

# HCC ◆ INNOVATIONS

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# Learning Objectives HCC ECHO Series

Upon completion of this activity, the participants should be better able to:

- Explain data on the prevalence and consequences of HCC
- Demonstrate strategies to incorporate classification, diagnostic and treatment updates into clinical practice to individualize treatment strategies
- Analyze recently approved and emerging treatment options and understand how new agents are improving the standard of care for all HCC patients

# Disparities in Linkage to Care for HCC

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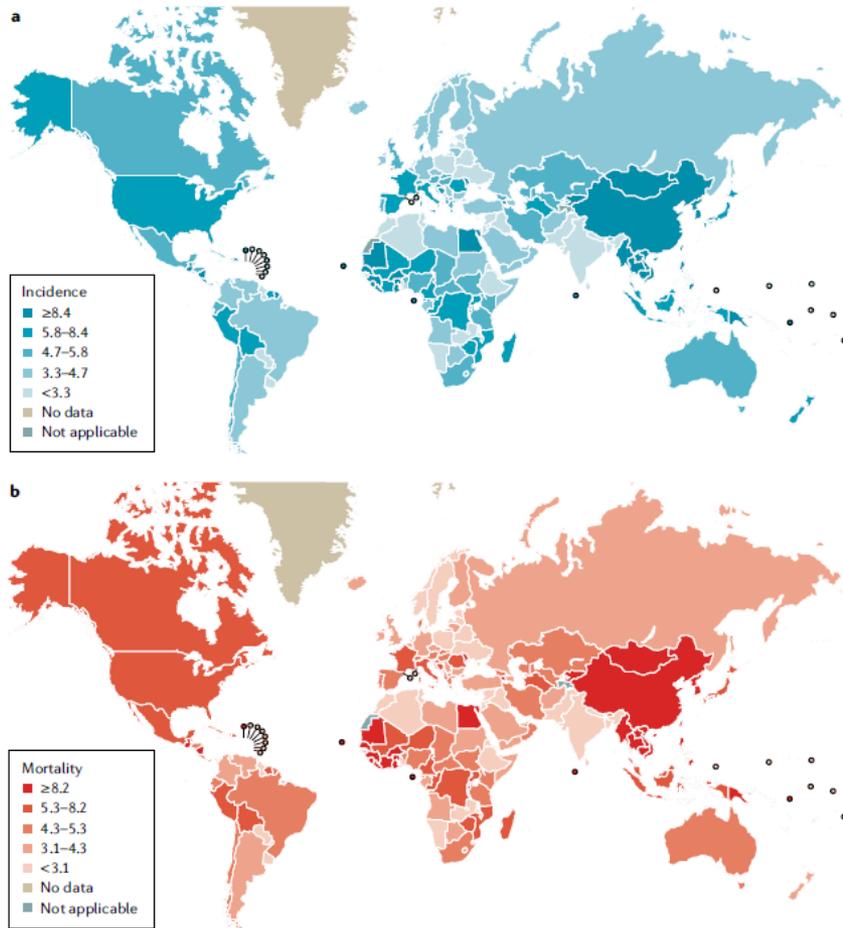
# Objectives

- Understand the complex steps in the HCC cascade of care
- Identify at risk groups who experience disparities in linkage to HCC care
- Explore some examples of innovative models of care delivery for HCC to mitigate disparities

# Summary of Key Facts Learned Thus Far

- HCC is the 4<sup>th</sup> leading cause of cancer-related deaths worldwide, accounting to 782k deaths in 2018 (WHO data)
- Majority of HCC occurs in Asian and African world regions
- HBV remains a leading cause of HCC in Asia/Africa, whereas HCV has been a leading cause in North American and European regions
- NASH is emerging as a major contributor to HCC epidemiology worldwide
- The success of managing HCC hinges of 3 key concepts
  - Prevention through targeting risk factors
  - Early diagnosis via effective screening and surveillance
  - Improved accessible treatment option

# Global HCC Data



- Nearly 85% of HCC occurs in low and medium resource countries, particularly in Eastern Asia and sub-Saharan Africa
- Significant variations in HCC incidence and HCC mortality reflect regional differences in risk factors, healthcare resources, access to screening, and availability of HCC therapies
- Dynamic changes in HCC epidemiology compounded by aging population, evolution of viral hepatitis therapies, and changing landscape of HCC risk factors

Chronic liver disease  
(e.g. viral hepatitis, NASH)

Access to care and treatment  
Disparate preventative care and  
disease screening

Cirrhosis and At Risk HBV

Sub-optimal HCC screening  
Poor linkage to care  
Disparities in HCC screening awareness

Initial HCC Screening

Continued engagement into care  
Access to effective screening modalities

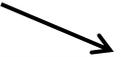
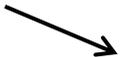
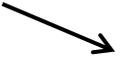
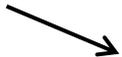
Continued HCC Surveillance

