

Global HCC Epidemiology, Changing Risk Patterns and Unmet Medical Needs

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Disclosures



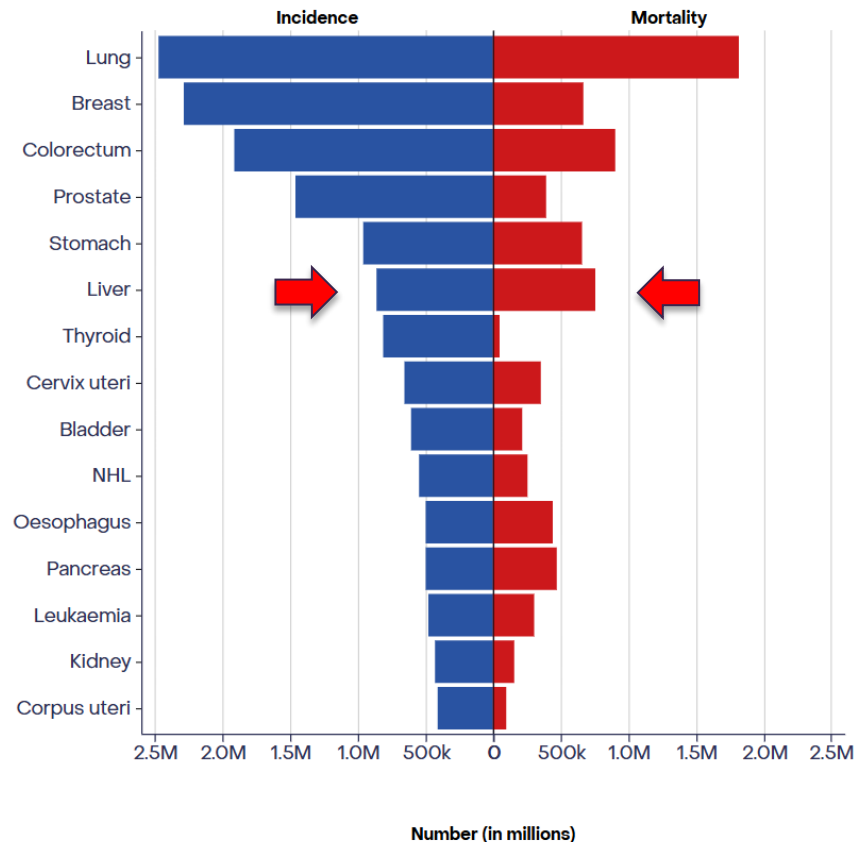
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Objectives

- Review current updates in HCC epidemiology globally
- Understand the evolving trends in underlying liver disease etiology contributing to HCC
- Highlight gaps in HCC care cascade, with a focus on gaps and disparities in HCC surveillance
- Identify the unmet needs and areas of high priority to address the global HCC burden

HCC is the Third Leading Cause of Cancer Deaths

- HCC is a major cause of cancer-related morbidity and mortality globally
- In 2022, WHO estimates ~900k new cases of HCC (6th leading cause) and ~800k HCC deaths (3rd leading)



- The highest burden and mortality is seen in Asia-Pacific and African regions
- In 2022, Asia accounted for ~71% of all new cases of HCC and ~70% of all HCC deaths globally.

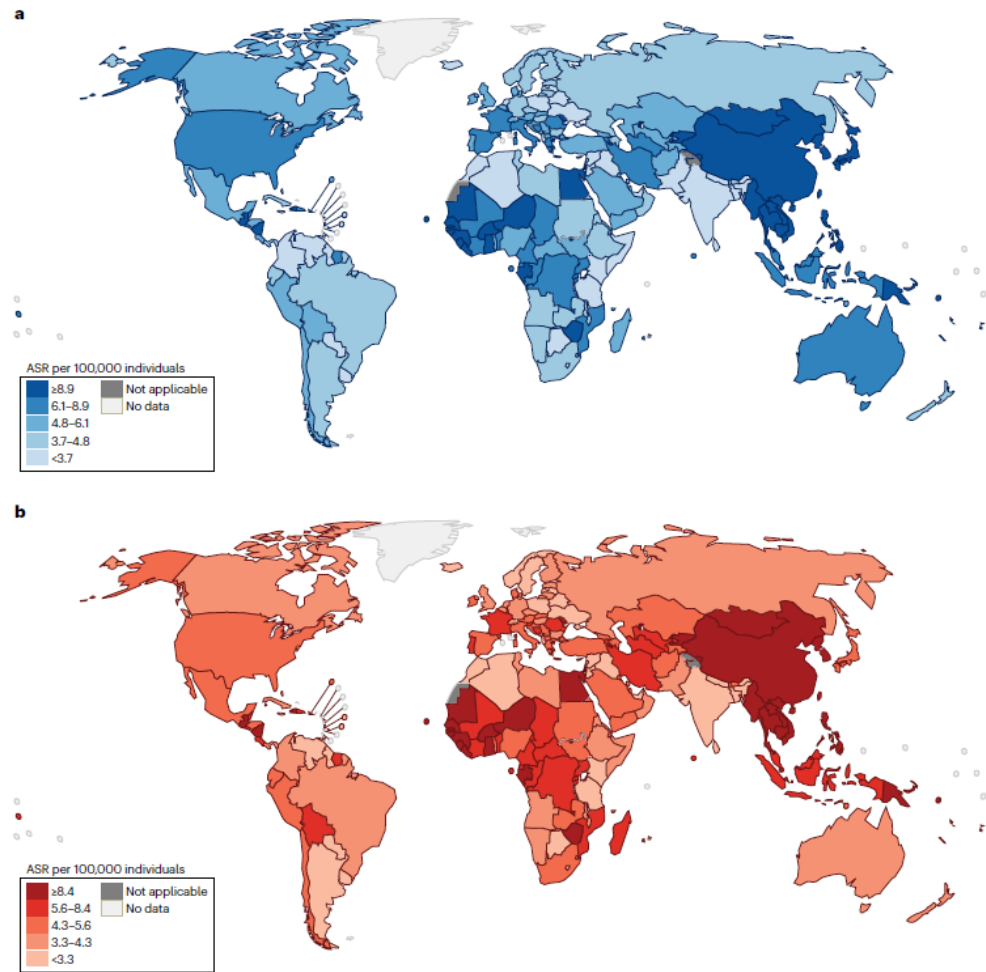


Fig. 3 | Global incidence and mortality of liver cancer. The shading indicates the estimated annual age-standardized incidence (part a) and mortality (part b) of liver cancer per 100,000 persons, regardless of age or sex, in 2020 across

countries worldwide based on data from GLOBOCAN 2020 (ref.1). Adapted with permission from GLOBOCAN 2020 (part a and part b), copyright International Agency for Research on Cancer. ASR, age-standardized rate.

