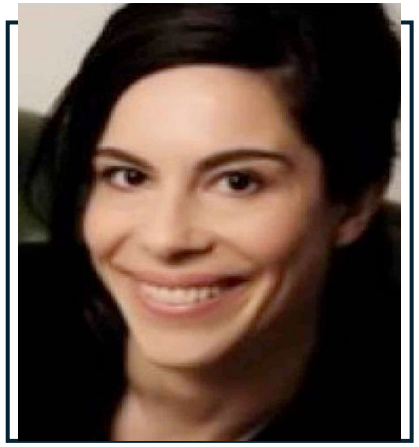
Name: Maud Lemoine



Country: United Kingdom/The Gambia

Affiliation: Medical Research Council (MRC)

Function:

Main expertise (1-2 lines): Professor Maud Lemoine is a Professor and Clinical Consultant in Hepatology at St Mary's hospital, Imperial College London, UK. Her research activities are mainly focused on the prevention and management of viral hepatitis in resource-limited countries, mainly in Africa. Since 2011, she has been working with the Medical Research Council (MRC) The Gambia unit, as part of the hepatitis B study, PROLIFICA (Prevention of Liver Fibrosis and Cancer in Africa) programme in The Gambia and Senegal.

Viral Hepatitis Prevention Board

Epidemiological Insights into viral-induced Hepatocellular Carcinoma within the Framework of WHO's Global Hepatitis Elimination Strategy

Prof. Maud Lemoine

St Mary's hospital, Imperial College London, UK

MRC @ the London School of Hygiene and Tropical Medicine, Gambia

MRC Unit The Gambia

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Imperial College London

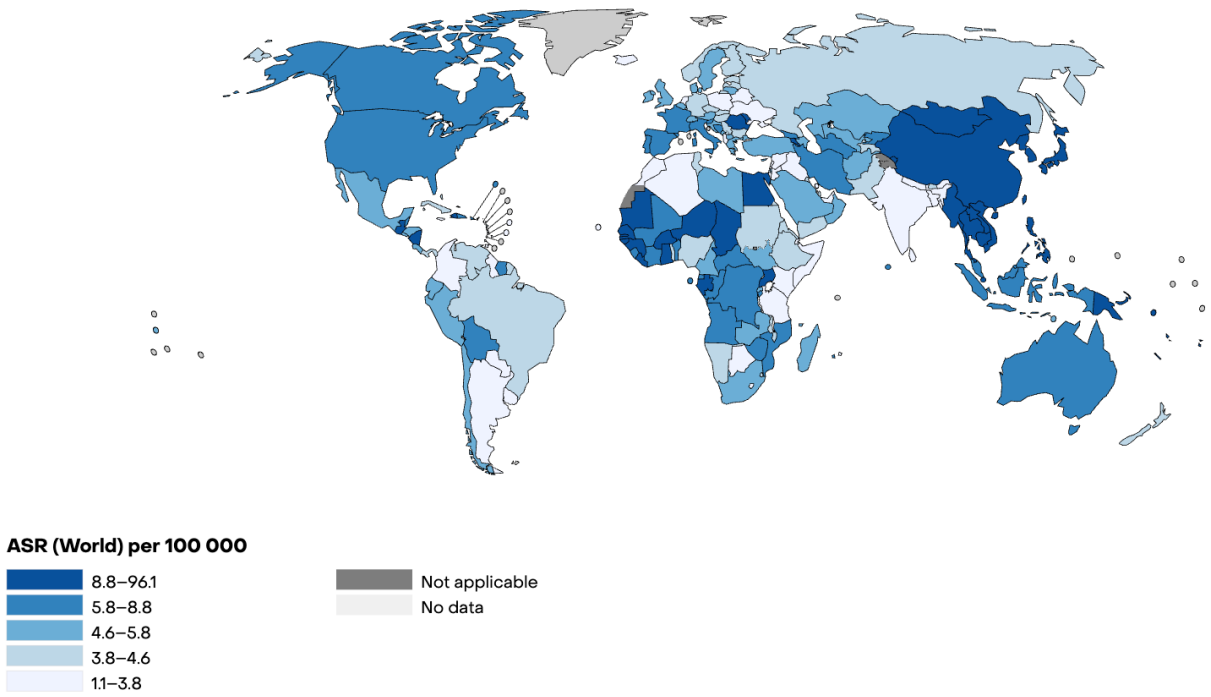
Global burden of hepatocellular carcinoma (HCC)

- Third leading cause of cancer-related death globally
- Poor prognosis: 5-year survival rate of approximately 18%
- Approximatively 800,000 annual deaths

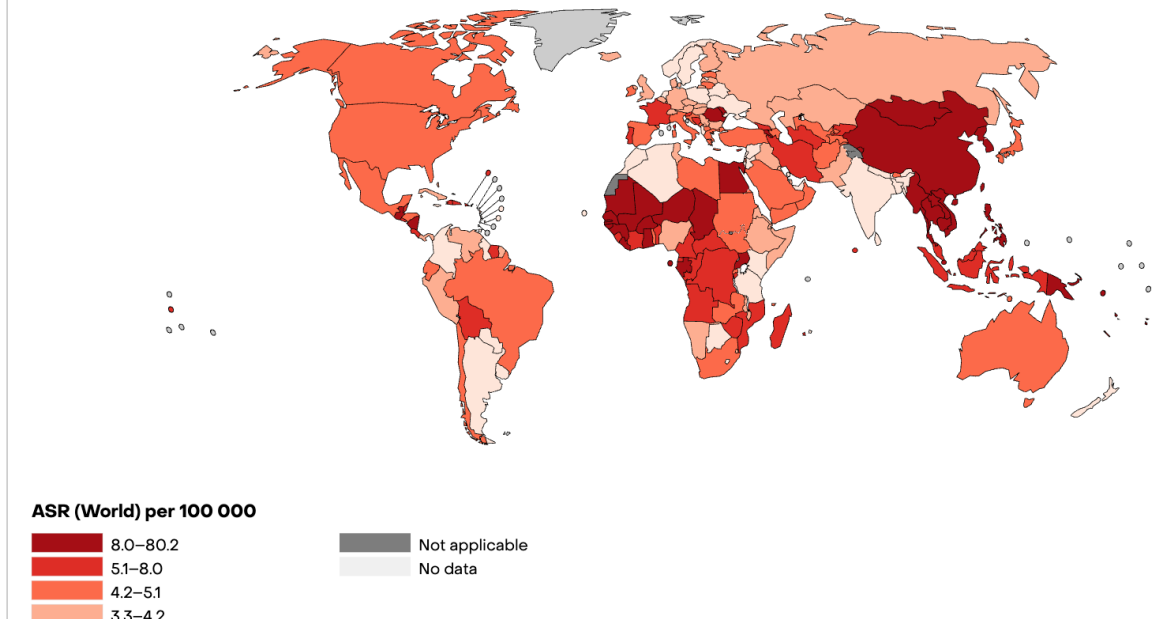
Siegel RL et al. Cancer statistics, 2022
WHO-IARC 2022 data

Africa and Asia: the most affected regions

Liver cancer AS incidence rate in both sexes (2022)



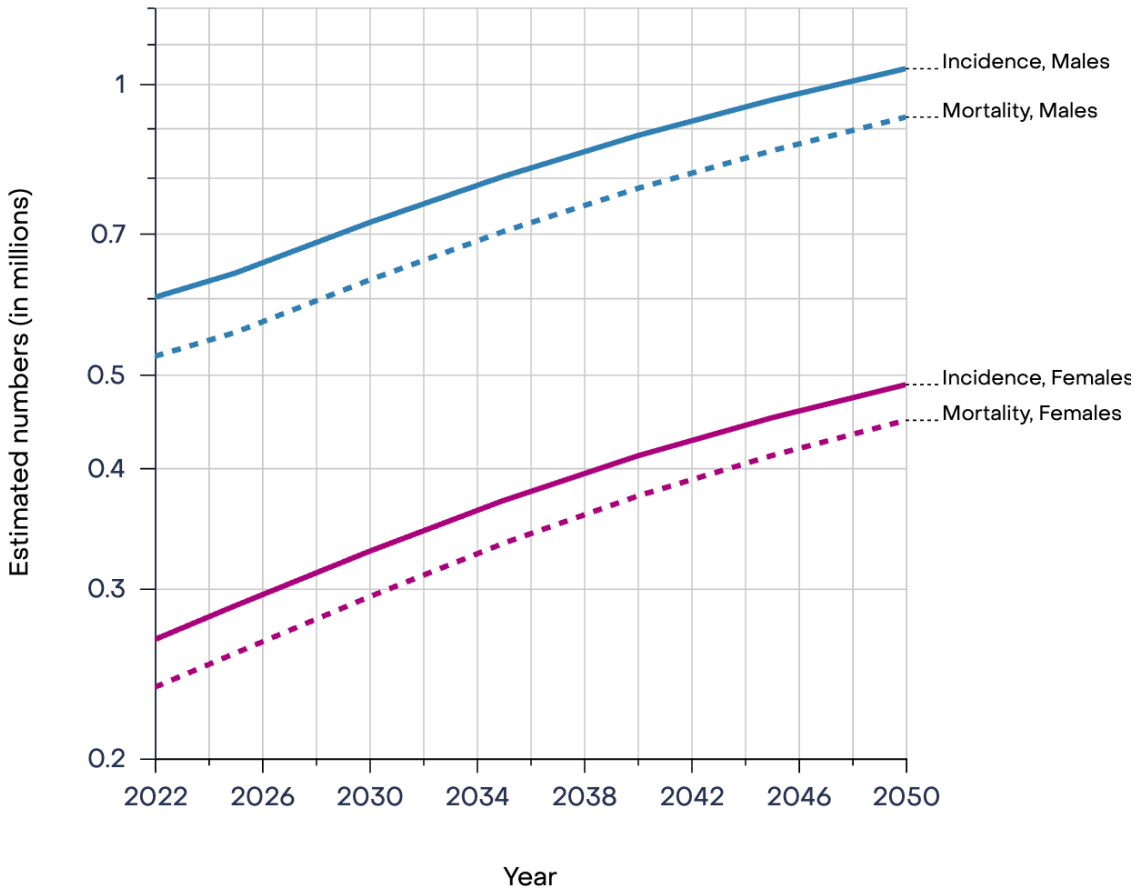
Liver cancer AS mortality rate in both sexes (2022)



Globocan 2022 data

Global burden of HCC: an anticipated increase by >55% by 2050 globally

Estimated numbers from 2022 to 2050, Males and Females, age [0-85+]
Liver and intrahepatic bile ducts