Availability of  
curative therapies

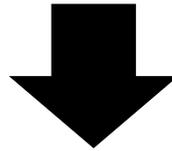
Early Stage HCC Diagnosis

Need for novel non-  
surgical therapies

HCC Therapies



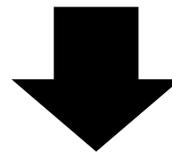
Timely HCC Diagnosis and Staging



Assessment of HCC Treatment Options via  
Multi-disciplinary Tumor Board



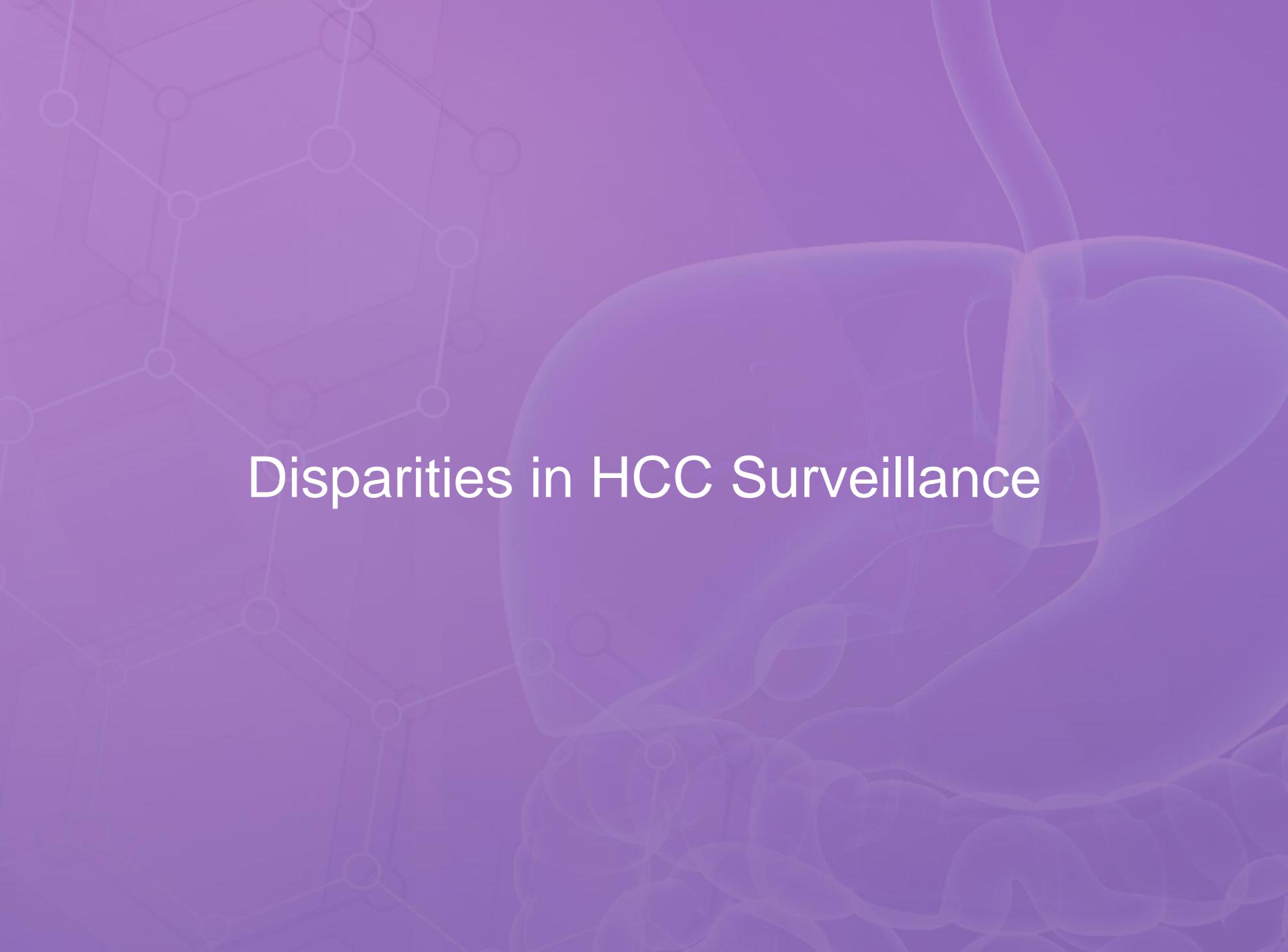
Timely Referral to and Receipt of  
Appropriate HCC Therapies



Continued Monitoring and Receipt of  
Adjuvant HCC Therapies

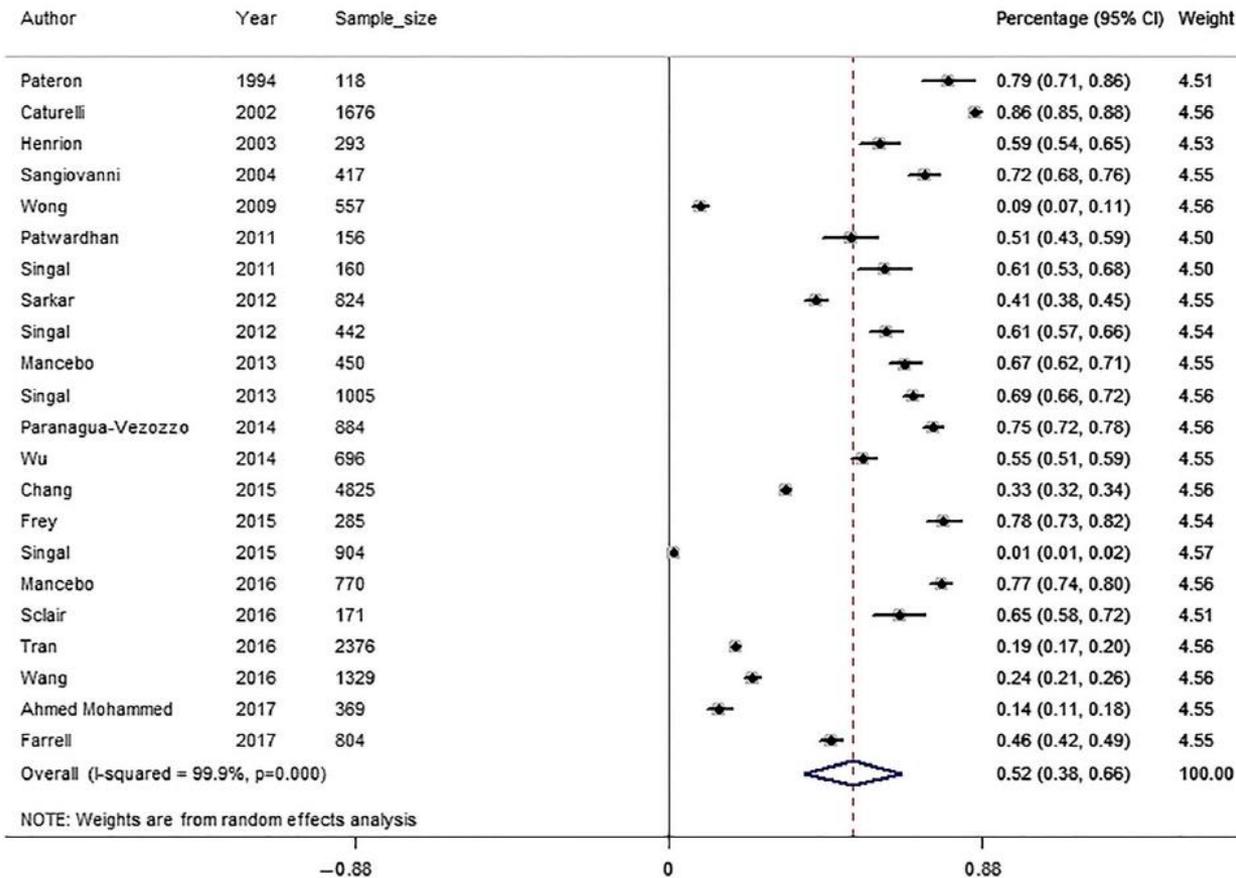
- Availability of HCC specialty providers
- Availability of patient navigators or HCC case managers
- Access to LT center and multidisciplinary tumor board/clinic