Global burden of primary liver cancer



905,700

people were **diagnosed**
with liver cancer in 2020



830,200

people **died** from liver
cancer in 2020



Liver cancer ranked among the
top 3 causes of cancer death in

46 countries
in 2020



The **number** of people
diagnosed with or **dying** from
liver cancer globally could

**increase by
more than 55%**
between 2020 and 2040 if
current rates do not change



Liver cancer is a major cause of death in many countries. Efforts to reduce the incidence of preventable liver cancer should be prioritised to avoid the predicted rise in people diagnosed with liver cancer.

- Modeling data from the Global Cancer Observatory estimated a **76% increase in new HCC cases** and **80% increase in HCC deaths** in 2050, which translates into **~1.5 million HCC diagnosed** and **~1.37 million HCC deaths**
- The vast majority of HCC diagnosed and HCC deaths remain in the Asia region, followed by Africa region

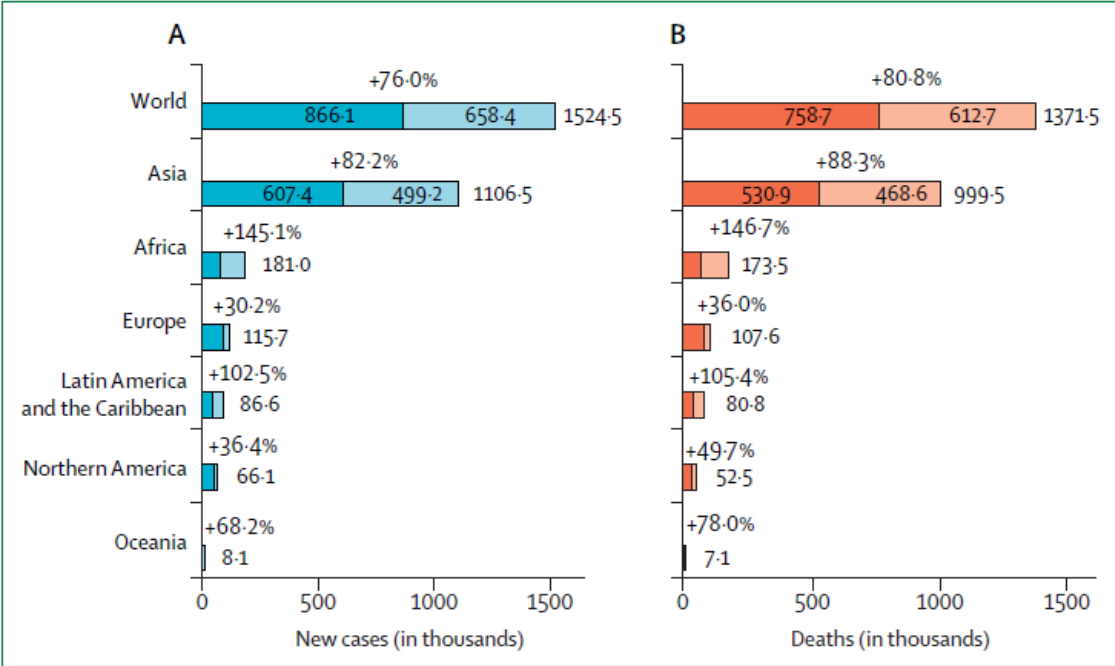
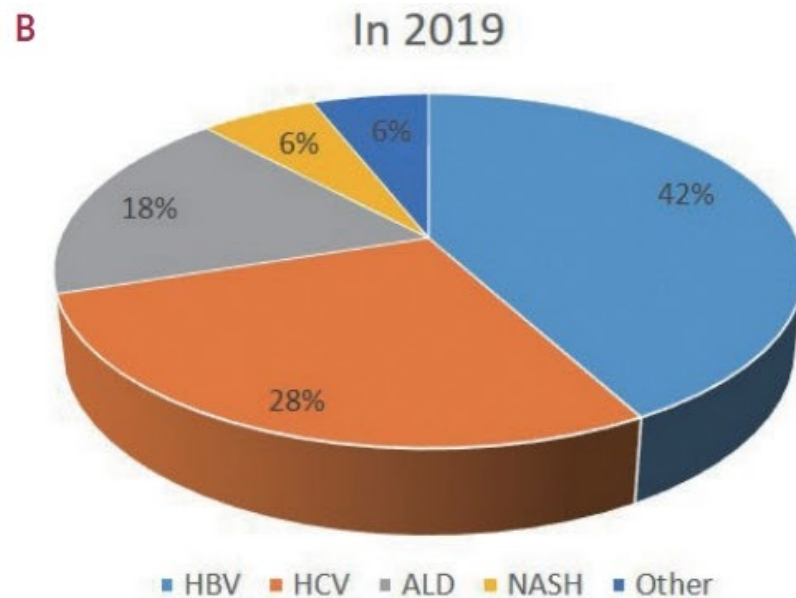
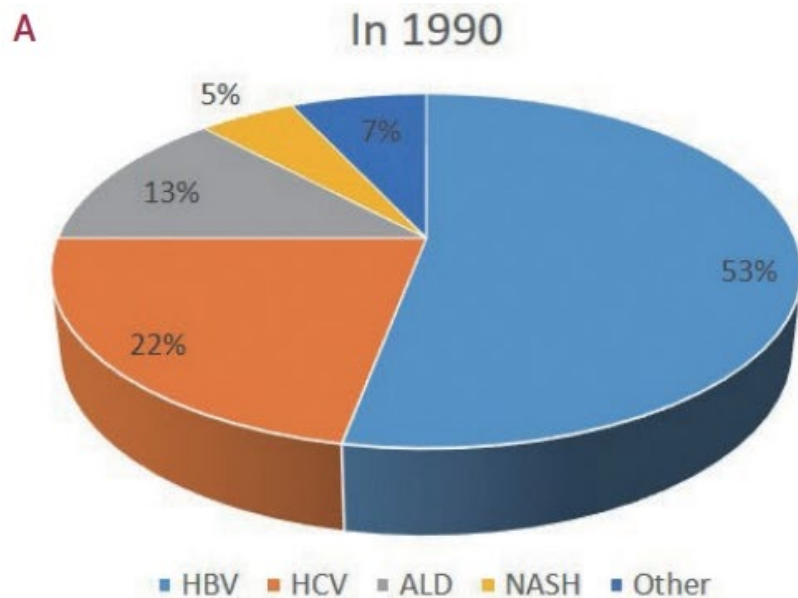


