated institutions.[11] Due to this comprehensive programming and disease management, viral hepatitis does not pose a large threat to liver health in the country. However, despite these improvements, viral hepatitis remains a leading cause of death by liver disease in Poland.[12]

There are a few autoimmune liver diseases predominant both in Poland and around the world. Polish patients with primary biliary cholangitis (PBC) have been studied closely and found to have a diminished quality of life as a result of the disease itself, lack of treatment, and lack of awareness. Female patients exhibited more severe cognitive effects compared to their male counterparts.[13] Each year, there are 300 new cases of autoimmune hepatitis (AIH).[14] Primary sclerosing cholangitis (PSC) is another similar liver disease in which the majority of cases are comorbid with ulcerative colitis, a disease for which 2-5% of those affected will develop PSC.[15]

Despite these improvements,

VIRAL HEPATITIS

remains a leading cause of death by liver disease in Poland.

Liver cancer only has a

one-year survival rate of 23%

and a

five-year survival rate of 7.9%

in Poland

Per WHO data, Poland, along with Western Europe, belongs to a group of nations with relatively low HCC incidence. Alcohol and obesity are identified as key risk factors, and prevention efforts should focus on decreasing alcohol consumption and promoting healthier lifestyles. Still, both incidence and mortality due to liver cancer in Poland seem to be slightly on the decline.[16] Liver cancer only has a one-year survival rate of 23% and a five-year survival rate of 7.9% in Poland.[16] With such a bleak outlook upon diagnosis, the prevention of liver cancer by addressing upstream factors like fatty liver disease and chronic hepatitis infection is critical.

Poland spent 2.3 billion euros on oncology in 2020,[17] of which a small amount could have been allocated towards the prevention and early diagnosis of liver cancer to mitigate its devastating impact. Each year, about 300 liver transplants from deceased donors are conducted in Poland, while only about 20 partial liver transplants are conducted from living donors. The five-year survival for those who receive a liver from a living donor is about 80%, and about 70% for those who receive a liver from a deceased donor. Both living and deceased donor liver transplantation have been transformative for liver health.

LACK OF WORKFORCE SPECIALIZATION, LIMITED INVESTMENT, AND LIFESTYLE HABITS HINDER LIVER HEALTH

Dr. Marek Hartleb is a gastroenterologist in Katowice, Poland. Dr. Hartleb is an active clinical researcher, involved in ongoing clinical trials, has published many hepatology papers, and serves as the president of the Polish Society of Gastroenterology, an affiliate of United European Gastroenterology (UEG).

While our spending on health in Poland has been slowly growing, GI concerns do not receive that attention. Oncology and cardiology are currently government priorities in Poland – with direction towards the overwhelming supremacy of oncology in a manner I think can be disproportionate.

A similar disregard for hepatology is reflected in the Polish healthcare workforce itself. Due to historical reasons in Poland, hepatology is a no man's land! Rather than a specialization, it is considered part of gastroenterology. However, many gastroenterologists focus more on endoscopy and bowel diseases, leaving liver care split between internists, surgeons, and infectious disease doctors, who took over much of liver care back when viral hepatitis was the major liver disease. Now that this is shifting, I anticipate that gastroenterology training should at some point be dichotomized to those focused on the gastrointestinal tract and those focused on liver diseases.

> Due to historical reasons in Poland, **hepatology is a no man's land!** Rather than a specialization,it is considered part of gastroenterology.
>
> DR. MAREK HARTLEB

The workforce issue extends beyond training, however. There is a large gap in collaboration between GPs and specialists. Patients want to be treated by specialists, and GPs are not motivated to keep them in their offices – even though many liver patients could be well managed in the primary care setting. That means that the wait time for a first visit with a specialist can be unreasonably long. Meanwhile, there is a massive exodus of gastroenterologists to the private sector, where work is less traumatic, requires less paperwork, and provides better pay.

There is also an ongoing quality issue. Financing of hospital gastroenterological departments is mostly based upon endoscopic procedures rather than their quality of consultation, clinical decision-making experience, or even scientific expertise. Gastroenterologists end up drifting into surgical medicine, while bureaucracy shifts attention away from patients towards computer monitors. At the same time, efficiency is lost and money is wasted from unnecessary examinations because doctors are not obligated to follow recommended standards. We need a strict application of standards and recommendations in management of gastroenterological disease.

At the same time, lifestyle patterns in Poland define the current landscape of liver disease prevalence, while features of our healthcare training and funding system impede the quality of care for patients. There has been a rise in the consumption of an unhealthy diet and sugary drinks – in many cases, for economical reasons. Unfortunately as a result, we are seeing a rise in metabolic syndrome, BMI, obesity, and type 2 diabetes. With the rise of these risk factors, it makes sense that in Poland, NAFLD is the most common chronic liver disease. Luckily, awareness of it is growing among general practitioners, diabetologists, and cardiologists. Over the years I have been practicing, there are now more treatment options. I have a lot more courage, now than before, in using antidiabetic, antihypertensive, and hypolipidemic drugs. So there are many more possibilities to influence a patient's metabolism.

Additionally, alcohol consumption is a real problem in Poland. While cigarette smoking is disappearing, the fight against alcohol will be much, much more difficult. While we know that alcohol is dangerous from a hepatology point of view, it is also associated with many cancers. This is especially true for women, who tend to be more predisposed to alcohol toxicity. From my perspective, alcohol-associated liver disease is probably the primary cause of liver-

related mortality in Poland, rates are increasing, and from the perspective of the transplant centers, alcohol-associated cirrhosis and hepatocellular cancer are becoming the leading indications for liver transplantation.

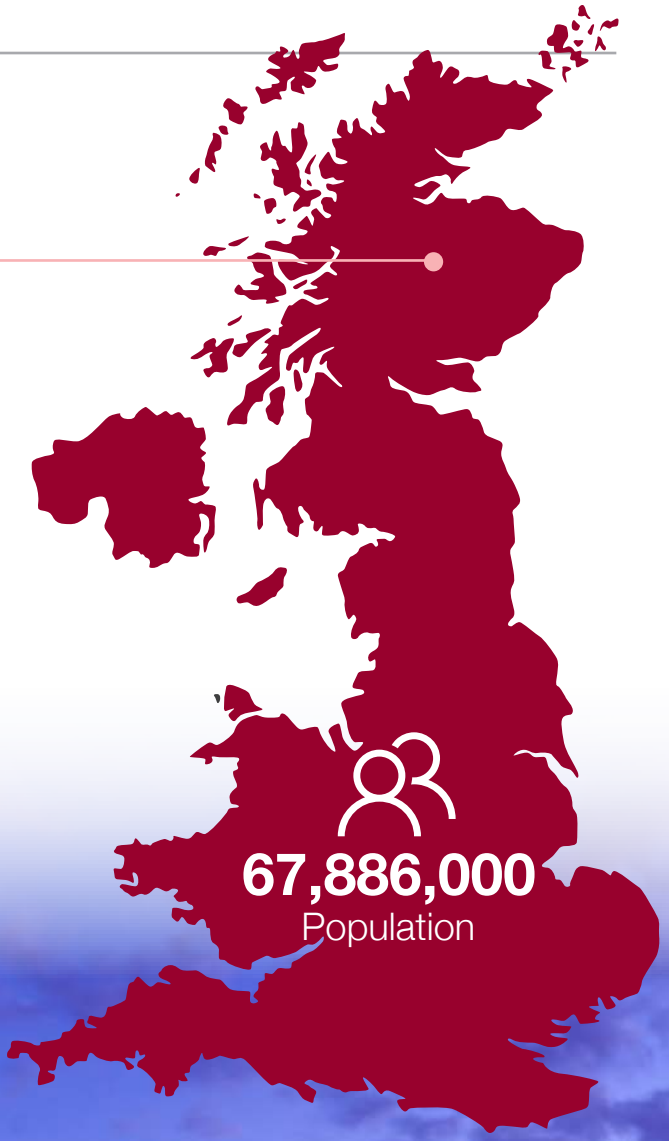
We can also track the success in viral hepatitis from the perspective of the transplant centers. Liver transplantation due to hepatitis C is clearly declining, while those due to alcohol-associated liver disease as well as NAFLD are increasing. At this point, neither acute hepatitis B nor acute hepatitis C are big problems in Poland, since there are few active carriers. With the current tests available, viral hepatitis is straightforward to diagnose and treat, but we are still awaiting efficient screening programs that search for HCV-infected individuals.

HCC, on the other hand, tends to have a low survival rate. Under-diagnosis of early stages of this tumor seems to stem from low adherence to clinical alcohol surveillance programs. It is largely under-treated in Poland because there is low availability and geographic scattering of the centers that can perform advanced therapeutic procedures like ablation and chemoembolization, important for treatment of advanced HCC.

It is interesting, but there is not a direct correlation between the actual prevalence of liver diseases and their economical burden with financial support for these diseases in Poland. As I've noticed in my involvement with UEG, ulcerative colitis and Crohn's disease, for example, have had significantly improved access to and quality of treatments in recent years in large part due to pressure from patient-led organizations. In part since Poland has a dearth of patient-led organizations, liver diseases remain scientifically and financially neglected.

OVERVIEW

UNITED KINGDOM



Population: 67,886,000 (2022)

GDP per Capita: $48,867 USD

Life Expectancy: 80.4 years (men)
83.8 years (women)

Healthcare Spending: 11.9% GDP

Healthcare Funding: Funded through general taxation and National Insurance contributions. Patients, with some exceptions, contribute via prescriptions costs and dental treatment. Private health insurance schemes are available, and most private hospitals accept a mix of private and the National Health System (NHS)-funded patients.

Source: World Bank

$48,867
Average Income
Per Household

79 years (men)
and **82.9 years (women)**
Life Expectancy

11.9%
of the GDP is spent
on Healthcare

Since 1970, deaths due to liver disease in the UK have increased by 400%–almost fivefold.[1] Overall, it is estimated that 600,000 people in the UK are living with serious liver disease. Liver disease itself is set to overtake CVD as a main cause of premature death in the UK.[1]

However, some areas of liver disease are better served statistically than others. Data are readily available on the prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) and prevalence of metabolic dysfunction-associated steatohepatitis (MASH) are generally estimates. With the rapid increase in obesity seen in recent years, these figures are generally accepted to represent a significant underestimation of the real statistical picture around MAFLD and the danger this represents.

Indeed, one in four adults in the UK are now classified as obese,[2] with adult obesity rates the sixth highest in the OECD (26.9% compared to an OECD average of 19.4%).[3]

The overall costs of MAFLD and MASH in the UK was estimated in 2016, as £5.24 billion of economic ('direct') costs and £26.03 of billion well-being ('societal') costs. MAFLD is set to overtake alcohol as the main cause of liver disease in the next few years.[4]

However, the UK government, similar to many developed countries, has continued to focus efforts and budgets on raising awareness of the link between obesity and type 2 diabetes (T2D) rather than obesity and MAFLD.

As a result, there is a real lack of awareness of the condition including the causes, comorbidities, and the consequences of the condition. Worryingly, this poor awareness is not just seen in the general public, who have a one in five risk of MAFLD, but also in high-risk groups such as patients with T2D who have a prevalence of MAFLD of around 70% (see page 64 for Pilot Study).[5]

180,000
PEOPLE

are living with chronic hepatitis B

Along with MAFLD, alcoholic-associated liver disease (ALD) accounts for much of the rise in the rates of liver disease in the UK, with the number of hospital admissions due to ALD increasing by 57% since 1970. In the last 15 years alone, admissions have nearly doubled, from 13,201 in 2004 to 24,544 in 2020/21.[6] According to the British Liver Trust, alcohol consumption is now the most common cause of liver disease in the UK, accounting for 60% of all liver disease cases.

However, although awareness levels of the risks of alcohol abuse have risen, alcohol consumption shows little sign of reducing, and the incidence of alcoholic-associated liver disease continues to rise.

Viral hepatitis is contained and well-managed in the UK with well-established and effective national strategies for prevention and control. The HBV vaccination program is available for all new-born babies as well as high risk adults. Vaccination against hepatitis A virus not usually offered as the rates are so low. Hepatitis E virus are low, with around 1,200 registered infections in 2019.[7]

Around 180,000 people are living with chronic HBV infection in the UK and 95% of new infections are now found in individuals who were infected overseas, including during early childhood.[8] The number of people living with chronic HCV infection in

England has fallen by 37% since 2015, to 81,000 in 2020.[9] Hepatitis D is rare in the UK.

The incidence of liver cancer is rising exponentially in the UK. Between 1993-1995 and 2016 and 2018, liver cancer increased by 141% in females and 171% in males.[10] Rates are still climbing and expected to continue to do so, driven by alcohol consumption and obesity.

Each year, around 6,000 cases of primary liver cancer are now diagnosed in the UK, making a once relatively rare cancer the 8th most common cancer. Outcomes are poor, with 40% of males and 36% of females surviving for one year after diagnosis, though five-year survival rates are 13%. There are 5,800 deaths each year.[10]

The UK spends less than almost any other western European country on cancer (and nearly half the amount of Austria, the top spending country).[11] This relatively low level of investment impacts on diagnostic services and medicines and, ultimately, on UK survival rates, which are lower than those in other similarly wealthy countries.

Autoimmune liver diseases are classed as rare and have, up until recently, been under-diagnosed and under-resourced. There are now guidelines for primary biliary cholangitis (PBC), (which is thought to affect around 20,000 people in the UK), autoimmune hepatitis (AIH) (10,000) and primary sclerosing cholangitis (PSC) (less than 1,000). However, some patient groups argue that these guidelines are not always followed, and good treatment can be sporadic and location-dependent.[12]

Each year, around

6,000

CASES

of liver cancer are diagnosed in the UK

Alcohol Consumption

is now the most common cause of liver disease in the UK

PILOT STUDY IN AN OUTPATIENT DIABETES CARE SETTING

A recent pilot study, led by Professor Saima Ajaz, carried out by Kings College Hospital London at an outpatient Diabetes Care Center in South London, set out to evaluate the awareness of NAFLD knowledge, the prevalence of it, and the prevalence of advanced fibrosis in patients with T2D who regularly attend a secondary diabetes clinic.

The pilot study used the Fibroscan method to examine the livers of 90 T2D patients and questioned them about their awareness of NAFLD/NASH.

In total, 85.6% (87) patients were unaware of NAFLD/NASH. Of the 87 valid scans, 56.3% of patients had steatosis and 27.6% already had advanced fibrosis, which required referral to a specialist liver center. The authors of the pilot study concluded that this group of high-risk patients were 'mostly unaware of this silent epidemic' and called for 'better screening of patients who are already in our healthcare system due to other pre-existing conditions.'

NAFLD, NASH AND ALD: A LOOMING CRISIS IN UK HEALTH

Dr. Saima Ajaz is a gastroenterologist at Kings College Hospital and Honorary Senior Clinical Lecturer at the School of Immunology and Microbial Sciences, Kings College London. She runs clinics for patients with NASH.

In the UK millions of pounds have been poured into raising awareness of T2D and CVD, yet the same has somehow not happened with NASH and NAFLD. As a result, we have a huge lack of awareness of these conditions and crucially, the link with obesity. This is not just true of the general public: A recent informal survey carried out at our hospital found that only 20% of hospital staff were aware of what NASH was, and, if indicative of clinicians as a whole, we can see that there is definite need for more education on these diseases.

Further, we are clearly underdiagnosing NAFLD and NASH, even in high risk populations as demonstrated by our recent pilot study. Additionally, we do not have an effective screening program. Even our high-risk populations, such as those with diagnosed T2D and metabolic syndrome are not being regularly screened, while others at risk populations – for example the overweight and obese – are extremely unlikely to be offered any liver screening until and unless they are admitted to secondary care. Finally, we have no established patient treatment pathways between primary and secondary care and, as a result, the specialists often don't see patients until the disease is quite advanced.

> Here in the UK **millions of pounds have been poured into raising awareness of T2D and CVD,** yet the same has somehow not happened with NASH and NAFLD.
>
> DR. SAIMA AJAZ

However, it is important to point out that preventing liver disease is only partially a clinical issue. In general, and as a society, we are not dealing well with obesity. It is still something we do not like to talk about or address, often the obese person and their family will be in denial. There is little education at school level and clinical advice usually consists of telling the patient to lose weight and come back when they have. That is not an effective way to see change.

In my experience, no one wants to be overweight, most people at least try to lose weight, but it can be a very difficult thing to do for a variety of reasons. It can be down to economic issues, or the person may be immobile and unable to exercise, and depression, or loneliness or stress can all lead to overeating.

Likewise, as a society we tend to look on alcoholic-associated liver disease as being the 'fault of the patient' rather than a manifestation of economic or mental health or life issues. This stigma discourages people from asking for help, or seeing their doctor, or attending alcohol support clinics. As a result sadly, we often onwly see patients with ALD when the disease is far advanced and much harder to treat.

AN EIGHT-POINT PLAN FOR AVERTING A DISASTER IN LIVER DISEASE

#1 FUND A ROBUST COST BENEFIT TRIAL

#2 RAISE AWARENESS OF NAFLD AND NASH

#3 TACKLE THE OBESITY CRISIS

#4 ESTABLISH AND RESOURCE AN EFFECTIVE DIAGNOSTIC SCREENING SYSTEM

#5 HARNESS NEW TECHNOLOGY

#6 REMOVE THE STIGMA OF ALCOHOL-ASSOCIATED LIVER DISEASE

#7 ENCOURAGE POINT-OF-CARE TESTING

#8 CREATE A CLEAR PATIENT PATHWAY FOR ALL HIGH-RISK PATIENTS

LATIN AMERICA

Many countries in the region can point to a **high quality healthcare.**

HEALTH OVERVIEW

Stretching from Cape Horn in the south to the Mexican US border in the north, and encompassing South America, Central America and the Caribbean, Latin America covers just over 19 million square kilometers – almost 13% of the Earth's landmass – and is home to nearly 650 million people.

According to a report by the United Nations, Latin America has some of the starkest inequity in the world, with GDP per capita in 2023 ranging from $17,093 USD (Chile) and $22,565USD (Uruguay) to under $7,000 USD (Bolivia, Ecuador and Paraguay).

This disparity is reflected in healthcare spending. In 2019, Uruguay allocated $1660.95 USD per capita to health, nearly seven times that of Bolivia, at $245.92 USD per capita.

The majority of Latin American countries provide some form of free state-sponsored healthcare. However, vast differences between the health funding systems from country to country results in wide variation in accessibility. Many countries require some level of patient financial contribution at point of care. According to a 2015 joint Pan American Health Organization/World Health Organization (PANO/WHO) report, approximately 30% of the population in Latin America and the Caribbean lack access to healthcare for economic reasons. In addition to this, the report found that 21% of the population do not seek care because of geographical barriers.

However, many countries in the region can point to a high quality healthcare network for those that can access it. Brazil, for example, boasts 6,642 hospitals (1 for every 32,000 people). Chile, which has over double the GDP per capita of Brazil has just 322 (1 for every 60,512 people).

Sources: TheGlobalEconomy.com, Pan American Health Organization, United States of America International Trade Administration, Statista

Despite limitations in available data on liver health, it is clear that one of the primary challenges to liver health in Latin America is obesity (as an etiology of metabolic dysfunction-associated steatotic liver disease, or MASLD).[1]

The 2022 Report 'Liver Diseases in Latin America: Current Status, Unmet Needs, and Opportunities for Improvement' notes:

'The high prevalence of liver diseases in Latin America is influenced by genetic factors, the elevated prevalence of obesity and metabolic syndrome, and environmental factors such as diet, low exercise and excessive alcohol intake.'[2]

Latin America is experiencing some of the highest obesity rates in the world, alongside the fastest growing rate of T2D.[3] In Mexico and Bolivia for example, 32.2% of adults (nearly one in three) are classed as obese, and a 2017 meta-analysis of 19 Latin America countries found that only five of the named countries could manage rates of obesity below 20%.[4] Given regional and global trends, it is likely that figures have increased since then.