- Availability of comprehensive HCC treatment options
- Access to HCC clinical trials



# Disparities in HCC Surveillance

# HCC Surveillance – Meta-Analyses



- Total of 22 cohort studies included with overall HCC surveillance rate of 52% (95% 38-66)
- Lower HCC surveillance rates observed for CHB (32%) compared to cirrhosis patients (52%)
- Significant heterogeneity between studies and differences were observed by world region, practice setting, type of surveillance modality used, and surveillance interval

# HCC Surveillance Disparities

- In a retrospective analysis of 904 cirrhosis patients from 2008-2011 at a single safety-net hospital, African Americans were 39% less likely to receive HCC surveillance vs. non-Hispanic whites (OR 0.61, 95% CI 0.42-0.99).
- Data from the VA HCV Clinical Case Registry of 13,002 HCV patients with cirrhosis demonstrated that African Americans had significantly lower rates of HCC surveillance compared to whites (15.5% vs. 68.1%; OR 0.60, 95% CI 0.45-0.81).
- U.S. national SEER-Medicare data also show African Americans have the lowest rates of HCC surveillance at only 12.2%.



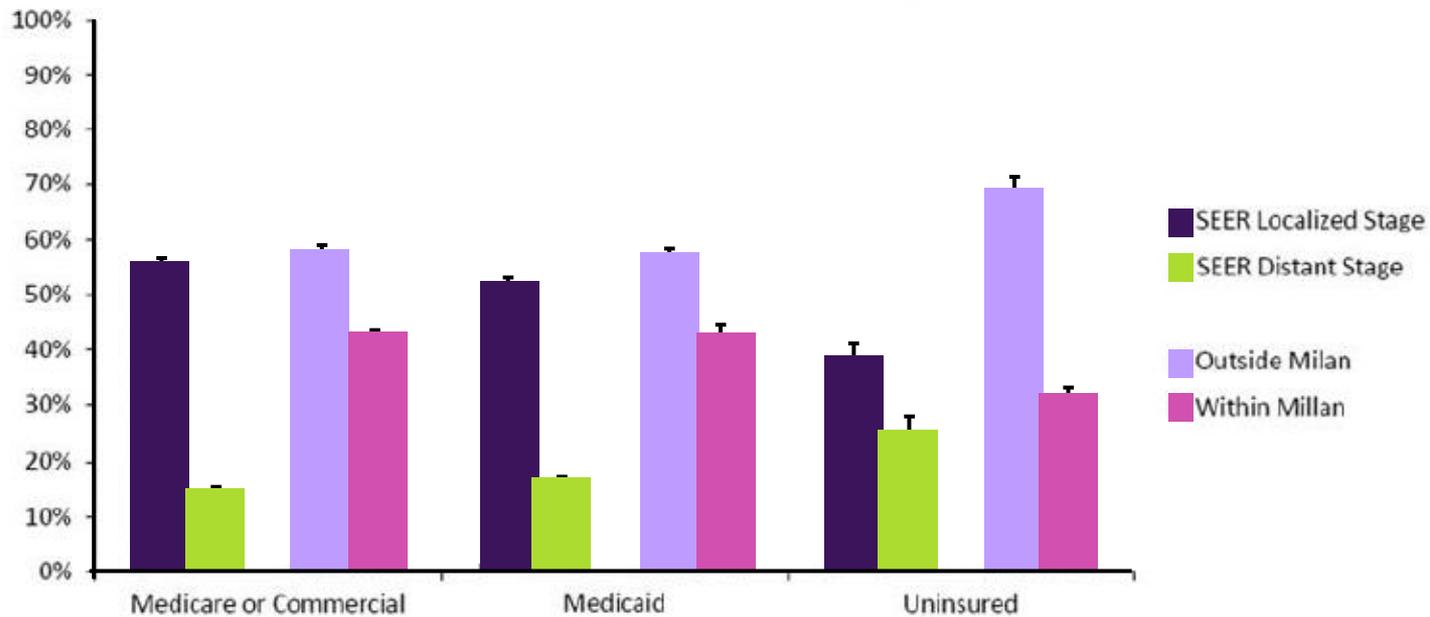
# Disparities in HCC Diagnosis and Staging

# HCC Diagnosis and Staging Disparities

- Data from the 2003-2011 U.S. SEER cancer registry observed African Americans had significantly more advanced tumor stage at diagnosis (OR, 1.20; 95% CI, 1.10-1.30;  $P < 0.001$ ) and were significantly less likely to have HCC within standard LT eligibility criteria at diagnosis (OR, 0.80; 95% CI, 0.75-0.85;  $P < 0.001$ ) compared to non-Hispanic whites
- Another study across two large health systems evaluated 1,117 patients with HCC from 2008-2017. Compared to non-Hispanic whites, African Americans (OR, 0.74, 95% CI 0.56-0.98) and Hispanics (OR, 0.75, 95% CI 0.55-1.00) were less likely to be diagnosed with early staged HCC

# HCC Diagnosis and Staging Disparities

## Hepatocellular Carcinoma Tumor Stage at Diagnosis



	Medicare or Commercial		Medicaid		Uninsured		P – Value
	Proportion (%)	Frequency (N)	Proportion (%)	Frequency (N)	Proportion (%)	Frequency (N)	
SEER Localized Stage	55.3%	11853	51.7%	3713	38.5%	553	< 0.001
SEER Distant Stage	14.9%	3208	16.2%	1166	25.4%	365	< 0.001
Outside Milan Criteria	58.1%	13402	57.2%	4433	69.3%	1089	< 0.001
Within Millan Criteria	41.9%	9663	42.8%	3318	30.7%	483	< 0.001

# HCC Diagnosis and Staging Disparities

- Patients from rural and low income households have sub-optimal access to high quality liver disease care, which affects timely receipt of HCC surveillance.
- Data from U.S. SEER database demonstrated that patients in rural geographic regions were 10% more likely to have advanced tumor stage at diagnosis compared to HCC patients in urban geographic regions.
- HCC patients from lower income households were also 15% more like to have advanced stage HCC compared to patients from higher income households.



