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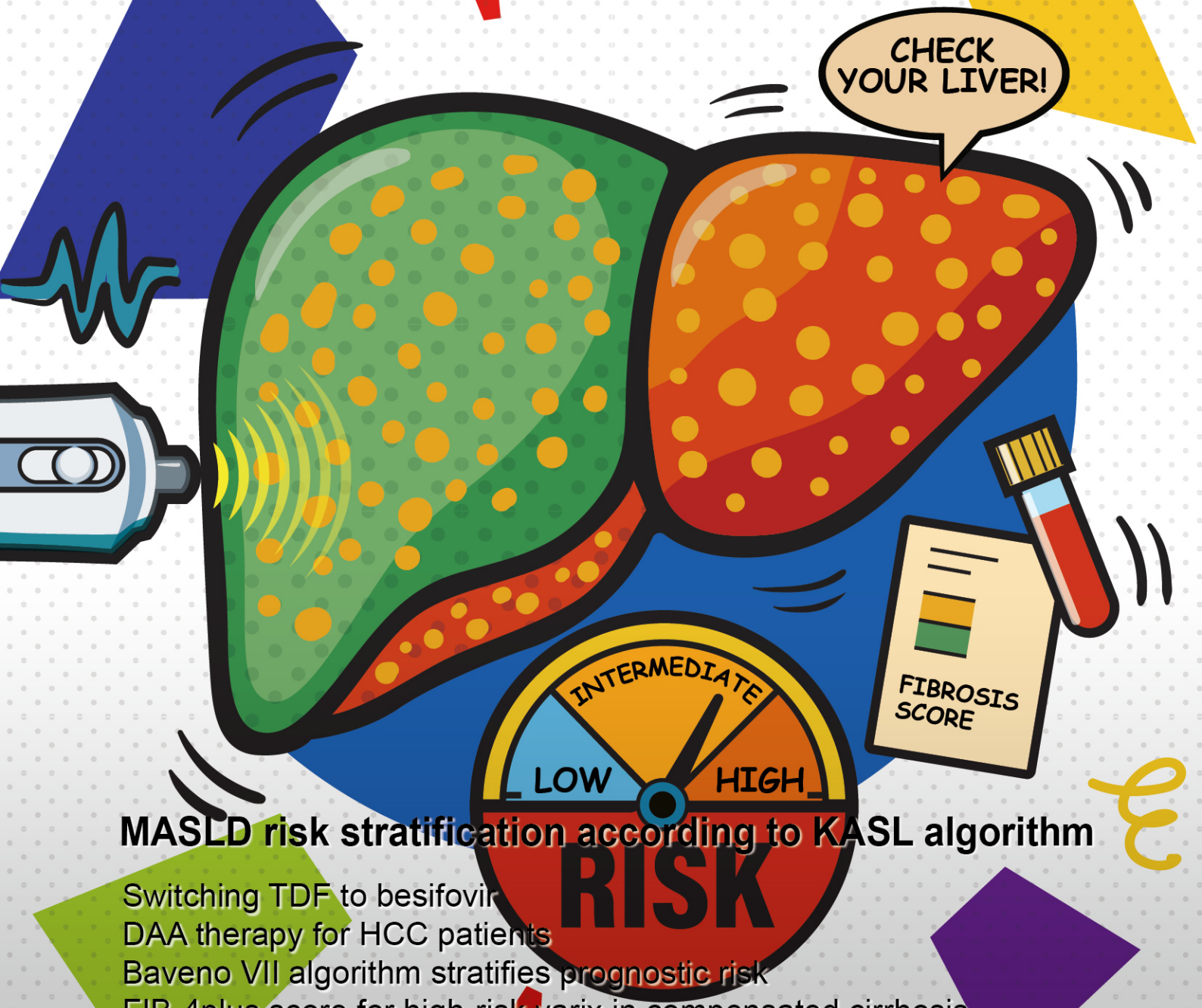

MASLD risk stratification according to KASL algorithm

Switching TDF to besifovir
DAA therapy for HCC patients
Baveno VII algorithm stratifies prognostic risk
FIB-4plus score for high-risk varix in compensated cirrhosis

KASL

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Special Review

Liver disease trends in the Asia-Pacific region for the next 50 years

Shuichiro Shiina[1], Javkhlan Maikhuu[1,2], Qing Deng[1,3], Terguunbileg Batsaikhan[1,4], Lariza Marie Canseco[1,5], Maki Tobari[1], Hitoshi Maruyama[1], Hiroaki Nagamatsu[1], Diana Alcantara-Payawal[6], Rino Gani[7], Yi-Hsiang Huang[8], Tawesak Tanwandee[9], Giovanni Galati[10], and Yoon Jun Kim[11]

[1]Department of Gastroenterology, Juntendo University, Tokyo, Japan; [2]Department of Radiology, The Second State Central Hospital, Ulaanbaatar, Mongolia; [3]Department of Ultrasound Imaging, Renmin Hospital of Wuhan University, Wuhan, China; [4]Department of Interventional Radiology, National Cancer Center of Mongolia, Ulaanbaatar, Mongolia; [5]Section of Gastroenterology, Department of Internal Medicine, De Los Santos Medical Center, Quezon City, Philippines; [6]Department of Internal Medicine, Fatima University Medical Center, Valenzuela, Philippines; [7]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, University of Indonesia, Cipto Mangunkusumo Hospital, Jakarta, Indonesia; [8]Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan; [9]Division of Gastroenterology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand; [10]Unit of Clinical Medicine and Hepatology, University Campus Bio-Medico, Rome, Italy; [11]Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea