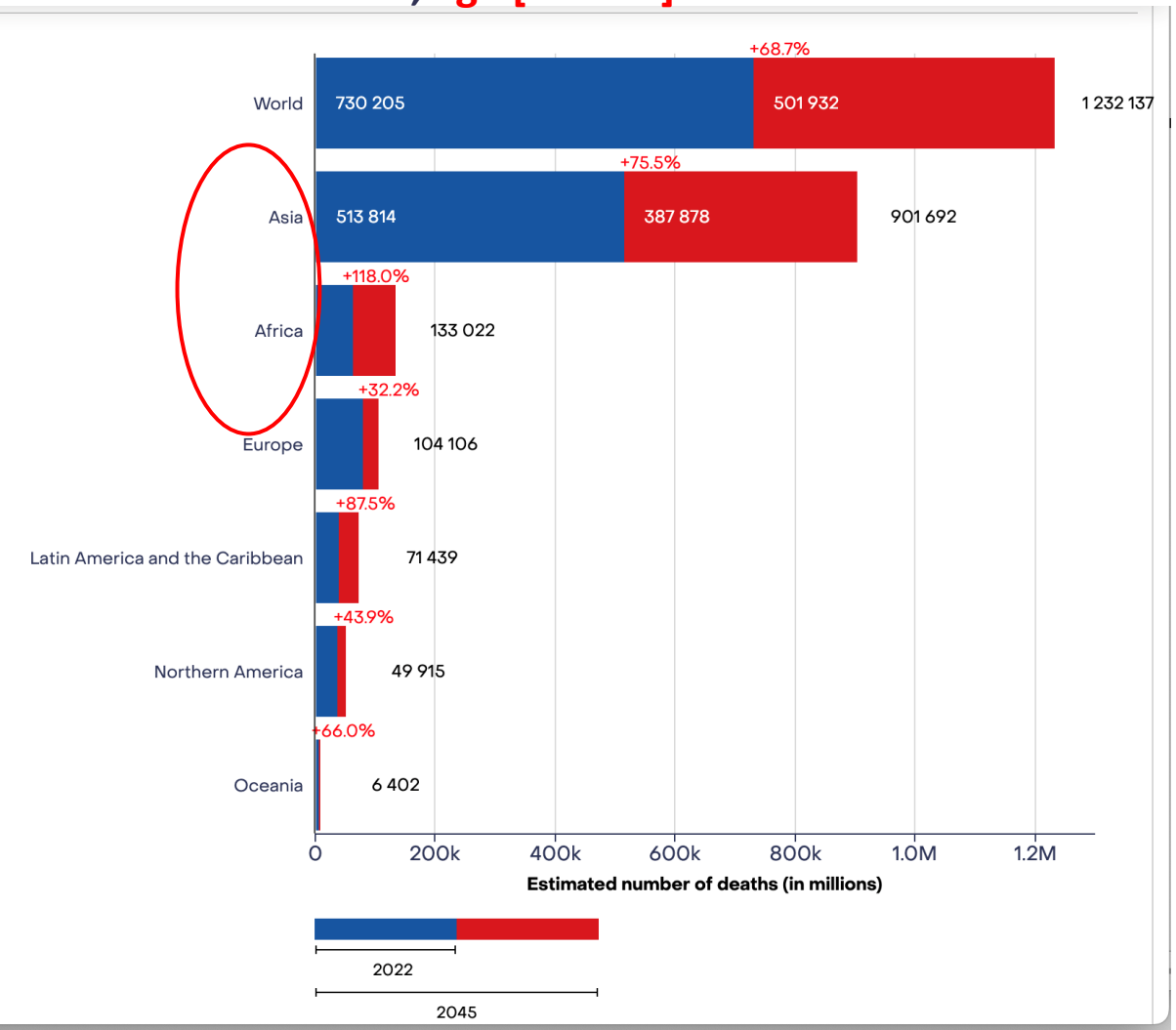


Globocan 2022 data
Rumgay et al. J hepatol 2022

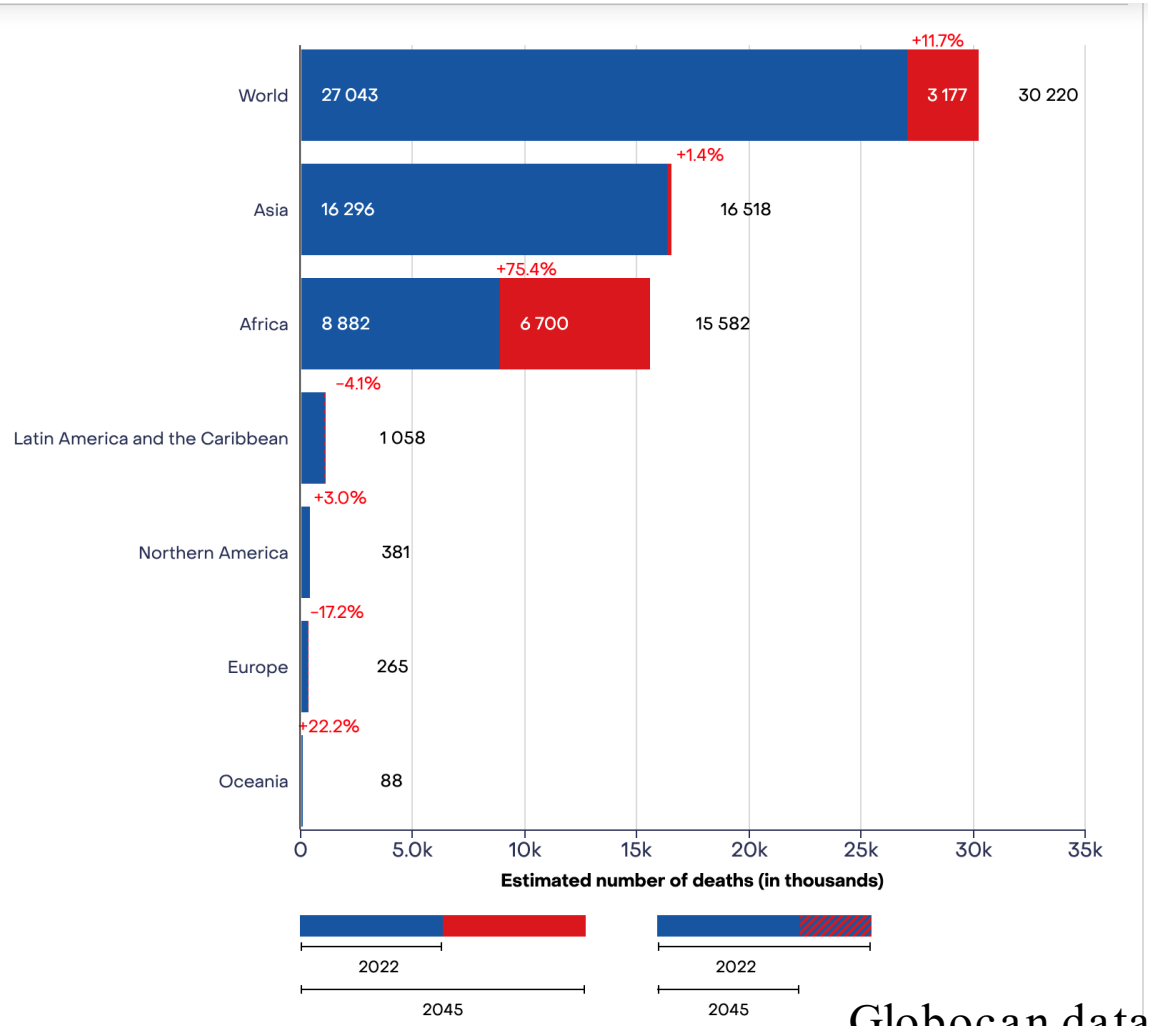
Increase in HCC mortality mainly observed in Asia and Africa in people >40 yo

Estimated number of deaths from 2022 to 2045

- **Both sexes, age [40-85+]**

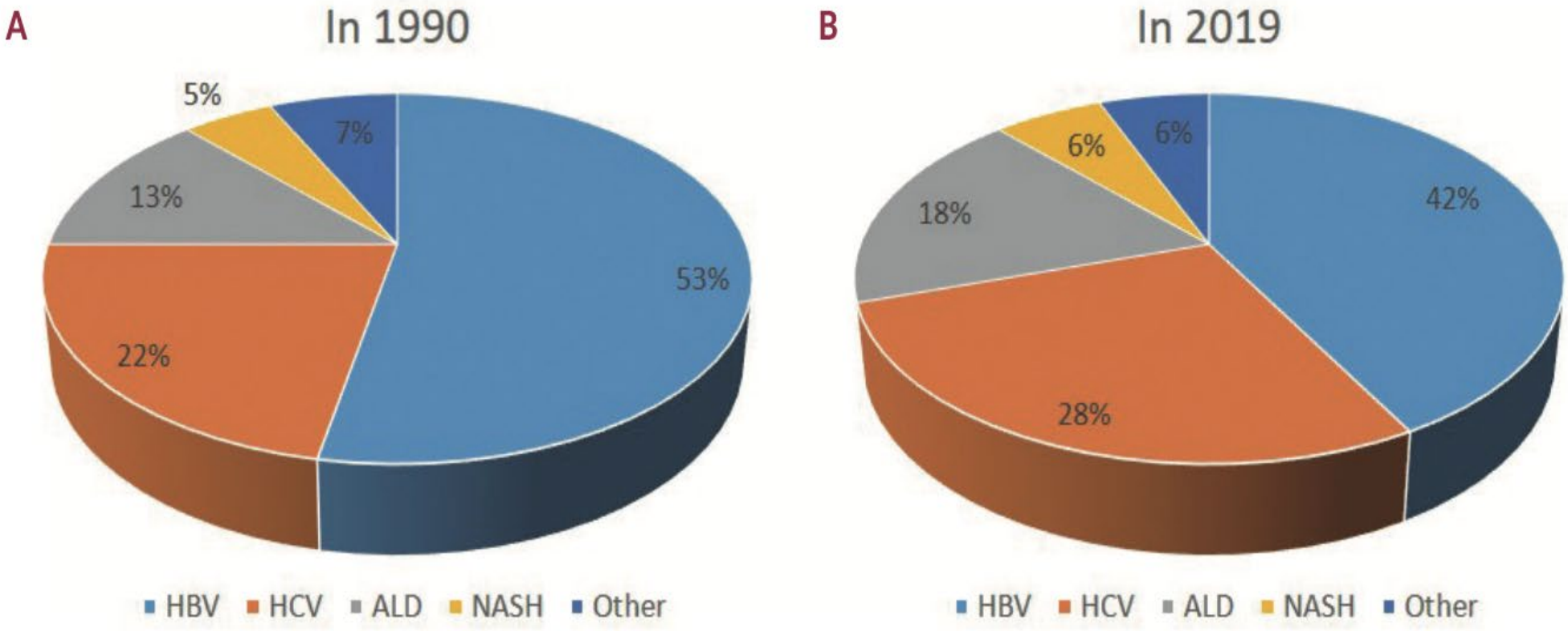


Both sexes, age [5-39]