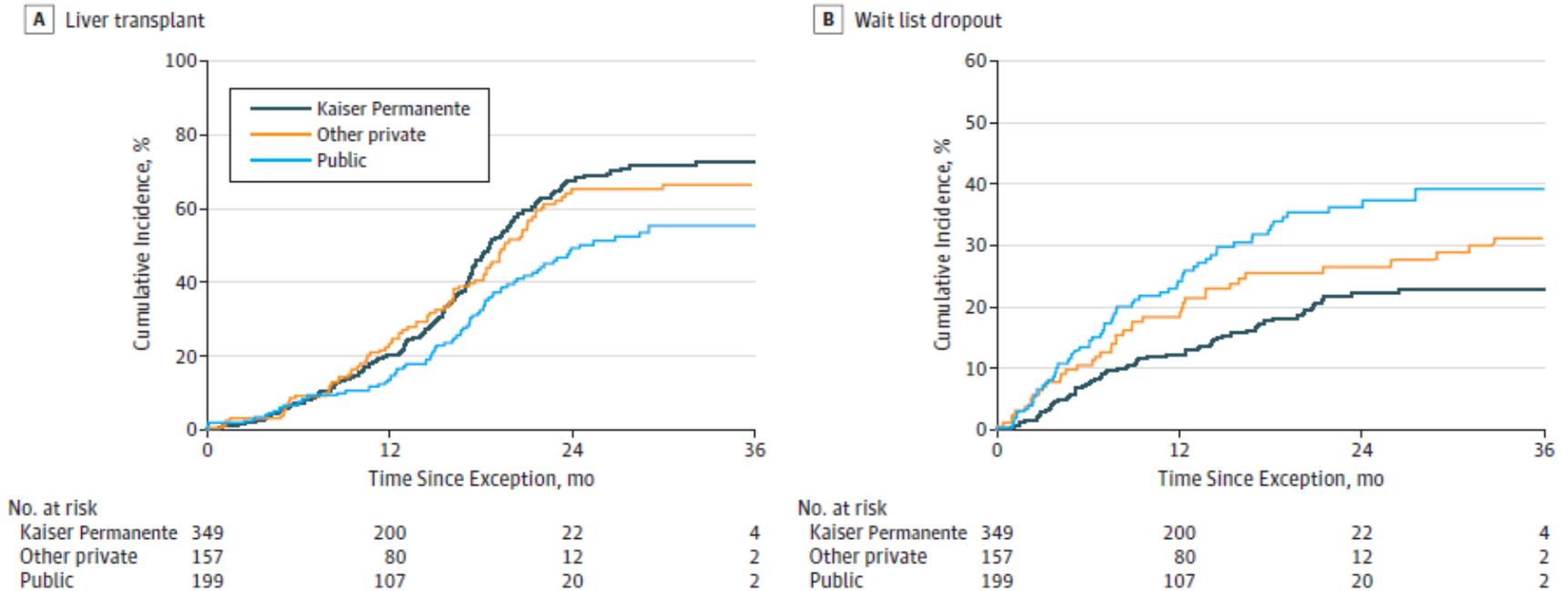
# Disparities in HCC Treatment

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- When evaluating U.S. SEER data, compared to non-Hispanic whites, significantly lower rates of HCC treatment were observed in African Americans (OR, 0.61, 95% CI, 0.56-0.66,  $p < 0.001$ ) and Hispanics (OR, 0.61, 95% CI 0.57-0.65,  $p < 0.001$ ).
- Data from UNOS Liver Transplant registry of HCC patients awaiting LT, observed that Hispanics were 49% less likely and Asians were 51% less likely to receive LT within 1 year of listing compared to non-Hispanic whites.

# Disparities in HCC Treatment

Figure 1. Cumulative incidence of Liver Transplant Waiting List Outcomes by Insurance Type

