WELCOME TO
AK LIVER DISEASE ECHO

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

NPAIHB
Indian Leadership for Indian Health

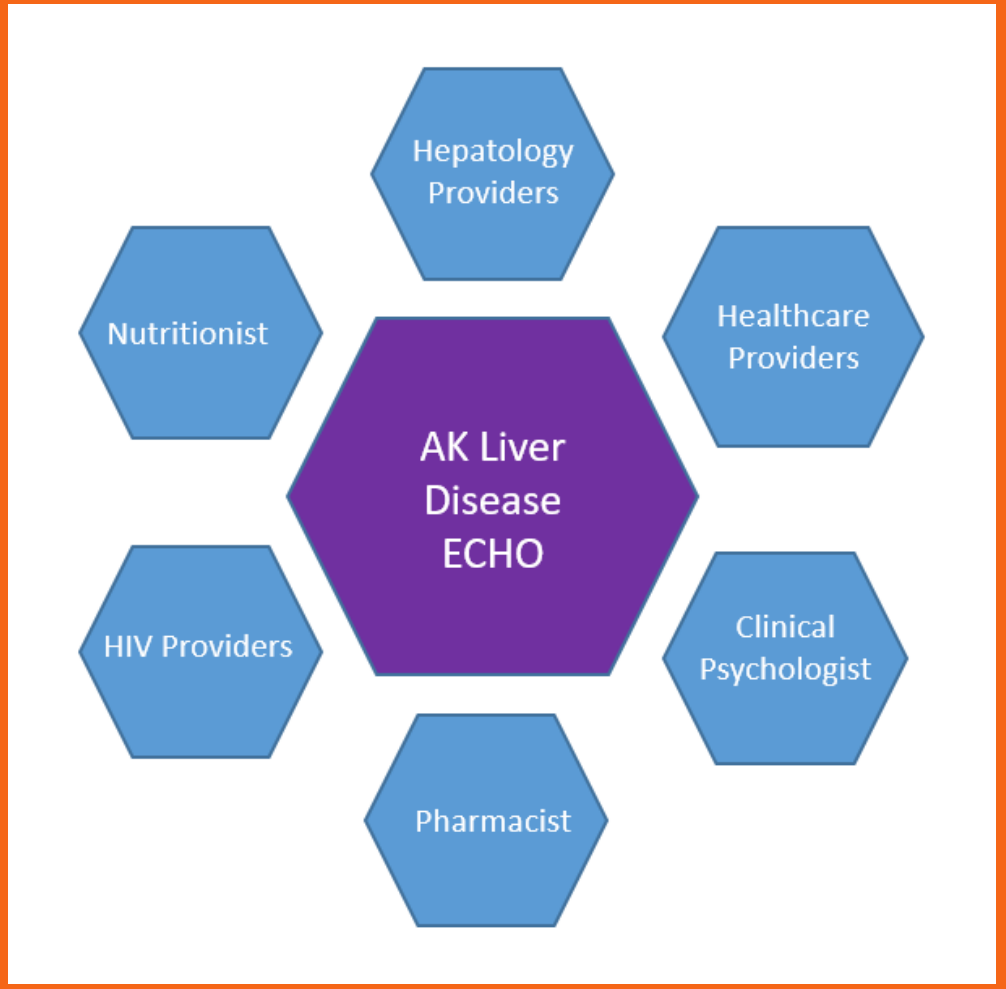
This project is supported by a grant from the Northwest Portland Area Indian Health Board and funding is provided from the HHS Secretary's Minority HIV/AIDS Fund.

WHAT WE DO

- Didactic Presentations pertaining to ECHO topics
- We're accepting **case presentations and questions pertaining to:**
  - Elevated Liver Function Tests
  - Cirrhosis
  - Managing Complications of Decompensated Cirrhosis – Ascites, encephalopathy, esophageal varices
  - Alcohol-related liver disease, including Alcohol Hepatitis
  - Autoimmune liver disease – Autoimmune Hepatitis, Primary Biliary Cholangitis, Overlap
  - Nonalcoholic fatty liver disease/Nonalcoholic steatohepatitis
  - Hepatocellular carcinoma
- Provide Expert Panelists

CONSULTANT TEAM

- Brian McMahon, MD Hepatologist
- Youssef Barbour, MD Hepatologist
- Lisa Townshend, ANP Hepatology Provider
- Annette Hewitt, ANP Hepatology Provider
- Leah Besh, PA-C HIV/Hepatology Provider
- Anne Fleetwood, MS, RDN, NDN
- Brittany Keener, PharmD, MPH, BCPS
- Rebecca Robinson, PhD Clinical Psychologist



Welcome to Alaska Liver Disease ECHO

Approved Provider Statements:

JOINTLY ACCREDITED PROVIDER™
INTERPROFESSIONAL CONTINUING EDUCATION

In support of improving patient care, Alaska Native Medical Center (ANMC) is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Contact Hours:

ANMC designates this activity for a maximum of 12 contact hours, including 3 total pharmacotherapeutics contact hours, commensurate with participation.

Financial Disclosures:

Youssef Barbour, MD & Lisa Townshend-Bulson, APRN / faculty for this educational event, are primary investigators in an ANTHC sponsored hepatitis C study funded in part by Gilead Sciences. All of the relevant financial relationships listed have been mitigated.

Requirements for Successful Completion:

To receive CE credit please make sure you have actively engaged in the entire activity, your attendance is recorded by the facilitator, and complete the course evaluation form found here: https://forms.gle/R8vibUZgMbRcoScw9.