The average prevalence of MAFLD in the general population is now estimated to be around 24%, though in high-risk groups, such as the obese and those with T2D, this figure soars to around 68%.[5]

However, despite the prevalence of MAFLD and the danger it represents to the liver health of Latin America, there are no prevalence figures for metabolic dysfunction-associated steatohepatitis (MASH) and no formal screening programs for high-risk groups.

Viral hepatitis continues to be a significant burden on liver health in Latin America. According to figures from WHO/PANO Mortality Information System 2008 and 2010, 10% of all deaths in Latin American countries were due to the effects of viral hepatitis.[6]

A 2021 report noted that less than half of Latin American countries collect data on the prevalence of HCV, and several have no national viral hepatitis program to provide estimates of the HCV disease burden.[7]

Figures from 2010 estimated that approximately 7.8 million (2010) persons were infected with HCV in Latin America.[8] Despite this high burden, rates of diagnosis of HCV range widely from 56% (Mexico) to 3% (El Salvador).[9]

HBV antibody prevalence among 12,000 people in 6 countries

21.4%	Dominican Republic
7.9%	Brazil
3.2%	Venezuela
2.1%	Argentina
1.4%	Mexico
0.6%	Chile[10]

Figures from an investigation into the prevalence of HBV antibodies in over 12,000 subjects in six countries found:

Additionally, in 2018 there were an estimated 38,400 cases of liver cancer in Latin America and 38,000 deaths with the highest rates seen in Honduras, Costa Rica and Cuba (1.4-1.9 per 1000,00) and Chile (1.00-1.39 per 100,000).[2]

The main cause of liver cancer in the region is still viral hepatitis, followed by alcohol consumption, although it is thought that MAFLD may soon become a predominant risk factor for the cancer.[11] Many studies refer to the challenge of late-stage diagnosis in liver cancer in Latin America, exacerbated by geographical distances and economic inequalities.[12]

Latin America has high alcohol per capita consumption, with those aged over 15 years drinking 6.8 liters of pure alcohol per year compared to the global average consumption (6.4 liters per capita).[13] Thus, excessive alcohol consumption is the leading cause of cirrhosis in Argentina, Brazil, Chile, Mexico and Peru with around 53% of cirrhosis attributable to alcohol.[2]

Despite the disparity in healthcare, Latin America also boasts a large number of tertiary hospitals with high levels of equipment and expertise. More than 2,500 liver transplantations are performed yearly – equating to 17% of global liver transplants.[14]

ARGENTINA

Population: 47,327,407 (08/2022)

GDP per Capita: $13,731 USD

Life Expectancy: 73.5 years (men) and 80.12 years (women) (2020)

Healthcare Spending: 9% GDP

Healthcare Funding: A mix of social security/union-run health insurance system, which covers 50% of the population, private medical insurance (Prepagas) (10%), and PAMI, a system which covers the elderly and disabled. Public hospitals are the responsibility of each province's Ministry of Health, and around 35% of the population relies on this free care.

Sources: United States of America International Trade Administration, SAHE

$10,729.20
GDP per capita

9%
of the GDP is spent on Healthcare

73.5 years (men)
and **80.12 years (women)**

In 2019, it is estimated that 15-20 people per 100,000 died of cirrhosis in Argentina.[1]

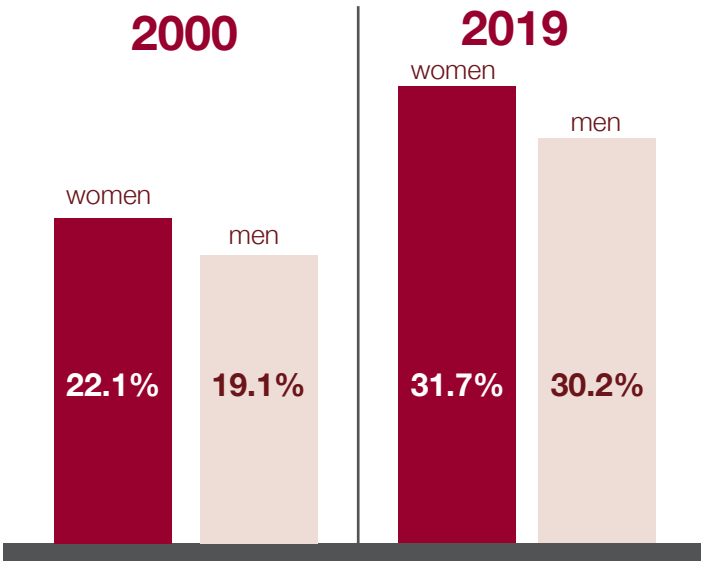
As in many Latin American countries, the most robust data for liver disease is related to viral hepatitis. It is estimated that 400,000 people in Argentina live with chronic HCV infection.[2]

A estimated that 326,000 people live with HCV infection, 9% of whom were diagnosed in 2019.[3]

Despite the decrease in incidence, hepatitis continues to take a toll on liver health. Of the 4650 liver transplants carried out in between 2006 and 2019,16.4% of them due to hepatitis.[4]

However, Argentina has been at the forefront of attempts in Latin America to reduce the rates of hepatitis. For example, following an outbreak of hepatitis A between 2003 and 2004, Argentina became the first country in the region to introduce a single-dose vaccine against hepatitis A in 1-year old children, resulting in a dramatic reduction in the virus. Today, there is an effective HBV vaccination strategy for babies, while clinics throughout the country provide free testing on demand for HBV and HCV.

The data on obesity demonstrate that rates are rising fast in Argentina. The Global Nutrition Report reports that in 2000,19.1% of males and 22.1% of females were classified as obese in Argentina. By 2019, those figures had risen to 30.2% and 31.7% of females.[5]



Classified as **obese** in Argentina

In 2019, it is estimated that

15-20

people per 100,000 **died of cirrhosis** in Argentina.[88,90]

As a result, there is increasing concern about the rates of metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction-associated steatohepatitis (MASH). Obesity is classed as high risk for MASLD, and studies across Latin America have put the rate of MASLD in high-risk for NAFLD, and studies across Latin America have put the rate of NAFLD in high risk populations at around 68%.[6]

The ongoing prevalence of early stage liver disease leads to many patients who develop liver cancer. A study of liver cancer found that although 37% of all cases of liver cancer was caused by HCV, ALD was the cause of 20.8% of cases and MAFLD was 11.4%.[7] Crucially, there was a sixfold increase in the percentage of MAFLD as a cause of liver cancer between the years of 2009 and 2016. Given that obesity rates have risen dramatically since the close of this study, it can be hypothesized that this percentage has increased commensurately.[7]

Non-complex CLD, for example, early stage hepatitis or MAFLD, is managed in primary care or clinic settings within the 22 provinces. Scans and diagnostics are carried out at secondary care hospitals, where treatments such as chemoembolization, radioembolization and hepatobiliary surgery, are also offered.

Complex care needs, including end-stage liver disease, liver cancer and liver transplant are referred to tertiary centers usually situated in the large cities such as Buenos Aires. There are 35 centers, albeit many based in the large cities, with the expertise to carry out liver transplantation in Argentina. In 2021, despite the burden placed on the health system by the COVID-19 pandemic, 377 liver transplants were performed, although there are currently 1523 patients waiting for transplants.[8]

BRAZIL

Population: 215,347,203 (2022)

GDP per Capita: $10,044 USD (2022)

Life Expectancy: 70.3 years (men) and 76.6 years (women) (2021)

Healthcare Spending: 10.5% GDP (2019)

Healthcare Funding: The Sistema Unico de Saude, or SUS (Unified Health System) is funded through general taxation and provides free access to primary, secondary and tertiary care, including medications, to all Brazilians. The private sector is accessed via pay as you go or insurance schemes.

Sources: Organization for Economic Co-operation and Development (OECD), 2020 Epidemiological Bulletin: Health Surveillance Secretariat of the Ministry of Health, Brazil Epidemiological Bulletins Ministry of Health

$10,044
GDP per capita

10.5%
of the GDP is spent on Healthcare

73.3 years (men)
and **80.3 years (women)**
Life Expectancy

In 2019, it is estimated that **15-20 people** per 100,000 **died of cirrhosis** in Brazil. [1,2]

In 2019, it is estimated that 15-20 people per 100,000 died of cirrhosis in Brazil.[1, 2] As with the other countries featured in this chapter, research and data on liver disease are disproportionately focused on viral hepatitis, which, in Brazil, is still the main etiology for deaths from liver disease.

In 2019, Brazil had

37,771

NEW CASES OF VIRAL HEPATITIS

2%	Cases of Hepatitis A
37%	Cases of HBV
60%	Cases of HCV
0.4%	Cases of Hepatitis D[3]

According to a 2021 report, there are currently 1,787,000 people living with HCV, equating to 0.9% of the population, of whom 8% were newly diagnosed in 2019.[71] There are up-to-date clinical guidelines on HCV, a universal screening program, a national registry and government financial assistance for treatment therapies.[4]

From 1999 to 2020, there were 254,389 confirmed cases of HBV in Brazil.[5] A 2016 modeling study found that the prevalence rate of HBV infection was 0.6%, of which only 28% of infected individuals were diagnosed and only 12% of the population was treated.[6]

HBV particularly affects people living in poverty and, although a relatively wealthy country within the Latin American region, remote areas of Brazil are some of the most deprived in the region. A study from the favelas in Goiás State, Central-West Region of Brazil, for instance, found that the prevalence rate of HBV exposure was more than ten times the national rate.[6]

Similar to other Latin American countries, obesity rates are soaring. Between 1990 and 2017, the prevalence of obesity increased by 244.1%, and 165.7% for men and wo men, respectively.[7] However, there are no registered figures on metabolic dysfunction-associated steatotic liver disease (MASLD), though prevalence is estimated to be about 38%.[1]

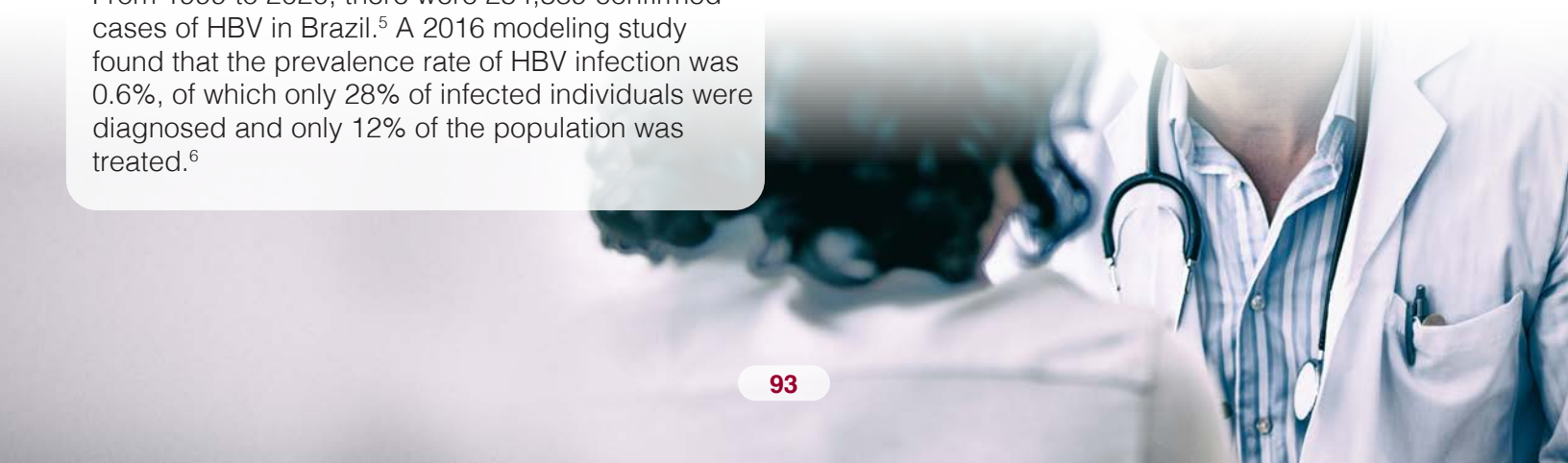
Brazilians drink around 7.5 liters of alcohol per year per person, which is on a par with their neighbors. When adjusted to those who actually drink alcohol, the amount rose to 19.2 liters per year. Alcohol-associated liver disease is one of the main causes of cirrhosis in Brazil.[8]

According to DATASUS, only 11% of cases of liver cancer were diagnosed at an early stage. 67% of diagnoses could only receive palliative care.[9]

Nonetheless, Brazil is a key center of expertise for liver transplant needs from across Latin America, and now carries out the second highest number of liver transplants in the world.[9]

2,033

Liver Transplants were performed in 2021.



AN URGENT NEED FOR EDUCATION, DATA AND DIAGNOSTICS

Dr. Bianca Della-Guardia and Dr. Marcio Dias de Almeida are hepatologists based at the Albert Einstein Hospital, San Paulo, Brazil. They specialize in liver transplantation.

The prevalence of NAFLD and NASH is growing fast in Brazil as in all countries, but while we have some individual pieces of research from universities or hospitals, there is no significant national data. All we can do is estimate the size of the problem.

All hepatologists are now regularly seeing patients with advanced cirrhosis because of NASH, and we think it could soon become one of the main reasons for liver transplant in the next decade. NASH is also impacting our liver cancer rates, which are rising fast.

Our government has put some effort into raising awareness of diabetes, which affects 12% of the population, and trying to tackle childhood obesity; but we really need to do the same and more for NASH and NAFLD. If we carry on as we are, and with the obesity rates we have, we are heading for a public health crisis in Brazil and very soon.

We believe that the government should prioritize health education, including funding a properly targeted national awareness program about NASH, NAFLD and liver disease. Secondly, we are in need of accurate and current data. We need a government-funded and supported research project to establish the extent of liver disease across Brazil. Once we know the extent of the challenge, we can show that we need action fast and can start to put focussed health policies into place.

Our viral hepatitis rates are high compared to other South American countries, particularly in the remote areas and away from the cities. This is partly because Brazil came too late to tackle this disease, but also because there has been a big national effort recently to raise awareness of hepatitis and to screen and diagnose hepatitis, so we are finding previously unrecorded cases.

Now, real efforts are being made by both the government and the World Health Organization to reduce the rates of viral hepatitis. In addition to awareness programs, there is a vaccination program for new-borns and infants, and anyone can walk into a clinic and have a free blood test for hepatitis. The problem, of course, is that in remote areas, where it can take a few days to get to a clinic, people may not go for a test until they feel ill – by which time the liver disease is much harder to manage. In an attempt to solve this problem, we are having conversations about self-testing, particularly in remote areas.

We believe that the government should prioritize health education, including funding a properly targeted national awareness program about NASH, NAFLD and liver disease. Secondly, we are very short of good quality data. We need a government-funded and supported research project to establish precisely the extent of liver disease across Brazil, especially NAFLD and NASH. Once we know the extent of the challenge, we can show that we need action fast and can start to put focussed health policies into place.

Finally, we need more diagnostic resources so that when we get more people coming forward, we can scan them within weeks, not months, to begin treatment as soon as possible.

> If we carry on as we are, and with the obesity rates we have, **we are heading for a public health crisis in Brazil and very soon.**
>
> DR. BIANCA DELLA-GUARDIA AND DR. MARCIO DIAS

OVERVIEW

COLOMBIA

Population: 52.3 million (2023)

GDP per capita: $6,960 USD (2023)

Life Expectancy: 71.6 years (men) 77.6 years (women)

Healthcare Spending: 6.55% GDP (2021)

Healthcare Funding: Colombia's healthcare operates under the General Social Security Health System, which provides universal health coverage through a mix of public and private funding, supported by payroll contributions and taxes. This system, managed by certified health insurers (EPS), offers services like medical care, maternity support, and basic dental coverage for all citizens and legal residents. Out-of-pocket costs for patients are low, with only 13.67% of healthcare spending coming from individuals in 2021. However, the system faces financial challenges; around 80% of EPS providers lack the necessary financial reserves, raising concerns about long-term stability. Therefore, despite significant progress, funding struggles to keep up with the growing demand.

Sources: International Monetary Fund, World Health Organization, World Bank, Center for Global Development, Lockton, Pan American Health Organization

$6,960
GDP per capita

6.55%
of the GDP is spent on Healthcare

71.6 (men)
and **77.6 (women)**
Life Expectancy

Liver disease poses a significant challenge to the population health in Colombia. This significant health burden is due to the prevalence of hepatitis, alcohol consumption, obesity, and other risk factors affecting the population. Recognizing these challenges, Colombia is making strides to address risk factors for liver disease through steps such as decreasing the cost for medicine like antiviral treatments for hepatitis, increasing accessibility, and launching vaccination programs.[1]

Approximately 12.14% of the general population in Colombia are living with diagnosed hepatitis B virus (HBV) infection.[2] Of those diagnosed, only 7.8% receive the appropriate treatment. The rate varies among vulnerable groups.[2] For example, in certain indigenous populations in the Amazon, HBV prevalence is notably higher, with studies reporting a prevalence of up to 3.6% among children and 30.9% among mothers.[3] Colombia has set goals to eliminate HBV as a public health threat by 2030 by expanding vaccination coverage, especially among newborns, and has achieved an 85% HBV birth dose vaccination rate reported as of 2022.[2]

Hepatitis C virus (HCV) infection, on the other hand, affects about 0.6% of the general population in Colombia, but a study found that infection rates are anticipated to be as high as 22.8% among people who inject drugs.[2,4] Despite improvements in blood safety practices to curb HCV transmission, efforts to expand access to testing and treatment remain challenging.[4,5] Although highly effective direct-acting antivirals are available, their historically high prices have posed financial barriers.[5] Colombia has initiated a centralized purchase process for HCV treatments via the Pan American Health Organization. To obtain treatment, patients are required to enroll in a program called, Cuenta de Alto Costo, overseen by public and private health insurers and regulated by the Ministry of Health.[1] This program oversees medication distribution, adherence to treatment guidelines, and systematic follow-up of patients.[1] While generic alternatives have lowered treatment costs, Colombia still faces obstacles in making these treatments widely accessible due to ongoing funding and infrastructure limitations.[1]

1 in 10

people in Colombia has **chronic HBV infection.**

In Colombia, metabolic dysfunction-associated steatotic liver disease (MASLD) affects about 26.6% of the population, a figure that mirrors rising trends across Latin America, where rates are around 31%.[6] From 2009 to 2016, over half of liver disease cases in Colombia were linked to metabolic issues like obesity and diabetes.[7] A study in Cartagena found that MASLD was the second leading cause of liver cirrhosis, accounting for 30.9% of cases, with most patients also struggling with diabetes or overweight.[8]

Obesity and diabetes, major contributors to MASLD, have become commonplace in Colombia. Around 29.3% of adult women and 20% of adult men have obesity, with rates especially high in cities, where healthier foods like fruits and vegetables tend to be expensive.[9,10] To help address these issues, Colombia introduced a tax on sugary drinks and processed foods in 2022 and passed a “Junk Food Law” in 2021 that requires clear labeling on food packaging to indicate high sugar or salt content.[9] Today, diabetes affects about 9.5% of Colombian adults, with rates steadily increasing over recent decades.[9,10] The COVID-19 pandemic further exacerbated these problems, as lockdowns limited physical activity and altered eating habits.[10]

With an average of 4.09 liters of alcohol consumed per person, Colombia has a lower drinking rate than neighboring Latin American countries.[11,12] However, alcohol use remains widespread. High cases of alcohol-associated liver disease (ALD) have been reported in areas that have high alcohol sales.[13] Young adults are particularly affected, with the average age of drinking initiation around 12–13 years of age.[14] Despite the legal drinking age being 18, many students between the ages of 12 and 18 report drinking at least once or twice a week, which indicates early and frequent exposure.[14]

In 2021 Colombia passed a "junk food law"

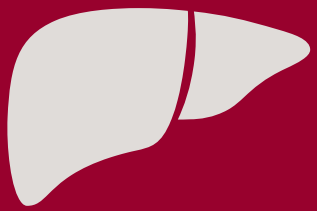
that requires clear labelling on food packaging, particularly on sugar and salt content.