Globocan data 2022

HepB and HepC are the leading causes of HCC worldwide



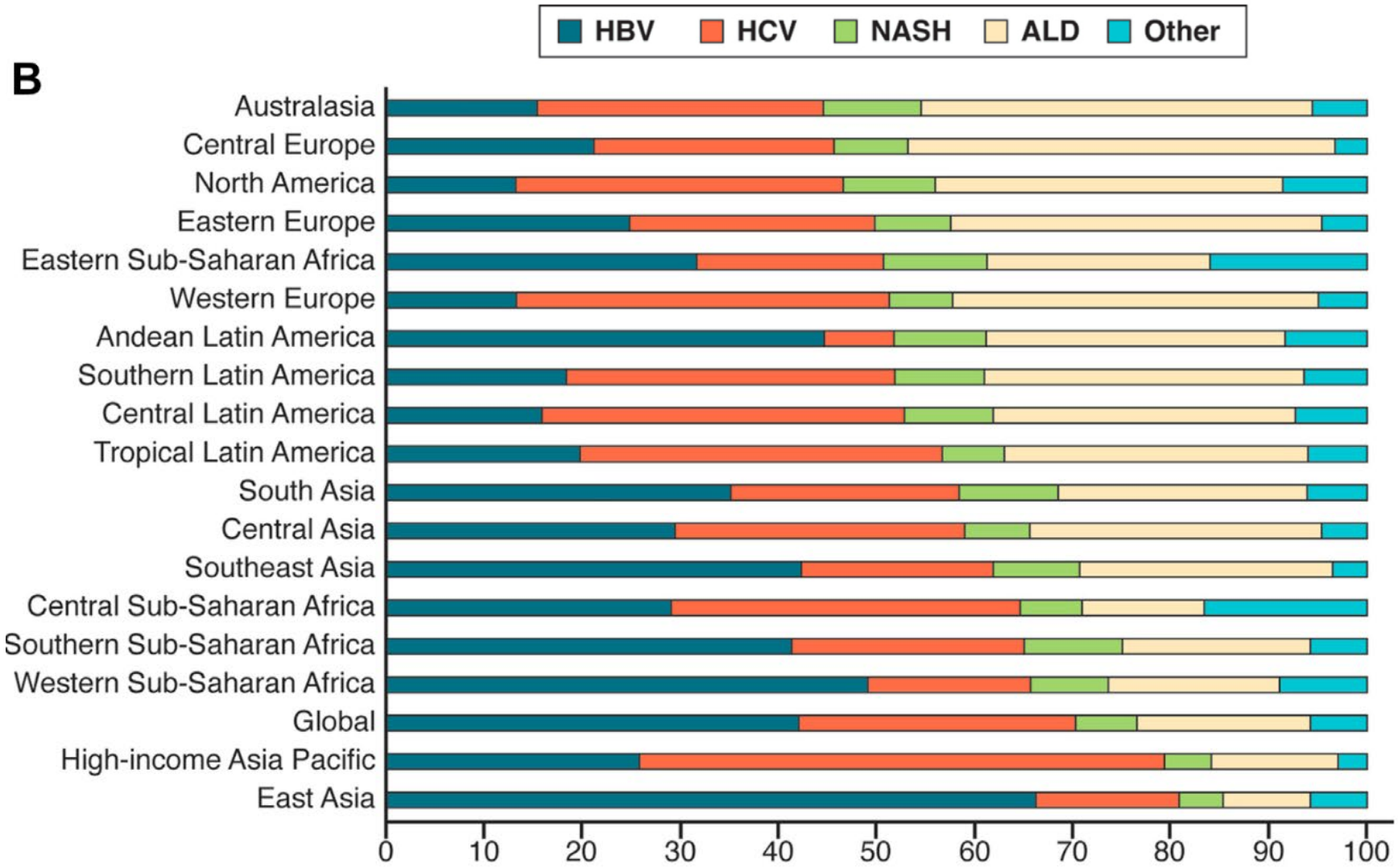
Proportion of HCC etiologies worldwide in 1990 (A) and 2019 (B) modified from Yang et al. and Toh et al.

Kim et al. *J Liver Cancer 2024*

HCC etiologies vary by regions (2019 data).

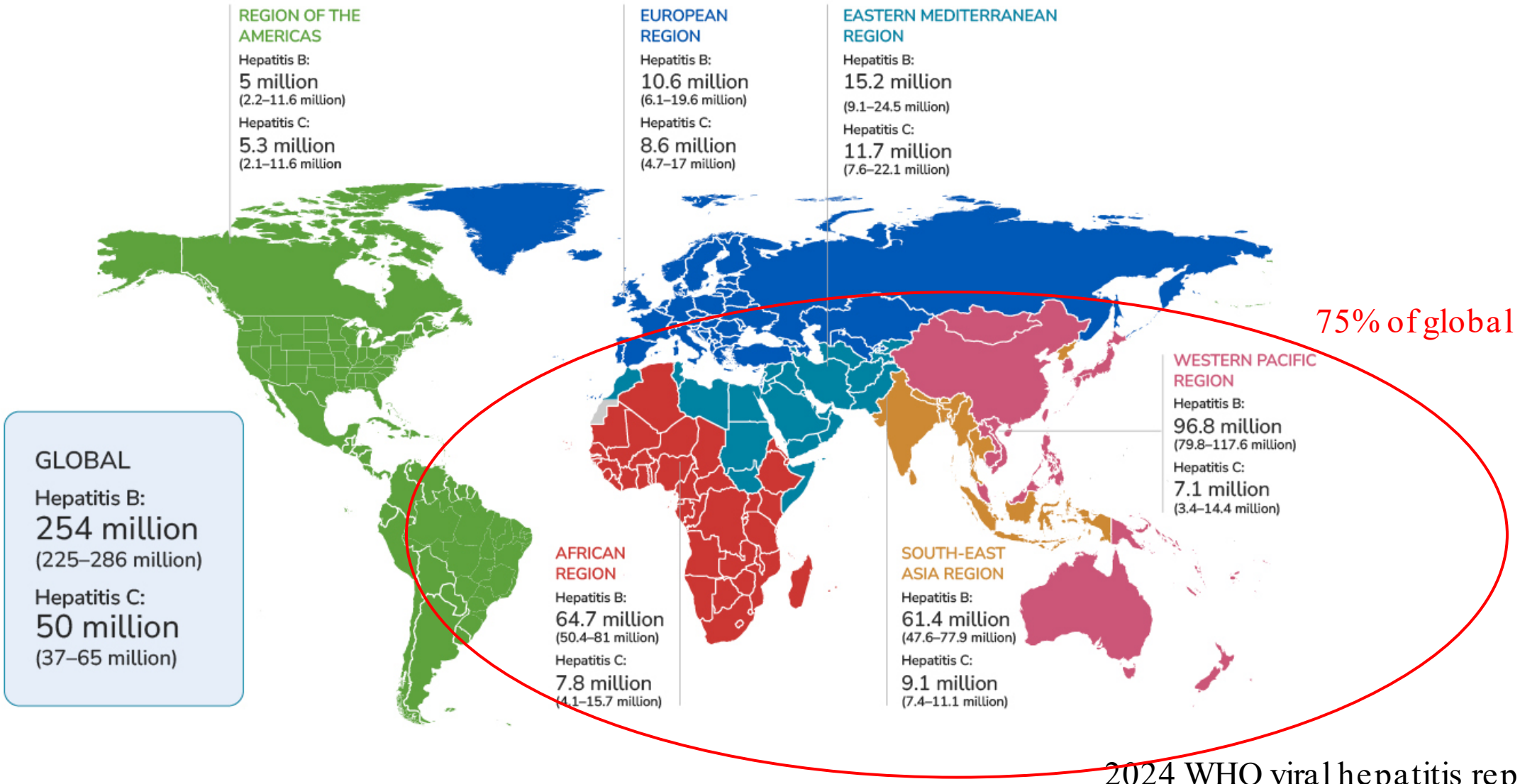
Nonviral causes,
contribute
to the majority of HCC in
North America & Europe,