Figure 1: Predicted number of new cases and deaths from liver cancer in 2050, assuming no change in the age-standardised rates of incidence and mortality
Data from the Global Cancer Observatory 2022.⁹ Population data from the World Population Prospects, the 2019 revision (accessed June 30, 2024).¹⁰ The percentage change was calculated by subtracting the estimated number of new cases and deaths in 2022, from the projected number in 2050, then dividing the difference by the 2022 value.

Changes in Etiology of HCC - Globally



Increasing Proportion of HCC Attributed to MASLD

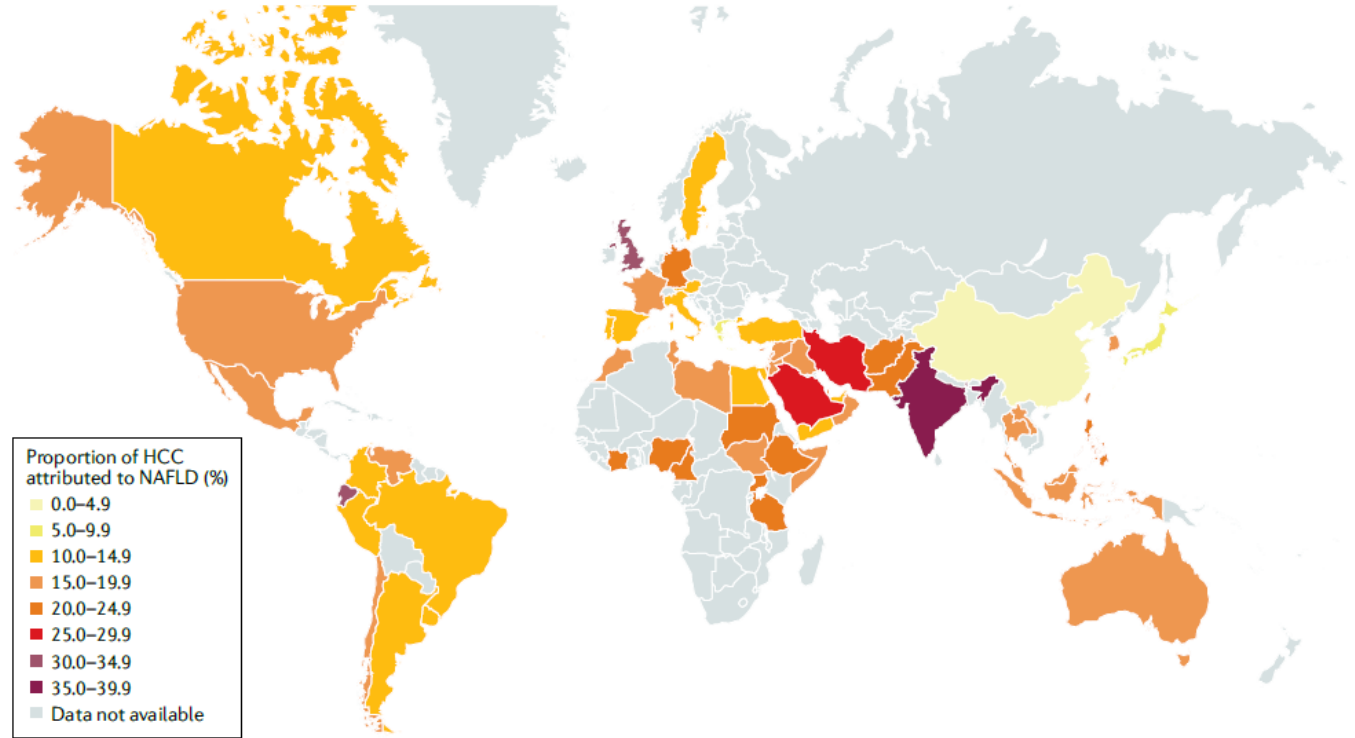


Fig. 1 | The estimated proportion of HCC attributed to NAFLD. The proportion of hepatocellular carcinoma (HCC) attributable to nonalcoholic fatty liver disease (NAFLD) is high in the UK, India, Germany and the Middle East

Changing Etiologies of HCC

- Using data from the Global Burden of Disease and population data from the World Population Prospects, Lancet Commission authors projected the distribution of causes of HCC in 2022, 2035, and 2050.
- Based on the latest trend of liver cancer incidence by cause, it is estimated
 - HBV-HCC decrease from 39.0% in 2022 to 36.9% in 2050
 - HCV-HCC decrease from 29.1% in 2022 to 25.9% in 2050
 - ALD-HCC increase from 18.8% in 2022 to 21.1% in 2050
 - MASH-HCC increase from 8.0% in 2022 to 10.8% in 2050