For more information contact
jlfielder@anthc.org or (907) 729-1387

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

HEPATOCELLULAR CARCINOMA (HCC): EPIDEMIOLOGY, SURVEILLANCE AND MANAGEMENT IN ALASKA NATIVE PEOPLE

Brian J McMahon MD

Liver Disease and Hepatitis Program

Alaska Native Tribal Health Consortium

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

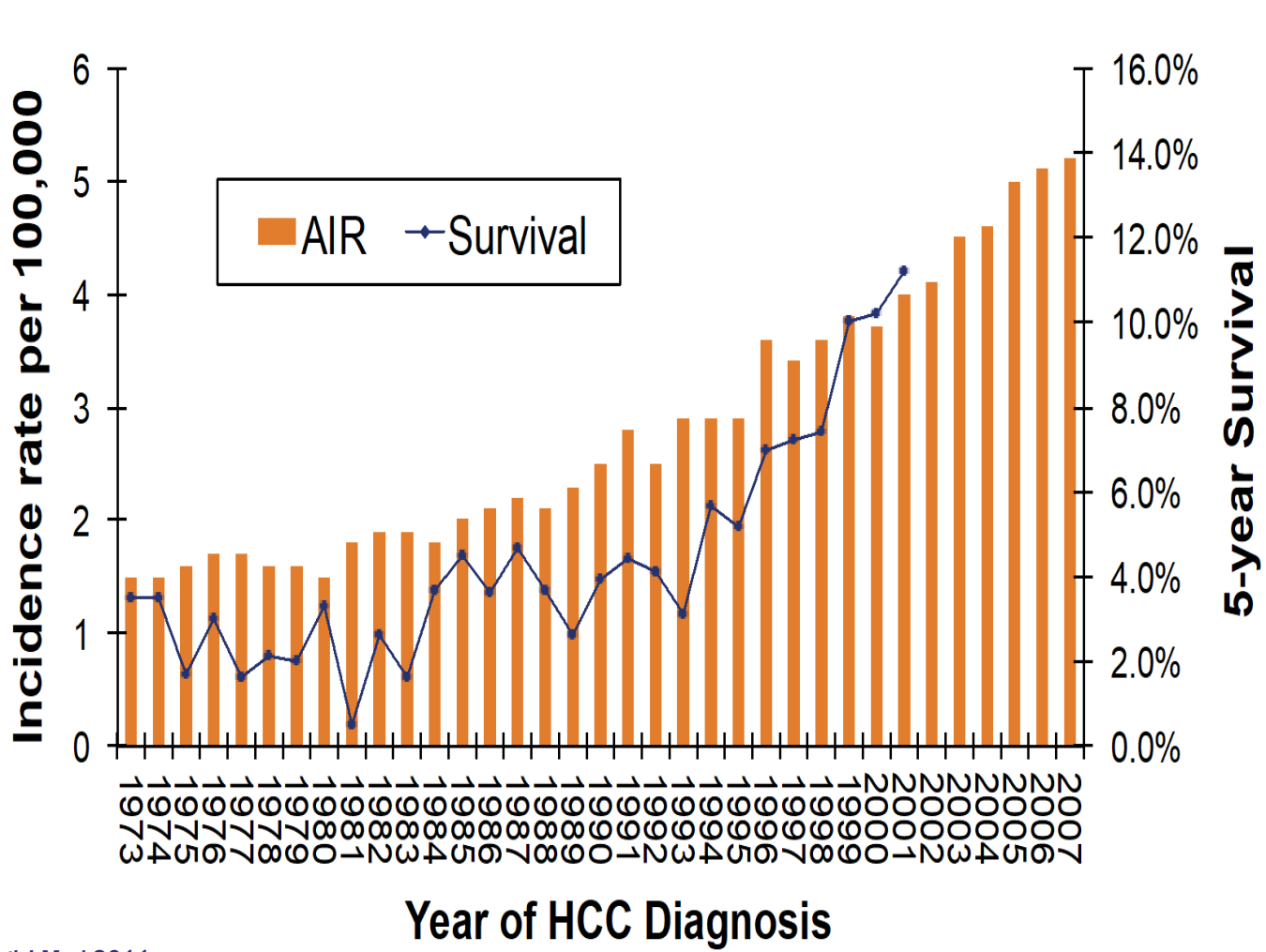
CONFLICTS OF INTEREST

- Brian McMahon: None
- Our Program has a research grant from Gilead Sciences which does not fund any of our salaries

GOALS OF PRESENTATION

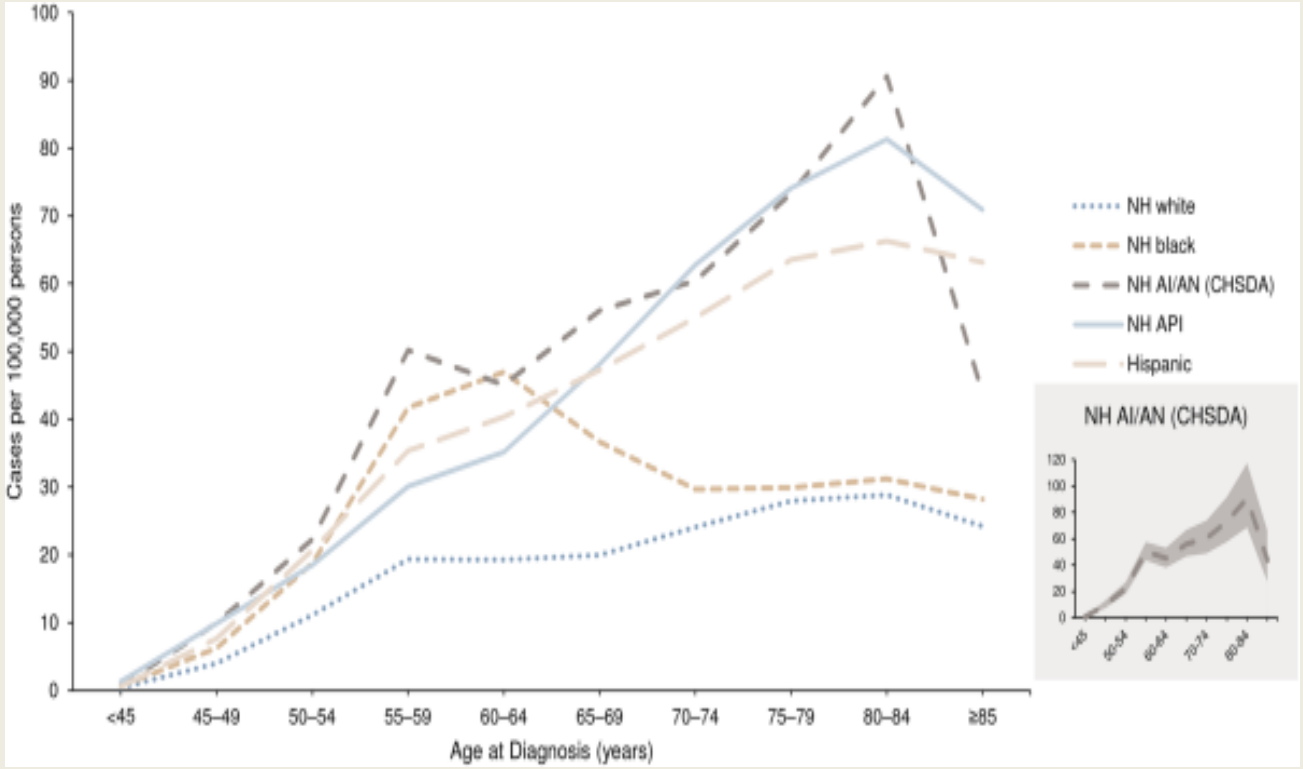
- Discuss the incidence of hepatocellular carcinoma (HCC) in Alaska Native People:
- Changes in the incidence and etiology in the decades
- Discuss major etiologies of cirrhosis and HCC
- Discuss risk factors for developing HCC in associated etiologies:
  - Hepatitis B virus (HBV)
  - Hepatitis C virus (HCV)
  - Metabolic fatty liver disease (MAFLD)
  - Alcoholic cirrhosis
  - Other etiologies of cirrhosis and HCC
- Reducing the incidence of HCC: What must be done
- How to improve rates of early diagnosis when HCC can be cured

