

HCC Epidemiology and Care Cascade Recommendations

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School of Medicine

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Objectives

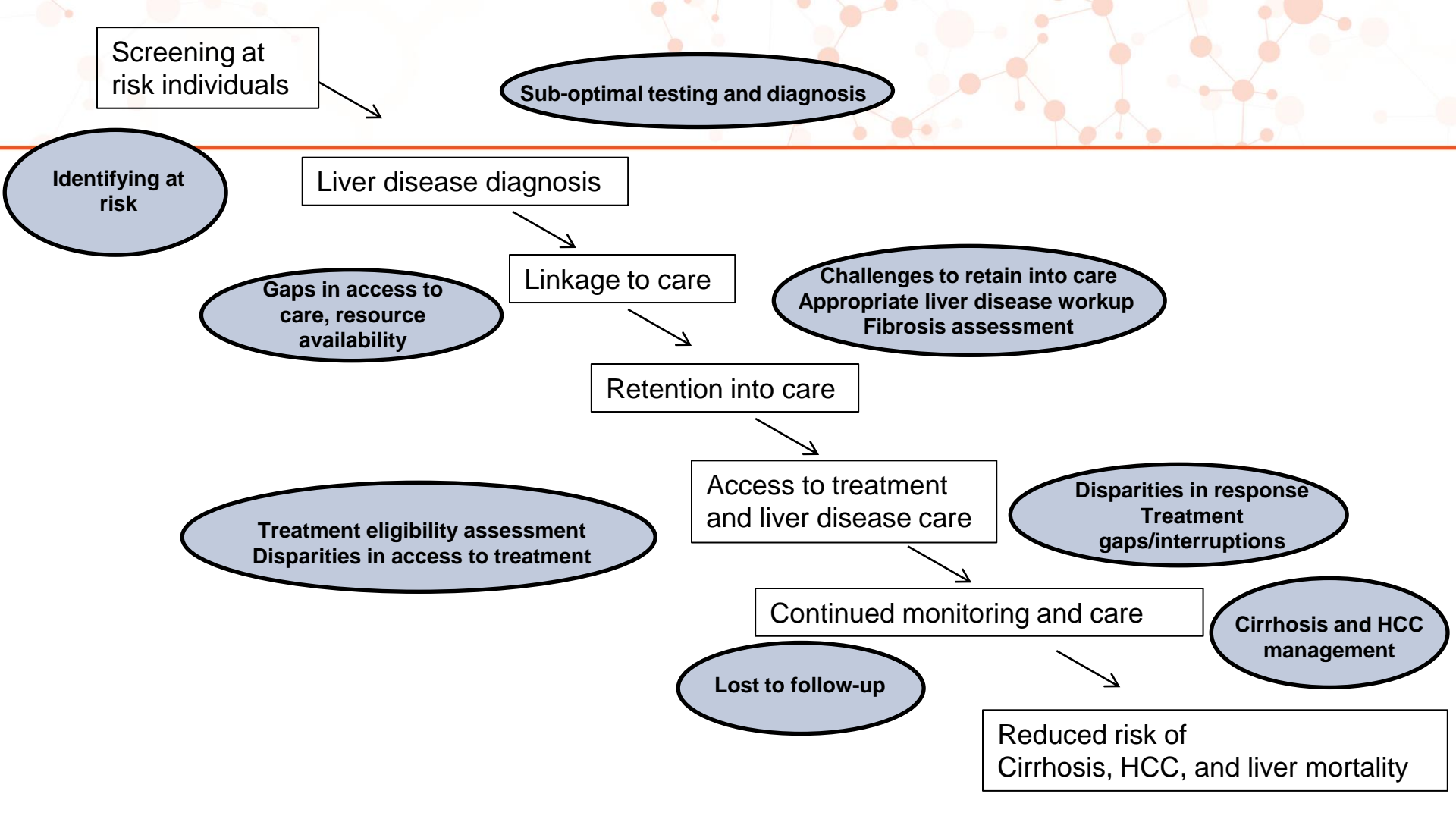
- Review recent updates in HCC epidemiology with a focus on highlighting disparities
- Review the CLDF HCC Care Cascade Decision Support Tool to improve management of patients with HCC