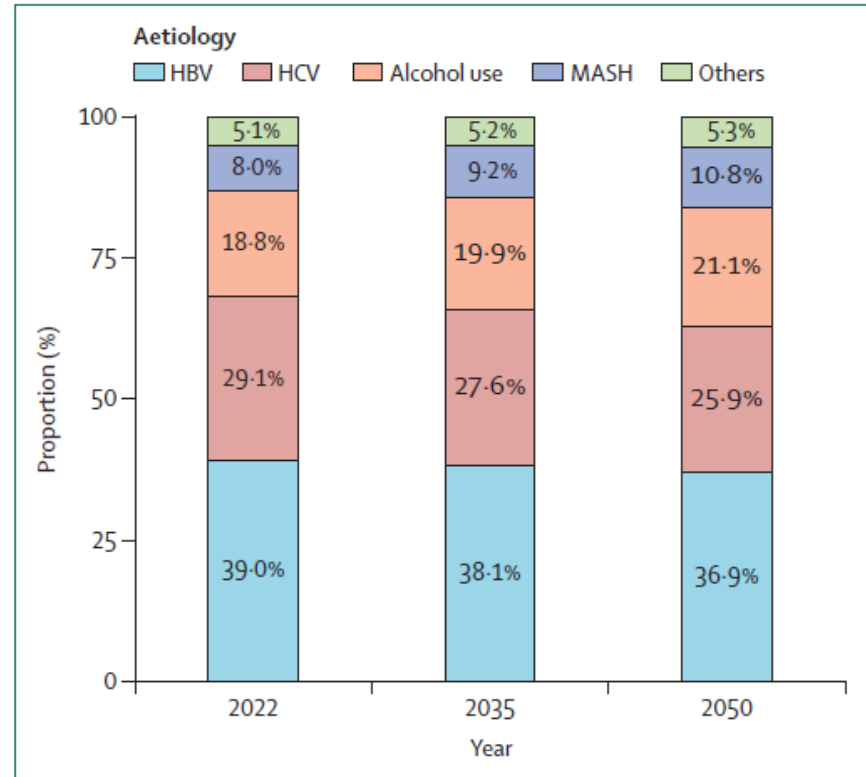
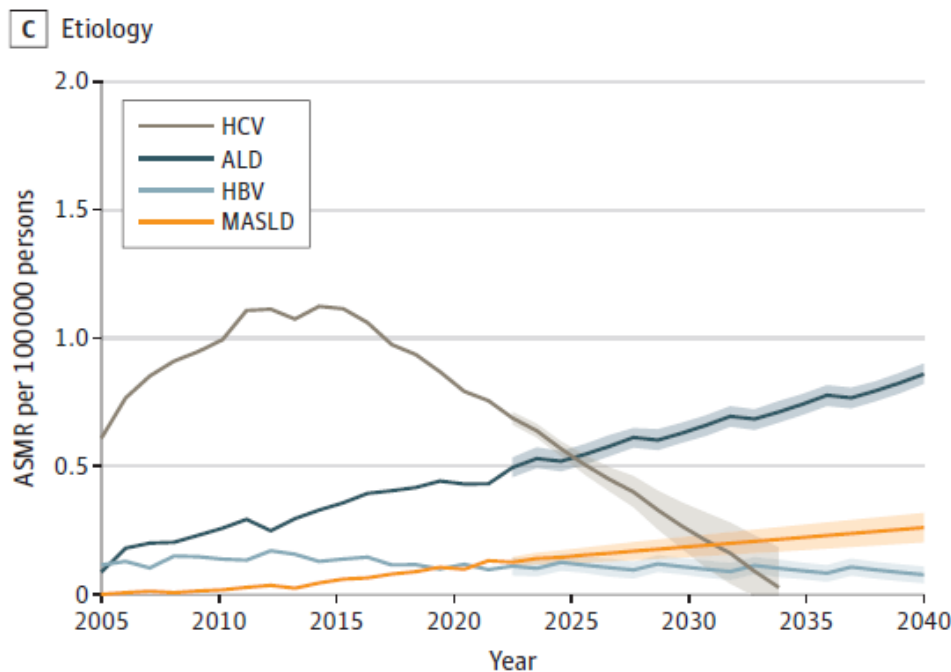


Figure 4: Projected distribution of liver cancer by cause in 2022, 2035, and 2050

Observed and Projected HCC Mortality by Etiology in the U.S.

- Using data from the Centers for Disease Control and Prevention (CDC) Wide-Ranging Online Data for Epidemiologic Research (WONDER) and National Vital Statistics System, **ALD** and **MASLD/MASH** are projected to become the leading etiologies of HCC deaths



MASH and ALD are Leading Causes of HCC Among Liver Transplant Waitlist Registrants in the U.S.