Liver disease has emerged as a critical and escalating public health concern worldwide, with the Asia-Pacific region at the forefront of this challenge due to its vast population and diverse socioeconomic landscape. Over the coming five decades, this region will experience profound changes in liver disease patterns, shaped by rapid urbanization, lifestyle modifications, advancements in medical technologies, and evolving public health strategies. This article offers an in-depth analysis of six transformative areas defining the trajectory of liver disease in the region. First, it highlights the alarming rise of metabolic dysfunction-associated fatty liver disease and metabolic dysfunction-associated steatohepatitis, diseases driven by modern lifestyle factors and inherent metabolic susceptibilities. Concurrently, it celebrates the declining burden of viral hepatitis, underscoring the success of sustained public health interventions. However, new challenges are emerging, such as the growing impact of environmental and occupational exposures on liver health. Breakthroughs in genomic and epigenetic research promise to advance precision medicine, offering targeted therapeutic solutions. Additionally, the integration of artificial intelligence, big data, and telemedicine is poised to revolutionize liver disease management, improving accessibility and personalized care. Finally, the article emphasizes the critical role of robust health policies, preventive strategies, and cross-border collaboration in shaping a healthier future. By synthesizing these insights, the study aims to guide innovative and effective responses to the evolving liver disease landscape in the Asia-Pacific region. **(Clin Mol Hepatol 2025;31:671-684)**

Keywords: Liver diseases; Epidemiology; Forecasting; Precision medicine; Asia Pacific region

Corresponding author : Shuichiro Shiina
Department of Gastroenterology, Juntendo University School of Medicine, 2-1-1, Hongo, Bunkyo-ku, Tokyo 113-8421, Japan
Tel: +81-3-3813-3111 ext. 70222, Fax: +81-3-5684-5960, E-mail: s.shiina@gmail.com
https://orcid.org/0000-0002-7314-7228

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INTRODUCTION

The Asia-Pacific region, home to more than half of the world's population, has historically borne a disproportionate burden of liver diseases, with viral hepatitis, alcohol-related liver disease (ALD), and hepatocellular carcinoma (HCC) ranking among the leading causes of morbidity and mortality.[1] However, over the next 50 years, the epidemiology of liver disease in the Asia-Pacific region is expected to undergo significant transformations, driven by demographic shifts, economic development, lifestyle changes, and advancements in medical technology.

Metabolic dysfunction-associated steatotic liver disease (MASLD) and its progressive form, metabolic dysfunction-associated steatohepatitis (MASH), are becoming dominant causes of liver disease in the Asia-Pacific region due to rising obesity, diabetes, and metabolic syndrome.[2] Concurrently, significant progress has been made in combating viral hepatitis through hepatitis B vaccination and direct-acting antivirals for hepatitis C, leading to reduced infections and liver-related deaths.[3] However, challenges in diagnosis, treatment accessibility, and prevention persist, especially in low- and middle-income countries. Additionally, environmental and occupational exposures, such as aflatoxin contamination, industrial pollutants, air pollution, and unique genetic predispositions in the region, amplify liver disease risks.[4] Addressing these multifaceted factors through tailored prevention and intervention strategies is essential to mitigate the growing liver disease burden.

Advancements in technology, particularly in genomics, epigenetics, and artificial intelligence (AI), are reshaping the landscape of liver disease research and management.[5] Genomic medicine offers the potential for personalized risk prediction and targeted therapies, while AI and big data are transforming diagnostic precision and disease monitoring.[6] These technologies, combined with regional collaboration and policy innovations, promise to address the diverse and evolving challenges of liver disease in the Asia-Pacific.

As we look toward the next 50 years, the trends shaping liver disease in the Asia-Pacific region demand a multi-disciplinary approach that integrates prevention, early detection, innovative treatment strategies, and health policy reform. By addressing these challenges proactively, the region can pave the way for reducing the burden of liver disease and improving public health outcomes for future generations.

RISING PREVALENCE OF MASLD AND MASH

MASLD, previously known as non-alcoholic fatty liver disease (NAFLD), along with its progressive form, MASH, is becoming increasingly prevalent in the Asia-Pacific region. This trend mirrors global patterns and is closely linked to rising rates of obesity, type 2 diabetes, and metabolic syndrome. Projections indicate that the worldwide prevalence of NAFLD is expected to rise from 38.9% in 2020 to 55.7% by 2040, representing a 43.2% increase over two decades (Fig. 1).[7] Recent studies have highlighted a significant rise in MASLD prevalence across various countries in the Asia-Pacific region. In China, cross-sectional studies have reported MASLD prevalence rates ranging from 20.4% to 48.4%, with most studies indicating rates above 30%.[8] In Japan, the estimated prevalence is projected to rise from 33.7% in 2020 to 39.3% in 2030 and 44.8% in 2040.[9] Similarly, the prevalence of primary liver cancer attributable to steatotic liver disease, including MASLD, is rising in the Asia-Pacific region.[10] This upward trend underscores the urgent need for public health interventions to address the modifiable risk factors associated with MASLD and MASH.

The increasing prevalence of MASLD and MASH can be attributed to several factors.[2] Obesity, particularly central obesity, is closely linked to metabolic dysfunction, leading to liver fat accumulation and inflammation. The dietary shift from traditional diet towards high-calorie, high-fat, and high-sugar foods, contributes to obesity and metabolic dysfunction. The rising incidence of type 2 diabetes mellitus and insulin resistance as well as other components of the metabolic syndrome, including hypertension and dyslipidemia, are also associated with an increased risk of MASLD

Abbreviations:

AI, artificial intelligence; ALD, alcohol-related liver disease; CB, carbon black; DDLT, deceased donor liver transplantation; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; MASLD, metabolic dysfunction-associated steatotic liver disease; MASH, metabolic dysfunction-associated steatohepatitis; NAFLD, non-alcoholic fatty liver disease; PAHs, polycyclic aromatic hydrocarbons; PM2.5, particulate matter 2.5 μm or less in diameter