THE INCIDENCE AND 5-YEAR SURVIVAL OF HCC IN UNITED STATES



El-Serag HB. *N Engl J Med* 2011

ANNUAL REPORT TO THE NATION ON THE STATUS OF CANCER, 1975-2012, FEATURING THE INCREASING INCIDENCE OF LIVER CANCER



Cancer
9 MAR 2016 DOI: 10.1002/cncr.29936
http://onlinelibrary.wiley.com/doi/10.1002/cncr.29936/full#cncr29936-fig-0002

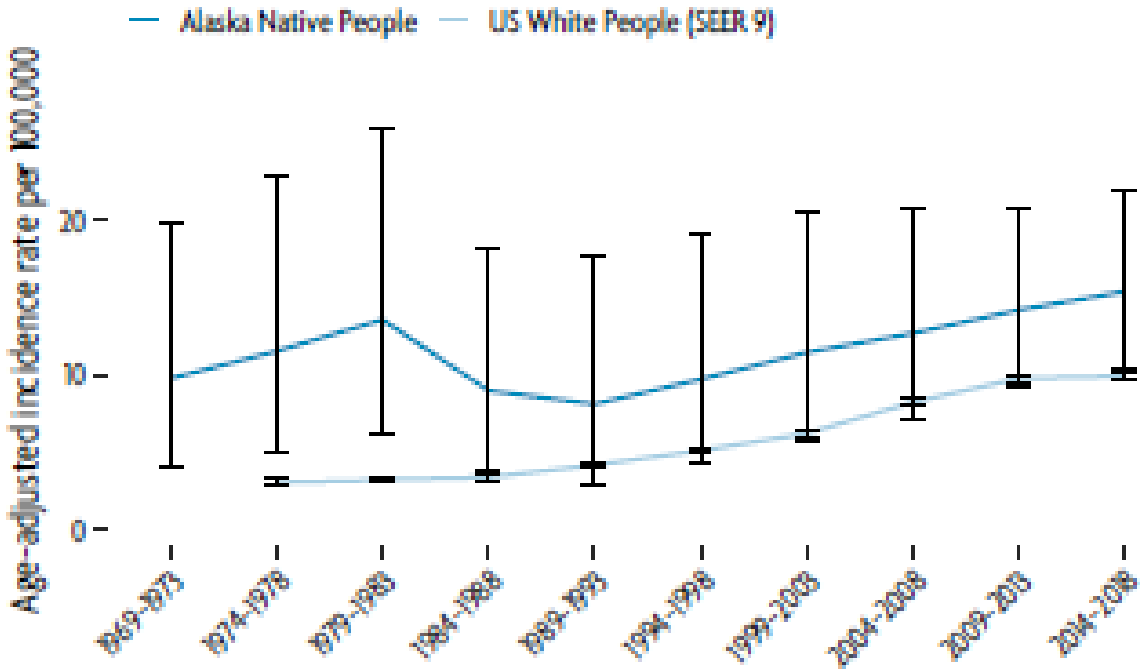
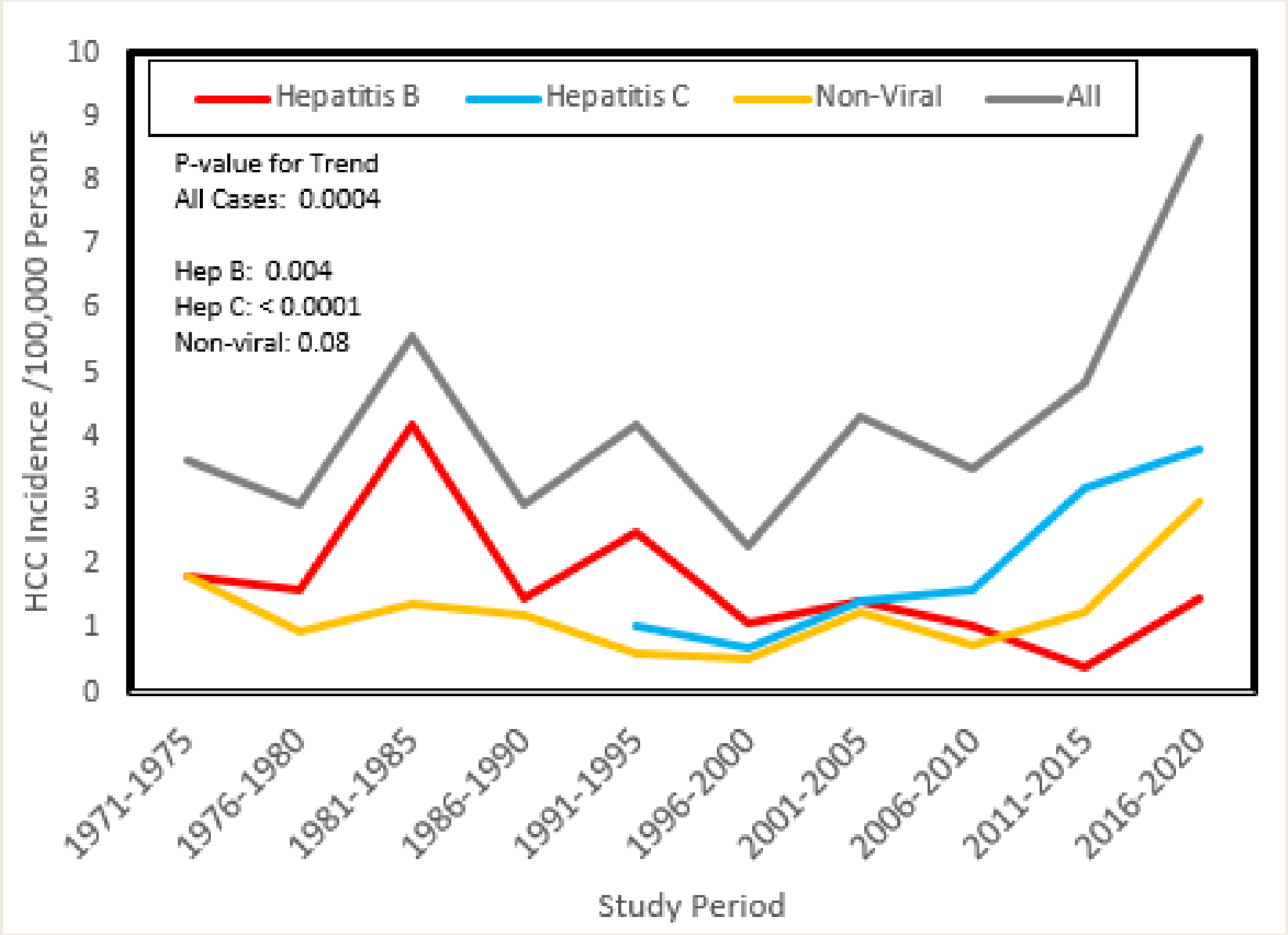