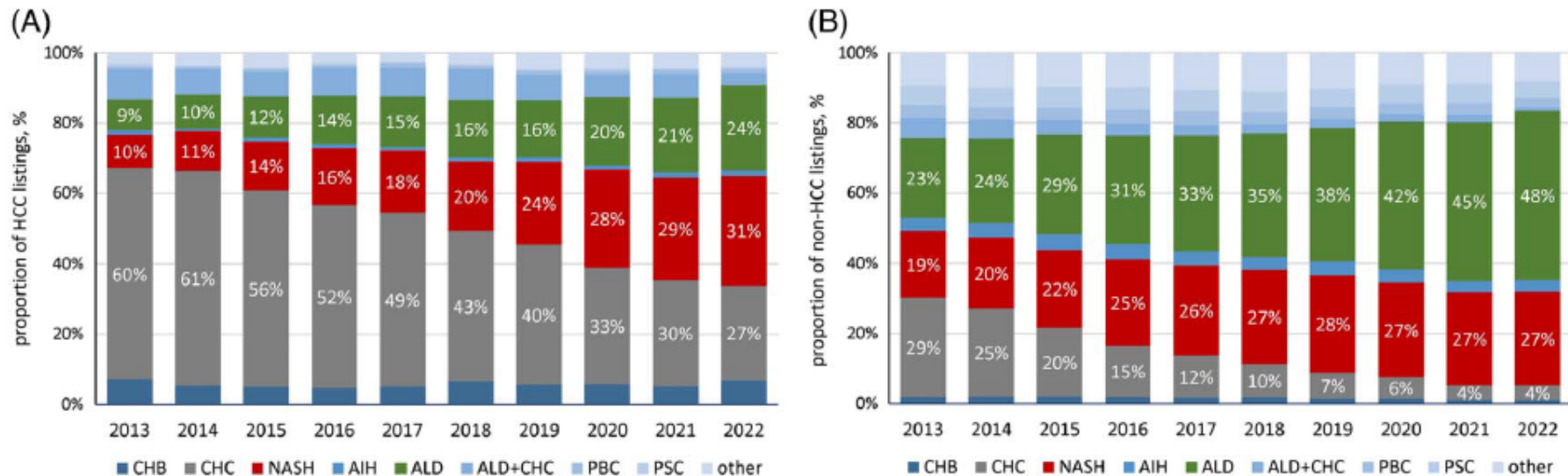
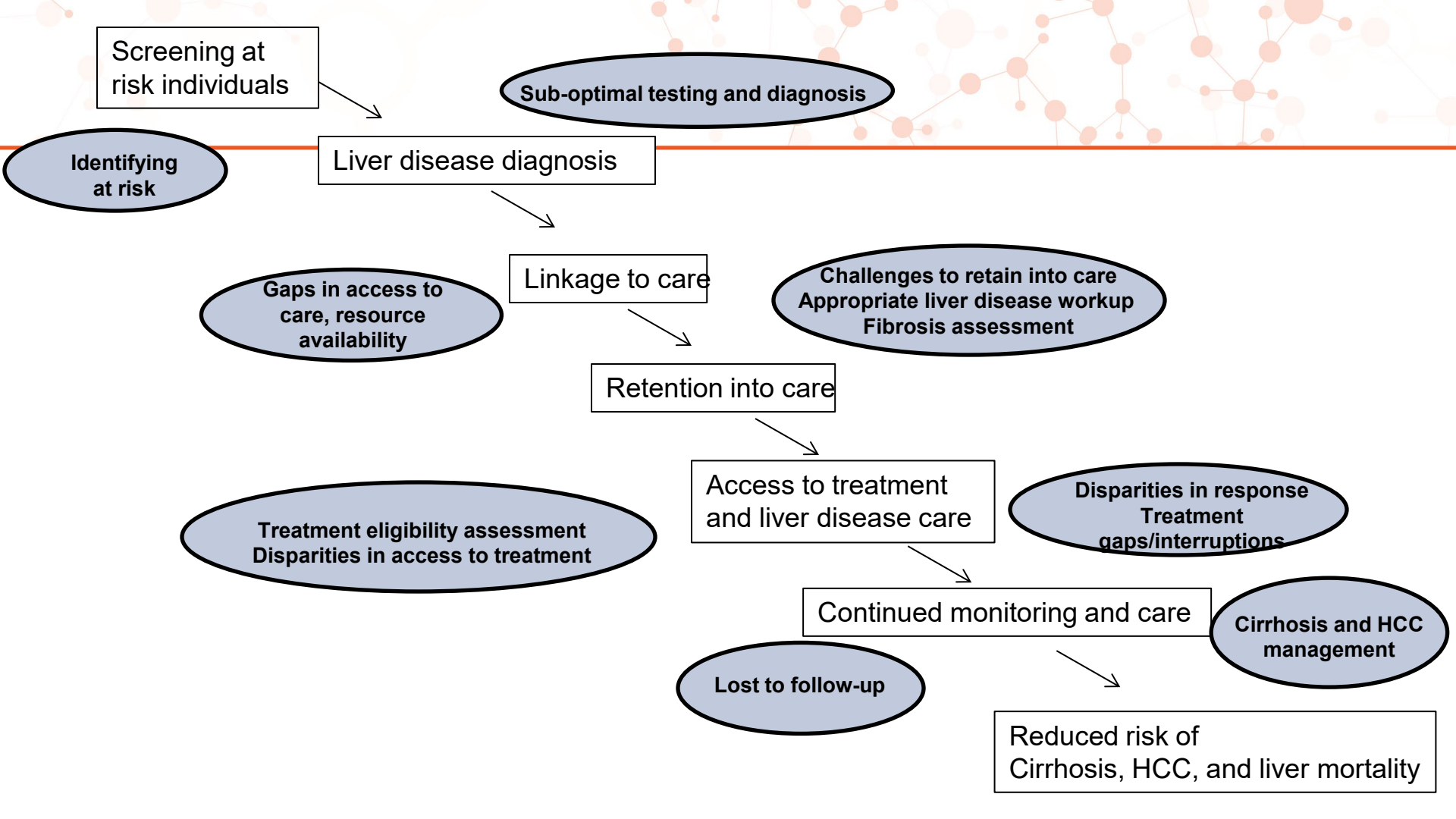


FIGURE 1 Distributions of CLD etiologies among adult candidates with and without HCC who underwent liver transplant. Abbreviations: AIH, autoimmune hepatitis; ALD, alcohol-associated liver disease; CHB, chronic hepatitis B; CHC, chronic hepatitis C; CLD, chronic liver disease; PBC, primary biliary cholangitis; PSC, primary sclerosing cholangitis.

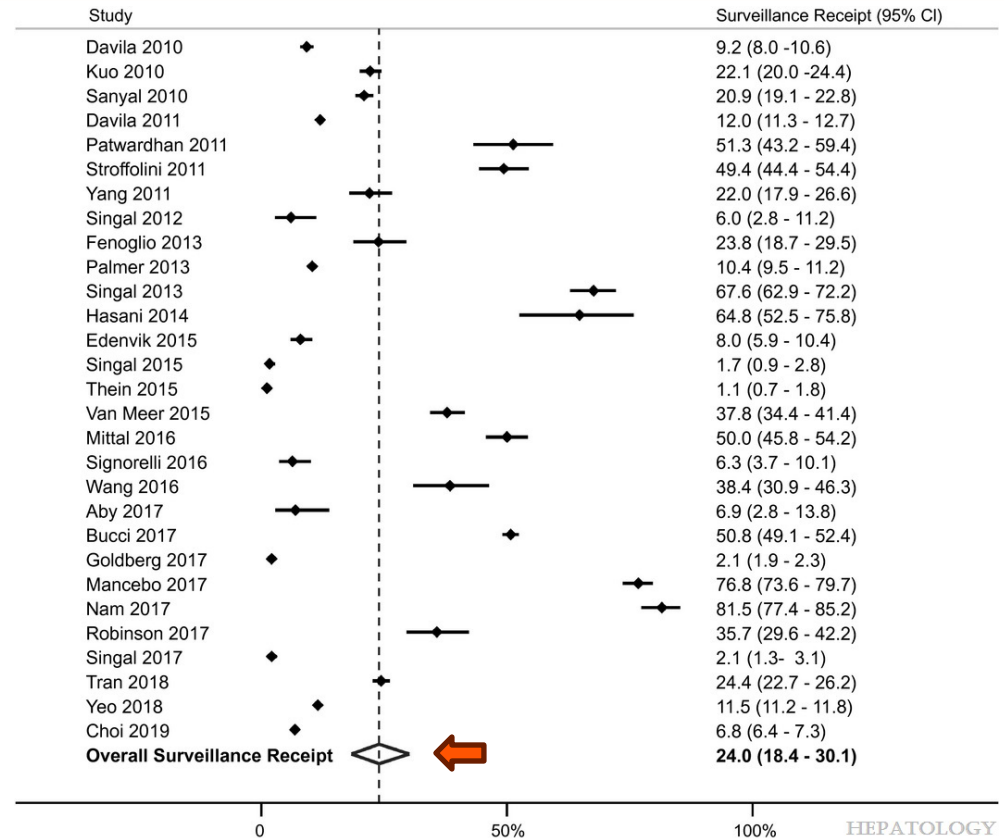


Effective HCC Surveillance is One of the Most Important Steps in the HCC Cascade of Care