Drinking has cultural roots in Colombia, especially in rural and indigenous communities, where sharing alcohol is common and occurs regardless of age or gender.[15,16] Prolonged use of alcohol from an early age raises the likelihood of developing long-term health issues, including ALD and eventually cirrhosis.[14,17]

In response, the government has partnered with alcohol companies like Diageo to reduce underage drinking through the "Alianza +18" project.[18,19] This initiative has trained thousands of retail staff to enforce age verification by placing reminders near cash registers and using software to prompt ID checks before selling alcohol.[19]

With rising rates of MASLD and alcohol consumption, liver cancer is becoming more of an issue in Colombia. In 2020, the International Agency for Research on Cancer reported that liver cancer affected about 2% of Colombians, with a mortality rate of 4%.[17] Between 2017 and 2021, 2,244 cases of hepatocellular carcinoma were reported in adults across the country.[20] Of those cases about 23.2% of patients had liver disease due to alcohol consumption, and 20.7% had cirrhosis with no known cause.[20]

Colombia has completed over



3,000 **liver transplants** since 1979.

Liver transplants in Colombia are most often needed for people with cirrhosis caused by hepatitis, alcohol use, MASLD, and liver cancer.[21] Since the first transplant in 1979, Colombia has completed over 3,000 liver transplants, making it the fourth-leading country for these procedures in Latin America after Brazil, Argentina, and Uruguay.[21] The Donation and Transplant Network of Colombia coordinates the system through a national organization and six regional offices, with 10 hospitals authorized to perform liver transplants.[21] Both deceased and living donor transplants are covered by the national health system, ensuring that cost does not prohibit anyone who needs a liver transplant from receiving one. Transplants from living donors, which are especially beneficial for children on the waitlist, have grown in recent years and accounted for 14% of all liver transplants in 2017.[21]

Challenges remain, such as an insufficient number of organ donors, donor health, culture reluctance to religion, and liver transplant costs.[21,22] A liver transplant can cost between $27,000 and $38,500, depending on complications, with additional expenses for those with end-stage liver disease due to more frequent hospitalizations.[22] Since Colombia has a universal healthcare system these costs are normally shared by both the government and the patient but the extent to which the patient covers is unknown. Despite these challenges, outcomes are promising, with recent studies showing a 5-year survival rate of around 71% and 80% for transplant recipients.[23] Building a stronger culture of organ donation and enhancing organ availability are key goals to sustain and expand Colombia's transplant program.

Efforts to improve liver health in Colombia reflect the country's commitment to expanding healthcare access and tackling complex public health challenges. Continued focus on preventive measures, early interventions, and community education could further enhance outcomes for those affected by liver disease.

OVERVIEW

MEXICO

Population: 131,873,500 (2022)

GDP per Capita: $13,926 USD

Life Expectancy: 71.5 years (men) and 78.2 years (women) (2021)

Healthcare Spending: 6.2% GDP

Healthcare Funding: A complex mix of several employment-based social insurance schemes managed by national institutions, an insurance funded private sector, pay at point of care and a public assistance scheme for the uninsured operated by both state and federal authorities and supported by a financial protection scheme. A 2020 WHO review found that 14% of the population lacked financial healthcare protection, and the other insured sectors are wildly varying in the amount and type of health cover they provide.

Sources: World Bank, WHO

$9,926.40
GDP per capita

6.2%
of the GDP is spent on Healthcare

71.7 years (men)
and **77.1 years (women)**
Life Expectancy

Liver disease poses a substantial burden for the people of Mexico. In 2019, cirrhosis of the liver was reported to be the fourth most common cause of death in Mexico, behind diabetes, CVD, and chronic kidney disease,[1] with more than 30 people per 100,000 living with the condition.[2]

Between 2012 and 2017, the most frequent causes of **liver cirrhosis** included

36.2% HCV
31.2% ALD
23.2% NASH[3]

The **least frequent** were

1.1% HBV
7.3% Autoimmune Disorders
1.0% Other Conditions[3]

It is impossible to discuss liver health in Mexico without discussing the country's obesity epidemic – Mexico currently has the highest rate of obesity in OECD.[4] Over the past two decades, adult obesity, morbid obesity, and even childhood obesity are all rising quickly.[4,5] In 2018-2019, 36.1% of the population were deemed to be obese, while only 23.5% of the population were of a healthy weight.[5]

In response, the Mexican government has implemented a series of measures to try to improve the eating habits of the population, including taxes on sugary drinks and non-nutritional high calorie foods, clear nutritional labeling on products and beverages as well as banning the use of cartoon characters on children's foods.

However, despite this emerging catastrophe, there is still no national register for metabolic dysfunction-associated steatotic liver disease (MASLD) or MASH. Based upon the current numbers of people with diabetes, an estimated 14.4 million people in Mexico have MAFLD, of whom approximately 4.3 million suffer from its more severe form, metabolic dysfunction-associated steatohepatitis (MASH).

2 MILLION
Mexicans will be living with chronic liver disease **by 2050.**

Studies into liver disease trends predict the outcome of this public health crisis. If present trends continue, two million Mexicans will be living with chronic liver disease by 2050 (see breakout).[6]

In 2016, Mexico joined the WHO global campaign for the elimination of viral hepatitis. Detection campaigns have been implemented in the open population and in at-risk groups that include sex workers, people who inject drugs, immigrants, and prisoners. The 'Specific Action Program' was launched within the WHO global framework with the aim of detecting 90% of all HBV and HCV cases.

Additionally, there have been concerted efforts by the Mexican government to reduce the burden of disease and mortality from HCV and associated diseases, including liver disease. In addition to patient education campaigns, the latest treatment regimens, rescue medications (in case of failure of the first treatment regimen), and tests to corroborate HCV elimination are all used regularly in Mexican hospitals today.

As noted in 2020 by the Epidemiological Surveillance Program, these efforts have paid off with a sharp downward trend – 57% reduction in total cases of HCV. Still, prevalence remains at about 1.5% of the general population.

Around three million adults are estimated to have acquired HBV, though 90% of these cases are inactive.[83] However, geography plays a role in these patterns: Higher rates of HBV infection are found in areas of dense populations and in regions with frequent itinerant populations.[7]

Average alcohol consumption in Mexico is around 5.05 liters per year, lower than that of many neighboring countries.[8] However, the rate of alcoholism is estimated to be around 3.4% of the population. Alcohol-associated liver disease currently accounts for around 30% of all liver cirrhosis in the country.[3] According to estimates, ALD will account for nearly a million cases of liver disease by 2050.[8]

LIVER HEALTH OVERVIEW

Mortality from liver tumors in Mexicans over the age of 60 is now the third most common cause of cancer deaths in the country for men and the second for women**.** In recent years, the mortality for HCC per 100,00 people in the country has more than doubled.[9]

To deal with liver disease, most patients must receive care from the specific network of doctors, clinics, hospitals, and pharmacies in their scheme. Within the state sector, non-complex CLD, early stage hepatitis or MAFLD is managed in primary care or clinic settings. Larger hospitals in bigger cities manage complex liver care through a system of referrals.

The private healthcare sector is well-resourced and sought after, and liver scans and complex treatments are carried out in private hospitals.

Though there is infrastructure to support liver transplants in the country, rates were affected by the COVID-19 pandemic. According to the Mexican National Transplant Registry, a total of 72 liver transplants were performed in 2020, which is only a third of those performed in 2019.[10] Of the 23 currently active liver centers, only seven performed 10 or more liver transplants each year. 22 centers were based in or around Mexico City, raising the question of geographic inequality.[10]

MEXICO AND THE COST OF OBESITY

The economic, social and physical costs that obesity represents for the people of Mexico was spelled out by the OECD Secretary General Angel Gurría, speaking at the 2020 Mexico City launch of the OECD study, *"The Heavy Burden of Obesity: The Economics of Prevention."* Mr. Gurria noted:

'According to our projections, overweight-related diseases will reduce life expectancy in Mexico by more than four years over the next 30 years … Our analysis estimates that overweight and related diseases will:

Reduce Mexico's labor force by the equivalent of 2.4 million full-time workers per year, as people with overweight and related conditions are less likely to be employed and, if employed, tend to be less productive;

Account for around **8.9% of health expenditure per year between** 2020 and 2050;

Curb Mexico's GDP by an estimated 5.3%, well above the OECD average of 3.3%, a figure that is already too high.

In fact, Mexico is the OECD country where overweight, obesity and related diseases will have the greatest impact on GDP between 2020 and 2050.'

OBESITY RATES SET TO OVERWHELM OUR HEALTHCARE SYSTEM

Dr. Alma Laura Ladrón de Guevara is a gastroenterologist at Hospital Angeles in Mexico City. She has a special interest in metabolic disorders and obesity.

Obesity is becoming a killer in Mexico. We saw that in COVID – although we lost elderly and vulnerable people - most of the younger victims were obese.

The causes are fairly obvious. In a few decades, we have gone from being a country that ate mainly vegetarian foods and only rich foods occasionally to one where over 40% of our diet is processed food which are full of carbohydrates, sugars and fat. Add to that a genetic preposition to metabolic disorders in some of our ethnic populations and a cultural love affair with eating and you have a recipe for disaster. As well as terrifying rates of obesity, we also have entire families who have T2D. We spend more on diabetes medication than any other country in the world.

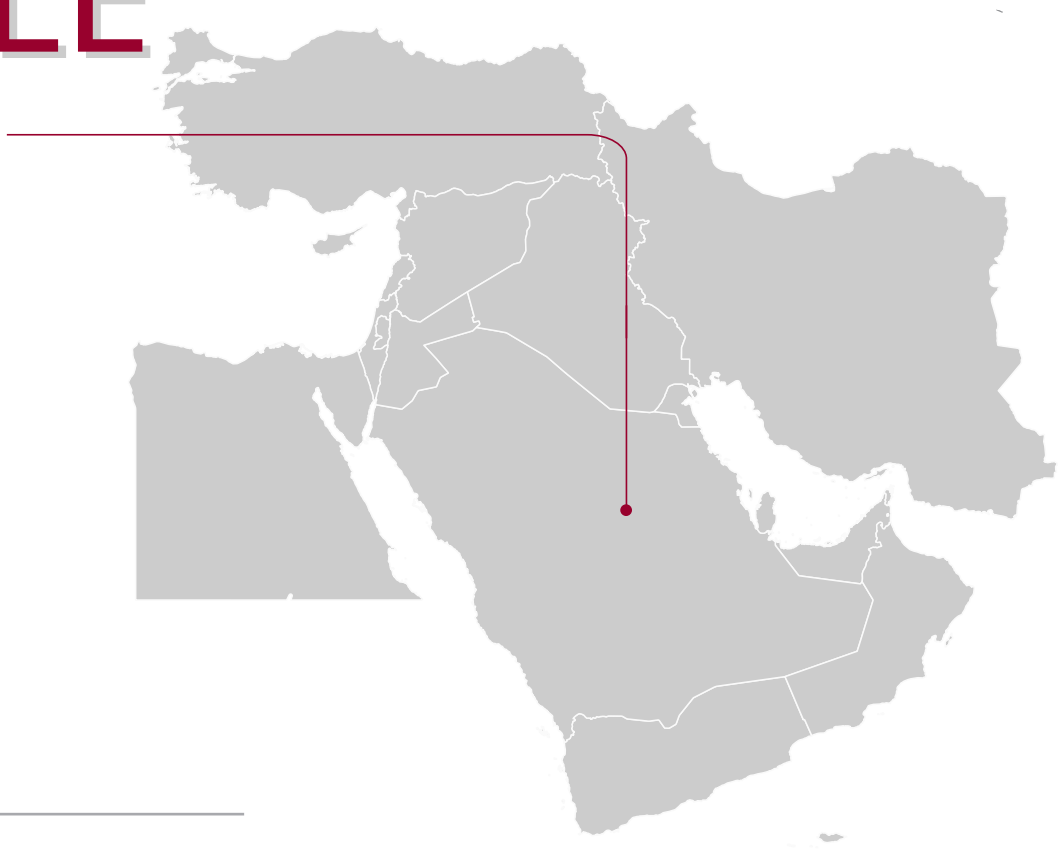
> **Obesity is becoming a killer in Mexico.**
>
> DR. ALMA LAURA LADRÓN DE GUEVARA

Even doctors and nurses are obese, which adds to the problem. If our clinicians are overweight, how can they tell their patients to lose weight? The government is talking about tackling obesity, but we do not see any effective plans.

In the past we have run successful health campaigns for breast cancer and diabetes. As a country we made a concerted effort to get on top of hepatitis, and over the last 20 years we have seen huge improvements in the reduction of hepatitis infections. However, it feels as if the government is not prioritizing health at the moment, much less liver health. We do not even have the resources to screen patients living with diabetes for NASH, even though we know it is present in around 50%-60% of these patients.

We need to make people understand the link between obesity and liver disease, and we can do that through a concerted effort to educate people from a very young age. If not, we will face a rising death rate and a health system overwhelmed by far too many people dying early of liver disease.

MIDDLE EAST



HEALTH OVERVIEW

Home to more than 400 million people, the Middle East is a transcontinental area that covers countries across western Asia such as Iran, Saudi Arabia and Türkiye, all the way through to North Africa, including Egypt and Libya.

Throughout this geopolitical region, there is a wide range of economies. Qatar and Israel are global economic leaders, while others, for example Iraq and Syria, are plagued by war and poverty. There are also a range of cultural and historical factors which engenders many different healthcare systems – and often uneven levels of health – in the region.

As expected, those countries with a stable and successful economy have well-funded healthcare centers, accessible to the majority of the population and even sometimes sought after by patients across the globe. This includes Qatar, which has an exclusively public healthcare system and is ranked 13th in terms of the best healthcare systems globally.

In contrast, Iraq's healthcare system has undergone a 90% funding cut due to war and the resulting economical and political instability; many healthcare professionals have left the country for a more stable home. This predicament is mirrored in other Middle Eastern countries such as Syria, where the healthcare system has been decimated by conflict.

Increasing rates of non-communicable diseases, such as heart disease, obesity and diabetes can be seen across the Middle East. As in other regions, this can be attributed to the recent and rapid adoption of Western diets and lifestyle patterns, placing a significant burden on the various healthcare systems.

Sources: Legatum Institute – Cloud Hospital, Prosperity Index, The World Bank

The Middle East has the **highest prevalence of NASH**

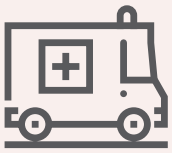
32%

when compared to worldwide figures.

As diarrheal and infectious diseases have decreased in prevalence over the last few decades across the Middle East, they have been replaced by gastrointestinal cancers and cirrhosis. Indeed, liver disease is now amongst the top four killers across all countries in this region, with Egypt having by far the highest mortality rates, followed by Yemen and Morocco.[1] Chronic liver disease is responsible for two thirds of hospital admissions in Iraq, most commonly hepatitis B, alcohol, hepatitis C, immune hepatitis and metabolic disorders.[1]

In parallel with the increase in obesity and diabetes, metabolic dysfunction-associated fatty liver disease (MAFLD) rates are also on the rise in the Middle East. A global analysis has found that the region has the highest prevalence for this condition (32%) when compared to worldwide figures, and approximately 20%-30% of these cases progress to MASH.[2] This is expected to continue to rise, with one study reporting that by 2030 there will be an increase of 48% and 46% in MAFLD cases for Saudi Arabia and the United Arab Emirates, respectively.[2] This pattern can largely be attributed to lifestyle changes: changes in dietary patterns, such as the adoption of more Western-based diets, as well as widespread physical inactivity. These factors must be addressed by policymakers to combat the growing burden of MAFLD.

Viral hepatitis has a wide range of prevalence across the Middle East, with hepatitis B ranging from 0.6% (Iraq) to more than 8% (Sudan).[3] For hepatitis C infection, Egypt has had the highest prevalence of HCV in the world (18%) until very recent successful efforts, whereas in Lebanon, Saudi Arabia, and Iran, prevalence is less than 1%.[3] The occurrence of extremely high rates of viral hepatitis infection indicates an urgent need for government and policymaker intervention. However, the broad disparity across the region, as well as in associated risk factors, calls for tailored solutions.