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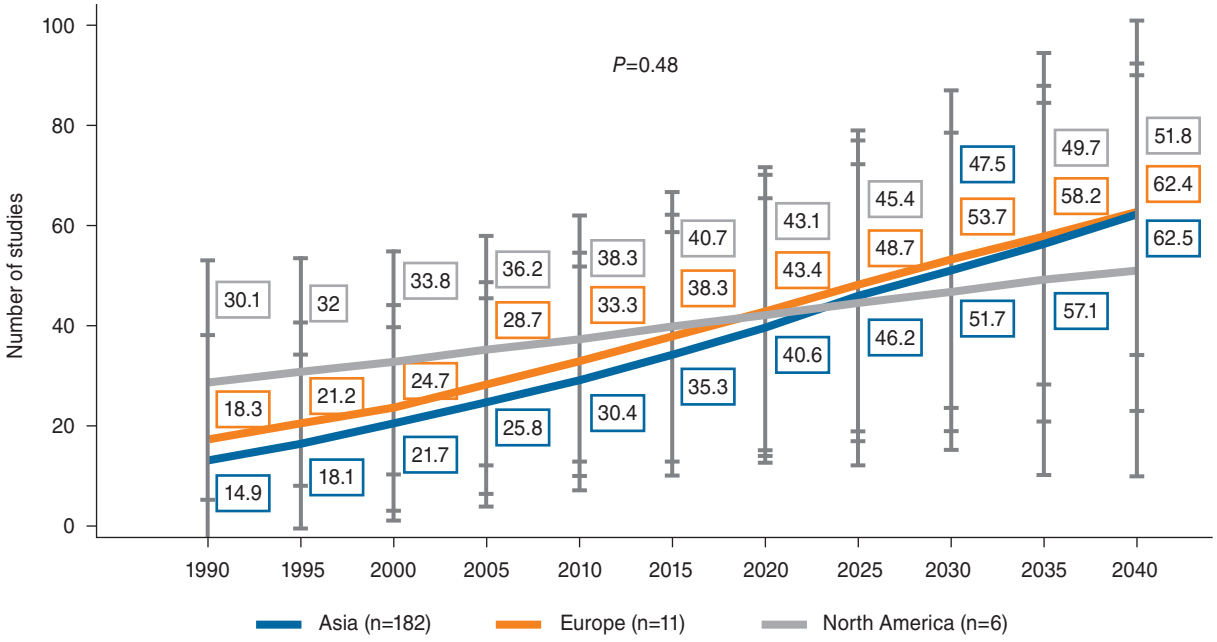

Figure 1. Forecast of metabolic dysfunction-associated steatotic liver disease prevalence for Asia, Europe, and North America.

and MASH. The clustering of these metabolic abnormalities exacerbates liver disease progression.

Certain genetic factors in Asian populations may predispose individuals to MASLD and MASH. For example, polymorphisms in genes such as PNPLA3 and TM6SF2 have been associated with increased susceptibility to these conditions.[11] Sedentary lifestyles are becoming more common in the region, contributing to obesity and metabolic dysfunction, which are risk factors for MASLD and MASH. Regular physical activity is protective against these conditions. Obstructive sleep apnea has been linked to the development and progression of MASLD and MASH.[12] Intermittent hypoxia associated with obstructive sleep apnea may exacerbate liver inflammation and fibrosis. Certain ethnic groups within the Asia-Pacific region may have varying susceptibilities to MASLD and MASH due to genetic and lifestyle factors. For instance, Asian populations are more susceptible to metabolic syndrome and MASLD than their Western counterparts.

Regarding implications for the future, the socioeconomic impact of MASLD and MASH in the Asia-Pacific region cannot be overstated. These conditions impose substantial direct costs on healthcare systems, including expenses related to diagnostics, pharmacological treatments, and management of complications such as cirrhosis and liver cancer. Indirect costs, such as loss of productivity due to illness and premature mortality, further exacerbate the economic burden. The challenges are particularly acute in low- and middle-income countries, where healthcare infrastructure and resources are often insufficient to manage the growing burden of chronic liver diseases. Addressing these issues will require comprehensive strategies encompassing prevention, early detection, and effective management. Prevention remains the cornerstone of MASLD management. Addressing modifiable risk factors, such as obesity, sedentary behavior, and unhealthy diets, is critical. Public health campaigns focusing on lifestyle modifications have successfully reduced risk factors. For instance, school-based programs aimed at promoting healthy eating and physical activity have proven effective in mitigating childhood obesity, a key driver of pediatric MASLD. Similarly, workplace wellness initiatives targeting physical inactivity and stress have shown promise in adult populations.

However, the scale of the problem necessitates a coordinated regional response that integrates these efforts with broader policies addressing urban planning, food security, and equitable access to healthcare services. Technological advancements are also playing a pivotal role in improving the diagnosis and management of MASLD and MASH. Non-invasive diagnostic tools, such as transient elastogra-

Table 1. Key pharmacotherapy breakthroughs for metabolic dysfunction-associated steatotic liver disease (MASLD) over the past decade

Drug/Therapy	Mechanism of action	Indication	Lifestyle integration	Study results
Resmetirom (THR-β Agonist)	Selective activation of thyroid hormone receptor β boosts lipid metabolism and lowers liver fat	MASLD with fibrosis (NASH)	Low-saturated fat diet, mediterranean diet, regular exercise	In the Phase 3 MAESTRO-NASH trial, resmetirom showed significant efficacy. NASH resolution without worsening fibrosis was achieved by 25.9% of patients on 80 mg and 29.9% on 100 mg, compared to 9.7% in the placebo group. Additionally, fibrosis improvement by at least one stage occurred in 24.2% and 25.9% of patients on 80 mg and 100 mg, respectively.[15]
Lanifibranor (PPAR Agonist)	Pan-PPAR agonist improves lipid and glucose metabolism and reduces liver inflammation	MASLD with fibrosis (NASH)	Weight loss, aerobic & resistance training	In the Phase 2b NATIVE trial, lanifibranor was effective for MASH. Among 247 patients, 55% of those taking 1,200 mg daily achieved a two-point SAF activity score reduction without worsening fibrosis, compared to 33% on placebo. In the 800 mg group, 48% met this endpoint.[16]
Semaglutide (GLP-1 Receptor Agonist)	Enhances insulin secretion, reduces appetite, and promotes weight loss	MASLD with obesity & diabetes	Caloric restriction, high-protein diet, physical activity	The Phase 3 ESSENCE trial showed that a weekly dose of semaglutide 2.4 mg significantly improved liver fibrosis and resolved steatohepatitis in adults with MASH and moderate to advanced liver fibrosis. After 72 weeks, 37% of those on semaglutide saw at least a one-stage improvement in liver fibrosis without worsening steatohepatitis, compared to 22.5% on placebo. Furthermore, 62.9% of participants on semaglutide achieved resolution of steatohepatitis without worsening liver fibrosis, versus 34.1% on placebo.[17]
Tirzepatide (GLP-1/GIP Agonist)	Dual agonists promoting glucose control and significant weight loss	MASLD with metabolic syndrome	Low-carb diet, intermittent fasting	SURMOUNT 1 and 4 Trials underscore tirzepatide's potential for improving metabolic health by reducing weight and enhancing serum biomarkers.[18,19]
Pegbelfermin (FGF21 Analog)	Improves insulin sensitivity reduces hepatic steatosis	MASLD with fibrosis	Balanced macronutrient intake, increased physical activity	Phase 2b study (FALCON 1 trial): Pegbelfermin failed to significantly reduce liver fibrosis in patients with NASH.[20]
Efruxifermin (FGF21 Analog)	Reduces liver fat and improves insulin sensitivity & lipid profile	MASLD with fibrosis	A diet rich in unsaturated fats, exercise	In the Phase 2b HARMONY trial, efruxifermin (EFX) improved liver histology in MASH patients. Fibrosis improved by ≥1 stage in 39–41% of EFX-treated patients vs. 20% on placebo ($P<0.05$). NASH resolution occurred in 76–79%, and fibrosis improved by ≥2 stages in 14%, outperforming placebo. These results suggest efruxifermin's potential as a therapy for MASH.[21]
Obeticholic Acid (FXR Agonist)	Modulates bile acid metabolism and reduces fibrosis progression	MASLD with fibrosis (NASH)	Alcohol restriction, fiber-rich diet	In the REGENERATE study, obeticholic acid improved liver histology, including fibrosis reduction, in patients with NASH.[22]
Aramchol (SCD-1 Inhibitor)	Reduces hepatic de novo lipogenesis and enhances fatty acid oxidation	MASLD with insulin resistance	Mediterranean diet, weight loss	In a 52-week, double-blind, placebo-controlled Phase 2b trial, Aramchol showed a placebo-corrected reduction in liver triglycerides and improvement in liver histology in MASH patients. These results highlight its potential as a metabolic and antifibrotic liver disease therapy.[23]