Burden of Liver Disease

- Globally, liver disease accounts for ~2 million deaths per year
 - ~1 million due to cirrhosis-related complications
 - ~1 million due to viral hepatitis and liver cancer
 - Cirrhosis and liver cancer account for 3.5% of all deaths worldwide
 - Liver cancer is third leading cause of cancer-related deaths
- In the U.S., liver disease and cirrhosis account for ~52k deaths per year
 - 12th leading cause of death in the US
 - HCC is ~5th leading cause of cancer deaths in the US (~31k deaths estimated in 2022)
 - HCC 5-year overall survival < 30%, due to delays in timely diagnosis and treatment

Understanding Gaps and Disparities Can Guide Targeted Interventions

- Poor clinical outcomes are preventable
 - Identify and address modifiable factors
 - Early detection and timely access to effective therapies
 - Early intervention through education and prevention of both patients and providers
- Socio-economically disadvantaged and vulnerable populations experience the majority of healthcare disparities
 - Compounds existing inequities (e.g., insurance, education/health literacy, household income, geography/transportation, language barriers, bias/discrimination)
 - Identify “low-hanging fruit” that can have a significant impact on liver disease outcomes



Screening at risk individuals

Sub-optimal testing and diagnosis

Identifying at risk

Liver disease diagnosis

Gaps in access to care, resource availability

Linkage to care

Challenges to retain into care
Appropriate liver disease workup
Fibrosis assessment

Retention into care

Treatment eligibility assessment
Disparities in access to treatment

Access to treatment and liver disease care

Disparities in response
Treatment gaps/interruptions

Continued monitoring and care

Lost to follow-up

Cirrhosis and HCC management

Reduced risk of Cirrhosis, HCC, and liver mortality

Multi-factorial Barriers to Effective HCC Surveillance

Patient Factors

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

Provider Factors

- Knowledge and up to date with guidelines
- Attitudes & bias
- Experience with patients with viral hepatitis and chronic liver disease
- Perception of barriers to screening and treatment

Timely and
Appropriate
HCC
Surveillance

System Factors

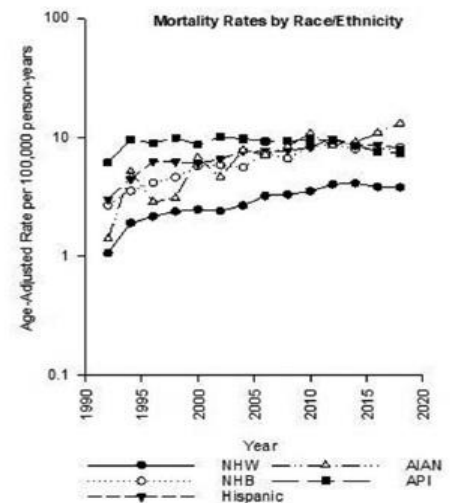
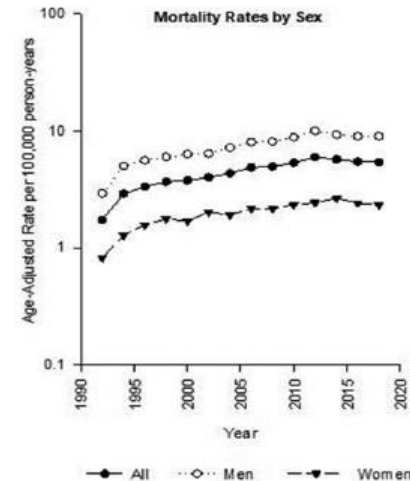
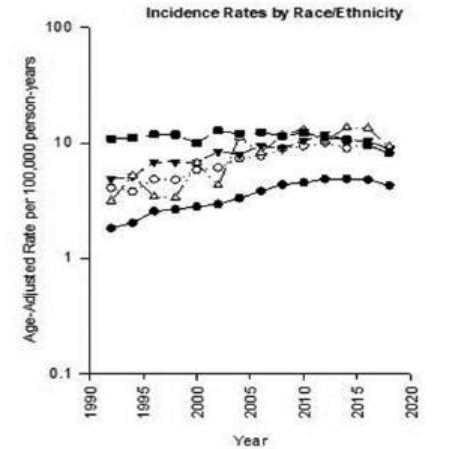
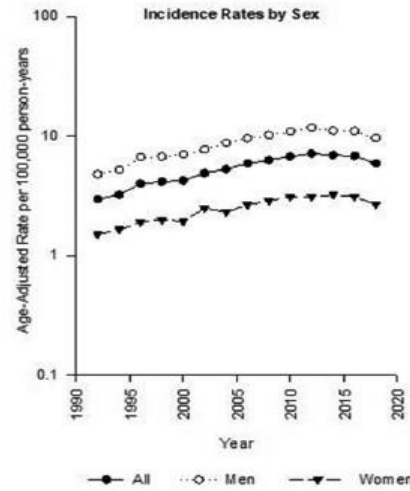
- Availability of providers
- Type of providers (primary care vs. GI/liver)
- Location of services
- Type of practice setting
- Costs