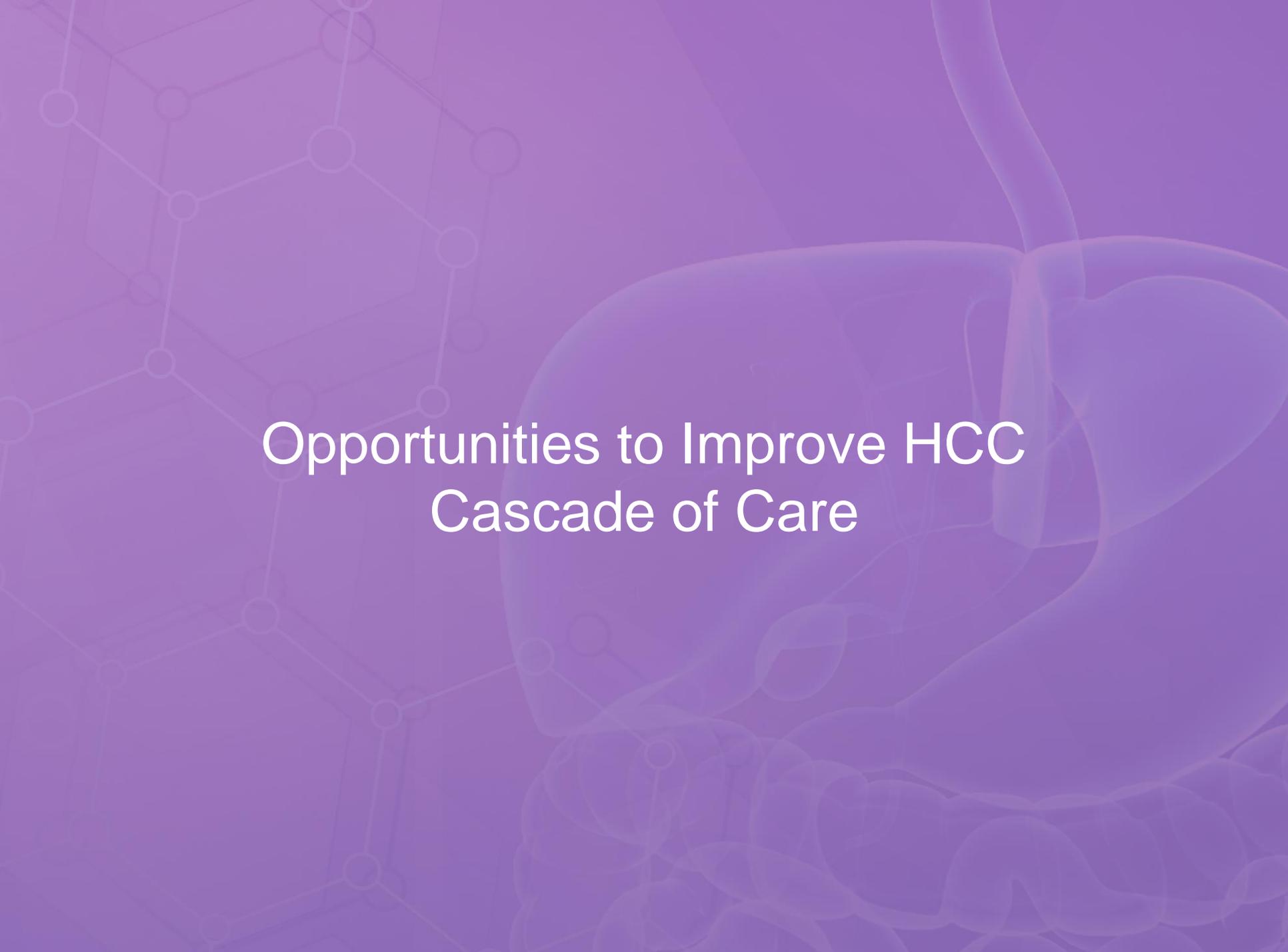


# Disparities in HCC Treatment

- Sarpel, et al evaluated 137 patients with advanced stage HCC ineligible for surgical therapy at a single tertiary care center in the U.S. and observed that patients with higher socioeconomic status (as measured by median household income) were significantly more likely to receive sorafenib compared to individuals in lower socioeconomic status backgrounds (OR, 2.05, 95% CI 1.19 – 3.54,  $p < 0.01$ )

# Disparities in HCC Survival

- The cumulative effects of disparities along the HCC cascade of care leads to more advanced tumor stage at diagnosis, fewer options for curative therapies, and ultimately lower overall HCC survival

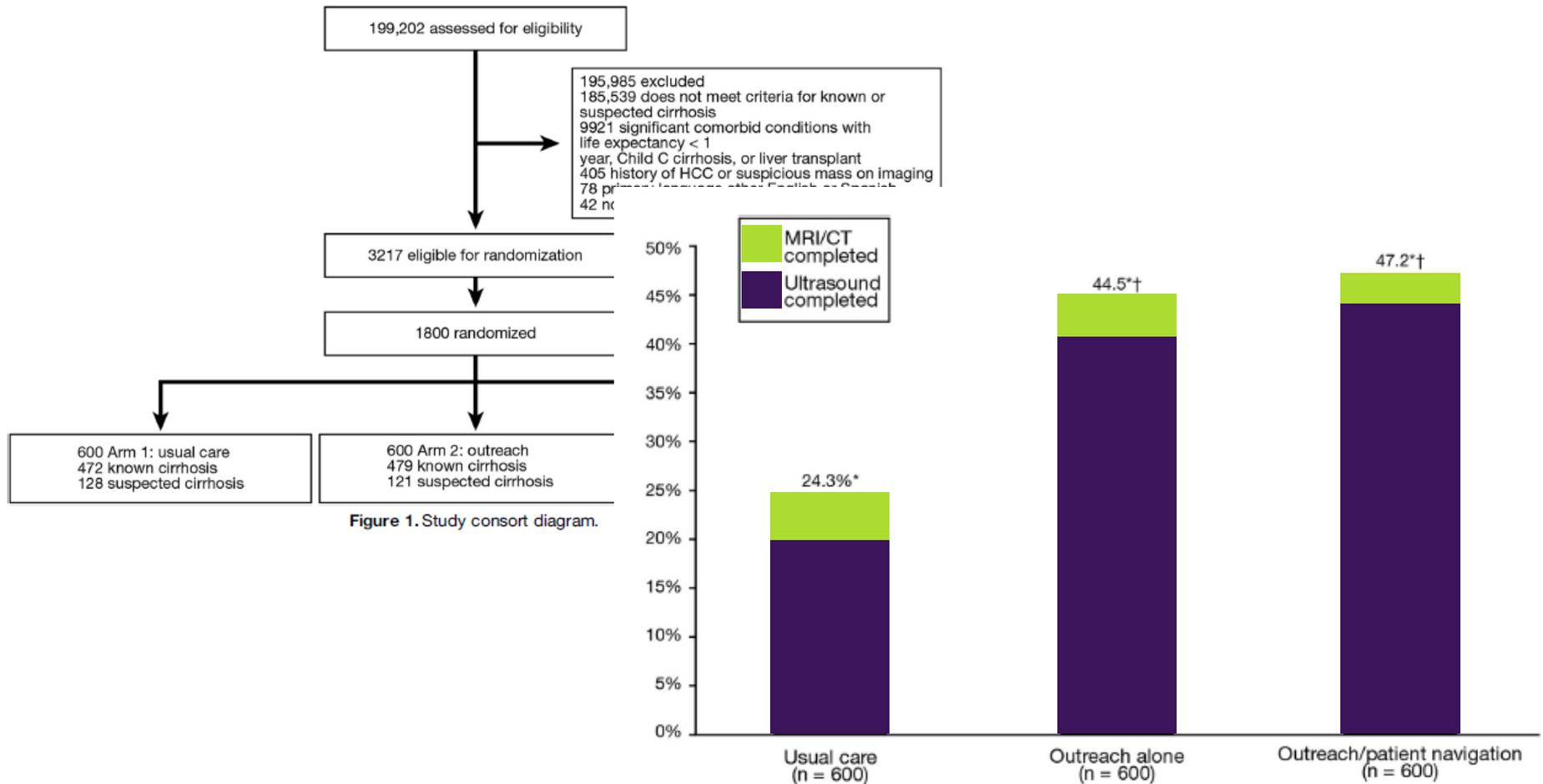


# Opportunities to Improve HCC Cascade of Care

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- Existing studies have demonstrated several factors associated with increased HCC surveillance
  - Patient education to improve knowledge and awareness
  - Provider education to improve familiarity with HCC screening guidelines
  - Improving patient engagement with PCPs
  - Patient navigators
  - Best practice alerts and integrated EHR reminders