- Effective HCC Surveillance leads to earlier tumor stage at diagnosis
- Tumor stage directly correlates with HCC treatment options
- More options for curative intent leads to better long-term survival
- Understanding and addressing disparities in HCC surveillance is important to reduce downstream disparities in HCC outcomes
- Complex interplay between patient, provider, and system level factors

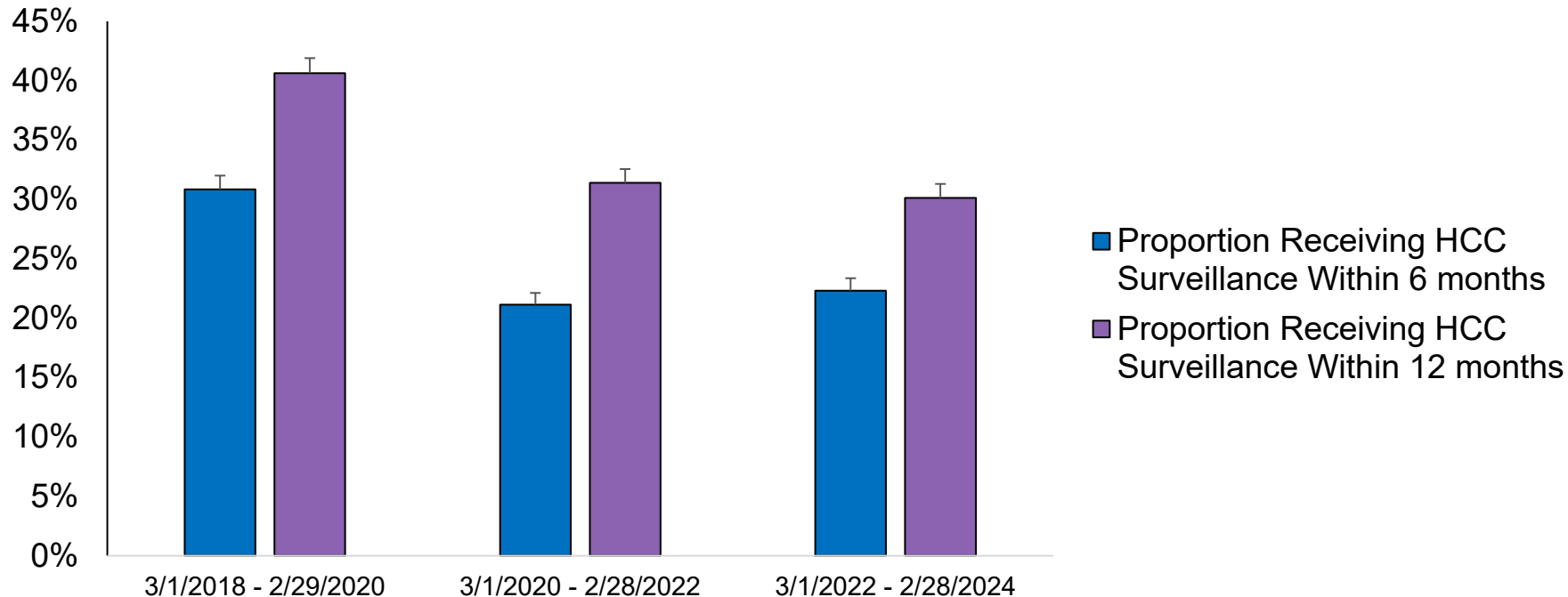
Suboptimal HCC Surveillance

- Wolf, et al performed a systematic review and meta-analysis (2010-2018) of 29 studies, inclusive of 118,799 patients
 - Pooled estimate of HCC surveillance among cirrhosis patients was **24% (18.4-30.1)**