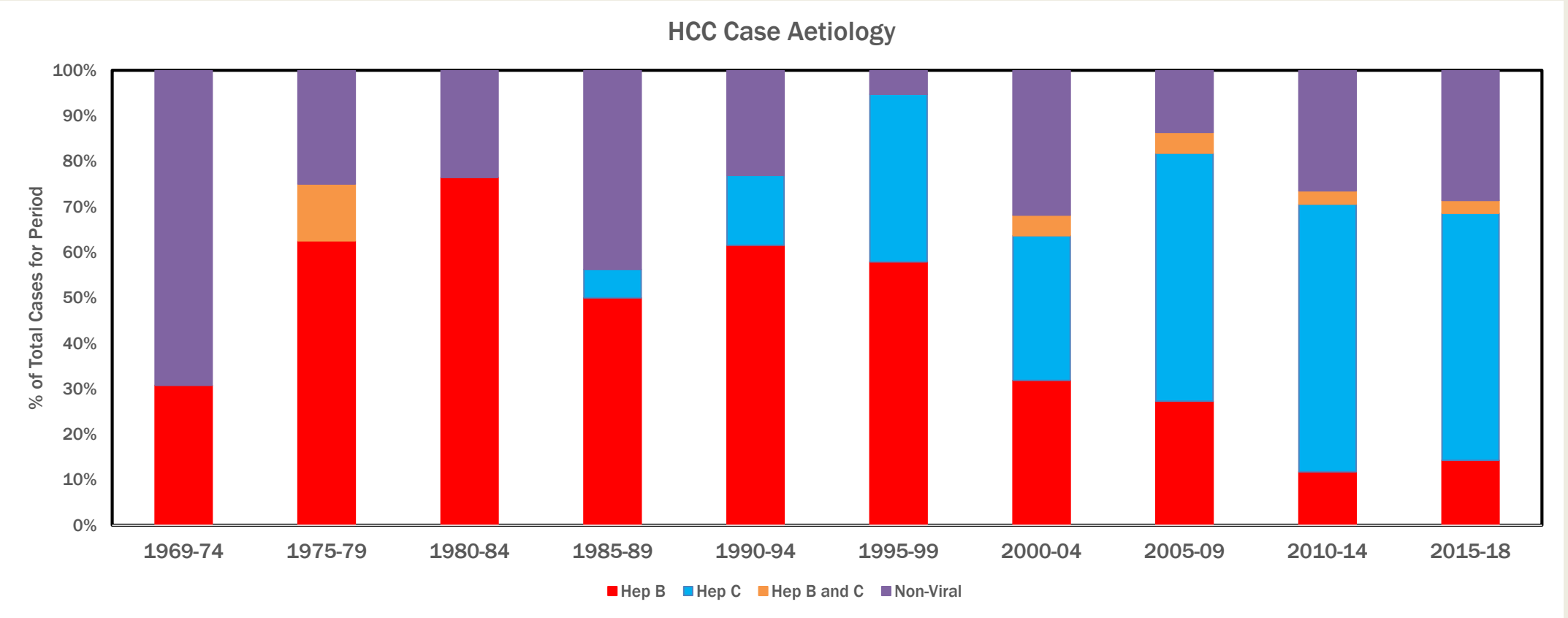
Figure 4.20: Comparison of trends in average annual age-adjusted cancer incidence for liver, men, 1969–2018.

Alaska 50 year Cancer Registry Report: http://anthctoday.org/epicenter/http



Unpublished Data. Do not share

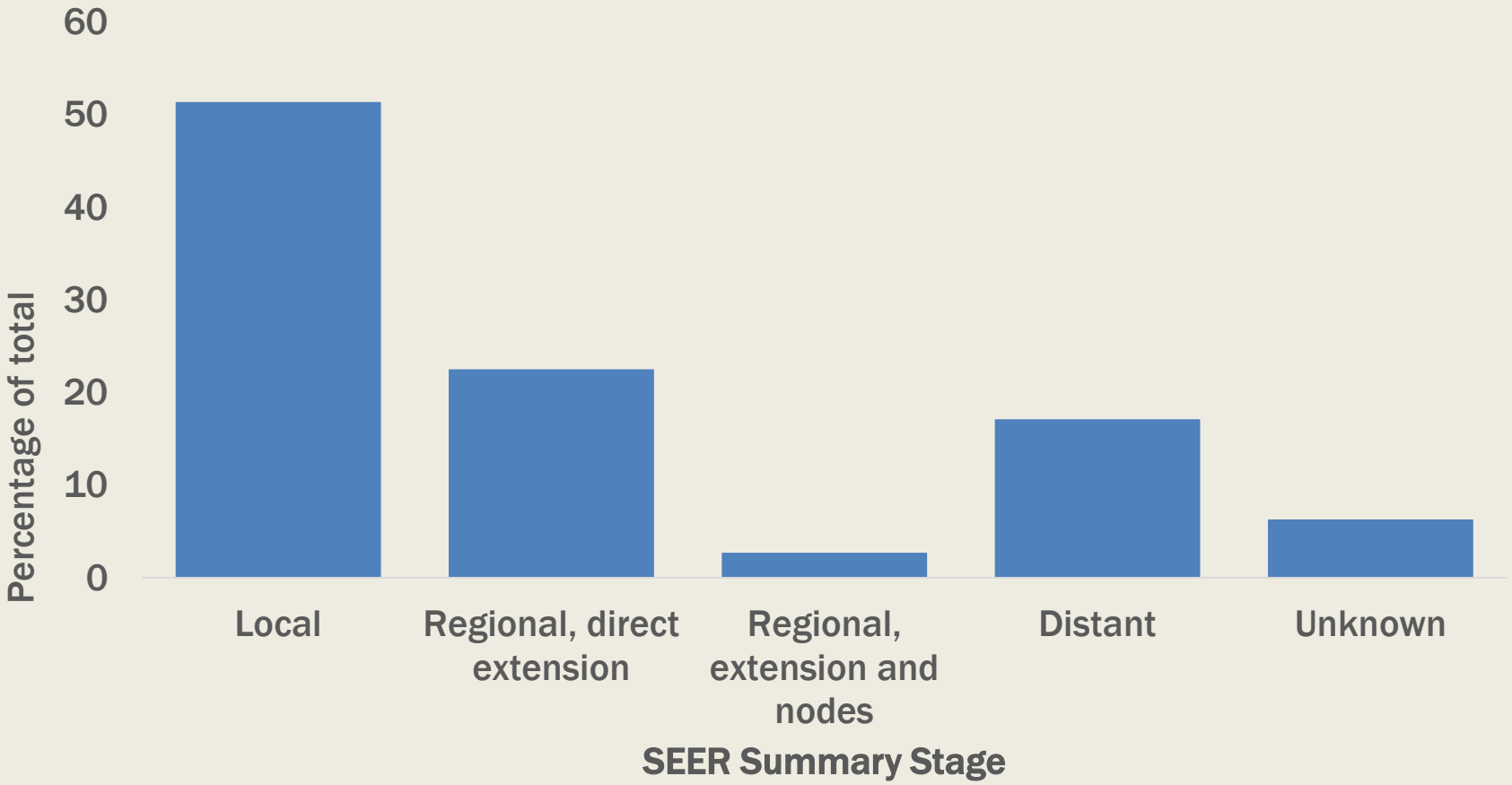
FIGURE 2. PERCENTAGE OF ALL HCC CASE IN ALASKA NATIVE PERSONS BROKEN DOWN BY VIRAL ETIOLOGY AND NON-VIRAL CASES, 1969 – 2018