Viral hepatitis is the
main cause of HCC
in **Asia & Africa**



Toh et al Gastroenterology 2023

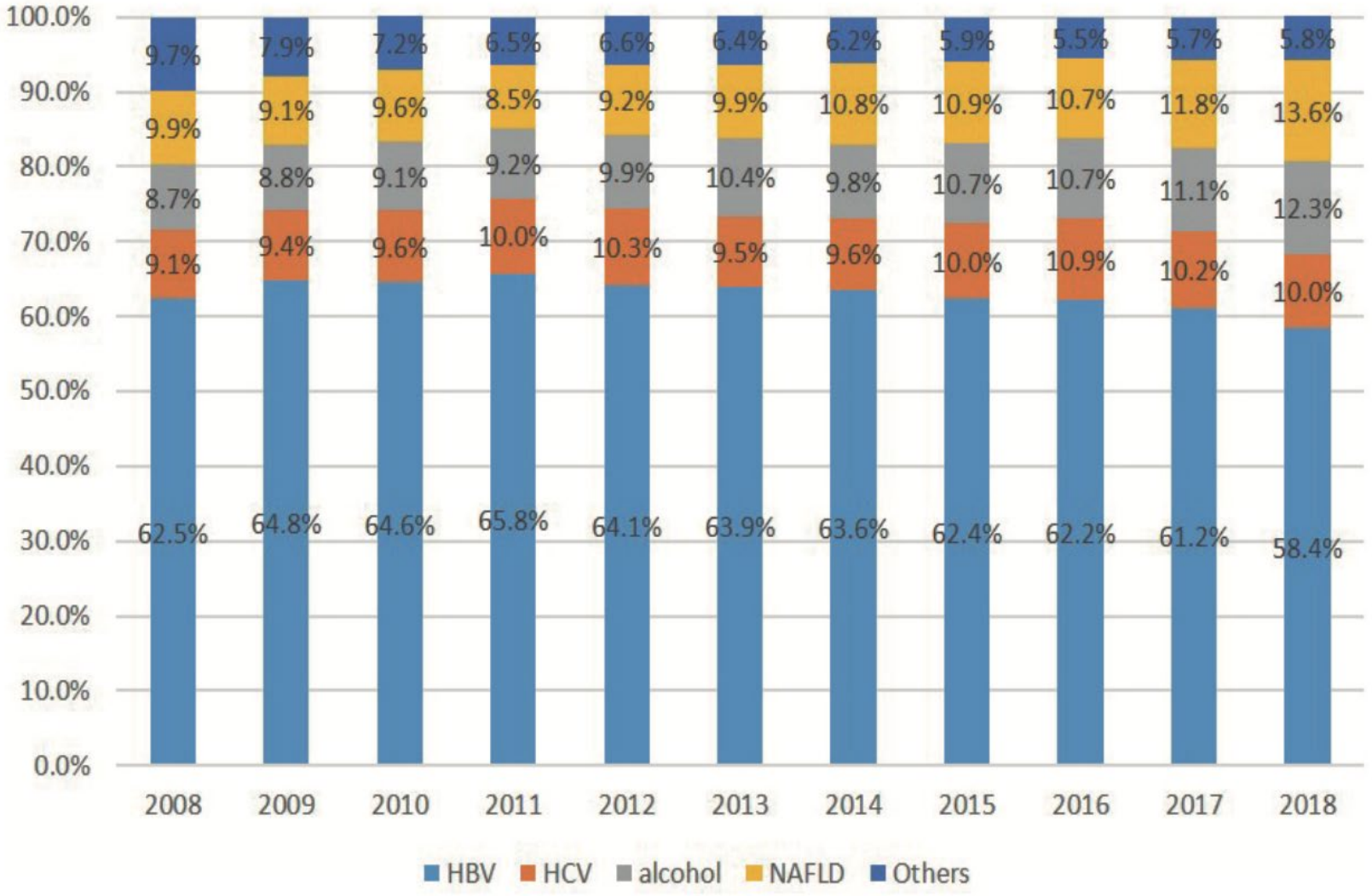
Africa and Asia carry the highest prevalence of HBV & HCV



75% of global cases

2024 WHO viral hepatitis report

Anticipated shift in etiologies, even in endemic countries
The South Korea case



Increase in non viral hep etiologies

In 2018, viral hepatitis accounted for 2/3 of HCC

Kim et al. *J Liver Cancer 2024*

Figure 2. Distribution of HCC etiologies demonstrating increase of NAFLD between 2008 and 2018 in South Korea.

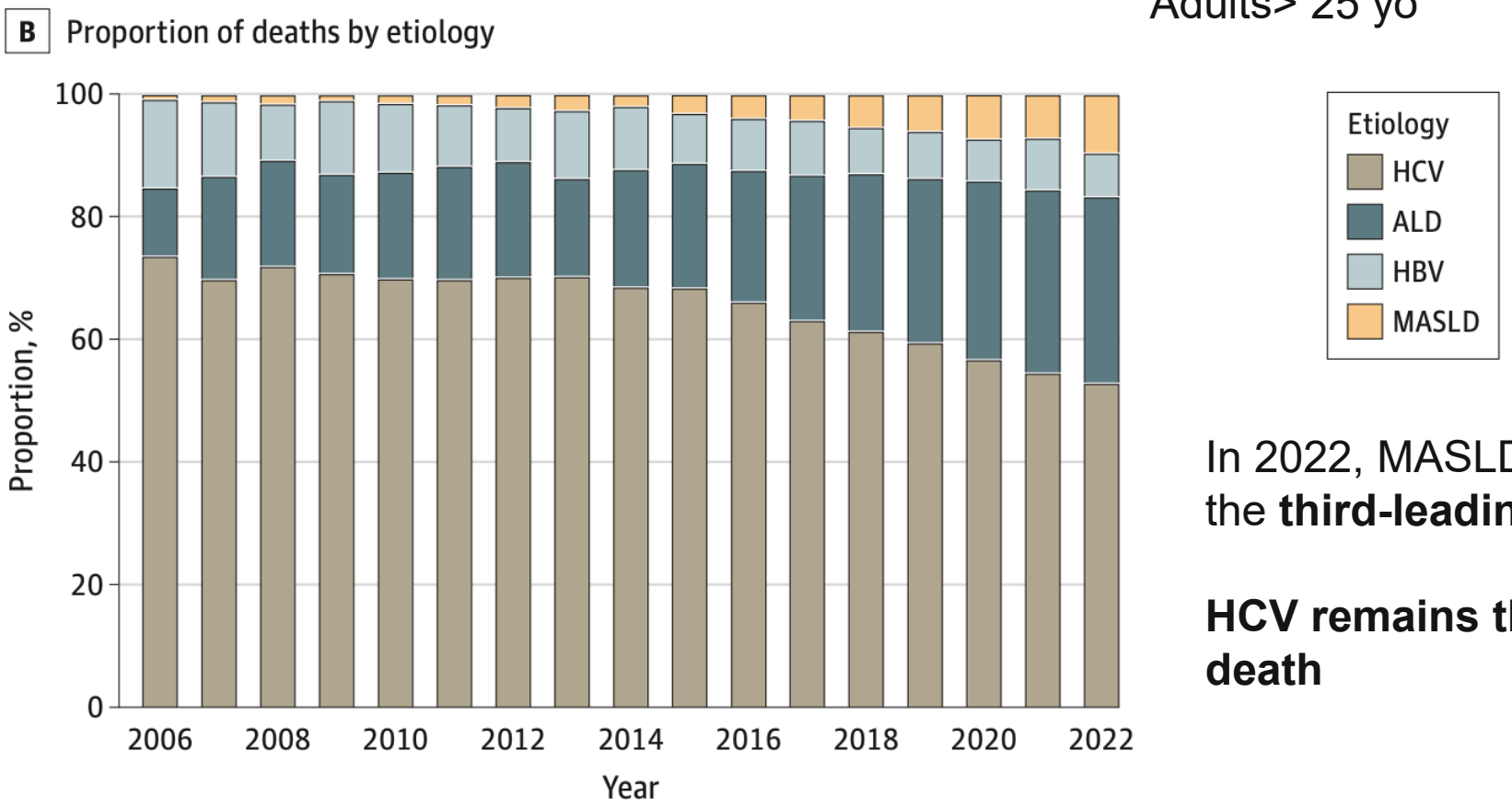
JAMA Network Open

Original Investigation | Gastroenterology and Hepatology

Trends in Hepatocellular Carcinoma Mortality Rates in the US and Projections Through 2040

Sikai Qiu, MM; Jiangying Cai, MM; Zhanpeng Yang, MM; Xinyuan He, MD; Zixuan Xing, MD; Jian Zu, PhD; Enrui Xie, MD; Linda Henry, MD; Custis R. Chong, MD; Esther M. John, MD; Ramsey Cheung, MD; Fanpu Ji, MD, PhD; Mindie H. Nguyen, MD, MAS

188 280 HCC-related deaths from 2006 to 2022
Adults> 25 yo



In 2022, MASLD surpassed HBV as the **third-leading cause of HCC-related death**

HCV remains the main cause of HCC-related death

An anticipated shift from viral hepatitis to non viral hepatitis HCC

JAMA Network Open

Original Investigation | Gastroenterology and Hepatology

Trends in Hepatocellular Carcinoma Mortality Rates in the US and Projections Through 2040

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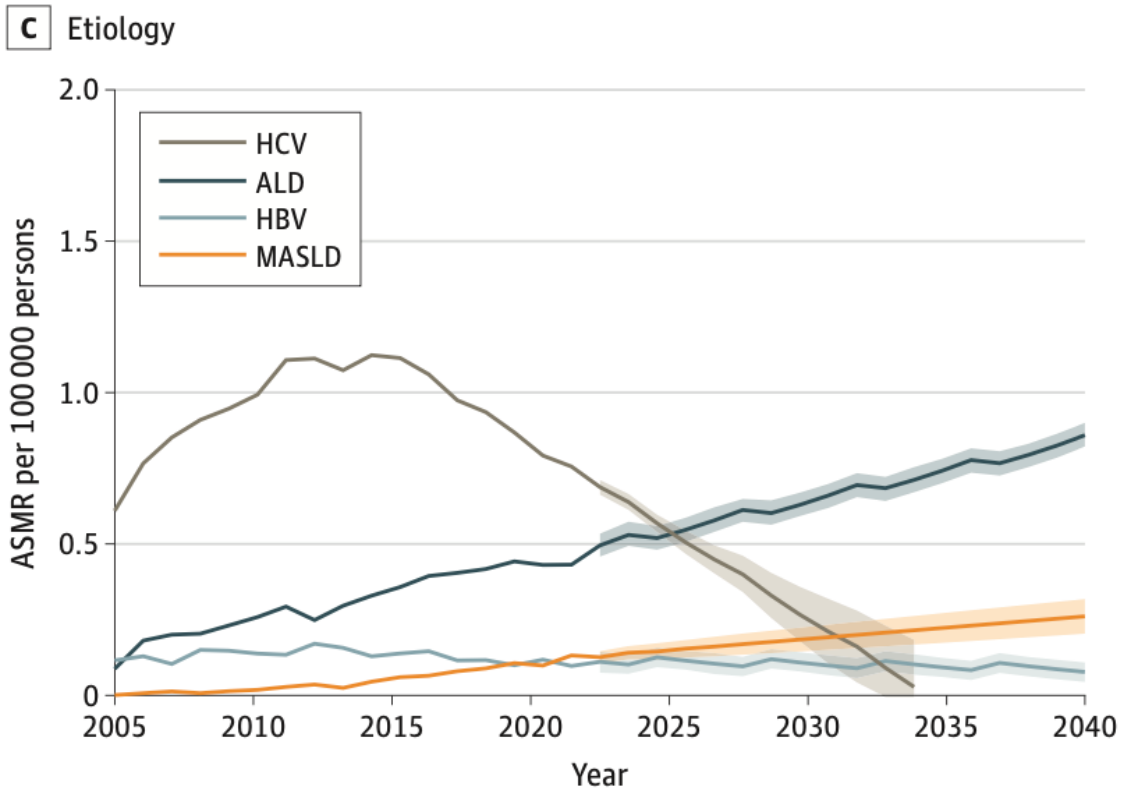


ALD is projected to be the leading cause of HCC-related death in **2026.**

MASLD is projected to overtake HCV in 2032 as the **second-leading cause of HCC death**

Qiu et al. JAMA Open 2024

MASLD: the fastest rising cause of HCC among patients listed for liver transplantation in the US