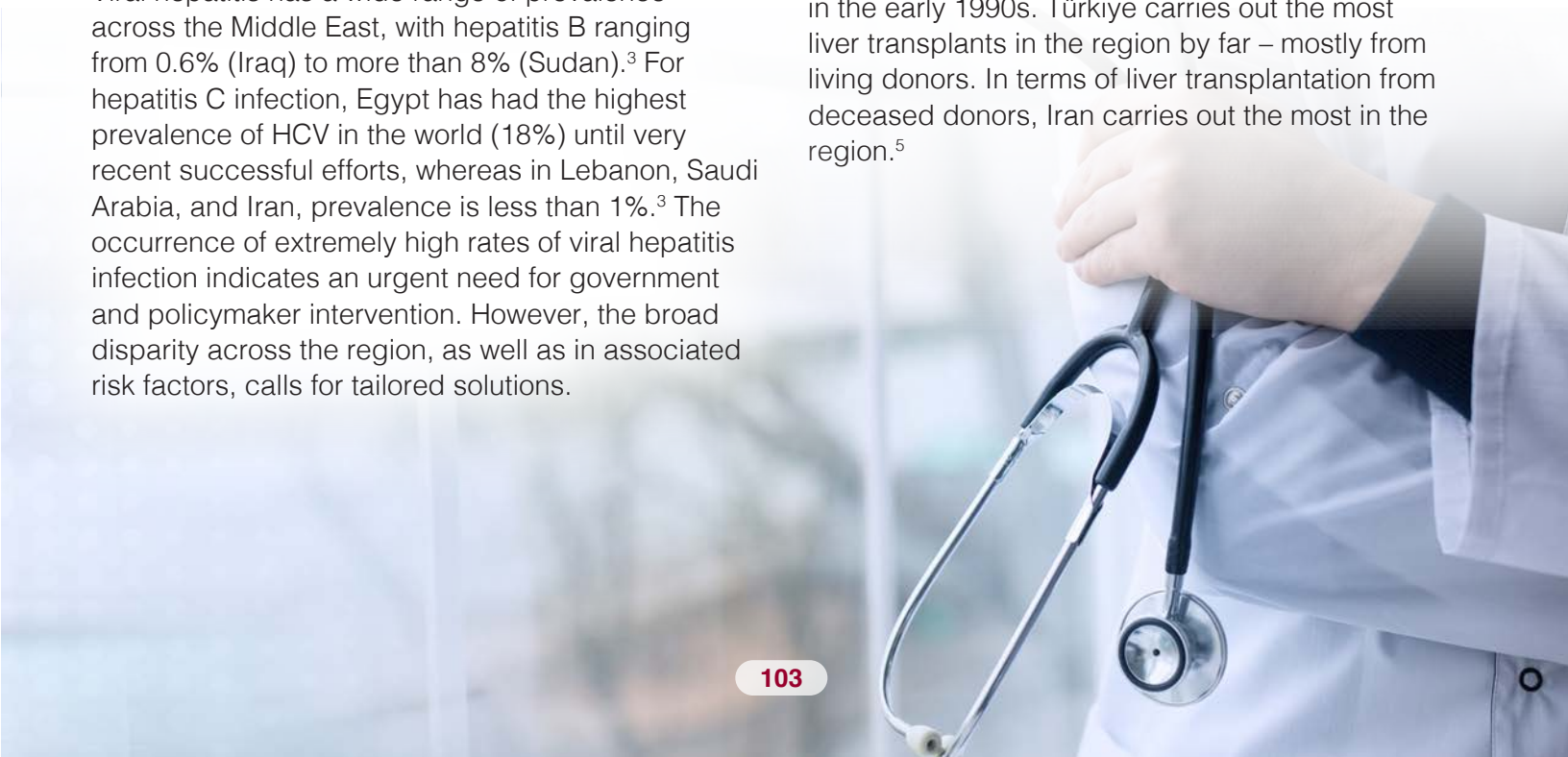
CHRONIC LIVER DISEASE

is responsible for **two thirds of hospital admissions in Iraq.**

Liver cancer is one of the top four causes of death in the Middle East, with hepatitis B and C infection being the main causes of hepatocellular carcinoma.[1]

Although the occurrence of hepatocellular carcinoma is lower than in East Asia, it is expected that it will increase in parallel with the rising incidence of MAFLD and HCV.[4]

More than other regions, religion also plays a critical role in liver health in the Middle East, given that Islam is the dominant religion and Islamic policymakers have complex views on organ transplantation from dead donors. However, in 1986, the Amman declaration was passed, which allowed for the recognition of brain death in Muslim countries.[5] This opened a door for organ transplantation in the region and kick-started programs in several countries in the early 1990s. Türkiye carries out the most liver transplants in the region by far – mostly from living donors. In terms of liver transplantation from deceased donors, Iran carries out the most in the region.[5]



OVERVIEW

LEBANON

Population: 6.77 million (2021)

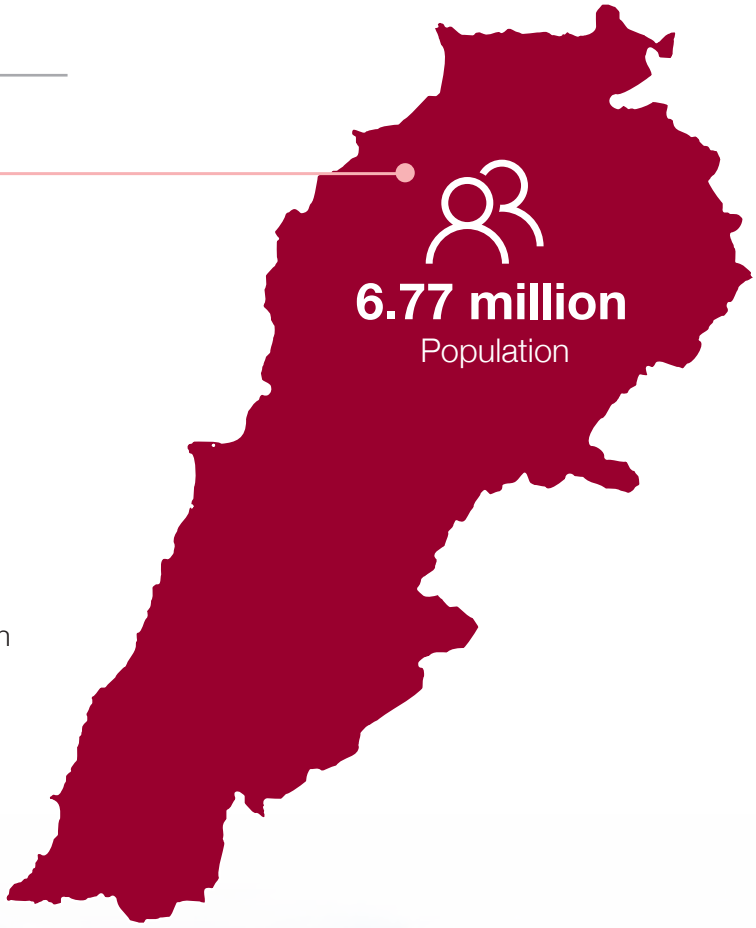
GDP per Capita: $3,350 USD

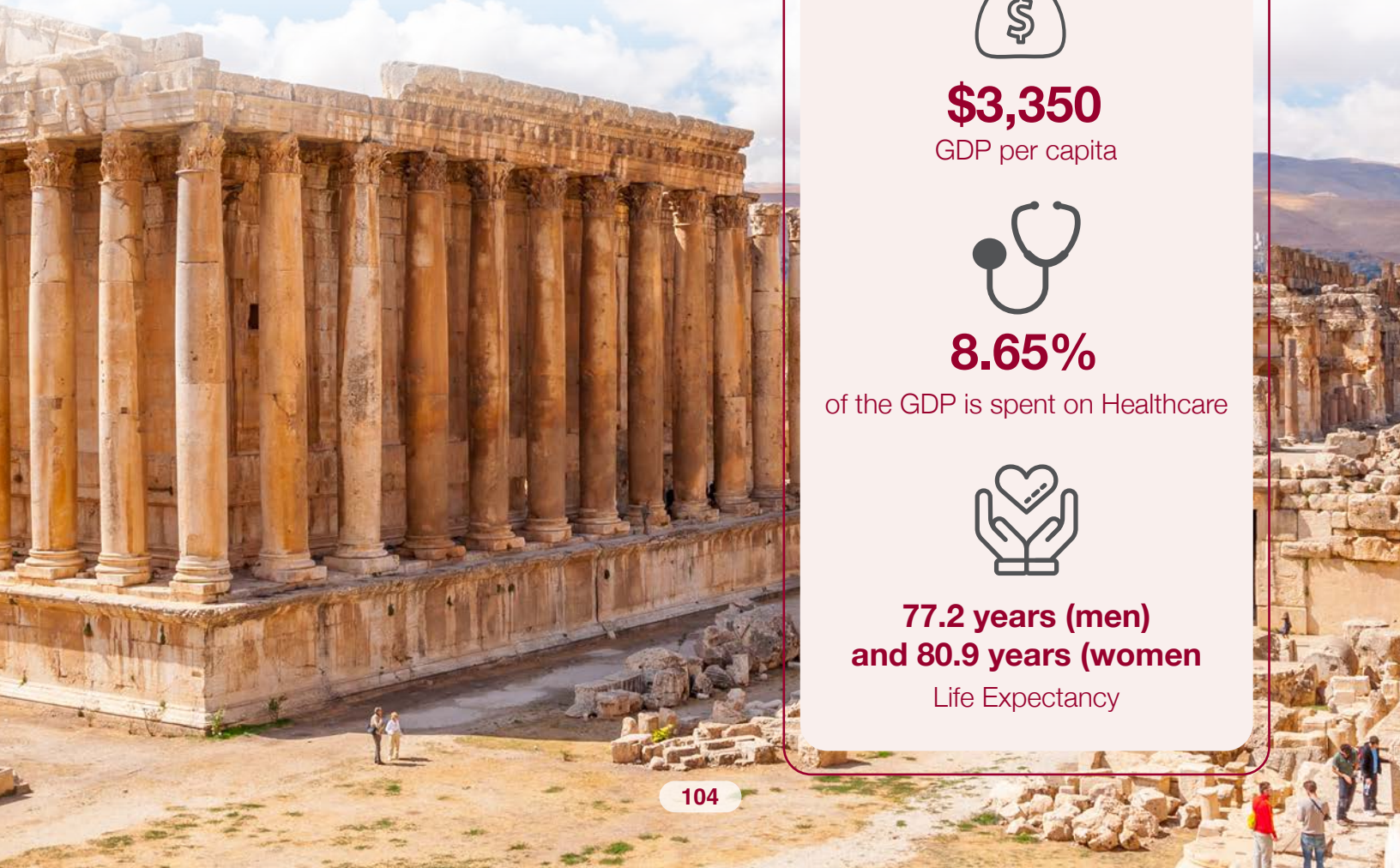
Life Expectancy: 72.2 years (men) and 76.6 years (women)

Healthcare Spending: 8.65% GDP (2019)

Healthcare Funding: The main source of funding is out-of-pocket payments from patients. Primary healthcare centers are mainly operated by non-governmental organizations through agreements with the Ministry of Public Health. However, secondary health care services, for example the majority of hospital beds (86%), are provided by the private sector. Lebanon's health sector has long been viewed as fragile, but over the last two years a combination of COVID-19, high levels of poverty, hyper-inflation and heightened security risks have inflicted major damage on Lebanese healthcare.

Sources: WorldData.Info, salaryexplorer, Data. WorldBank, LSE Middle East Center Blog





$3,350
GDP per capita

8.65%
of the GDP is spent on Healthcare

77.2 years (men) and 80.9 years (women
Life Expectancy

There is a limited amount of published data on the prevalence of liver disease in Lebanon. A study of patients who had undergone fibroscan in Beirut found that 58.3% had metabolic dysfunction-associated fatty liver disease (MAFLD).[1] Viral hepatitis infection was the second most common cause, with hepatitis B and C having a prevalence of 14.3% and 11.1% respectively.[1] Other causes included alcohol-associated liver disease (7.7%), drug-induced liver disease (3.3%) and autoimmune hepatitis (2.9%).[1] This provides a basis to begin to understand the leading causes of chronic liver disease in Lebanon, though its limitations in size and geography mean multi-center studies and epidemiologic surveillance efforts are necessary to further characterize liver disease in Lebanon.

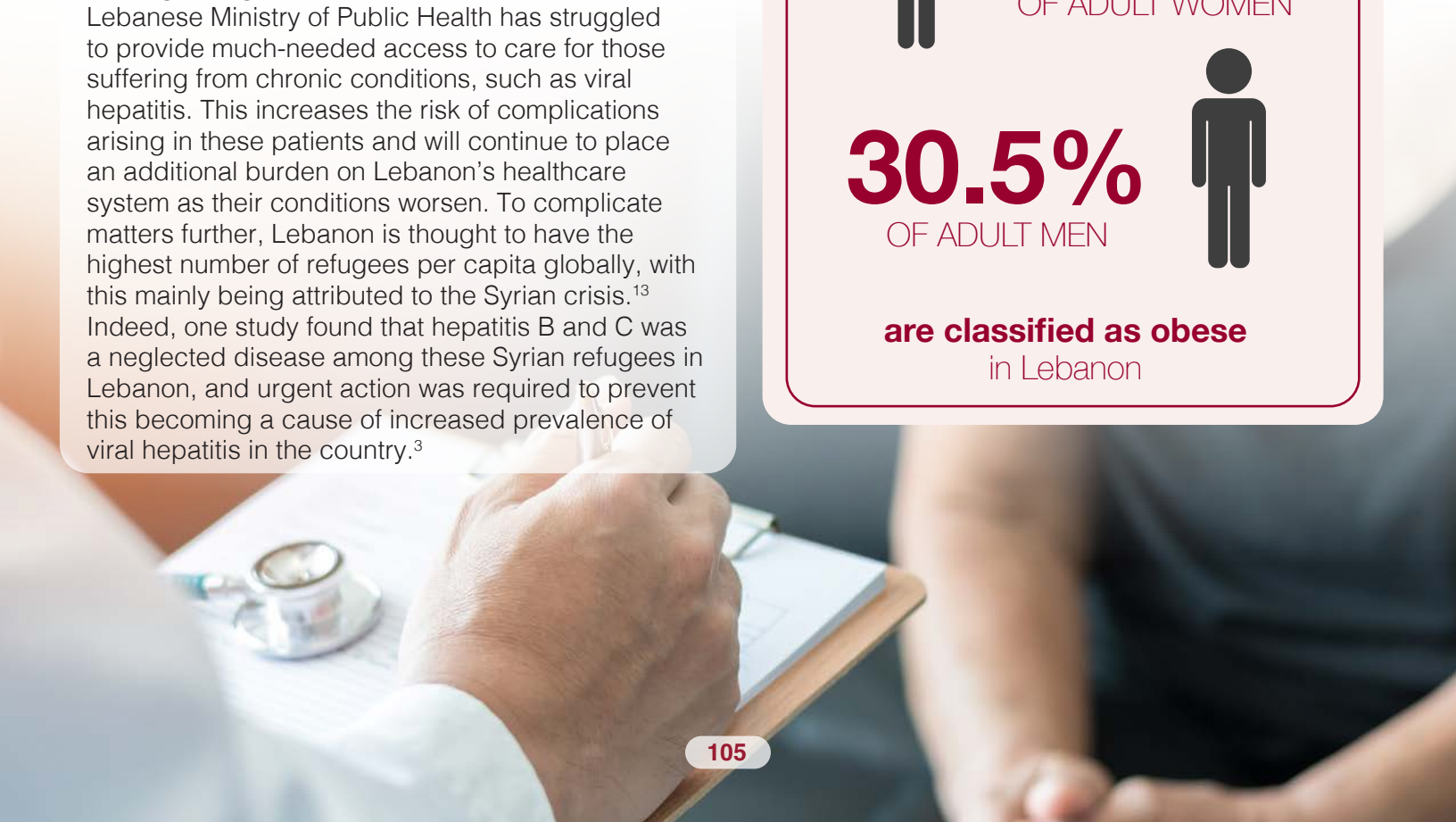
Lebanon is an area of moderate endemicity for both hepatitis B and C infection per several sources. Indeed, a 2016 study found that HBV and HCV prevalence of 1.74% and 0.21%, respectively.[2] This low prevalence can be attributed in part to the 1998 national hepatitis vaccination program for all newborns, in combination with an effective awareness campaign as well as active screening and vaccinations for high-risk groups.

However, it must be noted that due to a lack of funding, along with a volatile political situation, the Lebanese Ministry of Public Health has struggled to provide much-needed access to care for those suffering from chronic conditions, such as viral hepatitis. This increases the risk of complications arising in these patients and will continue to place an additional burden on Lebanon's healthcare system as their conditions worsen. To complicate matters further, Lebanon is thought to have the highest number of refugees per capita globally, with this mainly being attributed to the Syrian crisis.[13] Indeed, one study found that hepatitis B and C was a neglected disease among these Syrian refugees in Lebanon, and urgent action was required to prevent this becoming a cause of increased prevalence of viral hepatitis in the country.[3]

Although health experts believe it is becoming a common cause of chronic liver disease, the prevalence of MAFLD in Lebanon is unknown.[1,4]

However, several Lebanese studies have analyzed dietary patterns of patients with MAFLD and found that their intake of Western diets of more meat, fruit and fast food was greatly increased compared to the more traditional, native diets.[4,5] An estimated 30.5% of men and 39.9% of women are classed as obese in Lebanon, which is significantly higher than the global national average of 7.5% and 10.3% for men and women respectively.[6] These figures may give an indication of the consequential health burden that MAFLD is and will continue to inflict on the Lebanese population.

Limited data on liver transplantation in Lebanon is available, although one center in Beirut recorded 10 liver transplants between the years of 1998-2010, with an acceptable 10-year survival rate of 67%.[7]



WE MUST USE WHAT LITTLE HEALTHCARE RESOURCES WE HAVE EFFICIENTLY AND EFFECTIVELY

Dr. Jacqueline Kassouf Maalouf, PhD is the Founder and President of the National Diabetes Organization (DiaLeb). She is a certified diabetes educator and member of the International Diabetes Federation.

In Lebanon, we are facing an unprecedented economic collapse, which is impacting our healthcare system tremendously. Although, in theory we have a free or low cost primary healthcare system, along with a form of free secondary care, the reality is that many specific treatments are no longer available in the public health system. This is forcing people into the private health sector where they have to pay for treatment and medicines, often in US dollars.

At the same time, the costs of many medicines are rising exponentially so, for many Lebanese people, finding the money to pay for medicines and treatment is extremely difficult. As a result, many patients will avoid going for essential tests until they feel very ill. This is particularly relevant for liver conditions such as viral hepatitis, where regular checks are essential to maintaining good control of the disease, and cirrhosis, which often needs rapid and urgent treatment. Unfortunately, we have no way of knowing exactly how the current economic situation is impacting the health of the Lebanese people.

Another major challenge for our healthcare system is a lack of accurate and up to data on many of our key health issues, including liver disease. For example, there are no figures on NAFLD or NASH rates, while our figures on liver cancer date from 2016 and the latest figures on diabetes are from 2018. These almost certainly represent an underestimate of the true picture.

The truth is we really do not know how many people are living with or dying of liver disease in our country and, because we have no national liver transplant program or liver donation registry, we cannot even look to end stage liver disease for guidance in this area.

We do know however that obesity rates are rising, as are the number of people with diabetes, so we can assume that NAFLD and NASH rates will also be rising.

> Reducing the number of people who are obese will not only reduce the rates of T2D, but it also represents our best chance of **preventing a huge rise in liver disease.**
>
> - JACQUELINE KASSOUF MAALOUF

However, while there are government-run awareness campaigns around diabetes, few people are aware of the link between obesity and liver disease. This lack of awareness is even found within health care professionals – I have spoken to nurses and medical students who have never heard of NASH and NAFLD, much less how to treat it.

To improve this situation, we must be realistic about what resources we have and use them as efficiently as possible. It seems logical that if we tackle obesity, which is a cause of both T2D, NAFLD and NASH, we could make some progress in both these disease areas. I would like to see our government focus on reducing obesity, perhaps through a national campaign where national experts visit schools, perhaps with initiatives on healthy eating in the workplace and training programs for healthcare professionals to support their patients to lose weight safely. Here at DiaLeb, we have been successfully running similar programs, although at a very small scale, so we know it can be done.

Reducing the number of people who are obese will not only reduce the rates of T2D, but also represents our best chance of preventing a huge rise in liver disease cases. With the few resources we have, and are likely to have for the foreseeable future, this is our only realistic chance of salvation. It is as simple as that.