Many cases prior to 1980 were not fully investigated and unknowns are listed as non-viral

Unpublished Data. Do not share

STAGE DISTRIBUTION OF LIVER CANCERS AMONG AN PEOPLE, 2004-2016



ESTIMATED PROPORTION OF ALASKA NATIVE AND US POPULATION WHO HAVE LIVER CONDITIONS

Liver Condition	Alaska Natives Proportion %	Alaska Native Number	US Population Proportion %	US Number
Hepatitis B	1%*	1100	Less than 1%	
Hepatitis C	3-5%	5,000 to 7,000	2-3%	5 to 7 Million
Metabolic Fatty Liver Disease (MAFLD)	20%-25%	Estimate 40,000; 7,000 persons with NASH	30%^	100 Million
Alcoholic Liver Disease	Unknown	Unknown	5%-7%	15 to 21 Million
Autoimmune Liver Diseases	2%	210	Rare, less than 0.5 %	<5,000

*Down from 3% in 1985; prevalence is still > 2% in Western Alaska

^NHANES; 10.3% had advanced fibrosis or cirrhosis PloS One 2017;12e0173499. doi: 10.1371/journal.pone.0173499

UNDERLYING CAUSES OF LIVER CANCER IN ALASKA NATIVE PEOPLE

- Hepatitis B: in men 40 years and older, women 50 years and older, those who have family members who had liver cancer and those who have a cancer cause type (F)
- Hepatitis C: Those persons with cirrhosis, even if they have been cured
- MAFLD: NASH with advanced fibrosis or cirrhosis
- Alcoholic Liver Disease: most patients die of liver failure prematurely. HCC rate lower
- Other: Autoimmune Hepatitis/PBC
- What to do
  - Identify these persons early
  - Treat their underlying condition
  - Asses the level of fibrosis
  - If they have F3 or F4 fibrosis, initiate surveillance

INDEPENDENT RISK FACTORS ASSOCIATED WITH PROGRESSION OF HCV

- Heavy alcohol usage: Strongest factor
- Male sex
- Diabetes
- Presence of hepatic steatosis
- Older age at time of infection
- HCV genotype 3
- Co-infection with HIV or HBV
- Not associated:
  - HCV RNA level
  - Presence of Anti-HBc without HBsAg

McMahon et al. Gastroenterology 2010;138:922-31 and Clinical Gastro Hepatology 2017;15:431-7

Risk of Developing HCC from Time of Liver Biopsy by Fibrosis Stage

Outcome	Time Period	None/Mild (Metavir 0-1) (n = 150)	Moderate (Metavir 2) (n = 131)	Severe (Metavir 3) (n = 88)	Cirrhosis (Metavir 4) (n = 38)
HCC	3-Year	0.0% (0.0, 3.2) (n = 118)	0.0% (0.0, 3.4) (n = 103)	1.1% (0.2, 7.7) (n = 65)	3.3% (0.5, 21.4) (n = 25)
	5-Year	1.0% (0.1, 6.9) (n = 95)	1.0% (0.1, 6.6) (n = 87)	1.1% (0.2, 7.7) (n = 54)	13.4% (4.4, 36.7) (n = 16)
	7-Year	1.0% (0.1, 6.9) (n = 81)	2.3% (0.6, 9.1) (n = 72)	6.0% (1.9, 18.2) (n = 42)	35.0% (16.5, 64.4) (n = 11)
	10-Year	1.0% (0.1, 6.9) (n = 52)	4.6% (1.4, 4.8) (n = 44)	8.4% (3.1, 21.6) (n = 27)	
	# of Cases	2	4	7	9

Bruden D et al. Hepatology 2017;66:37-45

METABOLIC ASSOCIATED FATTY LIVER DISEASE (MAFLD FORMALLY NAFLD)

- Incidence is not well described
- Some studies suggest increase risk HCC in persons without cirrhosis independent of fibrosis
- Once cirrhosis is well established, life style changes of weight loss and exercise even if successful might not reduce subsequent risk of HCC

WHAT MEASURES MIGHT REDUCE RISK OF HCC

- HBV:
  - Universal vaccination starting at birth
    - Studies for Taiwan, Alaska and Thailand clearly show reduction in HCC in children 10-20 years after universal vaccination
    - However significant impact will not be seen for 3-4 decades (Goldstein)
  - Diagnosis of HBV in asymptomatic persons and linkage to care and treatment
- HCV:
  - Diagnosis, CDC recommends universal screening and treatment (cure) in persons with HCV
  - Programs to reduce acquisition of HCV, including opioid addiction treatment, clean needles
- MAFLD:
  - Progress in reducing obesity including diet, exercise, drugs such as appetite suppresses, obesity surgery, drugs that block hepatic steatosis and hepatic fibrosis
  - Determine which MAFLD patients have NASH and identify stage fibrosis (FibroScan)
  - Other conditions including hemochromatosis, AIH, PBC etc.: early diagnosis and treatment