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Table 1. Continued

Drug/Therapy	Mechanism of action	Indication	Lifestyle integration	Study results
Belapectin (Galectin-3 Inhibitor)	Reduces fibrosis and inflammation	MASLD with advanced fibrosis	Lifestyle changes with a focus on liver protection	In a Phase 2b trial, belapectin did not achieve its primary endpoint of reducing fibrosis in MASH-related cirrhosis. However, subgroup analysis indicated potential benefits for patients without esophageal varices, suggesting a possible role in early-stage disease.[24]

THR-β, thyroid hormone receptor β; MASLD, metabolic dysfunction-associated steatotic liver disease; NASH, non-alcoholic steatohepatitis; PPAR, peroxisome proliferator-activated receptor agonist; MASH, metabolic dysfunction-associated steatohepatitis; GLP-1, glucagon-like peptide-1; GIP, gastric inhibitory peptide; FGF21, fibroblast growth factor 21; FXR, farnesoid X receptor; SCD-1, stearoyl-CoA desaturase 1.

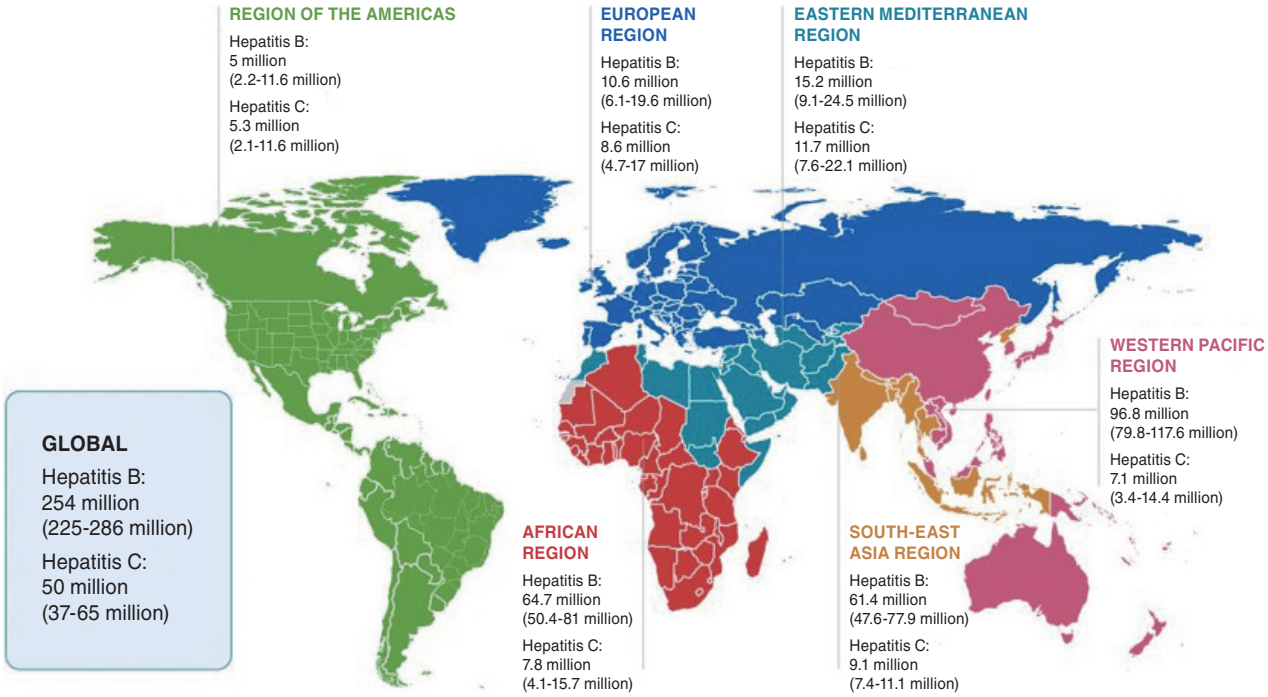

Figure 2. Prevalent cases of chronic hepatitis B by WHO region, 2022. WHO, World Health Organization.

phy and serum biomarkers, are increasingly being used to identify fibrosis and monitor disease progression, reducing reliance on invasive liver biopsies.[13] In addition to lifestyle modifications and diagnostics, pharmacological treatments are gaining traction in the fight against MASH. Current clinical trials evaluate therapeutic targets, including insulin sensitizers, anti-inflammatory agents, and antifibrotic drugs (Table 1).[14-24] Advances in precision medicine, underpinned by insights from genomics and epigenetics, further hold the promise of tailored therapeutic approaches that maximize efficacy while minimizing adverse effects.