Updates in HCC Epidemiology and Trends

- Declining incidence of HCV-related HCC due to effectiveness of HCV cure regimens
- Increasing burden of NAFLD/NASH-related HCC as the large population of patients with fatty liver are aging and developing liver-related complications
- Despite improvements in HCC treatment options, overall 5-year HCC survival remains less than 30%

Racial/Ethnic Disparities in HCC Incidence and Mortality

- NCI SEER data from 1992-2018 evaluating HCC incidence and mortality
- HCC incidence and mortality appears to have peaked in 2015 and have been declining since
- However, significant race/ethnicity-specific disparities were observed
- Trends may reflect improved treatment of viral hepatitis and the emergence of NASH and ALD as leading contributors to HCC incidence and mortality



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)**
- 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

TABLE 2. Race/Ethnicity-specific Variations in Stage of HCC at Diagnosis

Variables	Distant vs. Localized HCC			Within Milan Criteria		
	OR	95% CI	Pe	OR	95% CI	P
Non-Hispanic white	1.00	Reference	—	1.00	Reference	—
Hispanic	0.94	0.87-1.01	0.08	1.02	0.97-1.07	0.503
Black	1.20	1.10-1.30	< 0.001	0.80	0.75-0.85	< 0.001
Asian	0.87	0.80-0.94	< 0.001	1.00	0.95-1.06	0.86

Treatment Categories	Total HCC		
	OR	95% CI	P
Any treatment vs. no treatment			
Non-Hispanic white	1.00	Reference	—
Hispanic	0.61	0.57-0.65	< 0.001
Black	0.61	0.56-0.66	< 0.001
Asian	1.23	1.15-1.31	< 0.001
Curative vs. noncurative treatment			
Non-Hispanic white	1.00	Reference	—
Hispanic	0.55	0.51-0.60	< 0.001
Black	0.60	0.55-0.66	< 0.001
Asian	1.21	1.12-1.30	< 0.001

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

A Digital, Interactive, Decision-Support Algorithm to Facilitate and Improve the Hepatocellular Carcinoma Care Cascade in Adults: Integrating the Barcelona Clinic Liver Cancer (BCLC) Staging System and United Network for Organ Sharing(UNOS) Down-Staging Criteria into One Tool

The screenshot shows the CLDF website interface. At the top, the CLDF logo is on the left, with the tagline "Unparalleled expertise, unprecedented access" to its right. On the far right of the top navigation bar are links for "Home | Contact Us | Bookmark". Below this is a secondary navigation bar with categories: HEPATITIS, CIRRHOSIS, NASH, CHOLESTATIC, HCC, ALCOHOL LIVER DISEASE, and PEDIATRIC LIVER DISEASE. The "HCC" category is highlighted in orange. To the right of these categories are two more orange buttons: "About CLDF" and "Embassy of Education".