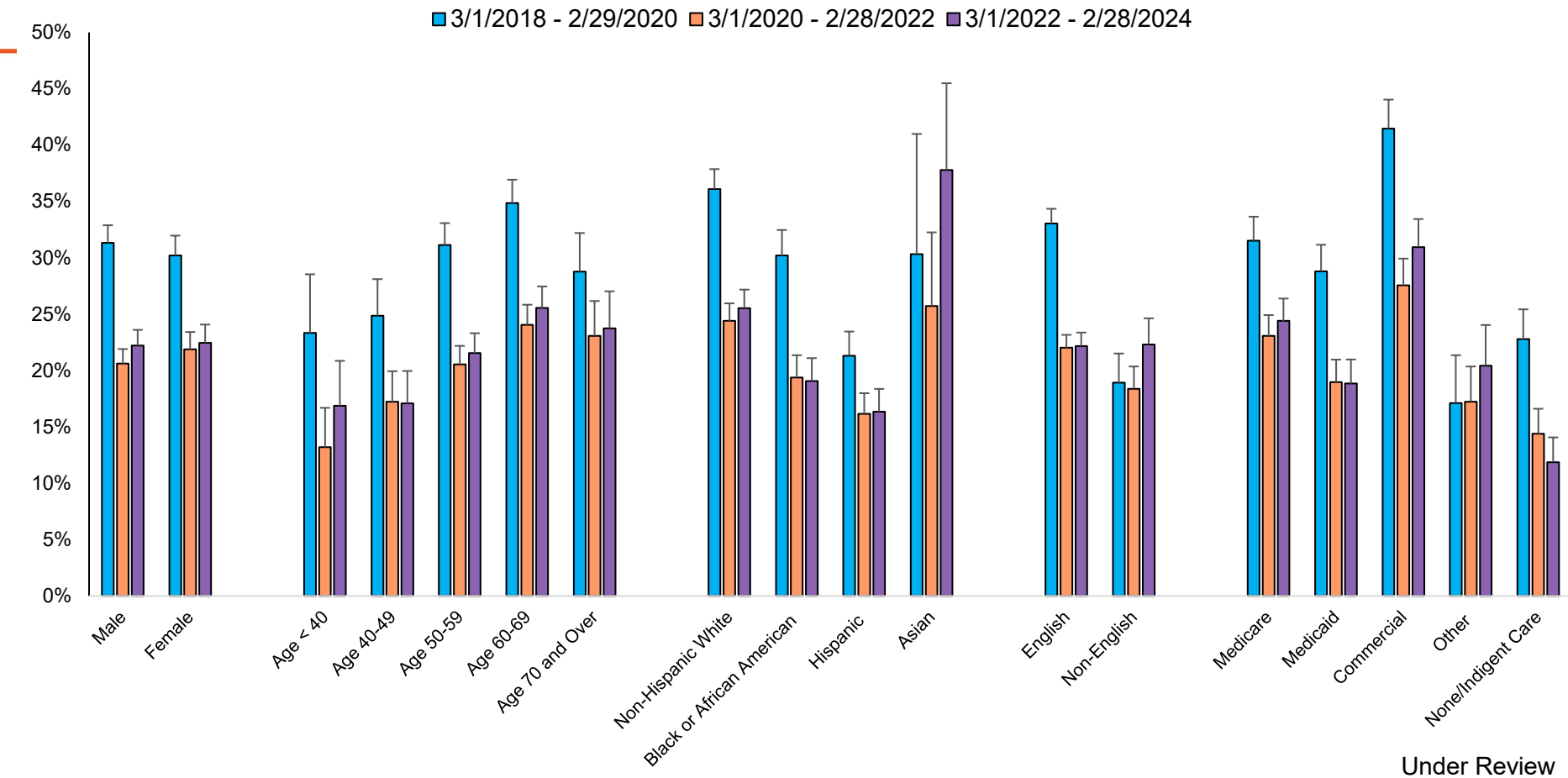


Persistently Low HCC Surveillance Following Pandemic-Related Disruptions in Cirrhosis Care

HCC Surveillance Before and Following COVID-19 Pandemic Across Five Safety-Net Health Systems in the U.S.



Proportion of Patients Receiving HCC Surveillance Within 6 Months



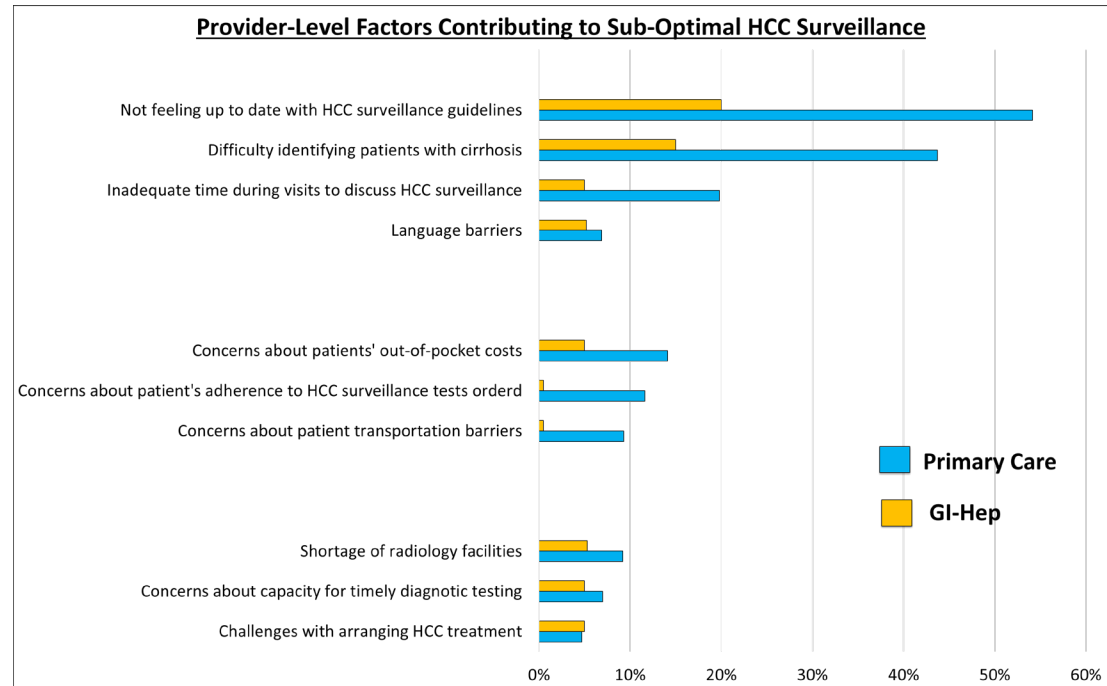
Disparities in HCC Surveillance Exacerbate Inequities in HCC Outcomes

- Data from our team and others have demonstrated that ethnic minorities, particularly African Americans and Hispanics consistently have lower rates of HCC screening compared to non-Hispanic whites
- Suboptimal screening leads to more advanced tumor state at diagnosis and fewer treatment options for ethnic minorities
- Using SEER NCI data, African Americans and Hispanics were more likely to have advanced tumor stage at diagnosis, less likely to receive treatment, more likely to experience delays in treatment, and had worse survival.