OVERVIEW

SAUDI ARABIA

Population: 36.4 million (2022 year)

GDP per capita: $33,040 USD

Life Expectancy: 75.7 years (men) 77.4 years (women)

Healthcare Spending: 5.97% GDP (2021)

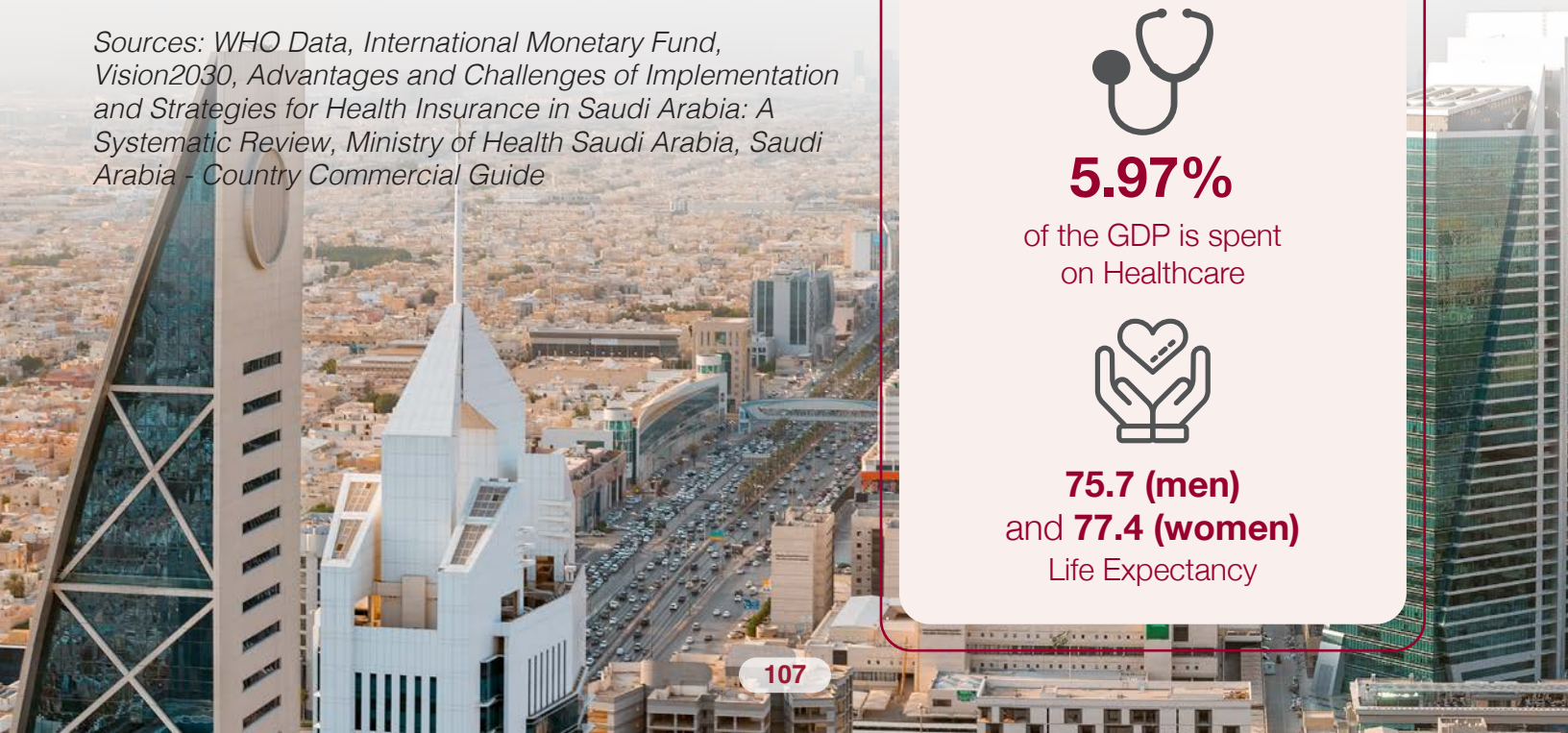
Healthcare Funding: Saudi Arabia's healthcare system, predominantly funded by government revenues, provides free universal healthcare to its citizens. In 2023, the government allocated approximately $50.4 billion, or 16.96% of its total budget, to healthcare and social development, with the Ministry of Health receiving 7% of the state budget in 2024. However, to reduce reliance on government funding and promote private sector involvement, Saudi Arabia has introduced mandatory health insurance for private sector employees, including expatriates. Saudi Arabia's residents currently spend about 4% of their monthly salaries, 191 SR (~$51 USD), on healthcare expenses. As a result of the aging population and rising chronic diseases, Saudi Arabia is implementing reforms under Vision 2030 to reshape the healthcare system. These reforms focus on improving healthcare quality, promoting preventive care, ensuring financial sustainability, and boosting private sector involvement. With plans to invest over $65 billion in healthcare infrastructure and e-health services, Saudi Arabia is opening new commercial opportunities for global companies.

Sources: WHO Data, International Monetary Fund, Vision2030, Advantages and Challenges of Implementation and Strategies for Health Insurance in Saudi Arabia: A Systematic Review, Ministry of Health Saudi Arabia, Saudi Arabia - Country Commercial Guide

$33,040
GDP per capita

5.97%
of the GDP is spent on Healthcare

75.7 (men)
and **77.4 (women)**
Life Expectancy



Liver disease is a growing public health issue in Saudi Arabia, now ranking as the seventh leading cause of death.[1] Although viral hepatitis cases have been steadily decreasing, major contributors such as environmental toxins, obesity, and undiagnosed metabolic dysfunction-associated fatty liver disease (MAFLD) continue to pose significant threats to liver health. However, efforts are underway to combat these challenges. Initiatives like the Rashaka program, aimed at reducing obesity, and childhood vaccination campaigns have shown positive results in improving liver health.[2] Although early diagnosis of MAFLD remains limited, increasing public education and awareness are gradually addressing this gap. Despite the persistent rise in obesity, prevention and early intervention strategies remain key priorities in improving liver health outcomes.

Viral hepatitis, particularly hepatitis B virus (HBV) and hepatitis C virus (HCV), has long been a public health concern in Saudi Arabia, ranking as the second most common viral disease after chickenpox.[3] Historically, the country was considered highly endemic for HBV, with studies in the 1980s showing that 5% to 10% of the population was infected.[4] Because close personal contact is necessary for most transmission, children under 12 faced some of the greatest risk of infection – around 7%.[5] However, starting in 1990, all Saudi children were required to be vaccinated before school entry, leading to a significant reduction in HBV prevalence to around 1.3% in the population as of 2019.[5,6]

Studies from Saudi Arabia suggest that HBV infection makes up the slight majority of viral hepatitis cases – with HBV more common in individuals under 44, and HCV more common in older individuals.[7] Although the incidence of viral hepatitis has decreased due to widespread vaccination and improved healthcare, a large number of individuals infected before the vaccination era continue to develop chronic liver conditions.[8] Also, many healthcare professionals and hospital staff in Saudi Arabia often have limited awareness of current treatment protocols and vaccination guidelines for managing HBV.[5] Comprehensive surveillance, targeted prevention, and access to treatment remain imperative.

HCV has remained relatively low in Saudi Arabia, with prevalence ranging from 0.4% to 1.1%.[9] Generally, most HCV infections in the country are caused by blood transfusions or other medical procedures like hemodialysis rather than by intravenous drug use. Patients undergoing maintenance hemodialysis are at heightened risk of contracting HCV due to their weakened immune systems and the need for frequent blood transfusions.[10] In 2011, the introduction of direct-acting antivirals marked a significant improvement in HCV treatment, with a response rate of over 90%.[11] To further work towards eradicating HCV, the Ministry of Health launched a national campaign in 2018 focusing on early detection, treatment, enhancing diagnostic services, and increasing public awareness among healthcare professionals.[11]

While viral hepatitis poses a significant health challenge, alcohol-associated liver disease (ALD) remains rare. Except for in diplomatic areas, the sale of alcohol has been banned in the country since 1952 until recently.[12] The country's strict legal penalties for the consumption, sale, and distribution of alcohol have limited the availability of the product.[12,13] This has contributed to a low prevalence of alcohol consumption and alcohol-related disorders.[13] According to the World Health Organization (WHO), the per capita alcohol consumption among individuals aged 15 and older was only 0.2 liters in 2016.[13] Additionally, less than 0.5% of men and 0.1% of women are estimated to have alcohol use disorders in the country.[13]

Given the extremely uncommon nature of alcohol consumption, the Saudi Association for the Study of Liver Diseases and Transplantation medical guidelines recommend routine screening for HCV in high-risk populations, such as individuals who consume alcohol regularly or use intravenous drugs.[14]

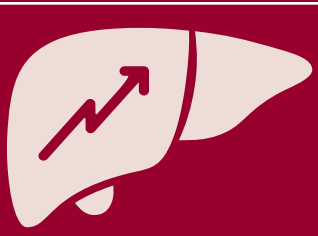
In Saudi Arabia, several environmental toxins pose significant risks to liver health, with heavy metals and cyanotoxins being prominent concerns. In regions with intensive agriculture and industrial activity, such as farms around Riyadh, soil samples have shown high concentrations of mercury, arsenic, and uranium.[15] These heavy metals can accumulate through ingestion or inhalation, leading to liver damage over time.[15] Additionally, cyanotoxins such as microcystins have been detected in freshwater sources like the Tendaha dam reservoir that provides irrigation and drinking water for the Asir region.[17] Prolonged exposure to these toxins presents a growing risk for liver-related health issues in affected communities.[17]

Metabolic factors like obesity and type 2 diabetes (T2D) are now contributing heavily to the rising burden of liver disease in Saudi Arabia.[1] The prevalence of obesity is approximately 38%, with projections estimating it could reach 45% by 2025.[17] The country's trends are consistent with the Middle East and North Africa region, where T2D has become highly prevalent, affecting 12.3% of the population and as many as 32% certain parts of Saudi Arabia.[17] These two conditions significantly increase the risk of developing MAFLD.

One of the key impacts of this trend is the rising burden of MAFLD in Saudi Arabia. MAFLD has seen a sharp increase in prevalence, affecting over 33% of the population in 2019.[1] From 2011 to 2019, MAFLD overtook HCV as the leading cause of liver transplants, accounting for 29.7% of cases.[17]

In response to the increasing burden of MAFLD, Saudi Arabia has implemented several prevention and educational strategies aimed at raising public awareness about these chronic conditions. One such initiative is the Rashaka program, which aims to reduce obesity rates in the general population by 5% by 2020.[2] This program was launched in the 2016–2017 academic year targeting national schools.[18] This program led to a 2.7 reduction in BMI among students, with girls' schools experiencing a more pronounced decrease in BMI compared to boys' schools.[18]

Hepatocellular carcinoma (HCC) is the third most prevalent cancer in Saudi Arabia, and liver-related deaths are estimated to increase by nearly 70% by 2030.[19,20] One of the major challenges in managing HCC in Saudi Arabia is frequent late-stage diagnosis of the disease due to a lack of comprehensive screening practices.[21] Most patients remain asymptomatic until the disease has progressed to advanced stages, at which point treatment options are limited. While surgical interventions, such as liver resection or liver transplantation (LT), are effective for treating HCC, less than 5% of patients in Saudi Arabia are diagnosed early enough to be eligible for curative options.[21] Other treatment options, like transarterial chemoembolization (known as TACE), have demonstrated some success, though survival rates decrease significantly beyond two years.[21] To address these challenges, the Saudi Association for the Study of Liver Diseases and Transplantation recently updated HCC management guidelines, which are endorsed by the Saudi Oncology Society.[21,22]



By 2030, liver-related deaths are estimated to **increase by nearly**

70%

Liver transplantation in Saudi Arabia has seen remarkable progress since the first successful transplant in 1990.[23] The country formally launched its LT program in 1994, focusing initially on transplants from deceased donors.[23] However, due to growing demand, the program expanded to include living donor liver transplants for children in 1997 and adults in 2001.[23] By 2017, the country had completed 2,233 liver transplants, with 1,133 involving living-related donors, 95 from living-unrelated donors, and 1,005 from deceased donors.[23] Despite these achievements, there are still not enough donor organs to meet the demand, partly because many adults are overweight, obese, physically inactive, or have T2D, which affects the quality of their organ donation.[23,17] This leads to more complications for both donors and recipients — since overweight donors are more likely to have fatty livers that can fail early — and raises concerns that the pool of potential donors may shrink even more in the coming years.[17]

In response to these issues, the Ministry of Health introduced a joint initiative in 2017 aimed at boosting organ donation and transplantation rates.[24] This program, developed in collaboration with the Donation Transplantation Institute and Saudi Center for Organ Transplantation, implemented a quality management system influenced by successful organ donation models from Europe and the U.S.[23,24] A key part of this initiative was the creation of an electronic alert system that improved communication between donor hospitals and intensive care units, ensuring more efficient coordination for organ donation.[23.24] While the living donor transplant rate reached 7.22 per million population (pmp) by 2019, the rate of transplants from deceased donors lagged at 2.33 pmp, reflecting the ongoing need for further improvements in organ donation infrastructure.[24]

In Saudi Arabia, liver disease remains a major public health issue due to factors like viral hepatitis, environmental toxins, and rising obesity rates. While vaccination efforts have successfully reduced hepatitis cases, challenges such as limited organ availability and late-stage liver cancer diagnoses persist. Ongoing initiatives, including public health programs and improved organ donation systems, aim to address these issues and improve liver health outcomes.

In Saudi Arabia, liver disease remains a major public health issue

due to factors like viral hepatitis, environmental toxins, and rising obesity rates.

FATTY LIVER DISEASE HAS SWIFTLY ECLIPSED VIRAL HEPATITIS AS SAUDI ARABIA'S MAIN THREAT TO LIVER HEALTH

Mahmoud S. Desoky, MD, is a Consultant Internist / Gastroenterologist at Sultan Bin Abdulaziz Humanitarian City (SBAHC) in Saudi Arabia as well as an Assistant Professor of Medicine at Minia University. Through a strong career throughout the Gulf Area, he has contributed to the elimination progress of hepatitis C in Egypt and has continuously advanced patient care, medical education, and research.

In practice, the most concerning threat to liver health is the increasing prevalence of obesity and fatty liver disease: the management and the awareness of the condition. I have a very big concern about the swift rise of obesity and overweight that has occurred after the COVID era and the impact this will have on liver health in Saudi Arabia.

Fatty liver disease is a new dilemma in liver health, but we know that it can be controlled through weight reduction, for instance through anti-obesity medication or bariatric surgery. However, people might not know to seek this treatment unless they are aware of the risks of liver disease.

Unfortunately, awareness about liver disease among the general public is low. People do not seek treatment until they have symptoms, which often does not occur until they develop cirrhosis. Right now, awareness focuses on other diseases: obesity, diabetes, hypertension, hyperlipidemia, cardiovascular disease, gout, and fatty liver disease is at the very end. It is underestimated. As we raise awareness, we can increase early screening, early detection, and early treatment – needed to improve outcomes for fatty liver disease as well as liver cancer.

I am confident that we will get the country to a healthier level in this era of controlling fatty liver disease. We have a strong liver transplantation center here that is well-recognized worldwide. Also, Saudi Arabia had a very impressive response to the last major threat to liver health and has seen success with hepatitis B and hepatitis C. Since they were introduced, patients have been able to access the treatment. The success of these efforts, as well as the national programs against diabetes and obesity, suggest that the treatment of metabolic-associated fatty liver disease will see great success in the future.

These efforts have to be multi-level, not only by specialists but also by primary care, students, and schools. Everyone who can share information or awareness should contribute, and then it is the government's job to ensure medication is available to stop the progression of the disease.

TÜRKIYE

Population: 85.04 million (2021)

GDP per Capita: $12,986 USD

Life Expectancy: 75.4 years (men) and 81.5 years (women)

Healthcare Spending: 4.34% GDP (2019)

Healthcare Funding: Taxes (41%), insurance premiums (31%), and out-of-pocket payment (28%) fund the healthcare system, along with a combination of national and private health insurance. The coverage offered by compulsory health insurance provided by social security foundations, namely the Government Employees Retirement Fund to serve pensions for civil servants, the Social Insurance Organization for blue-collar workers, and Bag-Kur for the self-employed, is comprehensive. The private sector is rapidly growing and complements, rather than competes with, the state system.

Sources: WorldData.Info, Global Data,WorldBank, Ministry of Health (Türkiye)

$12,986
GDP per capita

4.34%
of the GDP is spent on Healthcare

75 years (men)
and **80.8 years (women)**
Life Expectancy

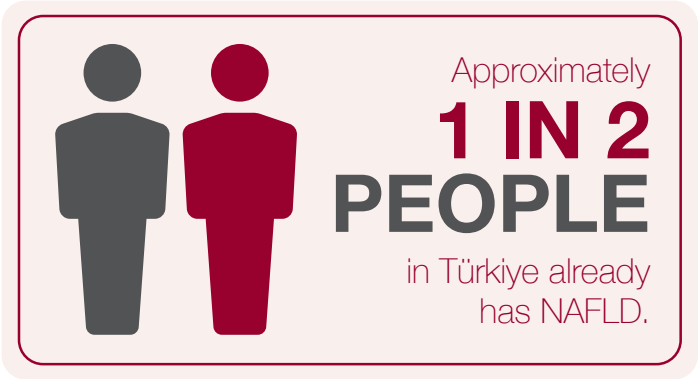
Türkiye faces many obstacles to liver health, including both unique challenges and those of broader global shifts.

Türkiye has high rate of obesity – a prevalence of approximately 32.1% according to 2016 data from the WHO.[1] Consequently, metabolic dysfunction-associated fatty liver disease (MAFLD) is a major public health concern with some studies estimating that almost half of the Turkish population currently have MAFLD, with prevalence expecting to continue its upward trajectory over the next decade.[1,2] Between 2007 and 2016, there was a 22% rate of increase of the prevalence of MAFLD to 53.1% of the population in 2016.[2]

Additional data from this study show that the condition was most prevalent amongst men over 50.[2] Furthermore, it appears that MAFLD patients are at high risk of advancing to MASH. Another study found that, 90.4% of MAFLD patients screened at a Turkish healthcare center had MASH – much higher than the typical 20% – which highlights not only the severity of this epidemic but also the high risk of mortality due to advanced liver disease.[3]

Another key cause of liver disease in Türkiye is hepatitis B – about 56% of patients with HCC were infected with the virus.[4] Hepatitis B is also thought to be the cause of between 30%-40% of the country's cases of cirrhosis.[5] As of 2019, the estimated prevalence of hepatitis B in the Turkish population was estimated to be approximately 4.57%, or 3.3 million people.[6] An HBV vaccine was integrated into the Turkish child vaccination program in 1991 with two booster vaccines administered within 12 months of birth, which has resulted in a reduction of the incidence of HBV to less than 100,000 in children less than five years old.[5]

Although not as prevalent, hepatitis C infection is another major cause of cirrhosis and HCC in Türkiye, responsible for 20% to 25% and 25% to 30% of cases respectively.[5] Based on a national study carried out between 2009-2010, prevalence of HCV infection ranged from 0.5% to 0.96% of the population, with a higher concentration amongst the poor and older groups.[7,8] It is predicted that the burden of HCV infection will increase in the next decade, with an estimated 80,000 people being infected by 2030.[5]



An at-risk group that is somewhat unique to Türkiye are barbers due to their regular exposure to the bodily fluids of their customers. One study found that HBV and HCV had a higher prevalence in barbers when compared to the general population, making HCV and HBV infection an occupational hazard for this profession.[9]

To combat viral hepatitis, the Turkish government has established "The Turkish Viral Hepatitis Prevention and Control Program" with an aim to implement and improve policies and strategies targeting viral hepatitis. This includes raising awareness amongst the high-risk groups, along with the improvement of early diagnosis and preventative treatments.

Alcohol is considered to be a significant risk factor for liver disease in Türkiye, and an approximate 15.9% of HCC patients in the country have a history of heavy drinking.[4] However, given that the vast majority of the population is Muslim, alcohol consumption tends to be limited, though relevant data is limited as well.

In 1989, the Ministry of Health in Türkiye established a national organ-sharing program, followed in 2001 by the establishment of the National Coordination Centers for the allocation of deceased donors. Following on from these programs, liver transplantation has made great strides in Türkiye. Between the years of 2002-2013, almost 7000 liver transplants were carried out with an 83% success rate, which is highly competitive with global figures.[10,11] As it currently stands, there are now 45 liver transplant centers across the country, with treatment costs starting at $52k per transplant, much lower when compared to other countries.[11]

A HIGH QUALITY HEALTHCARE SYSTEM BUT LOW PRIORITY FOR LIVER HEALTH

Dr. Fulya Gunsar is Professor of Gastroenterology at Ege University School of Medicine in Izmir. She is the current president of the Turkish Association for the Study of Liver Disease (TASL).

The picture in Türkiye around liver disease is quite varied. For example, we have excellent transplant centers, our university hospitals and the public and private hospitals are generally well equipped with up-to-date diagnostic equipment and cutting edge treatments, and we have highly skilled hepatologists and gastroenterologists.

On the other hand – and with the exception of viral hepatitis – liver disease has not really been a priority for our government who have instead mainly focused on heart disease, diabetes and cancers rather than the links between obesity, NAFLD and NASH.