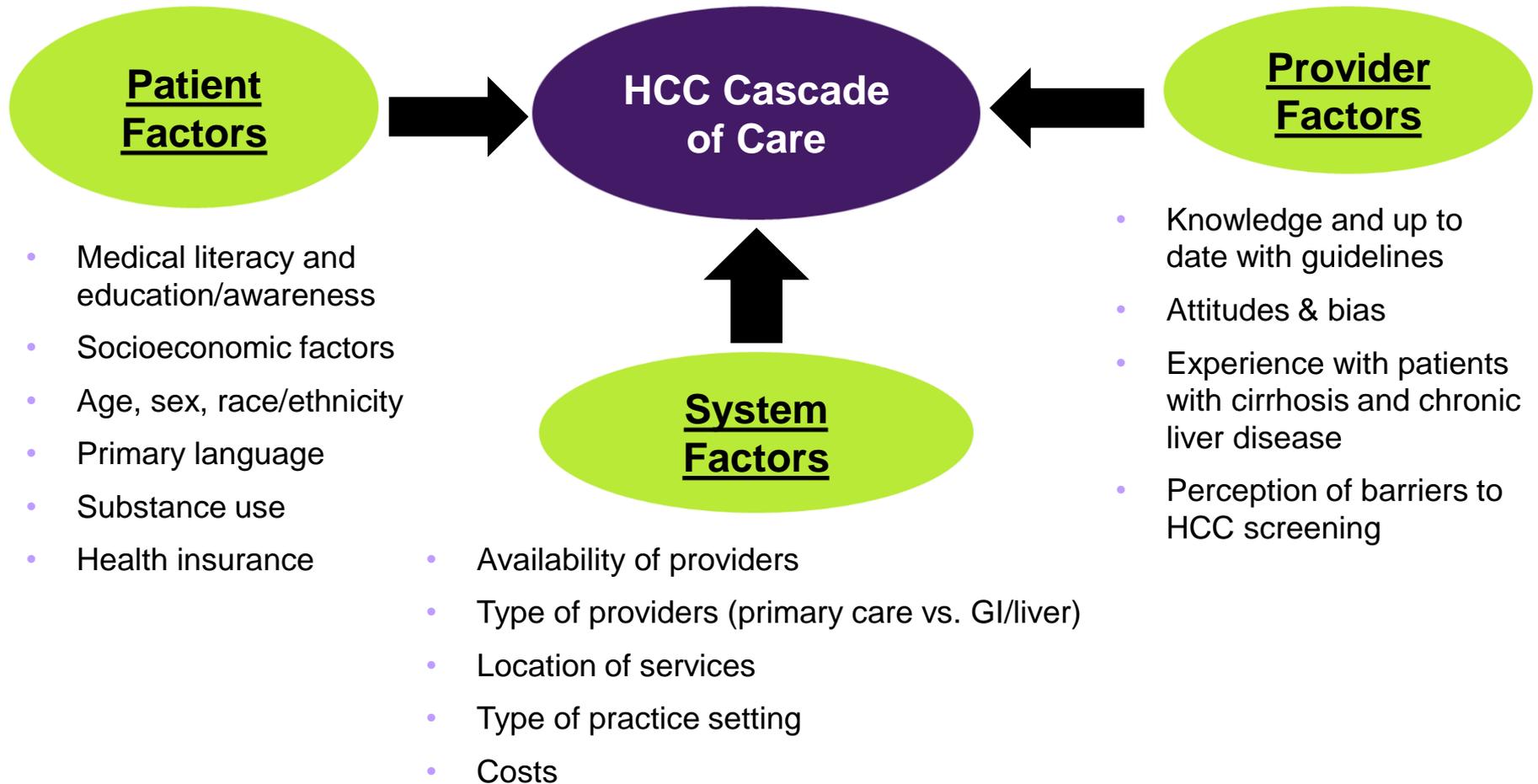
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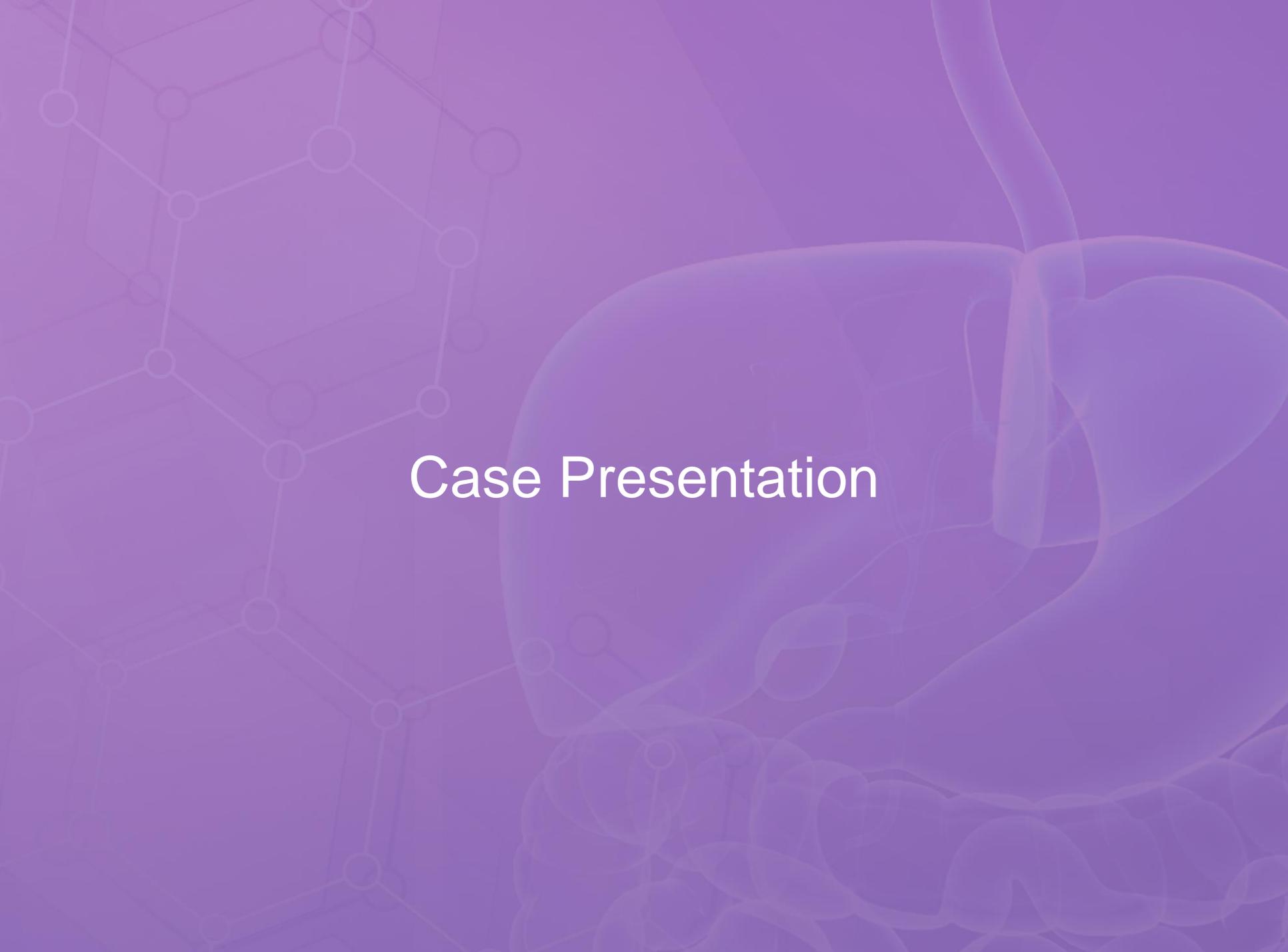
- Beste, et al evaluated the effectiveness of a primary care-oriented point of care clinical reminder to improve HCC surveillance among cirrhosis patients across 8 VA healthcare systems in the U.S.
- The EHR integrated clinical reminder intervention improved HCC surveillance by 51% from baseline.
- On multivariate regression significantly greater odds of appropriate HCC surveillance (adjusted OR 1.29, 95% CI 1.03-1.61,  $P = 0.02$ ) was observed.