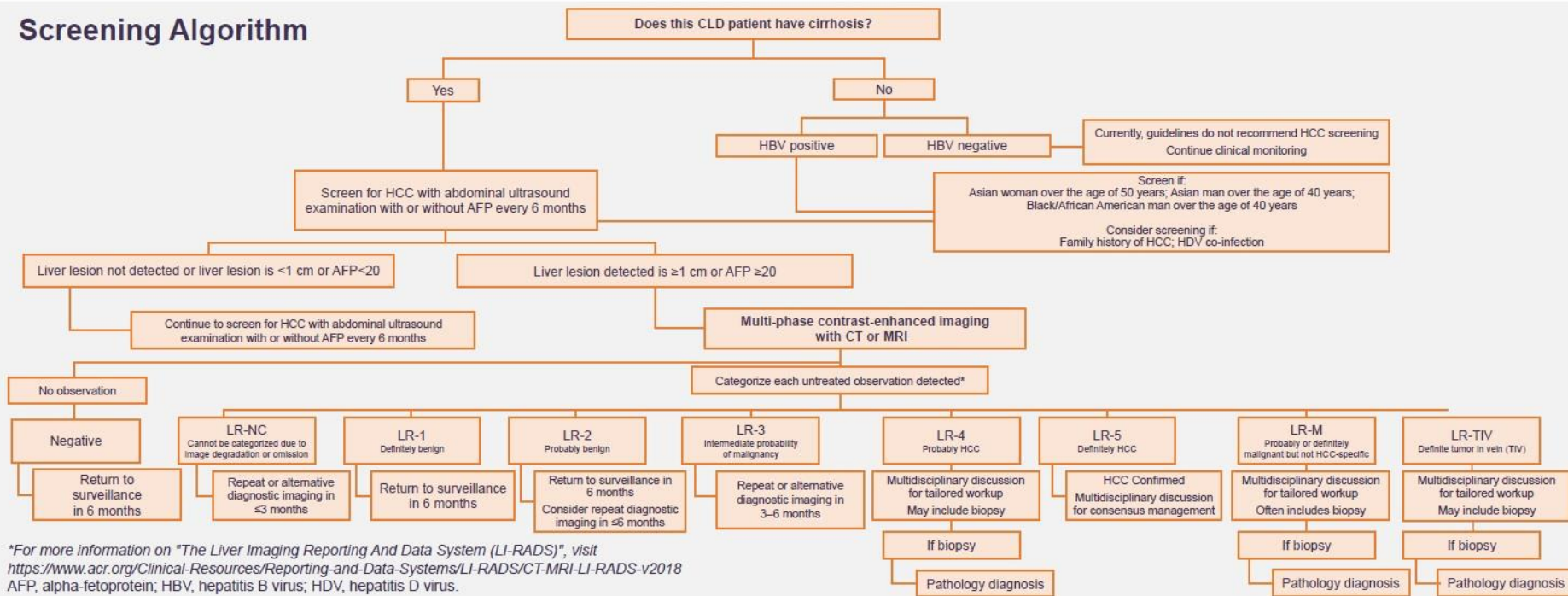
Below the navigation bar is a white bar with links: "Slide Library", "Publications", "Webcasts", "Abstract Library", and "Committee Members".

The main content area has a heading "HCC Care Cascade Decision-Support Algorithm" in orange. Below this is the CLDF logo and tagline. A light gray box contains the text "HCC Care Cascade - Introduction". Below that is a "History (0)" section with a plus icon and two small icons (a camera and a letter 'A').

The main heading "HCC Care Cascade" is centered. Below it is a blue header for a selected item: "HCC Care Cascade - Introduction". The content area below this header contains a paragraph: "The CLDF HCC working group has developed a practical, point-of-care, digital tool to assist healthcare professionals in the screening and surveillance, tumor staging, and treatment of patients with HCC that is based on the following resources:" followed by a bulleted list: "• The AASLD and EASL HCC guidance, which deliver data-supported approaches to the diagnosis, staging, and treatment of patients diagnosed with HCC (1, 2)."

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Screening Algorithm



*For more information on "The Liver Imaging Reporting And Data System (LI-RADS)", visit <https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/LI-RADS/CT-MRI-LI-RADS-v2018>
AFP, alpha-fetoprotein; HBV, hepatitis B virus; HDV, hepatitis D virus.

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Staging Algorithm

HCC Diagnosis Confirmed

Very Early Stage (0)
Single ≤ 2 cm
Preserved liver function*, PS 0

Early Stage (A)
Single, or ≤ 3 nodules, each ≤ 3 cm
Preserved liver function*, PS 0

Intermediate Stage (B)
Multinodular
Preserved liver function*, PS 0

Advanced Stage (C)
Portal invasion and/or
extrahepatic spread
Preserved liver function, PS 1-2

Terminal Stage (D)
Any tumor burden,
End-stage liver function (means Child-Pugh C
or ALBI grade 3), PS 3-4

Refer to Hepatology or Liver Transplant Program for consideration for:
Liver transplantation
Surgical hepatic resection

Refer to Hepatology or Liver Transplant Program for consideration for:
Liver transplantation
Surgical hepatic resection
Locoregional therapy

Refer to Multidisciplinary Liver Tumor Board for consideration for:
Locoregional therapy with or without subsequent liver transplantation
Systemic therapy
Experimental protocol
Palliative therapy

*PS refers to ECOG performance status
ALBI, albumin-bilirubin.

Take Home Points

- HCC remains a leading cause of cancer-related mortality in the U.S. and globally
- Disparities in timely diagnosis and treatment of chronic liver diseases contributes to continued HCC burden
- Gaps and disparities in timely HCC screening and surveillance persist
- Novel interventions are needed to improve the HCC care cascade to improve long-term HCC outcomes

Acknowledgements

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