ASSESSING LEVEL OF FIBROSIS IN AN PERSONS WITH LIVER DISEASE

- Non-invasive serologic markers of fibrosis
  - APRI
  - FIB4
  - NAFLD Fibrosis Score
  - Commercial markers: Expensive, not that much better than above free markers
    - Fibrosure, FibroSpect2, and others
- Vibration Controlled Transient Elastography (VCTE or FibroScan®)
- Other sonographic techniques such as sheer wave elastography
- Magnetic resonance elastography (MRE)
- Liver Biopsy

‘Simple Scores’ for Predicting Presence of Advanced (F3/4) Fibrosis

NAFLD Fibrosis Score

= -1.675 + 0.037 x **Age** + 0.094 x **BMI** + 1.13 x **IFG/diabetes** + 0.99 x **AST/ALT ratio** - 0.013 x **Platelets** - 0.66 x **Albumin**.

- A score of less than -1.455 excludes fibrosis (NPV 88-93%).
- A score of greater than 0.676 predicts fibrosis (PPV 82-90%). AOC 0.85

FIB-4 Score

= (**Age** * **AST**) / (**Platelets** * Sqrt (**ALT**))

- A score of less than 1.3 excludes fibrosis (NPV 95%)
- A score greater than 3.25 predicts fibrosis (PPV ~70%)

www.qxmd.com

ngulo et al, Hepatology 2007: 45(4) 846

Sterling et al, Hepatology 2006: 43, 1317; McPherson et al, Gut 2010: 59(9), 1265

WHICH AN PERSONS WITH CHRONIC HBV NEED SURVEILLANCE FOR HCC

- Persons with cirrhosis,
- Family history of HCC
- Men over 40 years and women above age 50 years
- Not effective for children <20 with the exception of those infected with HBV genotype F
  - Gounder et al. J of Pediatrics 2016:178:206-213

WHICH TO INITIATE SURVEILLANCE WITH CHRONIC HEPATITIS C

- All persons with F3 or F4 fibrosis need regular HCC surveillance
- It's important to establish fibrosis stage in HCV infected persons
  - FIB4 and APRI are good first steps
  - Serologic Fibrosis scores such as FibroSure, FibroTest and FibroSpect2 are expensive but a little better than FIB4
    - Important to note that these test have good specificity at the low and high ends but in between suggest flipping a coin for less expensive accuracy
  - Liver Ultrasound with portal vein flow study
  - Vibration-Controlled Transient Elastography; FibroScan®
  - MRI elastography or MRE
  - Liver biopsy

WHAT SCREENING METHODOLOGIES TO USE AND HOW FREQUENTLY

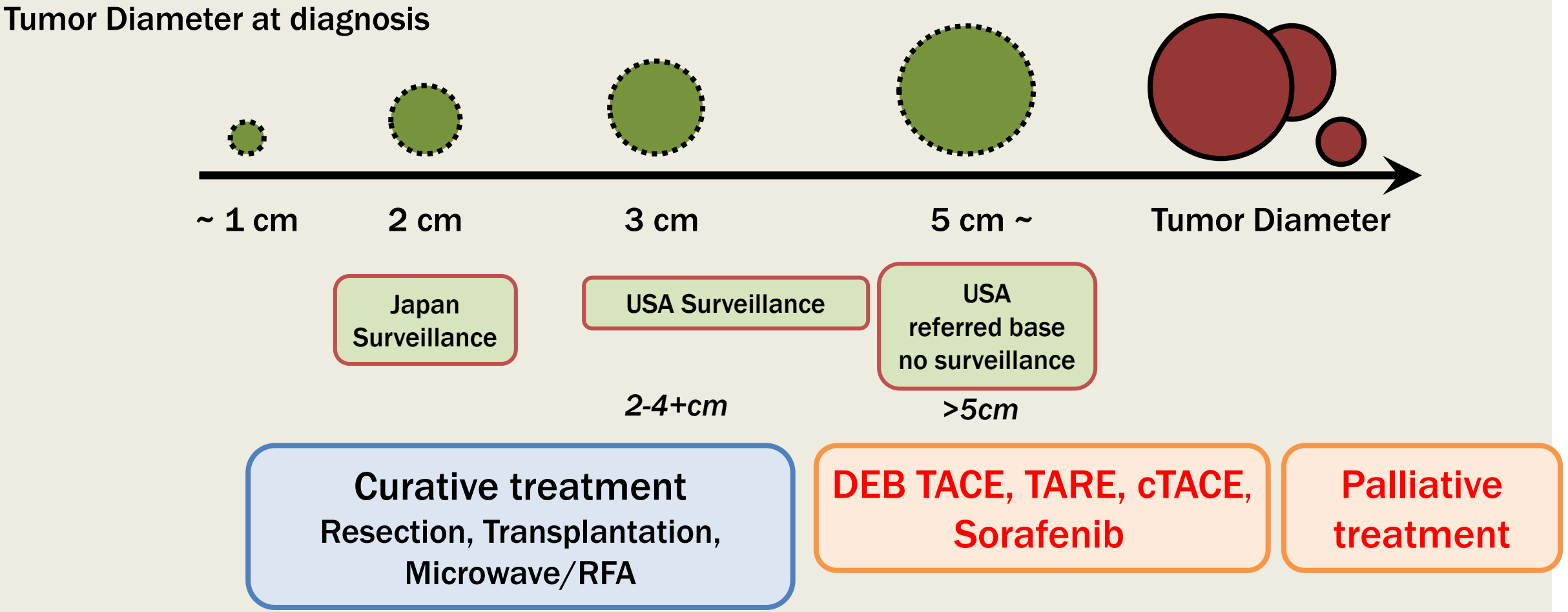
- Ultrasound of the liver and AFP every 6 months.
- Very difficult to get persons living in remote villages to get their US done and we have to rely more heavily on AFP
  - If AFP > 10ng/ml, we use every effort to get these persons in for radiographic studies

AASLD Guideline for HCC Hepatology 2018;67:358-380
Download for free at AASLD.org under practice guidelines

ABBREVIATED MRI

- New Technique using contrast but taking only 10-15 minutes
  - Multiphase with contrast: Non-contrast, arterial phase, venous phase, late phase
  - Can be done on any MRI machine
  - However, not yet studied enough to recommend
  - Since MRI is twice as sensitive as US in picking up small HCC lesions between 1 and 3 cm., could substantially improve early detection of easily curable lesions
  - We have received an NCI grant to study abbreviated MRI compared to US plus evaluate new bio and genetic markers for early detection of HCC with four other centers, UW, Fred Hutchinson both in Seattle, Cherokee Nation and SW Texas Medical School in Dallas