So currently we are in a situation where, although the rates of liver disease caused by viral hepatitis are falling, we are now dealing with increasing numbers of patients with NAFLD and NASH who need urgent interventions, often from a range of healthcare professionals.

However, this is an expensive system to maintain, and we know from the rates of obesity and the high rates of T2D in our population, that this cause of liver disease will continue to rise. The reality is that both clinicians and the government must work together to put strategies, including early detection, in place to deal with this upcoming crisis.

Currently the Turkish Association for the Study of Liver Disease is developing clinical guidelines for NAFLD which can be shared and used in both primary and secondary care. We sincerely hope that the government endorses and supports these guidelines. We really need to have national awareness of NAFLD and for everyone to understand that NASH can lead to cirrhosis or liver cancer.

> The reality is that **both clinicians and the government must work together** to put strategies, including early detection, in place to deal with this upcoming crisis.
>
> - DR. FULYA GUNSAR

Viral hepatitis is generally well managed, with a program for the elimination of HBV and HCV by 2023, and treatment and testing available for all. However, there are still concerns about the rates of awareness of hepatitis B or C. We believe that the key here is to educate the primary care physicians, not just to be alert for symptoms of hepatitis B, but also to encourage testing for patients who could be at risk and to refer for diagnosis as quickly as possible.

Ninety percent of the population in Türkiye is Muslim, therefore, alcohol consumption is generally limited. Despite this, we have many patients with alcohol induced liver disease, and as required for these patients, we will carry out liver transplants after six months' abstinence, or as an emergency if necessary.

Although our numbers on liver cancer are relatively low compared to other countries, we still see 70% of our patients at a late stage where curative treatments are often not an option. However, we have access to the latest medical advances, including radio frequency ablation, trans arterial radio embolization, chemoembolization, liver transplantation and liver resection for eligible patients with hepatocellular carcinoma. We generally use a multi-disciplinary approach with weekly input from radiologists, hepatologists, transplant surgeons and oncology.

Our national liver transplant program has been established for many years and is highly successful. Patients travel from many other countries to receive transplants. We have recently expanded our living donor program allowing us to increase our rate of transplantation. (See page 85).

A key consideration when we look to the future is the disparity between funding for the private and public hospitals. As the burden of liver disease continues to rise, the public sector, including the university hospitals are struggling to cope, often with basics such as bed space. Although the private system is very good, most people here cannot afford to pay for it. If we want liver health equality for all, not just for those who can pay, we need to invest in our public system once more.

BEST PRACTICE LIVING DONOR LIVER TRANSPLANTATION

‘Our national liver transplant program was established in 1988,’ explains Dr. Fulya Gunsar. ‘However due to the lack of donors from deceased patients, quite early on there was much clinical focus on living donor liver transplant (LDLT) as the most likely source of hope for patients awaiting liver transplant.

‘The first successful partial living donor liver transplant (LDLT) in children in Turkiye was performed by Haberal et al in 1990 and out of the 17544 liver transplantations performed in our country since 1988, 12839 (73%) of them have been from LDLTs.

‘All this experience has led to Türkiye becoming a center of excellence for LDLT. The one year patient survival rate after LDLT is between 80% - 90% and we have patients coming from all over the region and beyond to receive living donor transplants.

DID YOU KNOW?

The **first successful partial liver transplant** in Türkiye was performed in 1990.

‘One of the key issues when carrying out LDLT is the safety of the donor material and this was, unfortunately, a significant challenge during the Covid 19 epidemic. However, despite this, we have recently expanded our living donor program to allow us to increase our rate of transplantation and we expect this success to continue.’

NORTH AMERICA

HEALTH OVERVIEW

The third largest continent in the world geographically, with a population of around 370 million, North America comprises the northern portion of the Western hemisphere. With a combined GDP of over $20 trillion USD and GDP per capita income of $67,514 USD, North America is the wealthiest region on earth. 16.32% of the GDP is spent on healthcare in North America, with health spending per capita at around $10,000 USD a year, although around 11% of this amount comes from out-of-pocket payments.

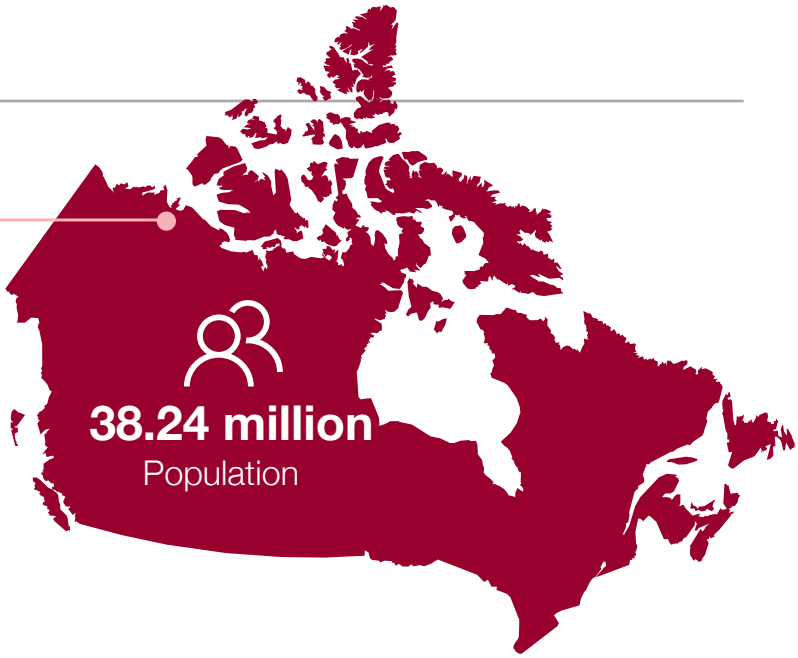
Despite its wealth, North America is also a region of great inequality, often along racial lines. In the United States for example, an estimated 28% of Black households and 26% of LatinX households had zero or negative net worth in 2019, twice the proportion of white communities. This inequality is particularly reflected in healthcare, especially in the United States where, unlike other developed countries, residents do not have universal healthcare access. Although North America has a highly developed medical infrastructure – world-class hospitals equipped with cutting-edge diagnostic equipment and staffed with globally-recognized experts providing the latest treatment therapies – many low-wage workers receive no health insurance, sick pay or pension plans. They have little hope of funding medical insurance costs and instead rely on emergency care facilities or poorly funded public clinics and hospitals.

North America is also a region of immigrants; 2017 saw a net migration of nearly six million people from around the world. This migration brings with it many health challenges, including chronic hepatitis, tuberculosis and HIV. At the same time, many of these immigrant communities begin their lives in North America living in areas of deprivation where often basic amenities, including access to healthcare, are unavailable and adding to their health burden.

Sources: World Bank, Institute for Policy Studies, US Census Bureau

OVERVIEW

CANADA



The second largest country in the world by area, 80% of which is uninhabited. Canada is a developed country divided into English speaking (58%) and French speaking (20%) territories. Around 5% of the population identify as native Indigenous people.

Population: 38.24 million (2021)

GDP per Capita: $53,372 USD

Life Expectancy: 79.7 (men) and 83.9 (women)

Healthcare Spending: As of 2021, Canada had a GDP of $1.99 trillion USD, and government spending on healthcare is approximately 10.8% of GDP (2019) equating to around $5,000 USD per capita. Domestic private health expenditure is around 29% of all healthcare spending.

Healthcare Funding: The Canadian Medicare system provides for universally available and free necessary primary and hospital care, administered and funded by the individual provinces supported by per capita assistance from the federal government.

Funding for other healthcare services, for example dental care and prescriptions, vary depending on the provincial funding but is usually available for certain low income groups such as pensioners, veterans and the Indigenous populations. Around two thirds of Canadians have some form of private insurance either through their employment, unions, or paid for privately, which also covers services such as optical and dental care.

Each province and territory is responsible for administering and overseeing its own health, and, as a result, there are wide variations in the focus on and availability of different healthcare services, including treatment pathways. Experts have cited this fragmented approach along with lack of federal leadership as one of the reasons why Canada was recently placed 10th out of 11 developed countries for the provision of good quality healthcare, ahead only of the USA.

Overall, the Canadian healthcare system provides a GP-led primary care which is available for all, although in some remote areas – which particularly affects Indigenous people – these services can be geographically difficult to access and may be nurse rather than doctor-led.

Secondary and tertiary care is provided by a mix of public and private (although usually not-for-profit) hospitals mostly overseen by local authorities or community boards. Specialist care can be accessed privately but is usually available via GP referral to the relevant tertiary care center.

Sources: World Bank, The Commonwealth Fund, WorldData.Info

$53,372
GDP per capita

10.8%
of the GDP is spent on Healthcare Spending

79.7 years (men)
and **83.9 years (women)**
Life Expectancy

A universal healthcare system, globally recognized research centers, and world class hospitals benefiting from the best diagnostic equipment and clinical expertise should, in theory, be good news for liver health. Yet Canadians are facing a crisis in liver health. Deaths from liver disease rose nearly 30% from 7.2 per 100,000 to 11 per 100,000 between 2000 and 2020 and, in 2013, the Canadian Liver Foundation estimated that one in ten Canadians were living with liver disease, with the number likely to have risen in recent years due to a rise in the rates of obesity and the corresponding emergence of metabolic dysfunction-associated steatotic liver disease (MASLD) and its more advanced form, metabolic dysfunction-associated steatohepatitis (MASH).[1,2]

Historically, viral hepatitis has been the main driver of chronic liver disease in Canada. This has been caused in part by relatively high rates of HBV found in immigrants arriving from developing countries, along with challenges in ensuring appropriate testing and treatment for Indigenous populations, who have a five-times higher incidence and prevalence rate of HCV than in the general population.[3,4]

A lack of federal initiatives has resulted in a fragmented approach to hepatitis control. For example, although childhood vaccinations for HBV have been in place since the 1990s, the age at which it is offered still varies widely between provinces and territories from birth to age 12.[4] Still, overall rates of viral hepatitis are showing a downward trend. Following a 14.4% rise between 2014 and 2018, between 2018 and 2019, the rates of HCV dropped by 10.2% in adults (although it rose in children). HBV rates also fell to their lowest in ten years between 2018 and 2019.[5]

Additionally, the introduction of widely available and fully funded antiviral therapies have transformed the outlook for HCV, which is now by and large considered to be a curable disease in Canada.[6] This is reflected in the liver transplant rate. Although the number of liver transplants in Canada per year increased from 251 in 2000 to 349 in 2018, the proportion of patients transplanted for HCV decreased from 31.5% in 2000 to 3.4% in 2018.[7]

However, as the danger from viral hepatitis slowly recedes, the transplant rates clearly demonstrate that another crisis is looming in liver health.

Canada, in line with the rest of the developed world, is beginning to suffer the consequences of the obesity epidemic on liver health. Just over one in four adults in Canada are now considered obese, with 62.6% either overweight or obese; MAFLD and MASH rates are soaring commensurately.[8] Estimates suggest that today 21.1% of all Canadians have some form of MAFLD and that 5.4% – just over 2 million adults – have MASH, the consequences of which are already being felt in liver health.[9] In 2000, just 0.4% of all liver transplants were performed due to MASH. By 2018 that number had risen to 12.6%, and by 2040 MASH is now expected to be the number one cause of liver cirrhosis in Canada.[7,10] However, despite this threat and the potential financial burden this represents to the health system, there appears to be little federal leadership around the liver health crisis, with no national guidelines and treatment pathways for MAFLD and MASH varying between individual provinces and territories.

There is also another danger looming with 22.2% of all Canadian adults classified as heavy drinkers, and, based on current trends, alcohol-associated liver disease is expected to become one of the main causes of liver cirrhosis (just behind MASH) by 2040.[8,10]

With increasing chronic liver disease upstream, the number of new cases of liver cancer in Canada is also increasing, with the percentage of transplants for HCC rising from 2.3% in 2000 to 32.4% in 2018 and a projected expectation of 3,500 new cases in 2022.[7,11,12]

There is little data on autoimmune liver disease in Canada. A 2018 study identified around 8680 cases of PBC across Canada, and another estimated the rate of PSC at 0.92 per 100,000.[13,14] There is no data on autoimmune hepatitis in the adult population.

In 2013, an estimated **one in ten Canadians were living with liver disease**

WE NEED TO BE PROACTIVE, INNOVATIVE AND MAKE OURVOICE HEARD

Dr. Mark G. Swain is Professor of Medicine and holds the Cal Wenzel Family Foundation Chair in Hepatology at the University of Calgary, Alberta, Canada. He is the current President of the Canadian Association for the Study of the Liver (CASL).

In Canada, as in many areas of the world, liver disease is shaping up to be one of the major health issues of the next few decades. Currently, at least a quarter of the Canadian population are living with NAFLD. However, with the rates of alcohol-associated liver disease, NAFLD and NASH, and liver cancer all projected to rise over the next few years, it is perhaps not an exaggeration to say that we are facing a tsunami of liver disease which will place an increasingly unsustainable burden on our healthcare system.

We can see the early waves of this tsunami lapping up on our shores already. For example, seven years ago I didn't need to hold a clinic specifically for NASH or NAFLD patients. Today, due to increased demands, we dedicate NASH and NAFLD clinics on a regular basis.

Alcohol-associated liver disease used to be considered a disease of older, male, lifelong heavy drinkers, and we rarely saw young people with severe alcohol-associated liver disease. Now, and especially since the pandemic when alcohol intake soared, it is common for me to be called in to hospital to deal with people in their 20s and 30s who have been admitted with acute alcoholic hepatitis or even liver failure. Even more striking, increasingly these are young women. Liver cancer, once a fairly rare cancer in Canada, has unfortunately become a 'growth industry', with incidence rates rising faster than any other cancer.

It is quite shocking for us as hepatologists to witness these dramatic changes in such a short period of time, and we understand that this situation cannot continue. Thus, we are working hard to try to be more proactive in making effective changes. For example, we don't currently have NAFLD or NASH guidelines in Canada, so CASL members are in the process of setting up a committee with primary care physicians, nursing and other specialists, to develop guidelines that will also include more multi-disciplinary approaches.
In Calgary, together with our primary care colleagues, we have co-developed an innovative screening and treatment pathway for NAFLD (see page 90 for more info). 'This model has been running since 2017 and has proven to be a great success. This type of primary care-based approach to liver disease case finding needs to be more widely employed across Canada.

> Our challenge then isn't so much in treating the patients with liver disease that we do see. **It's finding the patients - preferably as early as possible - that don't even know they have it!**
>
> - DR. MARK G. SWAIN

However, we are clinicians, not policy makers, and it is they who can make the big difference to liver health in terms of disease awareness, prevention, and early diagnosis. Unfortunately, possibly due to an established – and incorrect – narrative of liver disease always being the fault of the patient, there appears to be a lack of will, at the government level, to face up to and tackle the oncoming challenges of liver health.

We believe that it is imperative for liver disease to have a national voice, and to this end we are working with external partners to try to reach health policymakers in order to better achieve the big changes needed. To support this strategy, we also need accurate data to reinforce the message that prevention and early diagnosis can prevent the spending of healthcare dollars on liver disease further down the line, when people present for care with advanced cirrhosis, liver failure or liver cancer.

When I became a hepatologist in the early 1990s, we had very few effective liver treatments to help our patients. Today, while we have effective therapies and a growing number of care pathways for almost every type of liver disease, we can still only ever treat the patients we know about. Unfortunately, liver disease is typically a silent disease and many people do not know that they are living with it, so they do not ask for and receive help until it is often too late.

To a certain extent, our challenge then is not so much in treating the patients with liver disease that we do see. It is finding the patients – preferably as early as possible – that do not even know they have it!

BEST PRACTICES IN NAFLD CARE IN CALGARY, ALBERTA

A multi-disciplinary collaboration exists to develop a pathway for the screening and triaging of patients at risk of NAFLD within a primary care setting.[15]

Between January 2016 and December 2017, it was noted that around 40% of patient referrals to the Calgary hepatology service were for patients with NAFLD, to be assessed for the risk of liver fibrosis. Most were found to be of low risk and did not require further tertiary follow up.

Hepatologists, radiologists and primary care physicians in Calgary therefore partnered to co-develop an innovative screening pathway for those NAFLD patients at risk of fibrosis. Rather than referral, the primary care physician could directly order an ultrasound-based test called shear wave elastography (SWE), from a community ultrasound provider, assess the results, and, based on a pathway-based algorithm, advise on best treatment options which might then include referral or ongoing management in the primary care medical setting, in conjunction with management of common comorbidities including diabetes, high blood pressure and elevated cholesterol where relevant. Along with SWE-based screening blood serum, liver tests were also taken and, based on the pathway, other potential causes of liver disease were ruled out.

DID YOU KNOW?

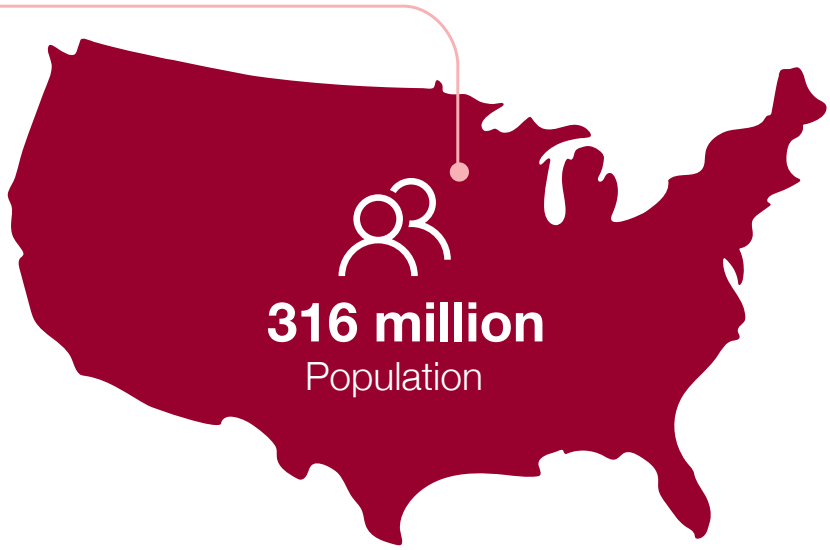
Between 2016-2017, it was noted that around 40% of patient referrals to the Calgary hepatology service **were for patients with NAFLD.**

The NAFLD pathway was implemented in January 2018 and made available to all primary care physicians in the Calgary Health Zone. Of the 2084 patients with suspected NAFLD who were initially evaluated in primary care using the pathway, 91.5% were found not to need referral to hepatology, 60.3% were classified as being obese, and 52.5% had elevated serum liver enzymes which would have previous qualified them for tertiary referral. The pathway is now standard practice in primary care settings across Calgary.

'Since January 2016 almost 14,000 patients have gone through this pathway,' explains Dr. Mark Swain who led the initiative. 'Of those, only around 7% of patients have needed to be referred to a liver specialist, with the remainder being effectively treated within their primary care setting.

'This innovative primary care-based case finding system has provided significant benefits, for both the tertiary care service and the patients who are now able to have their disease managed within a primary care setting, alongside their own primary care physician, in conjunction with any other health issues they may have.'

UNITED STATES OF AMERICA



The third largest country in size in the world, the US has the third largest population after China and India. The US is a federal republic made up of states, territories, and a federal district. There is no official language although English is the first language for around 79% of the population, and Spanish is spoken by around 13% of the population (equating to approximately 41 million people). 2% of the population (around 6.6 million people) identify as native Indigenous people

Population: 316 million

GDP per Capita: $81,695 USD

Life Expectancy: 74.8 (men) and 80.2 (women)

Healthcare Spending: As of 2021, the US had a GDP of $21.37 trillion USD, making it the world's largest economy. Government spending on healthcare is approximately 16.77% of GDP (2019) equating to around $10,92 USD per capita. Private health expenditure makes up over 50% of all healthcare spending.