# Multi-factorial Barriers to HCC Cascade of Care



# Take Home Points

- HCC cascade of care is a complex multi-step process that starts with appropriate recognition of at risk populations and implementing effective HCC surveillance
- Significant disparities exist from HCC surveillance, timely diagnosis and staging, to access to HCC treatment
- Comprehensive approaches that incorporate patient, provider, and system level challenges are needed to address these disparities



# Case Presentation

# Case DM

- 58 yo Hispanic women with compensated NASH cirrhosis.
- She had been following regularly in clinic until about 2 years ago and has since had several no-shows.
- She returns today to liver clinic. Last liver clinic encounter was 2018.

# Case DM, Cont.

- She reports that there have been a lot of complex issues that resulted in having not been seen in nearly 2 years.
- She is a single mother of two children and has difficulty taking days off for clinic visits. When she calls to reschedule, she has difficulty understanding as she is Spanish speaking and the clinic did not use an interpreter on the phone.
- She had an appointment 4 months ago, but due to COVID-19, she was afraid to go to the hospital. She tried calling to get more information, but could not get through to speak with someone.
- Her PCP left a voice message on her phone 3 months ago, but she hasn't found the time to call back as she is now working and also trying to help her children with school from home.

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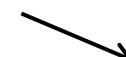
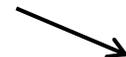
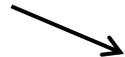
Continued engagement into care  
Access to effective screening modalities

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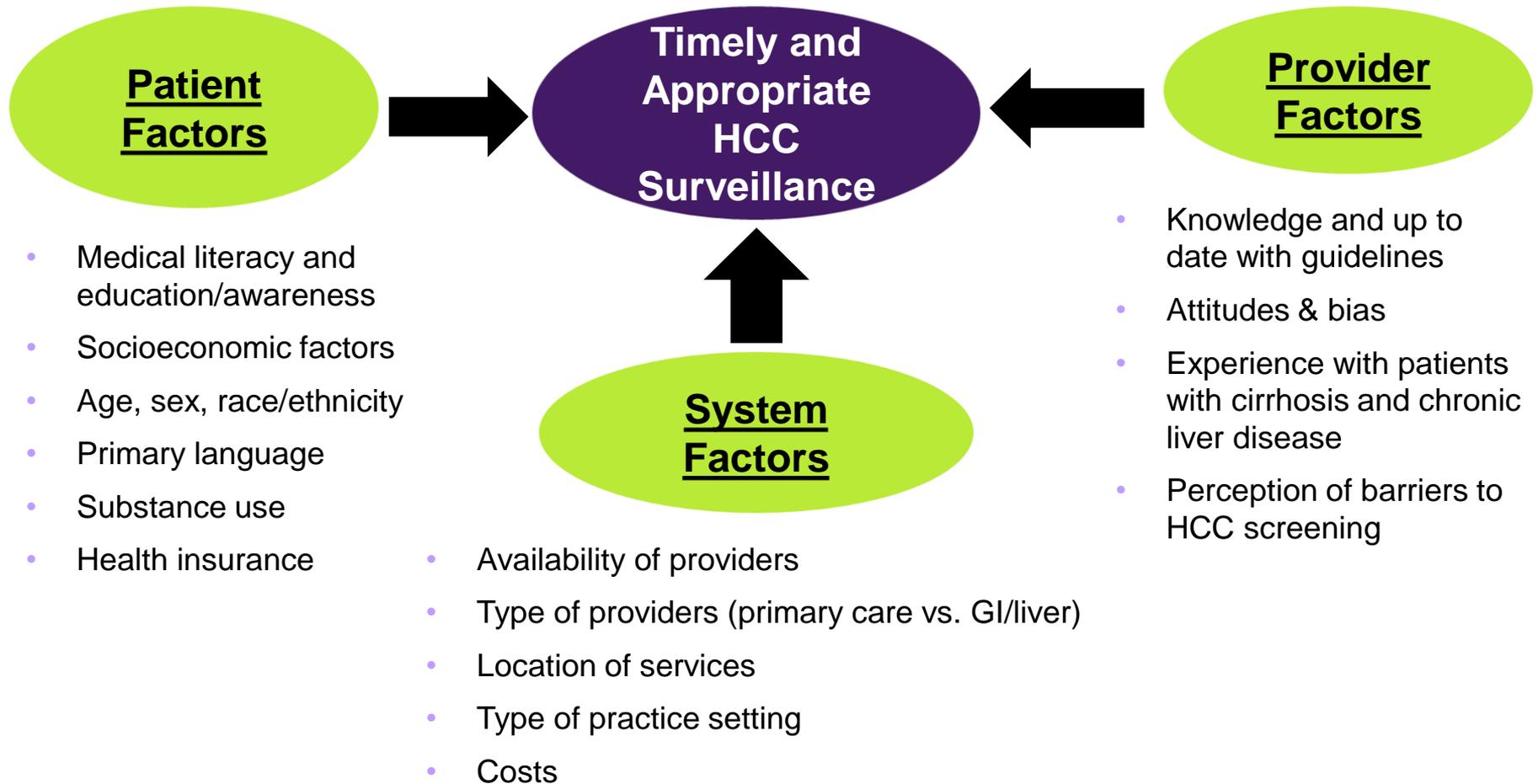
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surgical therapies