WHY IS HCC SURVEILLANCE BENEFICIAL?
HCC TREATMENT OPTIONS: EARLIER IS BETTER



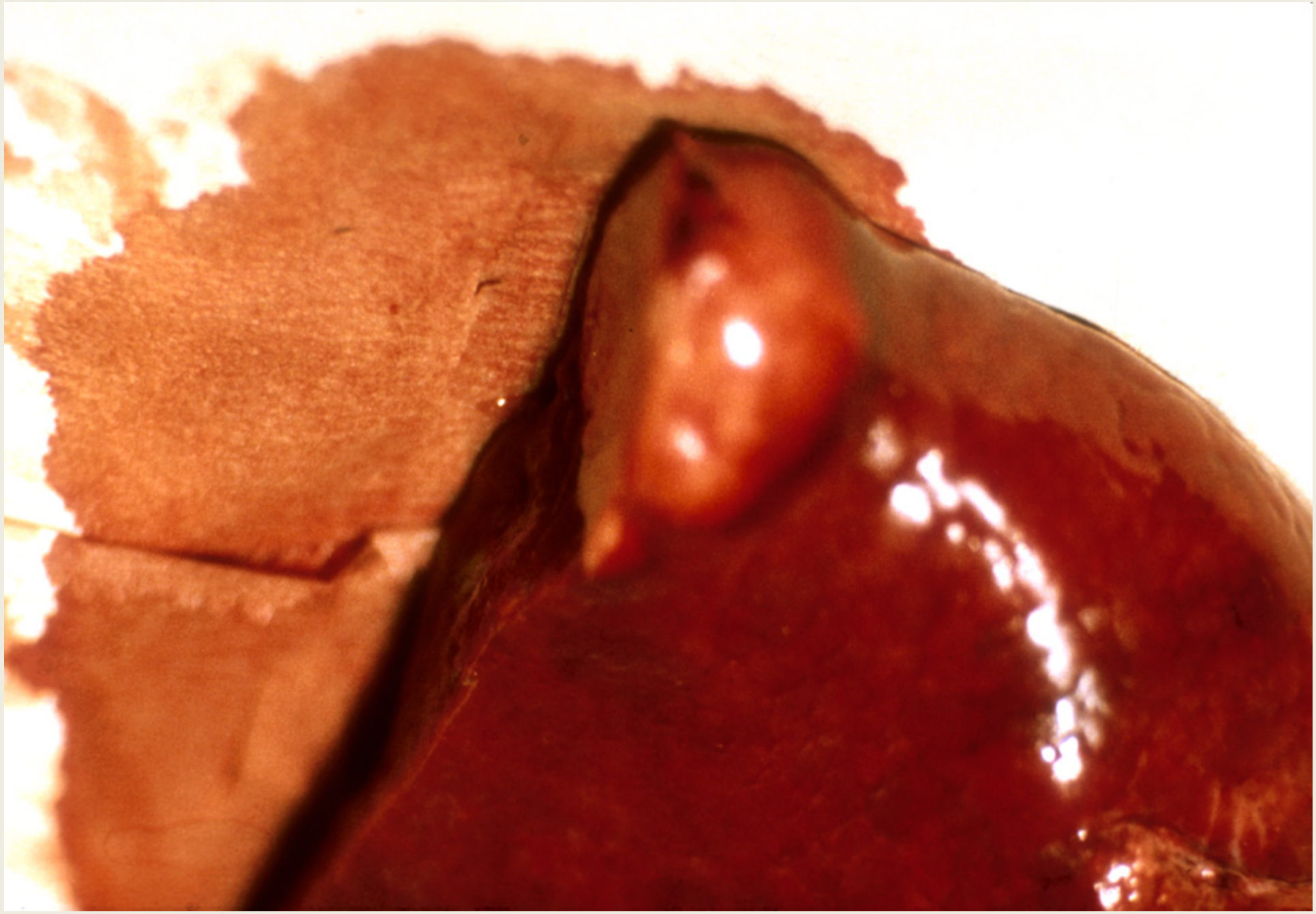
4/1/2014

SENSITIVITY OF HCC DETECTION

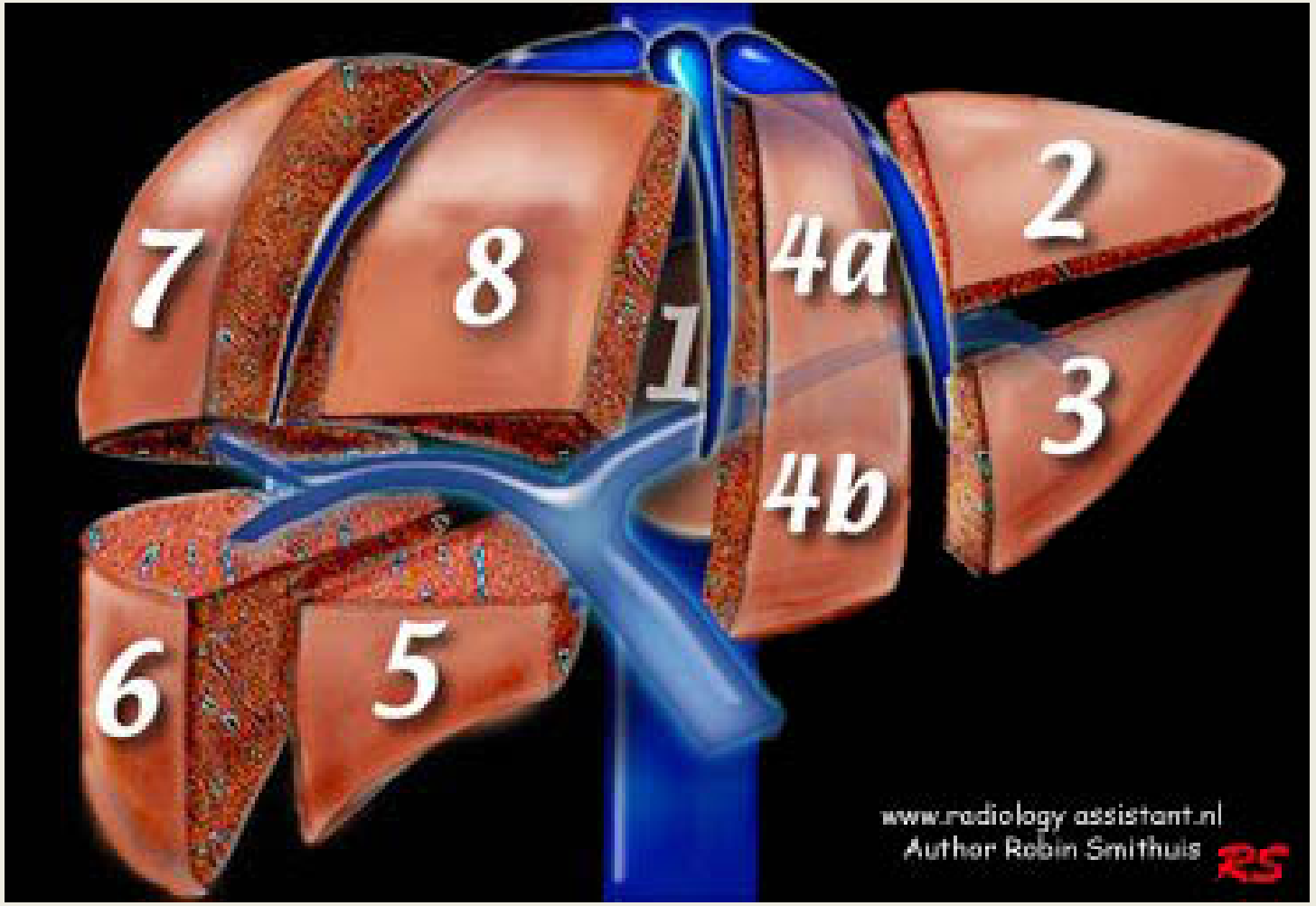
Size	US	CT	MRI
Per-nodule	92/200 (46%)	126/194 (65%)	126/175 (72%)
<2cm	20/96 (21%)	35/88 (40%)	33/70 (47%)
2-4cm	44/71 (62%)	59/74 (80%)	66/77 (86%)
≥4cm	28/33 (85%)	32/32 (100%)	27/28 (96%)
Per-patient	88/138 (64%)	113/149 (76%)	99/117 (85%)