Healthcare Funding: Uniquely in the developed world, the US has no universally available healthcare program. Private insurance, obtained as an employee benefit or privately purchased, provides health coverage for 67% of Americans, and the details of private coverage vary widely. Other forms of health provision include Medicare for those over 65 or with long-term disabilities and Medicaid for low income families, both of which are government-funded. There is no universal coverage for long-term health care, and few insurance policies provide this cover. Just over half of the hospitals are nonprofit, a quarter are for-profit and 19% are state-owned public hospitals. It is estimated that 8.5% of the population is uninsured.

Sources: World Bank, The Commonwealth Fund, WorldData.Info

$81,695
GDP per capita

16.77%
of the GDP is spent on Healthcare Spending

74.5 (men) and 80.2 (women)
Life Expectancy

The wealthiest and probably the most medically advanced country in the world is facing a crisis in liver disease of dramatic proportions. Currently, around 4.5 million adults in the US are living with a diagnosed liver disease and just over 50,000 people die of the condition every year, with 60% of these deaths attributed to alcohol-associated liver disease.[1] By 2030 however, it is predicted that liver deaths will have increased (since 2015) by 178% to an estimated 78,300 deaths, mostly attributable to metabolic dysfunction-associated steatotic liver disease (MASLD) and its more advanced form, metabolic dysfunction-associated steatohepatitis (MASH), which are expected to overtake alcohol-associated liver disease as the main liver-related cause of death.[2]

This dramatic change in the liver disease landscape is directly attributable to the high rates of obesity which has been a characteristic of American health for several decades. Indeed, 42.4% of Americans are now classified as obese, so the burden of fatty liver disease is translating into serious liver health issues including cirrhosis and decompensated liver disease.[3] A 2020 study of 100 physicians involved in treating liver disease found that MASH and MAFLD combined make up around 42% of specialists' and primary care physicians' liver patients.[4]

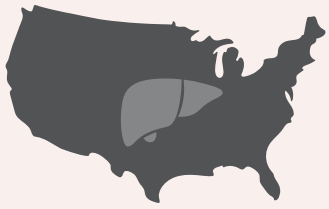
During the period 2015-2030, there are projected to be nearly 800,000 excess liver deaths with the accompanying social and economic costs.[2] A 2016 study estimated the annual medical costs of MAFLD in 2016 as $103 billion USD.[5] This figure is likely to have risen and to continue to rise exponentially over the next few years in parallel with the incidence of MAFLD and progression to MASH.

As with the rest of the developed world, liver health appears to be low on the list of priorities for both health administrators and health campaigners in the US. Obesity is regularly linked to diabetes and cardiovascular disease, but liver disease is rarely cited as a consequence of obesity. Thus 30% of physicians from across primary and secondary care were unable to name any national guidelines for the management of chronic liver disease.[4]

In 2020, Global Liver Institute and its MASH Council (known as the Fatty Liver Disease Council) released the U.S. MASH Action Plan to address MASH (now known as MASH), the most advanced form of MAFLD, and its impact on patients, families, public health, and the economy.

The U.S. MASH Action Plan, the first national MASH strategy, was a logical next step in the work of the GLI MASH Council to address the multiple challenges and barriers to better NASH screening, diagnosis, and treatment. Against the backdrop of MASH's prevalence and impact, each of these recommendations plays an instrumental role in elevating the disease to its rightful place on the public health agenda.

While the MAFLD/MASH epidemic continues to grow, alcohol-associated liver disease continues to be a significant cause of liver-related death. The age-adjusted death rate from alcohol-associated liver cirrhosis increased by 47.0%, from 4.3 deaths per 100,000 population in 2000 to 6.4 deaths per 100,000 population in 2019, with rates for white males increasing by 106%.[6]



4.5 MILLION

Adults in the US are **living with a diagnosed liver disease**

A 2019 national survey of around 25% of the adult population (aged over 18) reported binge drinking at least once in the previous month and estimates suggest 14.5 million people over the age of 14 have an alcohol use disorder.[7] At the same time, it is reported that less than one in ten people received any treatment for their condition.[6] In total, 29,505 people died from alcohol-associated liver diseases in 2020.[7] Further, between 2008 and 2019, alcohol-associated liver disease increased from 22% to 31% as a proportion of candidates for liver transplantation.[8]

On another hand, viral hepatitis is generally well controlled with effective vaccination and testing programs, combined with the latest available antiviral treatments which have kept acute case numbers stable for HBV and HCV (although infection rates for HCV are slowly rising).[8] Between 2010 and 2019, the proportion of candidates for liver transplant with a diagnosis of HCV dropped from 30.6% to 12.6%.[8]

However, it is not all good news. Both acute and infection rates of hepatitis A have been rising steadily since 2017 with an unprecedented spike in acute cases in 2019 attributed to a rise in needle-to-needle drug use and homelessness.[8] Overall, just under 4,000 people died from viral hepatitis in 2020, representing 1.2 deaths per 100,000 of population.[9]

The US carries out the highest number of liver transplants in the world and continues to be a center of global expertise. In 2019, there were 8,896 liver transplants were performed including 524 living liver donor transplants.[8,10]

Finally, it must be noted that the US benefits from numerous highly motivated and well-organized clinical and patient groups who have, between them, produced a large, high-quality and focussed database of relevant information on the current and future state of liver health. If there was any doubt before, there can be no more excuses for the government not to develop a national strategy on MAFLD and MASH as a matter of urgency to combat this potentially catastrophic public health crisis.

In 2019,

8,896

Liver Transplants

were performed, including **524 living liver** donor transplants.

MANY CHALLENGES IN LIVER HEALTH, BUT THE POSITIVES ARE WITHIN REACH

Professor Scott Friedman is the Chief of the Division of Liver Diseases and Dean for Therapeutic Discovery and Professor of Pharmacologic Sciences at the Icahn School of Medicine at Mount Sinai Hospital in New York.

We are facing several significant and interrelated challenges in liver health, all of which, if unresolved, are set to place a progressively larger burden on our healthcare system and providers over the next few years and even decades to come.

The first major challenge is that posed by NAFLD and NASH. Driven by our high obesity rates, there is every indication that the prevalence of these conditions is increasing fast and will continue to do so for the foreseeable future. Concurrently, and as a direct consequence of this, we are also facing rapidly rising rates of liver cancer. Primary liver cancer has the fastest rising incidence rates of any cancer, not just in the US, but globally.

There is a further danger to note here. Whereas with viral hepatitis, less than 5% of patients progress to liver cancer without at least some cirrhosis, the pathology pathway of NASH is somewhat different, and we estimate that around 30% of patients with NASH may progress to liver cancer without cirrhosis. This group of patients will have been far less likely to be in a screening program, and, therefore, their cancer is more likely to be diagnosed at a more advanced stage.

Currently we are not in a great position to counteract the effects of NAFLD and NASH through medications. The only approved treatment we can offer is to work with our patients to lose weight and exercise more, and in extreme cases bariatric surgery may improve NASH, as discussed below. However, as every clinician knows, weight loss can be extremely difficult for some patients to achieve – let alone managing and maintaining the weight – and is also a challenging therapy for the doctor to manage.

Additionally, there is a lack of regular screening for patients who are at high risk of NAFLD or NASH. In part, this is due to limits on capacity, but it is true to say that there is also a certain mindset amongst some clinicians, perhaps particularly in primary or general medicine, who feel there is little point looking for a disease for which there is no effective treatment. Even if the patient is included in a screening program, there is often uneven knowledge of 'what to do next' with someone who has elevated transaminases or high levels of fat around the liver. We need to change that clinical mindset – early detection always means better outcomes.

One potential solution to obesity is, of course, bariatric surgery, with many patients and their clinicians opting for this route in increasing numbers. However, while bariatric surgery is indeed beneficial for weight loss (along with providing some other metabolic benefits), it is an invasive and life-changing procedure, not to mention costly. As a result, this is not a solution that can be scaled up to an extent that it would provide a solution to the current US numbers of patients with NAFLD and NASH. Likewise, while we have a world-class liver transplantation program, with ongoing incremental improvement in transplant medicine, you simply cannot expect this complex and expensive procedure to provide a broad solution for the oncoming wave of medical need.

“We are facing several significant and interrelated challenges in liver health, all of which, if unresolved, **are set to place a progressively larger burden on our healthcare system.**”

- PROFESSOR SCOTT FRIEDMAN

MANY CHALLENGES IN LIVER HEALTH, BUT THE POSITIVES ARE WITHIN REACH

That leaves us with future pharmaceutical therapies, which have the advantage of being available to potentially treat large numbers of people. Probably our best hope of turning the tide of liver disease will come from treatments which directly work on the pathology of the liver to reverse the damage caused by NAFLD and NASH, and with several drugs currently undergoing late-stage trials we hope that at least one or two of these prove to be an effective therapy.

However, we cannot rely on the pharmaceutical industry to provide all the solutions to liver health. We have to consider that it may be time for a re-think of our current healthcare structure in order to meet this new type of health challenge.

Previously most liver disease was caused by viral hepatitis, or was alcohol-associated, with both conditions managed wholly within the specialty of hepatology. Now we have a situation where a patient who is at high risk for liver disease (i.e. an obese or T2D patient) may see a primary care doctor or a family practitioner. Then, depending on their most pressing medical need, they might be receiving specialist treatment from an endocrinologist, a cardiologist and other specialists.

Therefore, rather than being seen as a disease of just one speciality, NAFLD and NASH may be better managed via multi-disciplinary pathways effectively coordinated across all the various relevant specialities, supported by robust, widely approved clinical guidelines. This change would take a comprehensive conversation between clinicians and health care providers, and it is something we should think about sooner rather than later.

Apart from NASH and NAFLD there are several other areas of liver health that are challenges for hepatologists and their patients. Alcohol-associated liver disease continues to rise – especially during the COVID-19 pandemic – with little sign of slowing down. Pediatric liver disease may not affect the same numbers as NAFLD and NASH, but they can prove to be catastrophic for the child and, of course, devastating for their families. Unfortunately, we still have too few treatments and incomplete understanding of these often very complex conditions.

Drug-induced liver injury is another area of liver health which is often downplayed and while sporadic, is still a major unmet need. Often, we only reach diagnosis by exclusion of other conditions, and far too late to prevent severe damage from occurring. Hepatologists have also noted that COVID-19 can worsen liver function in patients with advanced liver disease, and we are continuing to see the effects of this in our patients, even while the epidemic is waning.

It is important, however, to remember that while liver disease presents a huge challenge for us all, we have many positives to think about. Firstly, most liver diseases are mostly either preventable or treatable, so if we focus on implementing effective preventative and awareness strategies then the burden should start to reduce. Secondly, we have some pharmaceutical therapies coming down the line which should improve outcomes of some liver conditions. Finally, and perhaps most importantly, uniquely of all our organs the liver has an amazing capacity to heal. All we have to do is give it a chance.

> Uniquely of all our organs **the liver has an amazing capacity to heal.** All we have to do is give it a chance.
>
> - PROFESSOR SCOTT FRIEDMAN

OCEANIA

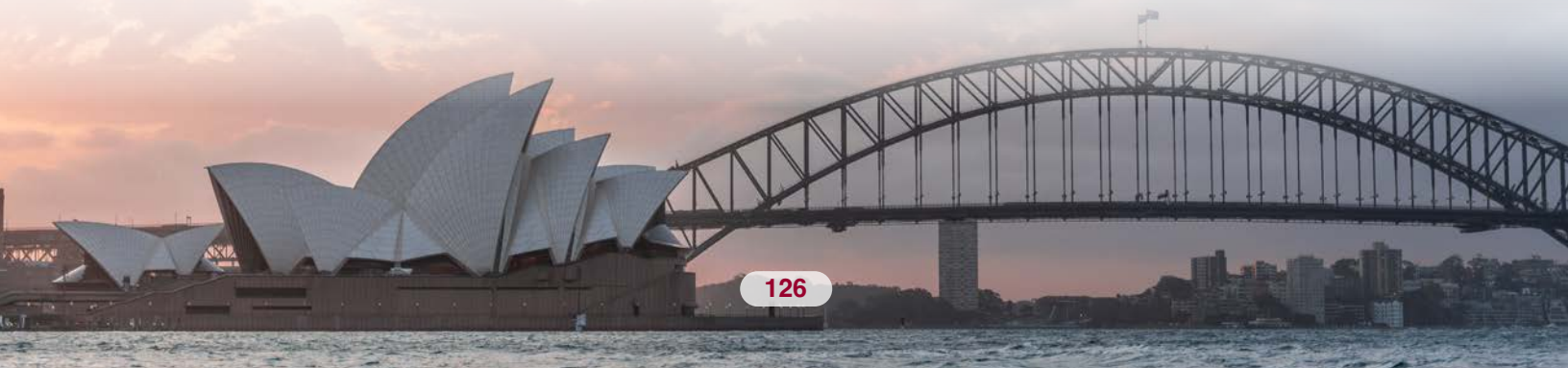
HEALTH OVERVIEW

Oceania, a vast region encompassing Australasia, Melanesia, Micronesia, and Polynesia, presents a diverse health landscape characterized by both challenges and successes. The health status across Oceania is influenced by factors such as geography, culture, socioeconomic conditions, and access to healthcare.

In Australia and New Zealand, two of the more developed countries in the region, health indicators generally reflect high standards of living. The healthcare systems in these countries are robust, providing comprehensive services and advanced medical technologies. Non-communicable diseases (NCDs) like cardiovascular diseases, diabetes, and obesity are prevalent, attributed in part to affluent lifestyles. Mental health is also a growing concern, prompting increased efforts to address awareness and support.

In the Pacific Islands, including Melanesia, Micronesia, and Polynesia, many health challenges become more pronounced. Many island nations face limitations in healthcare infrastructure, human resources, and accessibility. Communicable diseases such as tuberculosis and malaria persist in some areas, rates of obesity are high, and climate change poses additional risks to health, food security, and increased vector-borne diseases.

Sources: WHO Western Pacific Health at a Glance



The divide in health outcomes between Australia and New Zealand and the rest of Oceania persists in liver health as well. While Australia and New Zealand enjoy some of the lowest death rates due to liver disease in the world (New Zealand, for instance, has the third lowest death rate in the world), many island nations face mortality rates due to liver disease between 3 and nearly 10 times as high.[1]

The smaller island nations in Oceania face some of the highest rates of incidence and mortality due to liver cancer around the world, second as a region only to Asia.[2] Indigenous populations in Oceania, especially in the small island regions of Melanesia, Polynesia, Micronesia, and Papua, as well as from Australia and New Zealand, are over-represented for the burdens of infectious diseases (including viral hepatitis).[3] These communities face many challenges to positive health outcomes, including health system access and infrastructure, they also have some of the highest rates of obesity and fatty liver disease.

New Zealand has the
3rd lowest
death rate due to liver disease
in the world

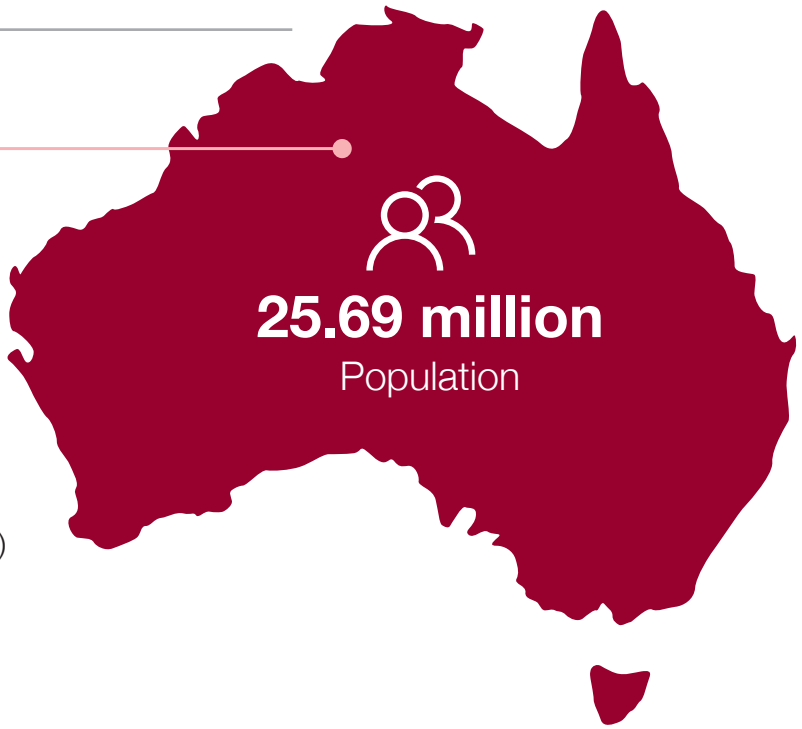
DID YOU KNOW?

Oceania has the
3rd highest NAFLD prevalence in adolescents.[5]

In fact, all of the nations with 50% or more people with obesity are found in Oceania – Nauru, Palau, the Marshall Islands, Tuvalu, and Niue.[4] Accordingly, Oceania has, for instance, the third highest metabolic dysfunction-associated fatty liver disease (MAFLD) prevalence in adolescents.[5] A similar pattern can be followed in the shared transplantation system of Australia and New Zealand, where NASH is increasing as the primary indication for liver transplantation.[6]

Viral hepatitis also poses a serious risk for the region, in which HBV causes more deaths than tuberculosis, HIV infection, and malaria, combined, and HCV leads to many cases of liver cancer.[7] Although Australia has implemented a remarkably successful HCV elimination strategy, there is still much work left to be done in the region.

AUSTRALIA



Population: 25.69 million (2021)

GDP per Capita: $64,712 USD

Life Expectancy: 81.2 (men) and 85.3 (women)

Healthcare Spending: 10% GDP

Healthcare Funding: Australia uses a combined system to achieve universal health coverage. Its universal public health insurance program (Medicare) covers care and prescriptions delivered outside of public hospitals and clinics. Public hospitals and clinics, are owned, operated, and funded by state, territory, and local governments. Medicare coverage is automatic for citizens and eligibility is available for permanent residents, people from countries with reciprocal benefits, and New Zealand citizens. Funding is financed through tax revenue and a government levy. About half of Australians purchase supplemental insurance for private hospital care, dental services, and other health services; this accounts for about a third of health spending in the country.

Sources: The World Bank, World Life Expectancy, The Global Economy, International Journal for Equity in Health

$64,712
GDP per capita

10%
of the GDP is spent on Healthcare

81.2 (men) and **85.3 (women)**
Life Expectancy

Liver disease affects more than six million people in Australia, leading it to become the 11th leading cause of death in the nation.[1, 2] Males account for approximately two-thirds of those deaths, suggesting a particular set of etiologies that affects the distribution of liver disease in the population.[2] Several global patterns that affect liver disease also appear in Australia.