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# Multi-factorial Barriers to Effective HCC Surveillance



## Case DM, Cont.

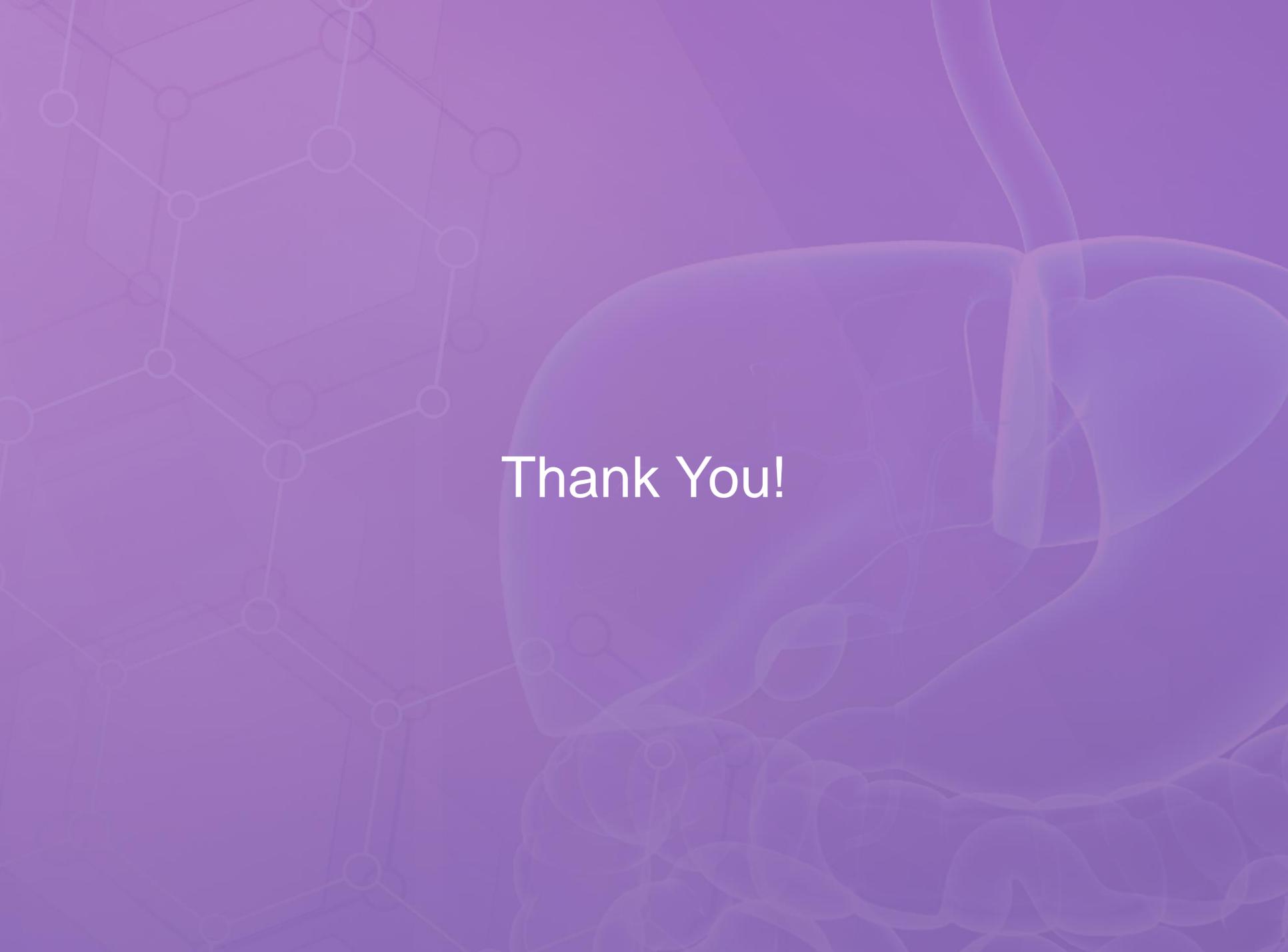
- As part of today's work-up, an US was ordered for continued HCC surveillance
- Due to issue with scheduling, the ultrasound is not completed until another 4 months later
- US demonstrates 2 lesions: 1.5cm and 3.2cm
- Follow up quad-phase CT confirms two HCC lesions LIRADS 5: 1.5cm and 3.4cm

# Barriers in the HCC Cascade of Care

- Challenges experienced by this patient in receiving continued HCC surveillance
  - Patient factors
  - Provider factors
  - Health System factors
- Disparities in HCC outcomes predominantly affect ethnic minorities and underserved populations (FQHC, safety-net)
  - Likely reflect other socioeconomic and situational barriers unique to these vulnerable populations

## Case DM, Cont.

- Tumor board recommended consideration of loco-regional therapy bridge to liver transplant evaluation.
- Patient attended initial transplant evaluation meeting but was scared about moving forward as she does not have a lot of family support, is raising 2 children alone, and was concerned about the complex transplant process.
- She proceeded with TACE at her local institution x 1 and will follow up in 2 months.
- For now, she hold off on pursuing further transplant eval.



Thank You!