638 Liver transplant 225 (35%) HCC,
23 excluded *(infiltrative, multifocal)*

Yu NC. et al Clin Gastroenterol Hepatol 2011;9:161-167



Segments of the Liver



ABLATION DEMO

rita animation.mpg

HOW TO DECREASE MORBIDITY AND MORTALITY IN AMERICAN INDIAN/ALASKA NATIVE AI/AN PEOPLE DUE TO HEPATOCELLULAR CARCINOMA (HCC) AND CIRRHOSIS

- Identify AI/AN Persons with underlying liver diseases early
- Determine the cause (etiology) of the underlying liver condition
  - Linkage to care
  - Prevent progression of this condition
    - Life style changes
    - Medication or other modalities
  - Cure condition if curative treatment is available
- Identify those with underlying liver condition at risk for HCC and initiate surveillance to detect HCC at an early and curable stage
    - Anyone with advanced fibrosis (F3) or cirrhosis (F4)
    - Persons with hepatitis B without cirrhosis at risk of HCC
- Apply most effective treatments for those who develop HCC
- Promote research, both scientific and community-based, to prevent and treat HCC

CONCLUSION

- Identify patients at risk for liver disease, determine etiology and initiate treatment
- Ascertain the stage of liver fibrosis
- Initiate every 6 month surveillance with liver US and AFP for those at highest risk of HCC including all persons with advanced fibrosis or cirrhosis
- Remember that there are significant limitations to our screening modalities and to keep a high level of suspicion
- Detecting HCC tumors early can lead to long-term survival
- HCC that is to advanced to ablate, resect or transplant is ultimately fatal as unlike other cancers, no chemotherapy for cure is available

CONCLUSIONS

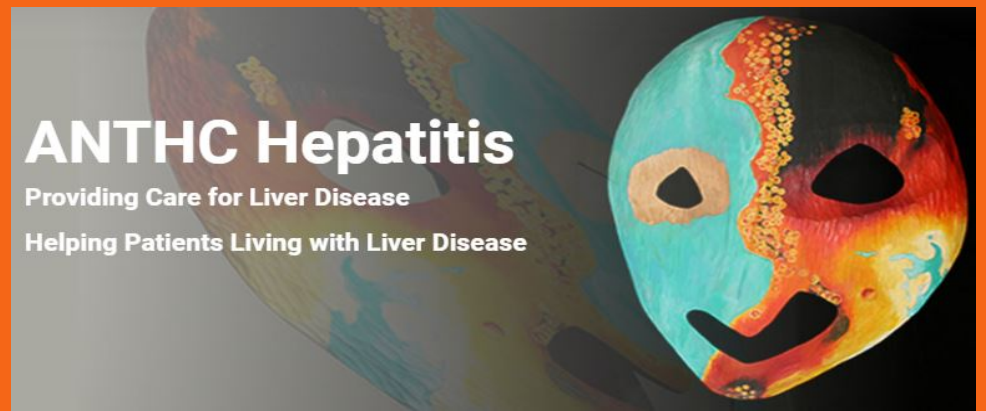
- Overall survival for HCC is poor due to under identification of persons at risk and inadequate surveillance.
- Need for better radiographic and biomarker tools to detect HCC earlier and reduce false positive lesions
- Can we combine risk factors (age, genotype, viral load etc.) to come up with better algorithms for frequency of surveillance
- We need better treatment modalities for treating non-curable HCC
- Globally to reduce HCC due to hepatitis B, Vaccinate all newborns and reduce aflatoxin exposure
- Treatment of active viral replication to reduce incidence in both HBV and cure HCV

LIVER DISEASE ECHO SCHEDULE AT A GLANCE

- September 16th HCC Surveillance – Brian McMahon, MD
- October 21st Treatment of Acute Alcohol Hepatitis – Brian McMahon, MD
- November 18th Nutrition & the Liver - Anne Fleetwood, RD
- December 16th Portal Vein Thrombosis – Youssef Barbour, MD

ADDITIONAL LEARNING OPPORTUNITIES

- AK ID ECHO: HCV, HIV, PrEP, STIs
  - The 2nd Tuesday of every month from 12:00-1:00PM Alaska Standard Time
    - 1CE/CME offered per session
  - anthc.org/project-echo/hcv-hiv-prep-stis-echo
- LiverConnect Webinar Program
  - Second Tuesday of every month 8:00-9:00AM Alaska Standard Time
    - Full Hour didactic topics on Liver Disease and related topics 1CE/CME offered
  - anthc.org/what-we-do/clinical-and-research-services/hep/liverconnect/



AK LIVER DISEASE ECHO -TEAM CONTACTS

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- ANTHC Liver Disease and Hepatitis Program: 907-729-1560
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Thank you

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