In Australia, non-alcoholic fatty liver disease is the most common cause of chronic liver disease – and cases are continuing to rise.[3] While accurate prevalence data is limited without population-based studies, estimates track with global estimates.[4] The epidemic of fatty liver disease follows the growing prevalence of overweight and obesity. One in four children and teens and two in three adults in Australia are considered overweight or obese.[4] Based on data from member countries of the Organization for European Co-operation and Development (OECD), Australia ranks 9th of 21 countries for prevalence of overweight and obesity over 15, greater than the OECD average. This proportion is even higher on the list for men than for women.[5] (metabolic dysfunction-associated fatty liver disease, or MAFLD is also more common in men than women in Australia.) Unfortunately, this trend in overweight and obesity has been on the rise for many years without signs of slowing down.[5] The prevalence of type 2 diabetes is also related to the rise of MAFLD and its more advanced form, metabolic dysfunction-associated steatohepatitis (MASH).[4] In parallel, prevalence of MAFLD is expected to increase by 25% by 2030, while MASH prevalence is expected to increase by 40%.[6] Prevalence in children is also on the rise – which, unfortunately, carries higher rates of progression to cirrhosis, liver cancer, or end-stage liver disease requiring transplantation than adults.[3, 4]

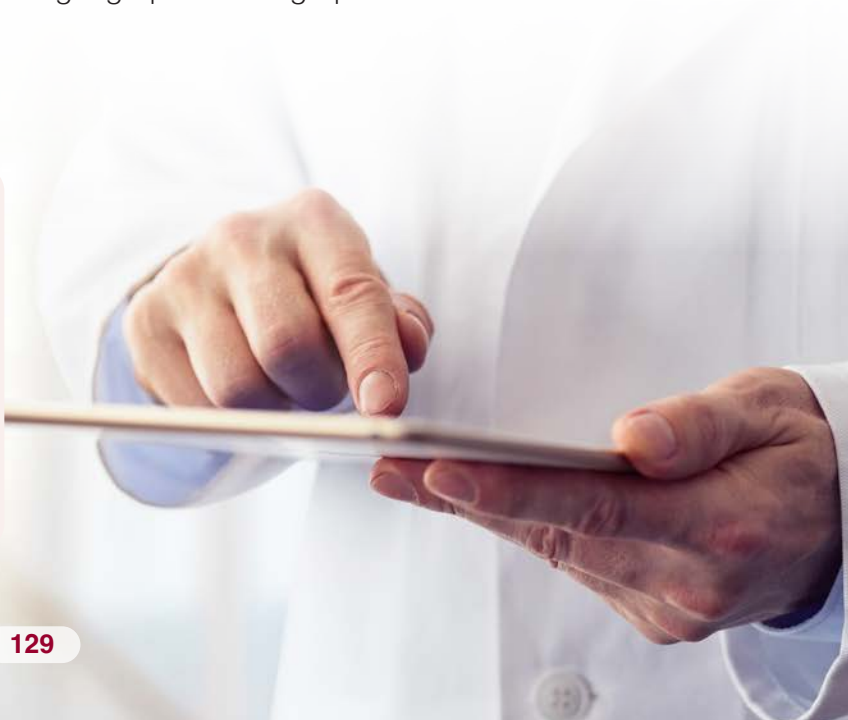
6 MILLION PEOPLE

(about 1 in 4) are affected by liver disease.

EXCESS ALCOHOL CONSUMPTION

is the leading cause of cirrhosis in Australia.

While MAFLD is the most common liver disease, excess alcohol consumption is the leading cause of cirrhosis.[3] Most Australians over the age of 14 have consumed alcohol in their lifetime, with the annual consumption rate of 9.5 liters of pure alcohol per capita for this age group, above OECD averages.[7] While there has been a decline in the proportion of people exceeding lifetime risk in recent decades, this improvement has paused since 2016;[7] about 1 in 4 men and 1 in 10 women exceed these guidelines today. Though this decline is positive, 25% of Australians 14 or older drink at a risky level at least monthly; this is also higher in men than in women.[7] An estimated 40% of liver cancer burden and nearly 20% of the chronic liver disease burden in Australia can be attributed to alcohol consumption – and liver disease is the most common cause of alcohol-induced death.[7] Notably, consumption is higher in regional areas than capital cities, which suggests geographic demographic differences in risk.



DID YOU KNOW?

Prevalence of NAFLD is expected to **increase by 25% by 2030,** while NASH prevalence is expected to **increase by 40%.**

Approximately 0.9% of the Australian population are living with hepatitis B, which represents a slight increase in the past two decades.[8] Hepatitis C has been about half as common.[9] However, since 2016, rates of new hepatitis C infections have declined, after highly effective direct acting antiviral treatments became widely available in a national scheme.[10] Hepatitis A, D, and E are known to be rare in the country, with A primarily caused by international travel.[11,12,13] Aboriginal and Torres Strait Islander people are at a greater risk of liver disease than other groups, in particular hepatitis B.[2]

There is a four-dose hepatitis B vaccination program for Australian newborns during the first four months of life, available freely through the National Immunisation Program, while eligible people under 20 years old, refugees, and other humanitarian entrants to the country can receive a free catch-up vaccination as well.[14] While the vaccination became available in the early 1980s, free infant vaccination began in 1990 and began nationally in 2000; as soon as 2017, 95% of Australian 1-year-olds were fully vaccinated against hepatitis B, and related hospitalizations have decreased since the vaccination programs began.[15]

While rare liver diseases do not receive widespread research attention, PBC incidence has been increasing, with women receiving the vast majority of diagnoses.[16] AIH cases are about 3 in 4 women, with about 1 in 4 having developed cirrhosis at time of diagnosis.[17] PSC is rare but present, with under a thousand cases diagnosed throughout the country annually.[18]

The total cost of cancer in Australia is 6 billion US dollars each year, and the country has nearly tripled its research spending in the last two decades.[19, 20] However, with only 1.8% of cancer cases being liver cancer, the diseases likely receive only a small portion of that allocation.[21] However, 5% of cancer deaths are attributable to liver cancer, disproportional to its prevalence.[21] Unfortunately, parallel to many other countries around the world, liver cancer only has a 22% five-year survival rate, and both preventive efforts as well as earlier diagnosis and improved treatment options will be important to increase survival rates.[22] Liver cancer is the most rapidly rising cause of cancer death in Australia.[2]

Liver transplants have been carried out in Australia since 1985, with one unit regulating liver transplantation in each state or region.[23] Almost all liver transplants are performed from deceased donors in Australia.[24] Because collaborative research is organized by the Australia and New Zealand Liver Transplant Registry and counts both countries, for which the most recent data available indicates that approximately 260 liver transplants across adults and children occur annually, though that number has likely increased following a growing trend.[23]

An estimated 40% of liver cancer burden and nearly 20% of chronic liver disease burden in Australia **can be attributed to alcohol consumption.**

AUSTRALIA'S SUCCESSFUL PROGRESS TOWARDS HEPATITIS C ELIMINATION

Dr. Simone Strasser is an Clinical Associate Professor in Medicine at the Central Clinical School at the University of Sydney and a hepatologist and researcher at Royal Prince Alfred Hospital A W Morrow Gastroenterology and Liver Centre in Sydney. Her work and research focus on transplantation and liver cancer, and she serves as the director of The Liver Foundation in Australia.

Overall, liver health is in a similar place in Australia as it is around the world. There is rapidly rising metabolic-associated fatty liver disease, which is becoming overwhelming here. While viral hepatitis is dropping as a cause for end-stage liver disease and liver cancer, the non-viral liver diseases are increasing (alcohol- and obesity-related liver disease). So we're trying to engage general practice more.

Hepatitis C itself is an absolute success story for Australia. At a time when, in the US and Europe, access to hepatitis C treatments were restricted to people with advanced disease, diagnosis rates were low, and prisoners and drug injection communities did not have access to treatment, everyone without restriction had access in Australia.

Now, the epidemiology of hepatitis C has changed drastically. We've seen a dramatic downturn in the amount of hepatitis C in the community; almost all patients with advanced liver disease have been treated, and the diagnosis rates now are 80%. So we have high rates of diagnosis, and the number of people with hepatitis C in the community is dropping quite quickly.

> "Everyone with hepatitis C in the bloodstream is **eligible for federally - funded treatment in Australia.**"
>
> - DR. SIMONE STRASSER

How the Program Works:

- The eligibility criteria was having the hepatitis C virus in the bloodstream – severity of disease, drug use, or imprisonment were not barriers to treatment.
- The program was federally funded, with **no direct cost to patients** to receive treatment.
- General practitioners (GPs), nurse practitioners, or other physicians, in addition to liver specialists were allowed to write prescriptions.
- The Gastrointestinal Society of Australia (GESA), launched a consensus; educated GPs, who were not confident treating this new, infectious, dangerous disease; and even set up a system where GPs could fax a form to liver specialists with patient details and receive sign-off on their treatment plan.
- Patients received a prescription for direct acting antivirals to their pharmacy of choice for two to three months of treatment, funded through the pharmaceutical benefits scheme (about $7.90 a month for pensioners or $35 a month for everyone else).

The story of hepatitis C treatment in Australia has been fantastic. Within the first year we had already treated 25% of the affected population. We have now treated at least 50-69%, including the majority of people with advanced liver disease. We are seeing the results now in reduced rates of transplant for hepatitis C, reduced liver cancer due to hepatitis C. Now there's a big shift in the population that we are transplanting – the driver for their progressive liver disease is often obesity and diabetes, and they've got multiple conditions. But with hepatitis C, we really opened up access universally for residents, with federally-funded therapy, and we've seen that it's been very effective.

CONCLUSION

Liver disease is a silent disease which often presents itself at a late stage. It is too often a chronic disease, sometimes requiring lifelong and costly therapies in which many populations cannot access. Across each region and examined country, the incidence of liver disease and liver deaths (from cirrhosis and cancer) has been rising quickly.

These findings confirm a daunting fear – that liver disease is set to become a global public health crisis to rival diabetes, cardiovascular disease and cancer. Yet at the same time, across the globe, liver disease is in no compelling instance treated as a major health threat by governments, policy makers, and the public – and, even, in some cases, by clinicians. Political mismanagement and even corruption is an ongoing issue, draining resources from where they are most needed and demoralizing healthcare professionals. Finally, this rise in liver disease has been a very recent phenomenon, comparable only to diabetes in its rapid and global onset.

In Europe, liver disease is now the second biggest cause of deaths of people of working age.[1] Chronic viral hepatitis affects over 70 million people in Africa, and dying from viral hepatitis there is becoming a bigger threat than dying from HIV/AIDS, malaria or tuberculosis.[2]

Latin America is experiencing some of the highest obesity rates in the world, alongside the fastest growing rate of T2D[3] with excessive alcohol consumption the leading cause of cirrhosis in Argentina, Brazil, Chile, Mexico and Peru.[4]

In 2015, for instance, almost two-thirds of global deaths due to liver disease occurred in the Asia-Pacific region.[5] In the US it is predicted that, by 2030, liver deaths will have increased (since 2015) by 178% to an estimated 78,300 deaths, mostly attributable to MAFLD/MASH.[6]

Nonetheless, advancements in technique and technology provide a promising outlook for the global state of liver health. Leading healthcare professionals are developing innovative ways to further advance the field. Many tools to address liver disease are available, and political will is builiding to deploy these tools. Patient groups and organizations continue to bridge the gap by leading awareness campaigns to educate the public, by providing patient perspectives on care, and by advocating for equity and accessibility to treatments. Since the majority of liver diseases are preventable and treatable, emphasis should be placed on public health strategies – including awareness and prevention – to reduce the rising tide of liver disease.

3 Throughout the report, **three major themes emerge:**

Obesity, no longer a disease of just the developed world, is now prevalent across many countries, **leading to greater incidence of MAFLD and MASH.**

Alcohol is losing its cultural stigma in some regions, while in other areas, heavy drinking across all age groups, sexes and demographics is becoming normalized – as several experts have noted that they now **regularly witness the tragedy of young people dying from alcohol-associated liver disease.**

Despite several preventative and curative tools available, **viral hepatitis** is well-controlled in many areas of the world, yet it is still **a major cause of liver disease and death in some countries.**

you can, **to improve the global state of liver health.**

WE CALL ON GOVERNMENT AND POLICY MAKERS GLOBALLY TO:

- Initiate a global coordinated program of good quality data collection to inform the above.
- Elevate liver health to take its place in the public health agenda commensurate with its prevalence and impact.
- Support regionally appropriate public awareness/education programs across the three main causes of liver disease.
- Commit to the value of prevention – education, screening, early diagnosis and treatment.

WE CALL ON CLINICIANS GLOBALLY TO:

- Recognize and understand the dangers of liver disease and tackle its causes and risk factors.
- Coordinate with liver colleagues to continue to produce high quality clinical guidelines.
- Instigate and support research into liver disease.
- Educate and inform patients to manage their own disease and to become a conduit for educating others.

WE CALL ON THE PUBLIC TO:

- Learn and understand their own liver health risk factors including weight, alcohol abuse or exposure to viral hepatitis and, where appropriate, commit to a preventative program including a testing and screening program if necessary.
- Support liver health organizations and/or patient groups.
- Become an ambassador/advocate for liver health in schools, community groups etc.
- Call upon your local/national politicians to support increased resources for liver health.

ENDORSING ORGANIZATIONS

AISF - Associazione Italiana per lo Studio del Fegato

ALEH - Asociacion Latino Americana para el Estudio del Hígado

APAC - Asia Pacific Liver Disease Alliance

Arizona Liver Health

CASL - Canadian Association for the Study of the Liver

Community Liver Alliance

ERN - European Reference Network

ESOT - European Society for Organ Transplant

Fatty Liver Alliance

Fatty Liver Foundation

Hepatology Society of the Philippines

Liver Action Network

Liver Coalition of San Diego

Liver Health Foundation

Liver Patients International

Mid South Liver Alliance

Nash Knowledge

Northeast Ohio Liver Alliance

PBC Foundation

SAASL - South Asia Association for the Study of the Liver

SAHGEED - Algerian Society of Gastroenterology and Digestive Endoscopy

TASL - Turkish Association for the Study of the Liver

Texas Liver Foundation

WHA - World Hepatitis Alliance

ENDORSERS

Dr. Alessio Aghemo, Former Secretary of AISF, Italy

Dr. Graciela Castro, ALEH President, Latin America

Dr. Raymond Chung, AASLD Past President, USA

Dr. Scott Friedman, AASLD Past President, USA

Dr. Fulya, Gunsar, TASL President, Türkiye

Dr. Phil Newsome, EASL Past President, EU

Dr. Diana Payawal, APASL Past President, ASIA/Pacific

Dr. Juanita Perez-Escobar, ALEH Secretary, Latin America

Dr. Shivaram Singh, INASL President Elect, India

Dr. Mark Swain, CASL President, Canada

Dr. Zobair Younossi, President of Inova Medicine, USA

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REPORT PRODUCTION:
Shakerra Bartley, Writer & Researcher, Global Liver Institute

Lily Benig, Manager, Communications, Global Liver Institute

Paige Brown, Graphic Design Coordinator, Communications, Global Liver Institute

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Donna R. Cryer, JD, Founder, Global Liver Institute

Giacomo Donnini, Program Director, Liver Health is Public Health, Global Liver Institute

Larry R. Holden, President & CEO, Global Liver Institute

Kayla Johnson, Graphic Designer, Global Liver Institute

Christine Maalouf, Director, Communications, Global Liver Institute

Roslyn Marano, Writer, Global Liver Institute

Jeff McIntyre, Vice President, Liver Health, Global Liver Institute

Isla Whitcroft, Health Journalist

REPORT ADVISORS:
Dr. Alessio AGHEMO, Former Secretary of AISF, Hepatology Unit Director at Humanities Research Hospital, Italy

Dr. Saima AJAZ, Clinical Research Fellow, King's College Hospital, Institute of Liver Studies, United Kingdom

Mr. Michael BETEL, President and Founder of the Fatty Liver Alliance, Canada

Dr. Cyrielle CAUSSY, Prof of Nutrition and Endocrinologist/ Diabetologist at Lyon 1 University, France

Dr. Bianca DELLA GUARDIA, Hepatologist, Hospital Israelita Albert Einstein, Brazil

Dr. Mahmoud Saad DESOUKY, MD, Consultant in Internal Medicine and Gastroenterology, University Lecturer, Founder of the Egyptian Hepatitis Alliance

Dr. Marcio DIAS DE ALMEDIA, Hepatologist, Hospital Israelita Albert Einstein, Brazil

Dr. Manal EL SAYED, Dr. Manal El-Sayed (Cairo, Egypt) is Professor of Pediatrics, Chair of the Pediatric department and director of the Clinical Research Center (MASRI-CRC) at the Faculty of Medicine, Ain Shams University, Egypt

Dr. Scott FRIEDMAN, Former AASLD President, Chief of the Division of Liver Diseases, Icahn School of Medicine at Mount Sinai, United States of America

Dr. Fulya GÜNSAR, Prof. of Gastroenterology, Ege Üniversitesi, President of TASL, Turkey

Dr. Dao Viet HANG, Vice General Secretariat of VNAGE, gastroenterologist and, hepatologist at Hanoi Medical University, Vietnam

Dr. Marek HARTLEB, President of the Polish Society of

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Ms. Vanessa HEBDITCH, Director of Communications & Policy, British Liver Trust, United Kingdom

Dr. Jacqueline KASSOUF MAALOUF, President & Founder of DiaLeb - The National Diabetes Organization, Lebanon

Dr. Aleksander KRAG, Aleksander Krag, MD, PhD, MBA Professor and Department Chair, Department of Gastroenterology and Hepatology Odense University Hospital, Denmark

Dr. Masatoshi KUDO, MD, PhD Professor and Chairman Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Japan

Dr. Alma Laura LADRON DE GUEVARA, Hepatologist, Centro de Investigación y Gastroenterología, México

Ms. Silvana Tsochkova LESIDRENSKA, Chair of Hepactive Patient Association, Bulgaria

Dr. Mbianke LIVANCLIFF, NCD Coordinator, VAHA, Cameroon

Dr. Josiah NANG-BAY, researcher and physician with experience in internal medicine, Ghana

Mr. Michael Ochieng NYAWINO, Executive Director, Christian Community Healthcare Foundation, Kenya

Mr. William J. OCRAN, Co-Founder of empowerment for Sustainable Livelihood, a charity that promotes disease awareness, prevention, education, advocacy, and research, Ghana

Dr. Linda Achieng ORUMA, Medical Officer, St. Elizabeth Mukumu Hospital, Kenya

Dr. Diana PAYAWAL, Professor, Fatima University Medical Center, Former APASL President, President of the Philippines Collegium of Physicians, The Philippines

Dr. Tung PHAM, Lecturer, researcher and curriculum fellow in the cancer epidemiology at the Harvard T.H. Chan School of Public Health, Vietnam

Dr. Shivaram P. SINGH, President Elect of INASL, President of SAASL, Gastroenterologist, India

Dr. Jörn SCHATTEMBERG, Director of Metabolic Liver Research Program, University Medical Centre Mainz, Germany

Dr. Wendy SPEARMAN, Head of Hepatology, University of Cape Town, South Africa

Dr. Simone STRASSER, Hepatologist, Clinical Associate Prof in Medicine, University of Sydney, Australia

Mr. Liam A.SWAIN, Dept of Community Health Sciences, Univ. of Calgary, Volunteer for the Fatty Liver Alliance, Canada

Dr. Mark SWAIN, CEO of CASL, Head of Gastroenterology, University of Calgary, Canada

Dr. Mónica TAPIAS, Hepatology Internist, Hospital Universitario Fundación Santa Fé de Bogotá

Dr. Laz UDE EZE, MBBS, MPH, CPH, FAPH, FCAI, Health Policy & Management Specialist| Sustainable Development Consultant, Founder/ CEO, Talk Health Real Media Ltd (talkhealth9ja.com), Founder, Make Our Hospital Work Campaign, Co-Founder, Sub-Saharan Brain Health Initiative (SSABHI), Nigeria

Mr. George WHITE, BSc, MSc Microbiology, University of Nottingham, United Kingdom

Dr. Marouan ZOGHBI, family medicine, Saint Joseph University, Lebanon

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CONCLUSION

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