DECLINE IN VIRAL HEPATITIS–RELATED LIVER DISEASE

Over the past few decades, the Asia-Pacific region has witnessed a decline in liver diseases associated with viral hepatitis, particularly hepatitis B virus (HBV) and hepatitis C virus (HCV).[25] Historically, the region bore a disproportionate burden of viral hepatitis, with countries like China, India, and Indonesia experiencing high prevalence rates (Fig. 2).[26] In 2015, chronic HBV was responsible for nearly 50% of liver cancer deaths in the Asia-Pacific region,[27] emphasizing the severity of the issue. However, the imple-

mentation of the Global Health Sector Strategy for Viral Hepatitis (2016–2021) has brought about substantial progress. Between 2015 and 2020, the prevalence of chronic HBV decreased from 4.69% to 4.30%, and HCV prevalence dropped from 0.64% to 0.58%.[3] The incidence of new hepatitis infections also fell, from 2.5 million in 2019 to 2.2 million in 2022.[28]

A key driver of this decline is the widespread adoption of hepatitis B vaccination programs.[29] Universal neonatal vaccination has dramatically reduced HBV transmission. For instance, countries like China have achieved vaccination coverage rates exceeding 95%, significantly lowering chronic HBV prevalence in younger populations.[30] The World Health Organization (WHO) Western Pacific Region aims to reduce the prevalence of chronic HBV infection in children under five to below 0.1% by 2030, a goal that now seems achievable.

Equally transformative are advancements in antiviral therapies. Nucleos(t)ide analogues such as entecavir and tenofovir have become the standard of care for HBV, suppressing viral replication and reducing risks of liver cirrhosis and HCC. Similarly, the introduction of direct-acting antivirals for HCV has revolutionized treatment, with cure rates exceeding 95%.[31] Countries like Japan and India have seen substantial reductions in HCV-related liver disease due to increased access to these highly effective therapies.[32]

Screening and early detection efforts have also been instrumental. Integrating HBV and HCV testing into routine health checkups and prenatal care has facilitated early diagnosis and timely treatment. South Korea, for example, has implemented robust screening programs targeting high-risk populations, including healthcare workers, pregnant women, and individuals with a family history of liver disease. These measures have significantly reduced disease progression and improved patient outcomes.[33]

Public health initiatives have further enhanced progress by addressing barriers such as stigma and limited awareness. Comprehensive campaigns have encouraged individuals to seek testing and treatment. Harm reduction programs targeting people who inject drugs, such as needle exchange initiatives and opioid substitution therapy in Australia, have successfully reduced HCV transmission in vulnerable populations.[34]

While the Asia-Pacific region has made remarkable strides in HBV and HCV control, persistent disparities in lower-income countries necessitate targeted research and policy innovations. For instance, cost-effectiveness studies in Cambodia and Papua New Guinea have demonstrated the utility of decentralized, community-driven testing models using rapid diagnostic tests to overcome infrastructural barriers.[25] Similarly, mobile health platforms, such as SMS-based reminder systems for vaccination and treatment adherence, have shown promise in rural India and Myanmar.[28] These approaches prioritize scalability and cultural relevance, critical in resource-limited settings.

At the policy level, international collaborations like the Global Alliance for Vaccines and Immunization have subsidized HBV vaccination programs in Laos and Nepal, achieving coverage rates exceeding 80% in previously underserved regions.[29] National policies in Bangladesh and Vietnam now integrate HCV elimination into universal health coverage frameworks, leveraging generic direct-acting antiviral procurement to reduce costs by 70–90%.[31] Looking ahead, novel therapeutic approaches, including immune modulators and therapeutic vaccines, offer hope for curing chronic HBV. Advances in genomic and epigenetic research may also enable personalized treatments, further reducing the disease burden. Strengthening international collaborations and leveraging regional partnerships will be critical for sustaining progress.

THE IMPACT OF ENVIRONMENTAL AND OCCUPATIONAL EXPOSURES

Heavy industrialization increases the release of liver-damaging toxins, such as aflatoxin, air-polluting toxic substances like particulate matter 2.5 μm or less in diameter (PM2.5), carbon black (CB), asbestos, polycyclic aromatic hydrocarbons (PAHs), and heavy metals. Previous studies have shown that specific environmental exposures, including aflatoxin, vinyl chloride, arsenic (a heavy metal), and PAHs, are hepatocarcinogenic in both humans and animals.[35]

Several studies demonstrated evidence of gene–environment interaction between serum aflatoxin and genetic polymorphisms in DNA repair genes (e.g., XRCC4),[36] highlighting potential biological mechanisms through which aflatoxin may impact the development of HCC and identifying indi-

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viduals who may be more susceptible to aflatoxin-induced liver cancer. Several animal models provide strong evidence that PM2.5 or CB, indicators of air pollution, can induce various diseases and act to exacerbate existing lesions in organs that are accessible to the constituents of air pollution. Among those organs, the liver is one of the vulnerable target organs since its microvasculature allows ready access to hepatocytes and inhaled PM2.5 pollutants can be translocated from the alveolar space into the bloodstream. Direct effects of PM or CB on hepatocytes include the induction of oxidative stress and DNA strand breaks. In addition, airborne PM2.5 contributes to the pathogenesis of steatohepatitis by altering lipid metabolism and inducing a pro-inflammatory milieu, exacerbating MASH.[37]

Environmental contamination from heavy metals primarily originates from industrial and agricultural activities, potentially promoting the development of MASLD through mechanisms related to inflammation and insulin resistance.[38] Exposure to arsenic and cadmium, polychlorinated biphenyl, and PAHs may also be associated with increased risk of HCC.[39]

Groundwater contamination, particularly near mining areas, should not be overlooked as a potential liver toxin. As the population grows, the demand for resources and products increases, pushing further industrialization. While work safety may improve over time and toxic exposure may be minimized, it will unlikely be eliminated in the next 50 years.

THE ROLE OF GENOMIC AND EPIGENETIC RESEARCH

The Asia-Pacific region faces a high burden of liver diseases, making innovative approaches in hepatology essential. Genomic and epigenetic research has become crucial in understanding the pathogenesis, progression, and treatment of liver disease. Over the next 50 years, advancements in these areas are expected to transform how liver diseases are managed.