MASLD indication rose

from 2.1% to 16.2% from 2000 to 2016

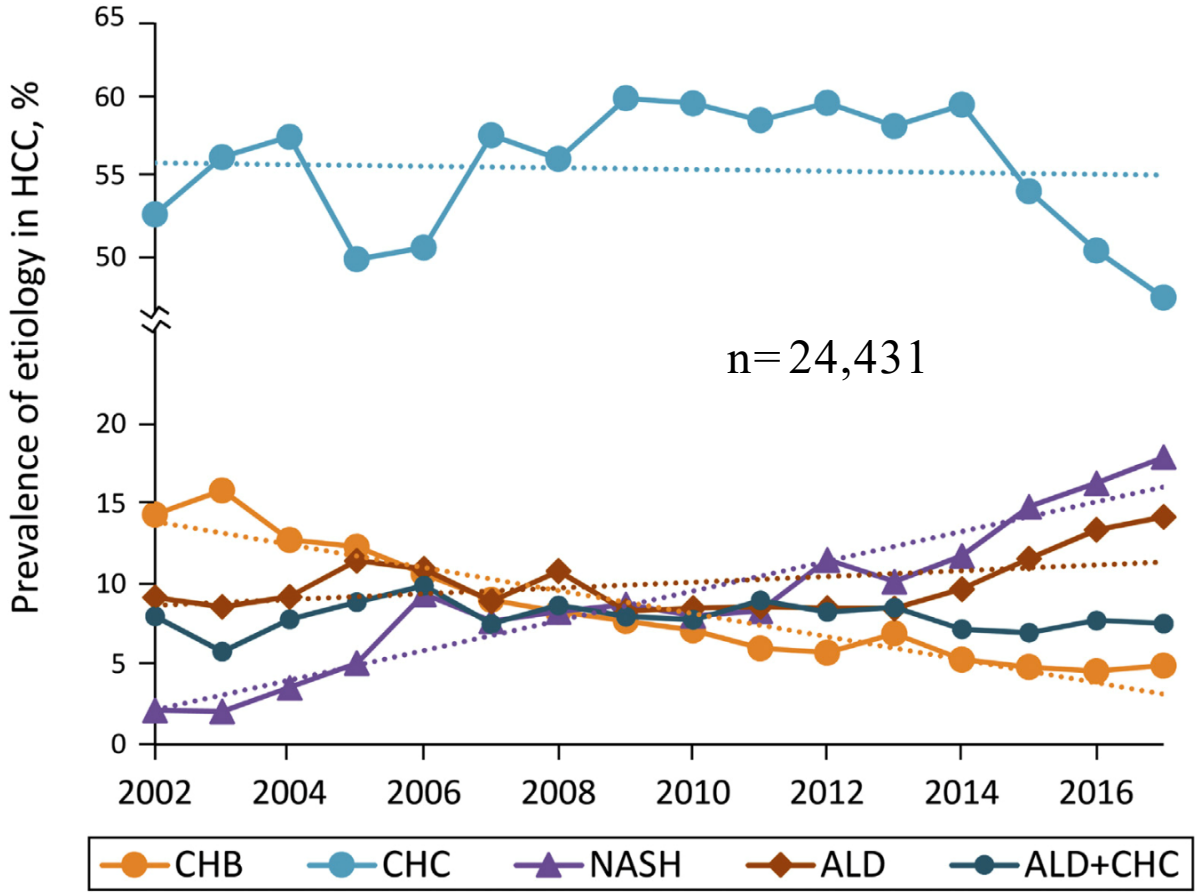


Figure 2. Prevalence of liver disease etiologies in patients with HCC and available etiology. *Dotted lines* represent linear trends.

Younossi, Z et al. Clin. Gastroenterol. Hepatol. 2019

Research Article
Genetic and Metabolic Diseases

JOURNAL
OF HEPATOLOGY

Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016–2030

- Dynamic Markov modelling for MASLD-HCC across **eight high income countries**
- **Predicted 122% rise in MASLD-HCC incidence by 2030**

- In England the incidence of NAFLD-associated HCC would increase by 88% between 2016 and 2030

Estes, C et al J Hepatol. 2018

? LMICs: an increasing burden of ALD and MASLD

Obesity

Obesity: Africa's new crisis

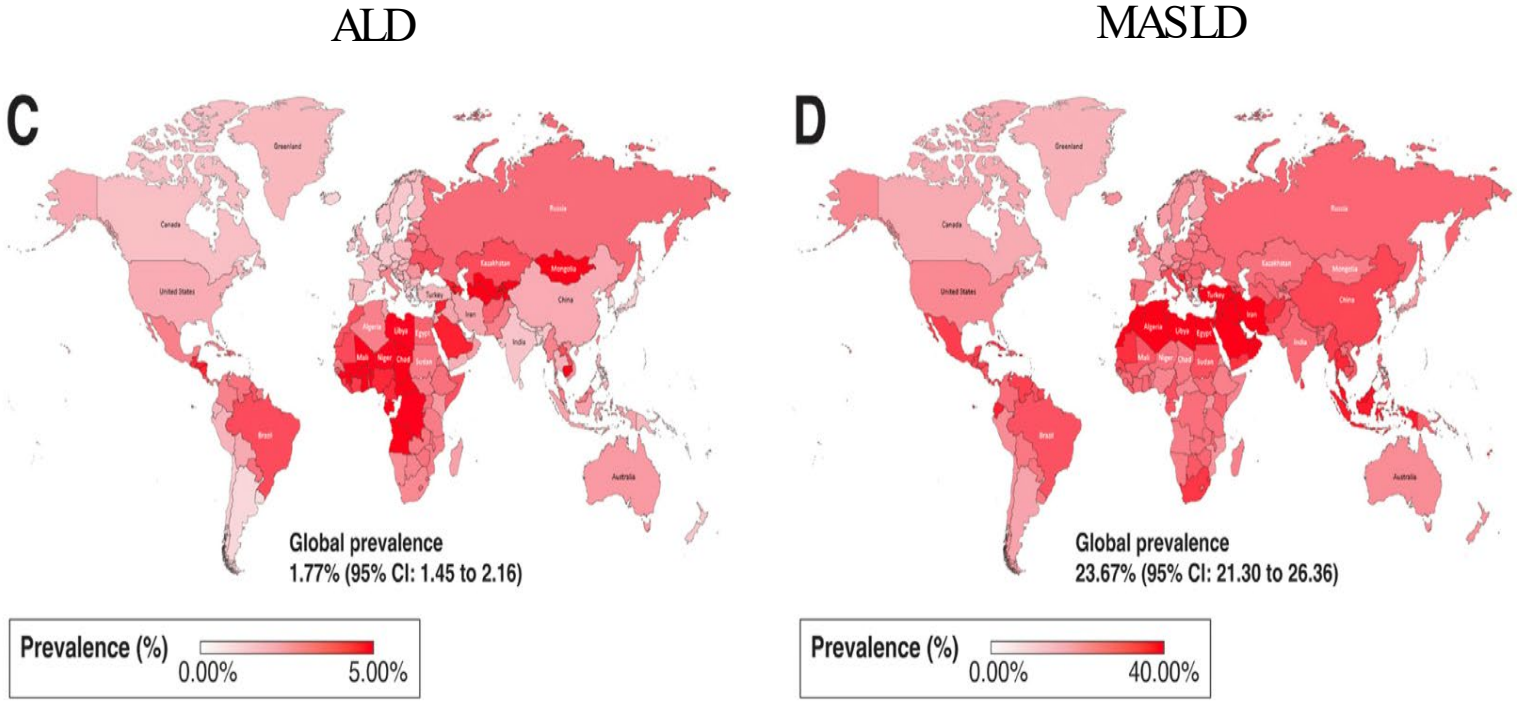
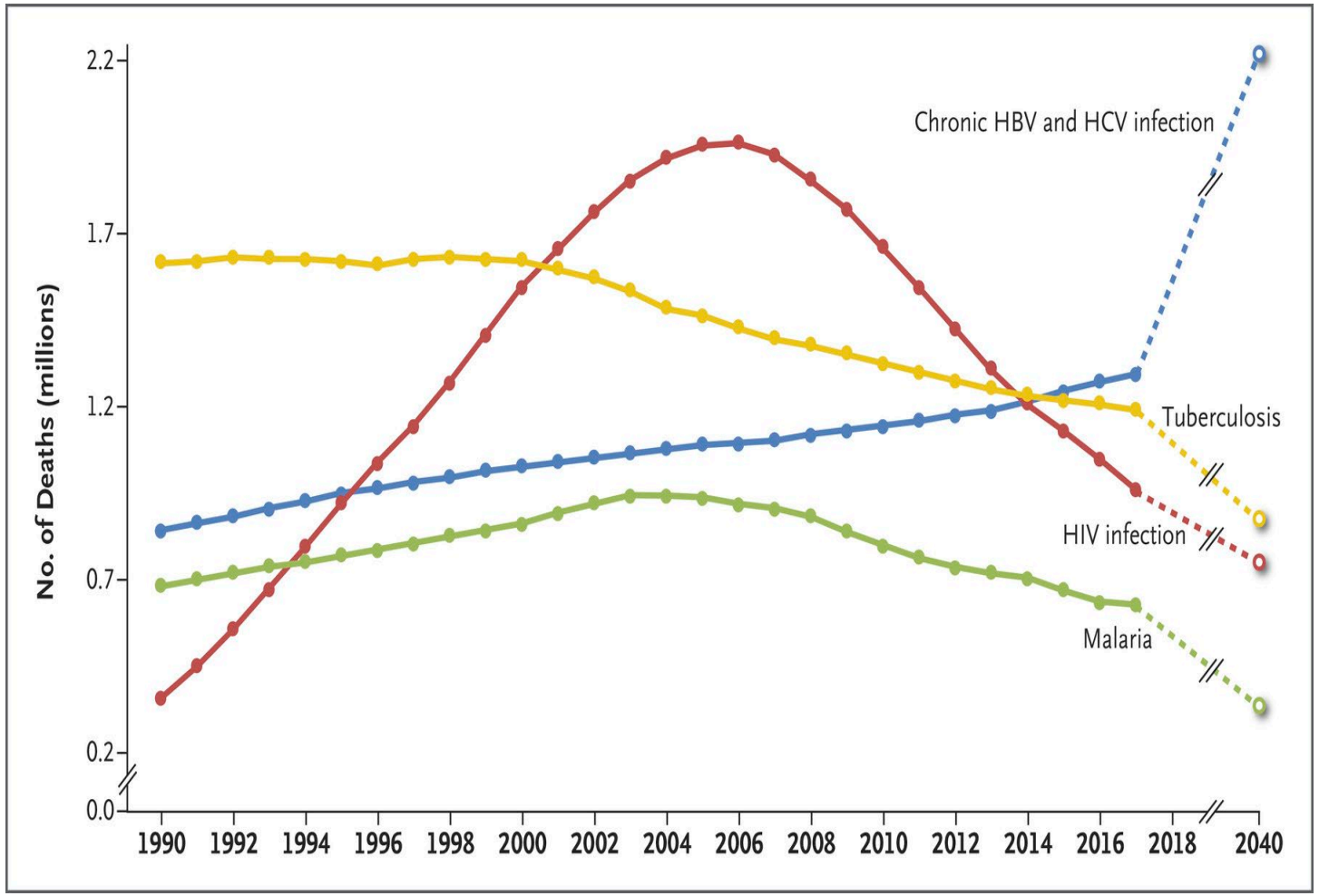


Figure 1. (*A*) Prevalence of hepatitis B virus, (*B*) prevalence of hepatitis C virus, (*C*) prevalence of alcohol-related liver disease, and (*D*) prevalence of nonalcoholic fatty liver disease (in adults age ≥20 years).