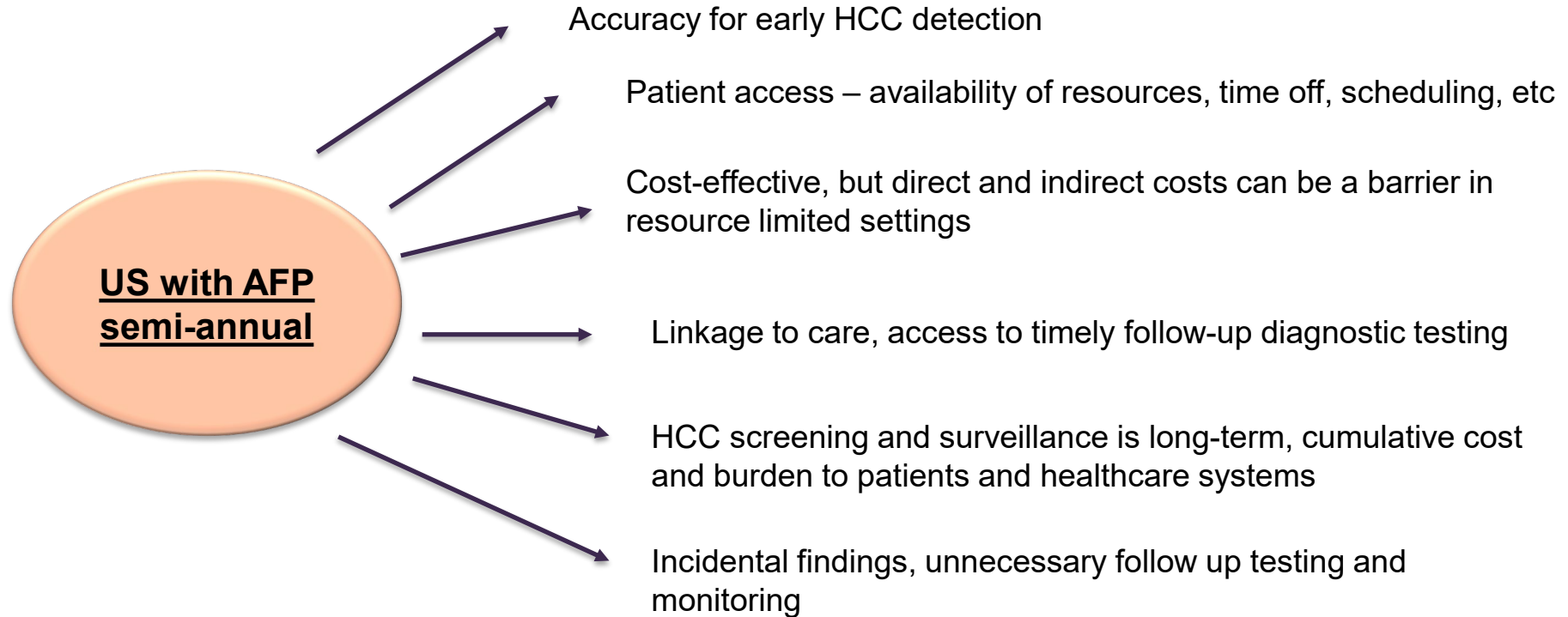
Race/Ethnicity	Localized Tumor Stage at Dx		HCC Treatment		Delays in HCC Treatment	
	<u>OR</u>	<u>95% CI</u>	<u>OR</u>	<u>95% CI</u>	<u>OR</u>	<u>95% CI</u>
Non-Hispanic White	Reference		Reference		Reference	
African American	0.84	0.81 - 0.88	0.77	0.74 - 0.81	1.12	1.05 - 1.19
Hispanic	1.09	1.05 - 1.13	0.84	0.81 - 0.87	1.45	1.38 - 1.52
Asian	1.09	1.05 - 1.14	1.19	1.14 - 1.24	0.93	0.88 - 0.99
AI/AN	1.01	0.89 - 1.15	0.85	0.75 - 0.99	1.59	1.34 - 1.89

Clinician-Level Knowledge and Barriers to Hepatocellular Carcinoma Surveillance

- A total of 347 clinicians across 5 safety-net centers surveyed to assess HCC screening knowledge, attitudes, perceived barriers.
- **Major gaps in HCC knowledge** were identified as potential contributors to low HCC surveillance
- Main barriers reported particularly by PCPs:
 - inadequate time to discuss HCC surveillance
 - difficulty identifying patients with cirrhosis
 - Not feeling up-to-date with HCC surveillance guidelines



Challenges of Current HCC Screening Approach



Role of blood-based biomarkers – what is the current status?

What Do Current Guidelines Recommend

AASLD 2023

10. HCC surveillance should be performed using ultrasound and AFP at semiannual (approximately every 6 months) intervals (**Level 2, Strong Recommendation**).
 - a. AASLD recommends use of interventions such as best practice alerts or outreach programs to increase HCC surveillance adherence given the underuse of surveillance in clinical practice (**Level 2, Strong Recommendation**).
11. AASLD does not recommend routine use of CT- or MRI-based imaging and tumor biomarkers, outside of AFP, for HCC surveillance in at-risk patients with cirrhosis or chronic HBV (**Level 5, Weak Recommendation**).
 - a. Alternative imaging modalities, such as contrast-enhanced MRI, may be considered for HCC surveillance in select patients in whom US-based surveillance is suboptimal (**Level 3, Weak Recommendation**).

EASL 2025

Recommendation

- An ultrasound examination of the liver every 6 months is recommended for screening of HCC. The combined use of ultrasound with AFP increases sensitivity while decreasing specificity and is a reasonable option. There is limited data to support the use of other promising imaging modalities such as abbreviated MR or serum biomarkers (**LoE 3, strong recommendation, consensus**).

Unmet Needs and Challenges to Improve HCC Care

– The Lancet Commission

Strengthening viral hepatitis prevention, screening, and treatment

Standardization of non-invasive diagnosis of HCC

Reduction of alcohol consumption

Facilitating access to treatment

Raising awareness of liver health

Addressing the East–West differences in clinical management

Preparing for the increase in MASLD and MASH

Control of environmental risk factors

Improving HCC survivorship

Improving early HCC detection

It Takes a Village to Address Challenges and Unmet Needs

Patient Factors

- Medical literacy and education/awareness
- Socioeconomic factors
- Age, sex, race/ethnicity
- Primary language
- Substance use
- Health insurance
- Access to care
- Stigma

Provider Factors

- Knowledge and up to date with guidelines
- Attitudes & bias
- Experience with patients with cirrhosis and HCC
- Perception of barriers to screening and treatment
- Competing demands

HCC Care Cascade

Health System Factors

- Availability of providers
- Infrastructure and resources to support screening implementation and linkage to care
- Location of services
- Type of practice setting

Payors

Patient Advocacy Groups

Industry Partners

Public Health Departments

Medical Societies

Take Home Points

- HCC remains a major global burden and a leading cause of cancer related deaths
- Viral hepatitis remains the predominant risk factor, but rising contribution of ALD and MASLD observed particularly among Western populations
- Major gaps in the HCC care cascade and unmet needs pose challenges to addressing the growing burden of HCC
- Novel and comprehensive interventions are needed and must incorporate a broad consortium of stakeholders

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