ALD is a growing concern across the Asia-Pacific region. Patterns of alcohol consumption vary widely, reflecting the diverse cultural, economic, and social landscapes of the region. As alcohol becomes more accessible and socially accepted in certain countries, its impact on liver health is anticipated to rise significantly. Addressing this issue will require culturally sensitive public health campaigns, stricter regulatory policies, and early detection strategies.

Genetic research has significantly advanced our understanding of ALD, highlighting the complex interplay between genetic predispositions and environmental factors.[40] These insights have paved the way for potential therapeutic interventions. Variations in genes responsible for alcohol metabolism influence an individual's susceptibility to ALD. For instance, certain polymorphisms can lead to the accumulation of acetaldehyde, a toxic metabolite, increasing liver damage risk. Genetic variants affecting oxidative stress responses and inflammatory pathways can modulate the severity of liver injury in ALD patients. Identifying these variants aids in understanding disease progression. Understanding the genetic underpinnings of ALD opens avenues for targeted therapies. Genetic profiling can identify high-risk individuals, enabling tailored prevention and treatment strategies. Furthermore, research into specific genetic pathways, such as those regulating oxidative stress and inflammation, has revealed potential therapeutic targets.

Genomic research has identified important variations in genes that affect liver disease risk. For example, the PNPLA3 I148M gene variant is linked to MASLD in Asian populations.[41] Variations in the HLA-DP and HLA-DQ genes influence whether someone clears or retains the HBV.[42] Genome-wide studies have found risk factors for liver cancer, which could help in developing new treatments. Epigenetic changes, such as DNA methylation, histone modification, and regulation by non-coding RNA, are key in liver disease.[43] For instance, hypermethylation of tumor suppressor genes like p16INK4a is linked to liver cancer. MicroRNAs, like miR-122 and miR-21, play roles in liver scarring and cancer development.[44] Moreover, many countries in Asia-Pacific regions will enter super aged societies where more than 20% of their population will be 65 years old or older. Aging itself may also affect all epigenetic mechanism including age-associated DNA methylation and age-related shifts in non-coding RNA expression.[45]

New technologies allow researchers to study the liver in detail, understanding changes in individual cells and their environments. Cost reductions and increased availability of next-generation sequencing technologies will enable large-scale population studies. Single-cell genomics and epigenomics can provide insights into cellular heterogeneity in

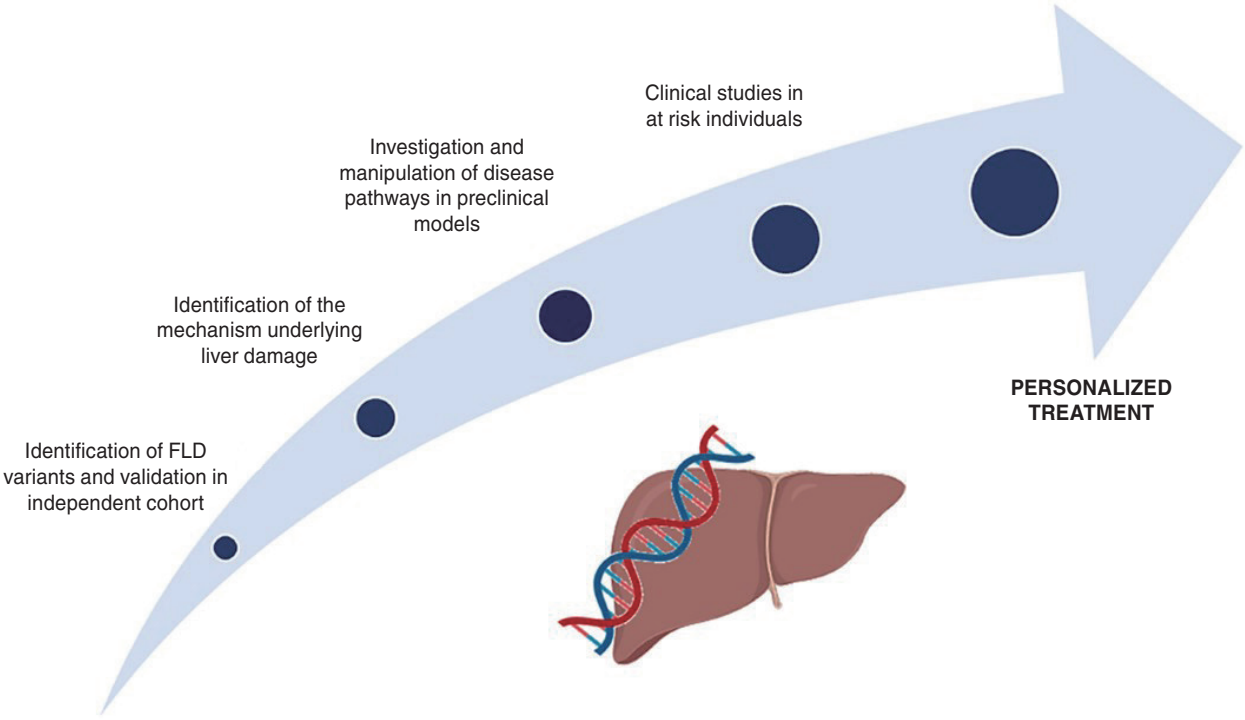

Figure 3. Genomic studies to develop new MASLD therapeutics and precision medicine approaches. MASLD, metabolic dysfunction-associated steatotic liver disease.

liver diseases. Gene-editing tools like CRISPR-Cas9 offer hope for correcting genetic mutations that cause liver diseases.[46] Epigenome editing, which involves precisely modifying epigenetic markers, is a promising new way to treat liver diseases. Combining data from genomics, epigenomics, and other omics fields can provide a more complete understanding of liver diseases and promote the development of personalized treatment (Fig. 3).[47]

Tailoring treatments to an individual's genetic and epigenetic profile could significantly improve liver disease outcomes. The Asia-Pacific region's genetic diversity requires studies focused on these populations to identify unique factors influencing liver diseases. AI tools can help analyze large genetic and epigenetic datasets, leading to better predictions and discoveries of new disease markers.[48] As genetic and epigenetic technologies advance, issues like data privacy and fair access to treatments will need to be addressed to ensure everyone benefits equally.