Younossi et al 2024
Clinical Gastroenterology and Hepatology

Viral hepatitis : a threat to global health



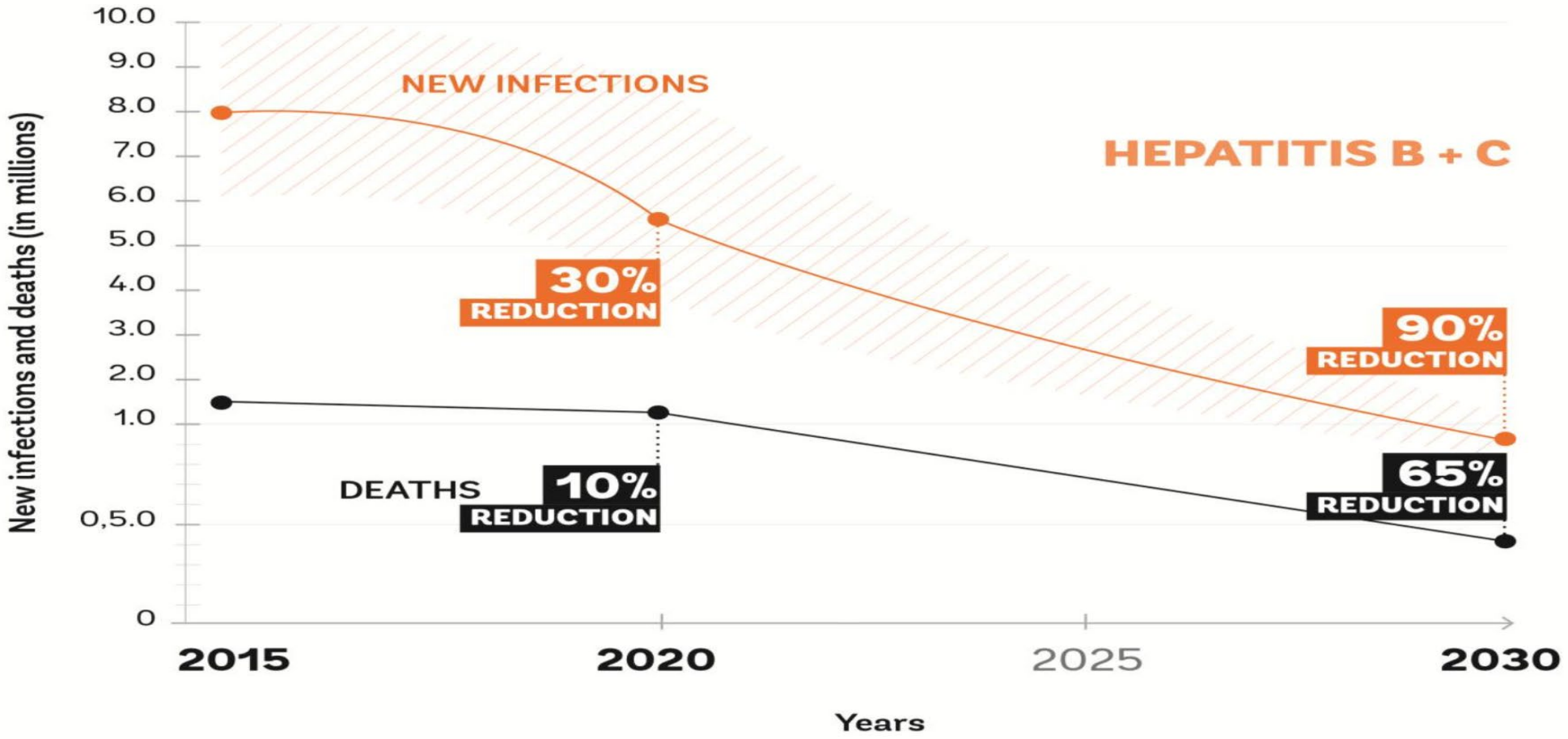
In 2022: **1.3 million deaths** due viral hepatitis

Mainly from HBV: 1.1 million deaths
(83% of all viral hepatitis deaths)

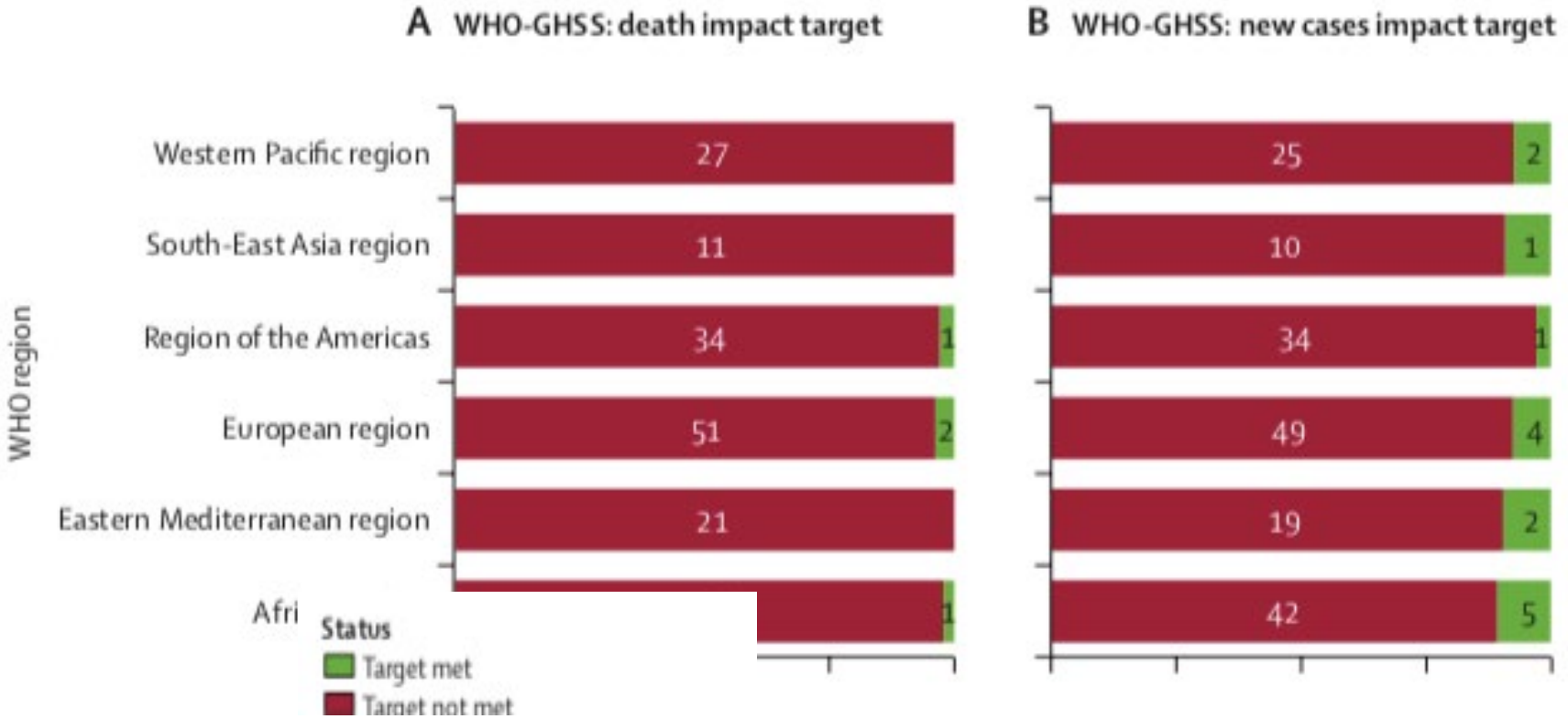
2014: the turning point

Thomas DL, NEJM, 2019
Global hepatitis report, 2017

2016: First WHO Hepatitis Elimination Targets



HBV2020-interim targets not met globally



Only four countries met or surpassed the 2020 WHO-interim target of reducing HBV-related deaths

Only 15 countries met or surpassed the 2020 WHO-interim target of reducing HBV incidence

GBD 2019 Hepatitis B Collaborators, Lancet Gastro Hep 2022

HCV elimination targets not reached in most high-income countries

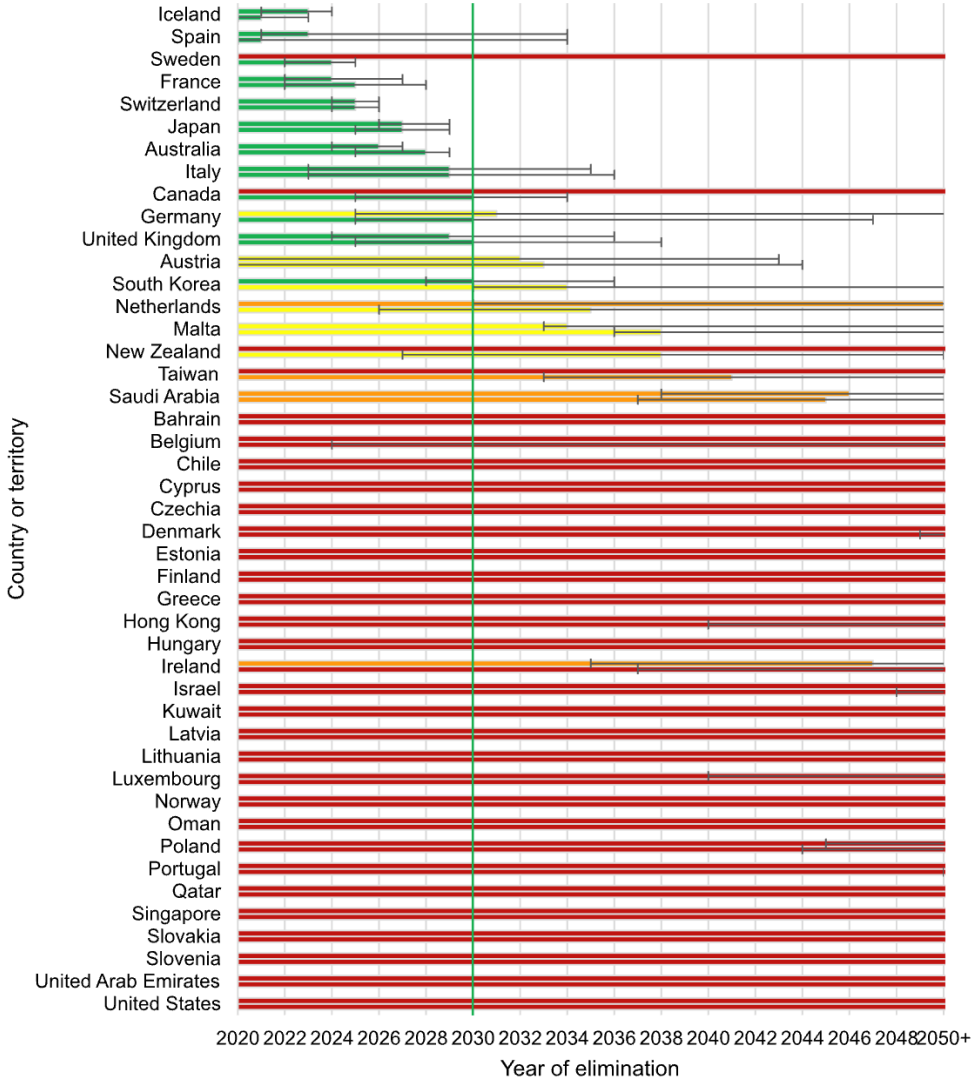


FIGURE 1 Progress towards the WHO's 2030 HCV elimination targets in high-income countries. Note: Green bars represent HCV elimination by 2030; yellow bars, after 2030, by 2040; orange bars, after 2040, by 2050; red bars, after 2050. The top bar represents the year of elimination at the 2017 status quo; the bottom bar, at the 2019 status quo. Error bars reflect the best-case (based on lowest starting chronic prevalence) and worst-case (based on highest starting chronic prevalence) years of elimination. HCV, hepatitis C virus

N=45 high income countries analysed

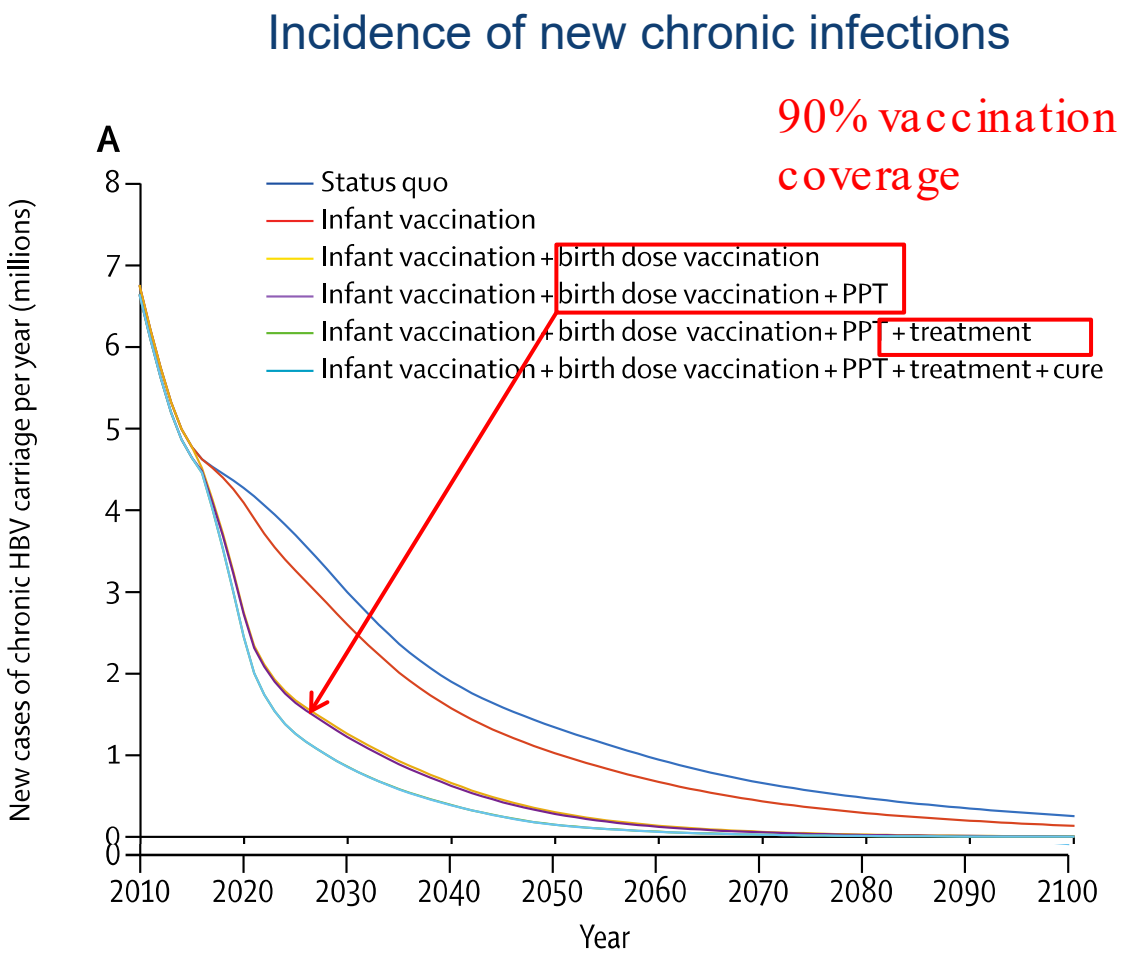
Only 11 countries on track to eliminate HCV by 2030

27 countries are not expected to achieve elimination before 2050.

Gamkrelidze et al. Liver international 2021

Can we accelerate viral hepatitis elimination and reduce the burden of viral hepatitis HCC ?

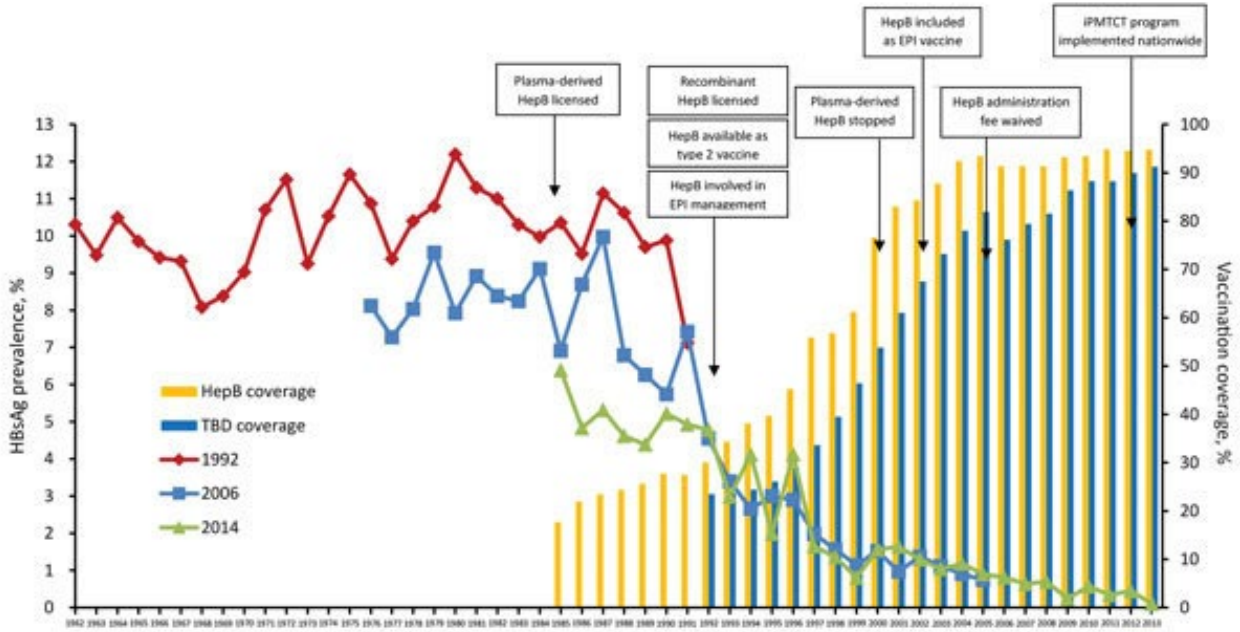
Scaling HBV vaccination and PMTCT is key