The future of genetic and epigenetic studies in hepatology is bright, especially in the Asia-Pacific region. With its high burden of liver diseases and genetic diversity, this region is well-positioned to lead new discoveries. Continued investment in research, technology, and ethical practices will be essential to make the most of these advancements.

THE IMPACT OF AI, BIG DATA IN LIVER DISEASE MANAGEMENT AND TELEMEDICINE

AI will help in the future in detecting liver diseases, from chronic inflammation and fibrosis to HCC onset, stratifying risk of disease progression and prognosis. Combining ultrasound, elastography, magnetic resonance liver imaging, histological and clinical data, AI will identify patients at risk of steatohepatitis and progression in the future.[49]

Recently, researchers employed a paired proteomics approach, using liver tissue and plasma, combined with machine learning that is a technique of AI to identify diagnostic and prognostic biomarkers of early ALD.[6] This advancement in molecular analysis is significant as it could provide a window for effective clinical intervention of ALD which is a growing concern across the Asia-Pacific region.

Primary liver cancer, predominantly composed of HCC, is a significant problem in the Asia-Pacific region. HCC is a

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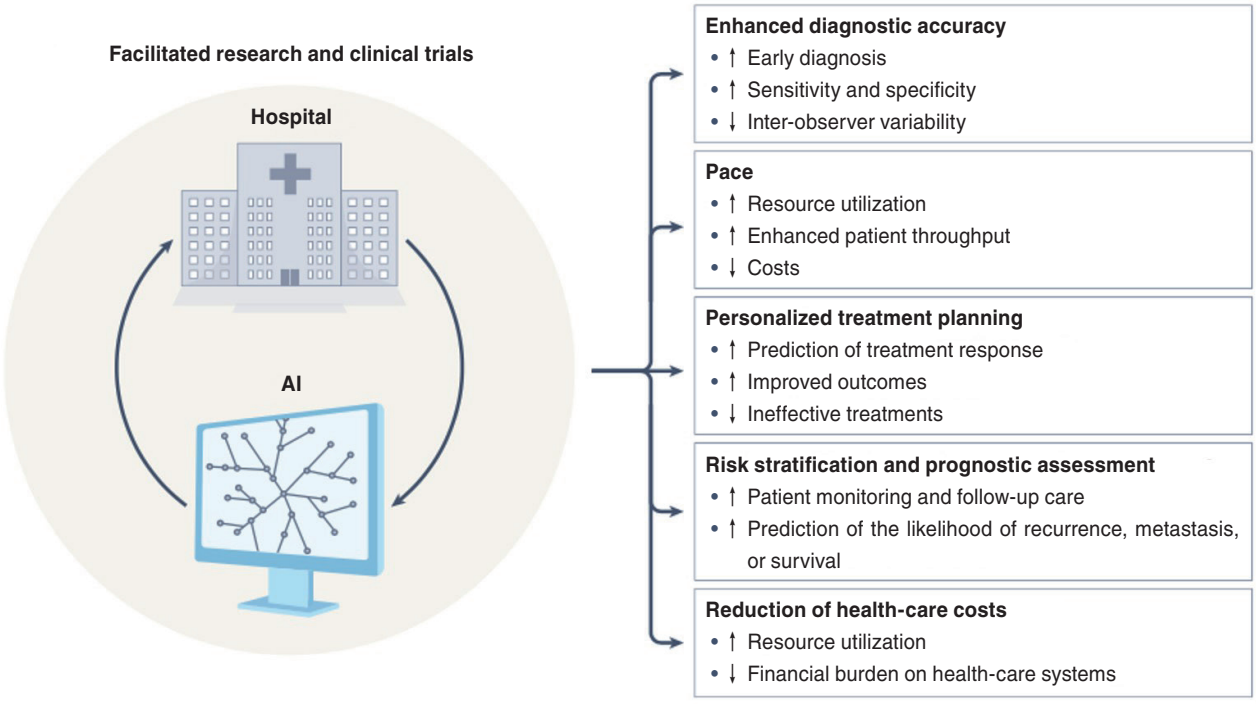

Figure 4. Conceptual model of the future of liver disease management. AI, artificial intelligence.

complex and heterogeneous cancer, with multiple potential etiologies, such as viral hepatitis, alcohol use, and metabolic syndrome, each impacting prognosis differently. The incidence of HCC associated with MASLD or ALD is expected to rise, while cases linked to HCV or aflatoxin exposure will notably decline.[10,50] Liquid biopsy tests (e.g., circulating tumor DNA, RNA) will be routinely used in early detection of HCC. AI is improving liver imaging in HCC by enhancing image reconstruction and diagnostic quality, and automating tasks like lesion segmentation and classification. AI is rapidly advancing from single purpose to multimodal applications that combine multiple data (e.g., histopathology, imaging, clinical features) to enhance HCC diagnosis, prognosis and recurrence risk (Fig. 4).[51,52] These advances require significant changes in the way clinicians, radiologists, and information technology specialists will work together.

However, several challenges, including data quality, management and security, model reliability, regulatory hurdles, and the need for explainable AI, must be addressed to ensure successful integration into clinical workflows. A well-rounded strategy, combining technical innovations and regulatory compliance, will be key to fully realizing AI's transformative potential in patient care.[53]

Telemedicine has the potential to provide and expand treatment access and might be able to reduce the need for hospital readmission.[54] AI aids telemedicine by offering real-time data analysis, facilitating language translation, and supporting healthcare professionals with patient clinical data. Additionally, the integration of wearable devices and health applications allows for remote monitoring and management of patient conditions.

High-quality, comprehensive data is essential for training effective AI models, and variability in clinical data can affect model performance. The use of AI in clinical settings must meet regulatory standards, which vary by region and require rigorous validation to ensure safety and efficacy.

THE IMPORTANCE OF HEALTH POLICY AND PREVENTIVE INITIATIVES

The global burden of MASLD is rising, with particularly severe consequences observed in low- and middle-income

countries, where higher levels of disability are prevalent.[55] Addressing this growing challenge requires a comprehensive policy framework that integrates workplace health interventions, skill-based multicomponent coaching or counseling, and community health worker engagement to enhance access and effectiveness.[56]

ALD remains a significant contributor to the global liver disease burden. Although various intervention strategies can be implemented to reduce alcohol use and its associated health consequences, public policy measures such as taxation, marketing restrictions, and public education campaigns have emerged as particularly effective for population-wide impact.[57]

The elimination of viral hepatitis necessitates the implementation of robust national policies focusing on the expansion of prevention, testing, and treatment services. Targeted interventions such as focused screening programs and treatment support initiatives, are critical to ensuring equitable healthcare access for high-risk populations and underserved groups.[58]

Disparities in the treatment of cirrhosis remain a pressing issue, with patients in low- and middle-income countries experiencing higher mortality rates despite adjusting for liver disease severity. These disparities are often exacerbated by inadequate healthcare infrastructure, including shortages of preventive medications, limited access to emergency endoscopy, and insufficient diagnostic tools.[59] Strong national policies are urgently needed to address these gaps by enhancing supportive care and ensuring the availability of essential services for affected populations.[60]

Screening policies for HCC vary widely across countries, with significant implications for mortality outcomes.[61] Country-specific strategies that improve the accessibility and affordability of HCC screening are vital.[62] Furthermore, structural and institutional inequities, particularly in liver transplantation, must be addressed through targeted policy reforms to mitigate the effects of systemic barriers such as racism and socioeconomic disparities.[63]

Liver transplantation has undergone intensive development in the Asia-Pacific region. Due to cultural and traditional factors, living donor liver transplantation has expanded more extensively than deceased donor liver transplantation (DDLT).[64] Notably, donor hepatectomy surgeries are now performed using advanced endoscopic techniques.[65] However, the high incidence of liver disease and a shortage of donors remain significant challenges.

To address this gap and expand liver transplant availability, scientists are developing various new technologies. While bioengineered artificial livers are under development, several challenges persist.[66] Nevertheless, within the next 50 years, it may become possible to create a liver dialysis system by decellularizing animal livers and integrat-

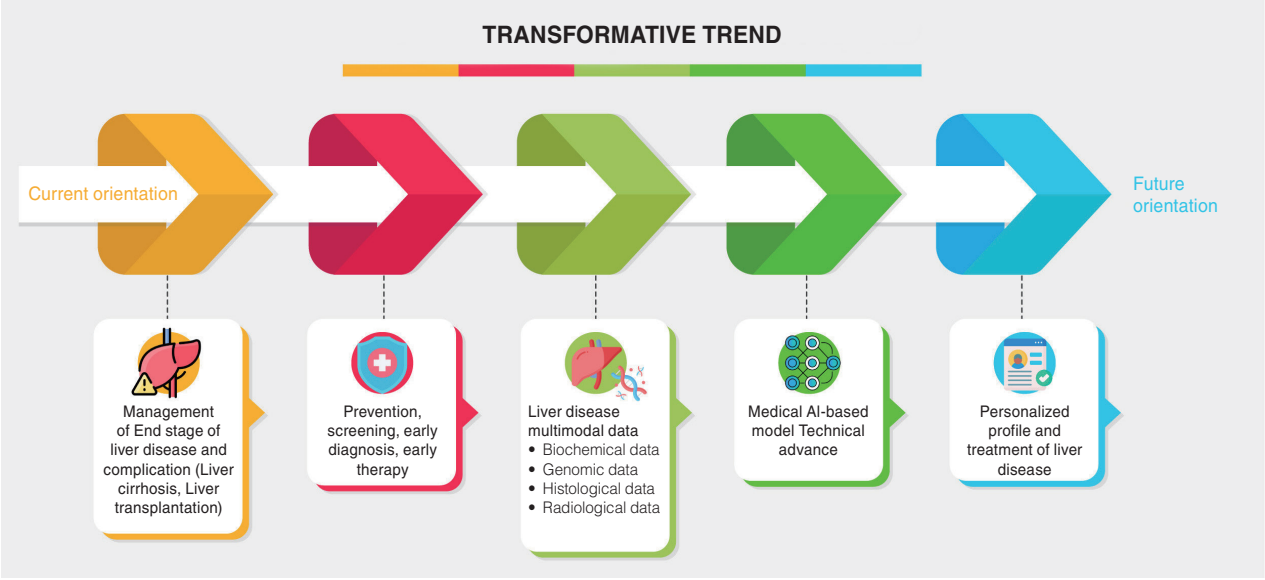

Figure 5. Transformative trends in liver disease management: from end-stage treatment to personalized precision medicine. AI, artificial intelligence.

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ing them into treatment protocols.[67]

In the future, as Asian countries become more globalized and societal perspectives evolve, DDLT may gain wider acceptance, potentially increasing donor availability. However, this development also carries the risk of increased organ trafficking, necessitating strict monitoring and preventive measures.

The future of liver cancer prevention and control will depend heavily on early detection facilitated by systematic screening programs, universal vaccination, lifestyle modifications, and advancements in personalized medicine. Public health initiatives aimed at promoting hepatitis B and C vaccination, raising awareness about the risks of alcohol consumption, and enhancing metabolic health management are expected to grow in prominence.

CONCLUSION

In the Asia-Pacific, in the next 50 years, we will likely see a reduction in viral hepatitis-related liver disease due to vaccination and antiviral treatments. However, lifestyle-related liver diseases like MASLD will continue to rise without significant lifestyle changes and public health intervention. In the next 50 years, the medical approach to liver diseases in the region will differ significantly from the present, and the transformation has already begun quietly (Fig. 5). Advances in genetic screening, AI, and environmental health policies could help curb the burden, but ecological challenges like pollution may exacerbate liver health risks in many areas. The future presents opportunities for significant progress in liver disease prevention and care. Region-specific research, regional collaboration, and leveraging digital health platforms can enhance healthcare access and impact. By prioritizing innovation, equity, and cooperation, we can reduce the liver disease burden and improve population health in the Asia-Pacific region.

Authors' contribution

Conceptualization and design: SS, JM, QD, TB, LMC; data curation, drafting of the manuscript: JM, QD, TB, LMC; review and editing of the manuscript: SS, MT, HM, HN, DAP, RG, YHH, TT, GG, YJK. The final version of this manuscript was approved by all the authors.

Conflicts of Interest

The authors have no conflicts to disclose.

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