Nayagam et al, Lancet Infectious Diseases 2016

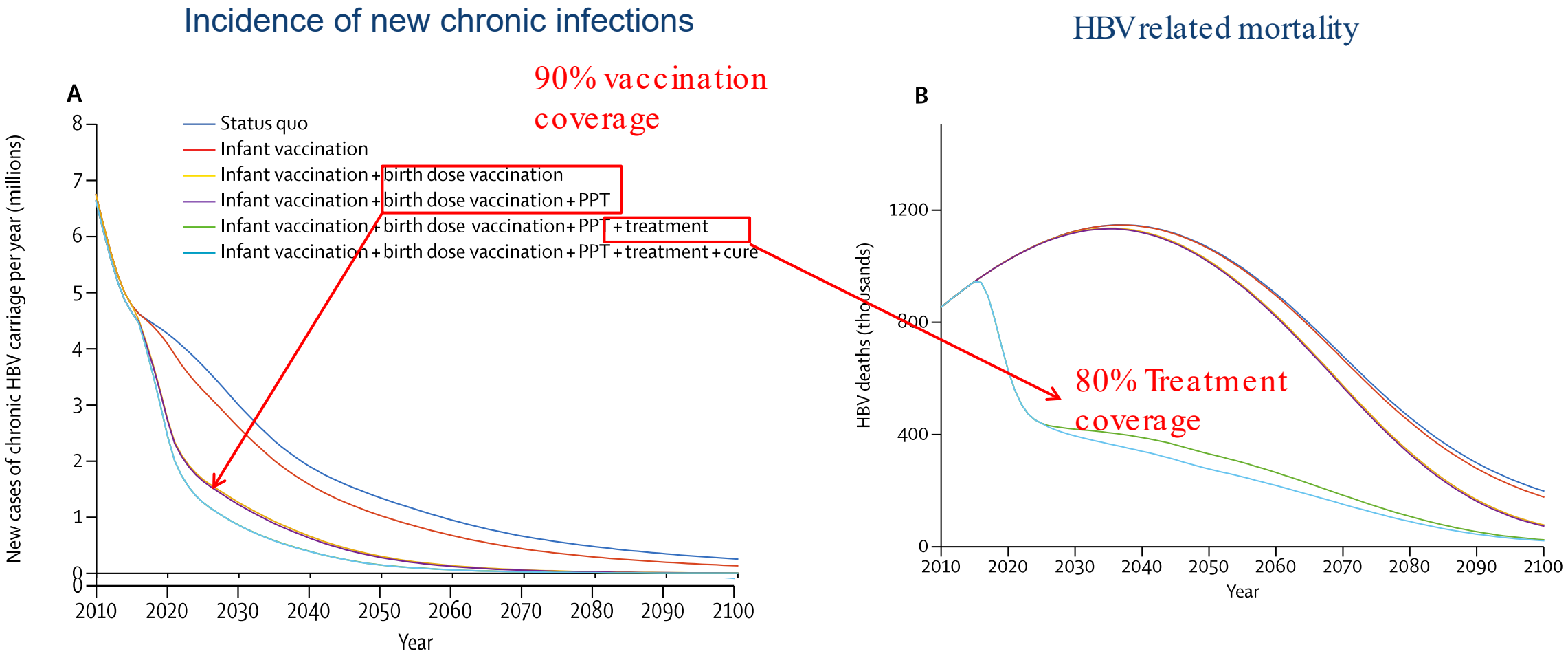
China – success story for HBV vaccination

- Very high burden country
- Has maintained high coverage of infant and birth dose vaccination and HBIG
- Fee abolished for patients & funding from GAVI
- Increased hospital births (rural reform policy)
- 5-year-old HBs Ag prevalence showed decline on national serosurveys; 9.67% (1992), 0.96% (2006), 0.32% (2014)
- Projected to reach elimination target (<0.1% in <5-year-olds) by 2030 (Hui Bulletin WHO 2021)



Cui et al, Emerging Infectious Diseases 2017

Scaling HBV treatment in addition to vaccination is key to reduce HBV-related deaths



Nayagam et al, Lancet Infectious Diseases 2016

Low coverage of interventions

Interventions	2022 estimates*				2030 Elimination Targets
	Globally	Europe	Africa	SE Asia	
HBV diagnosis (2022)	13.4%	**15.7**	**4.2%**	2.8%	90%
HBV treatment coverage amongst HBV eligible cases (2022)	2.6%	**1.9%**	**<1%**	<1%	80%
HBV vaccine infant coverage (3 doses) 2021 estimates	80%	**91%**	**71%**	91%	90%
HBV birth dose vaccine coverage (2022)	42%	**42%**	**18%**	58%	90%
Antiviral prophylaxis in pregnant women (2022)	<1%	**<1%**	**<1%**	**<1%**	80%

Barriers to HepB service delivery in LMICs

- ❑ >50% of the population live in **rural areas**
- ❑ 35% live in **extreme poverty**

- ❑ **Complex diagnostic and Tx algorithms**
- ❑ **Based on expensive and out-of-pocket** tests
- ❑ **Hardly accessible tests**
- ❑ Requiring high quality lab & stable electricity supply

Cirrhosis and HCC are diagnosed at advanced stages in endemic countries

Gambia case

- median tumour size 7.5cm at diagnosis
- median survival 1.5 months (IQR 1.1-2.

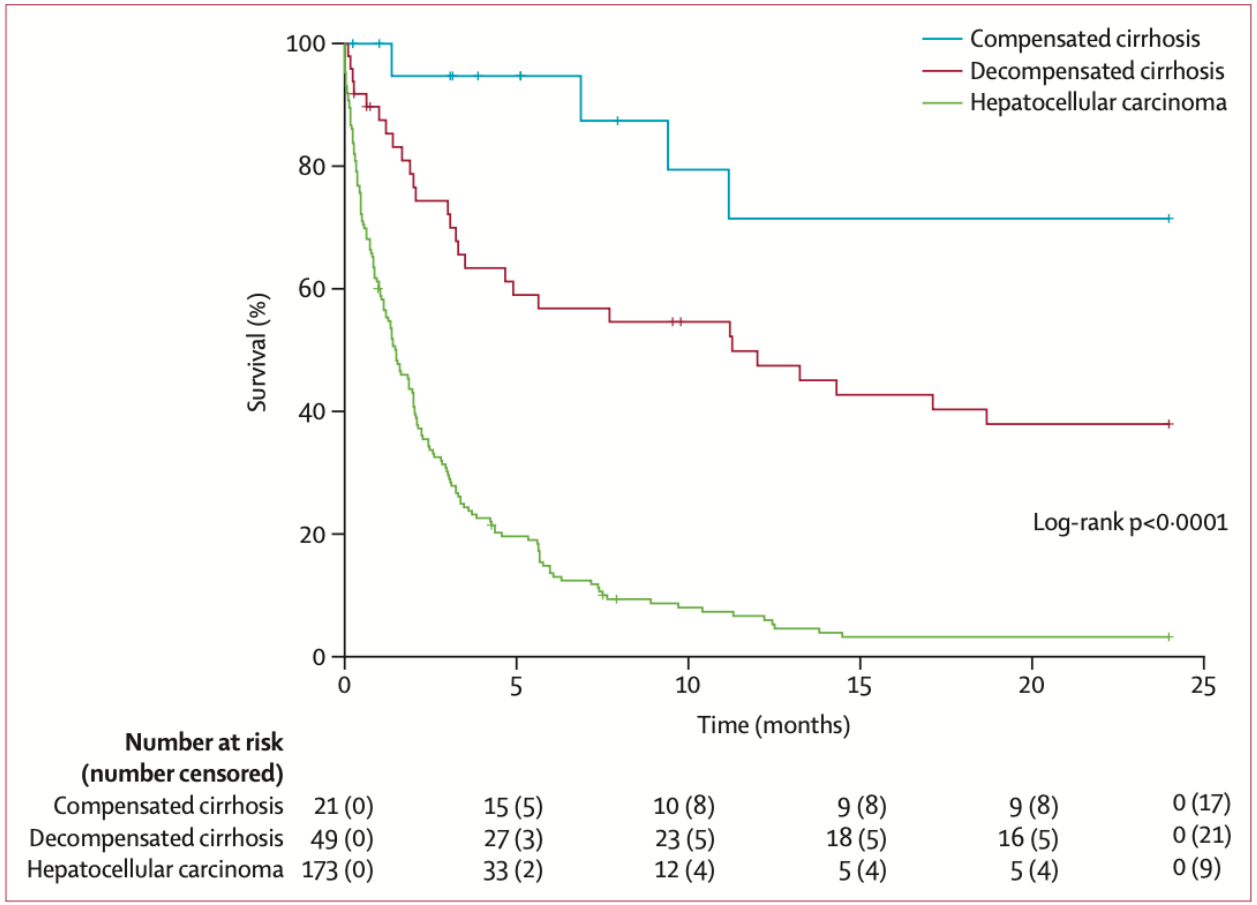


Figure 2: **Overall survival in 21 compensated cirrhosis, 49 decompensated cirrhosis, and 173 hepatocellular carcinoma cases**

Ndow, G et al. Lancet Global Health 2023

Need for early diagnosis of HCC in LMICs and HICs

- In high income countries, only **20% of patients with HCC are diagnosed at early stage**

- Surveillance for HCC is associated with improved detection of early-stage tumors and overall survival.

- No HCC surveillance programmes in most LMICs
- Adherence rate to **HCC surveillance is low (15-52%)** globally

Singal AG, et al J Hepatol. 2022

Costentin, C et al Gastroenterology 2018

Zhao et al. Liver international 2018

Aneed for improved surveillance tests to detect early HCC

- Ultrasound: low sensitivity (47%) for early-stage HCC detection

US alone missed more than a half of early HCC

- Using ultrasound with AFP improves the sensitivity (63%) for early-stage HCC detection

Tzartzeva K. et al Gastroenterology 2018

- Use of scores to identify persons at risk for HCC and enrolment in surveillance programs

REACH-B (Age, sex, HBeAg, HBV DNA, ALT)

PAGE-B (Age, sex, platelets)

Emerging HCC screening modalities

New Biomarkers and models

- AFP-L3 (Lens culinaris agglutinin-reactive fraction of AFP)
- DCP (Des-γ-carboxy-prothrombin)
- GALAD score (gender, age, AFP-L3, AFP, des-gamma carboxyprothrombin [DCP])
- GAAD score (GALAD without AFP-L3)

GALAD score > AFP alone in detecting HCC across various studies

Even better results when combined with ultrasound (e.g., GALADUS)

Johnson et al Cancer Epidemiol Biomarkers Prev,2014

Emerging HCC screening modalities

- **Abbreviated MRI:** a shortened MRI protocol with contrast

Reduced scanner time (10-15 min) and costs

High sensitivity and specificity for early-stage HCC

Park HJ. Et al. Liver Int 2022

- **Radiomics**: a novel technique that can extract quantitative features from medical images and translate them to minable data

- **Machine learning models**

Kim et al J Hepatol 2022

Summary,

- The global burden of HCC is high and will increase over the next decades
- Despite vaccination (HBV) and effective antiviral therapies, HBV and HCV remain the most common causes of HCC worldwide
- But there is a transition from viral to non-viral causes with an increasing incidence of alcohol-and MASLD-related HCC
- If interventions are not significantly scaled up, the burden of viral hepatitis related deaths will remain high especially in LMICs
- Putting at risk the 2030 elimination objectives

Thank you

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HEPSANET
HEPATITIS B IN AFRICA COLLABORATIVE NETWORK

Patients
The European Commission
MRC UKRI
Gilead US company
Echosens company

MRC Unit The Gambia
London School of Hygiene & Tropical Medicine
NIHR National Institute for Health and Care Research
EASL The Home of Hepatology
Imperial College London
Institut Pasteur
Gilead
ANRS France REcherche Nord & sud Sida-hiv Hépatites
Agence autonome de l'Inserm
UKRI Medical Research Council
wellcome trust
Abbott
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