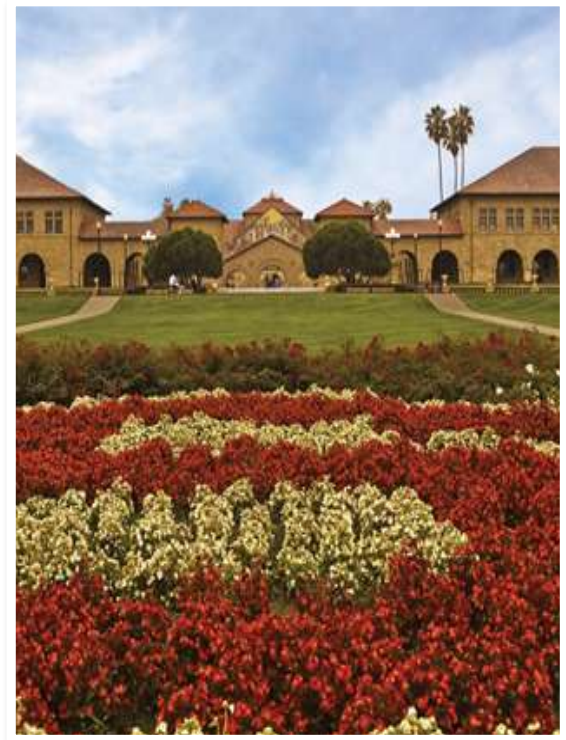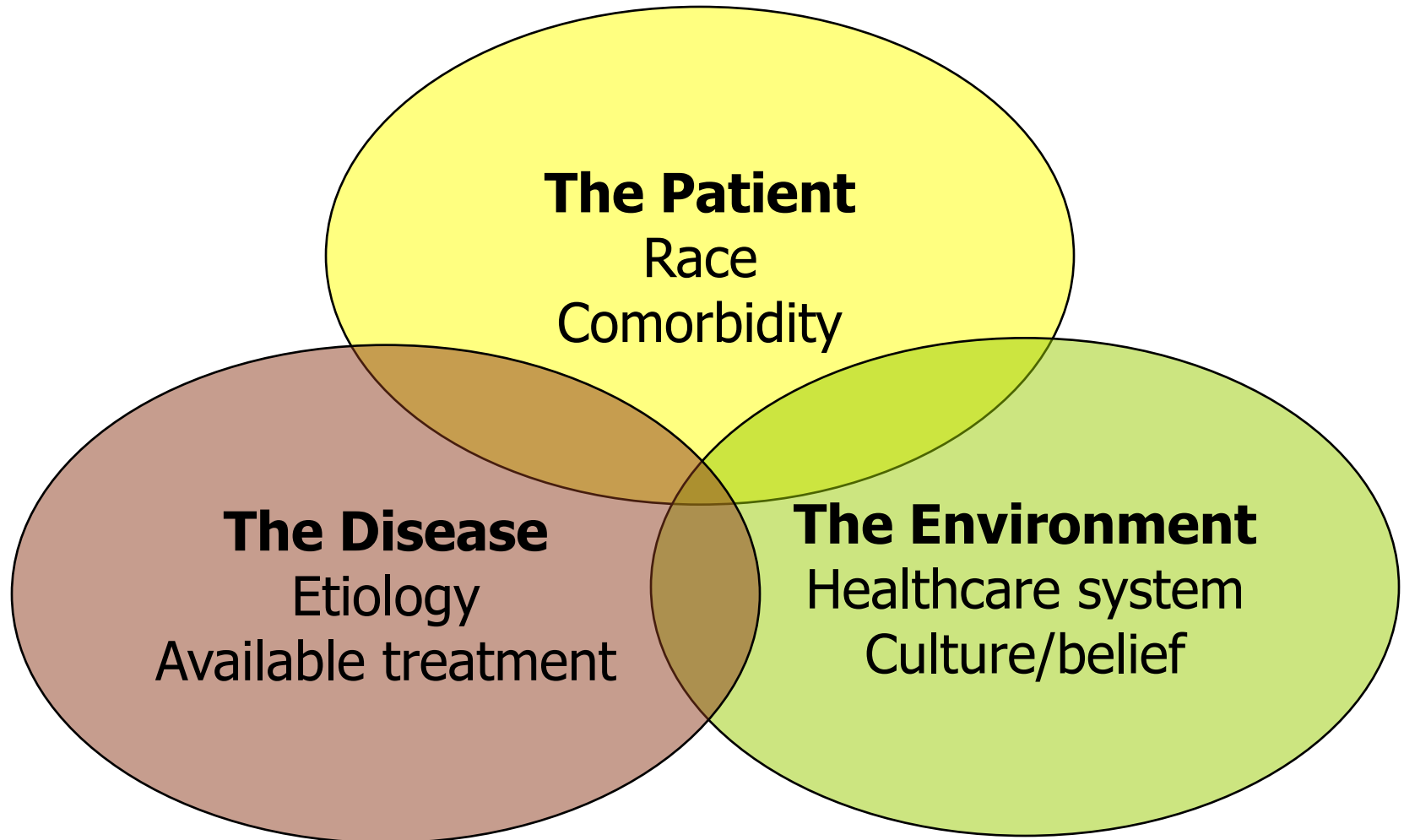# Clinical Staging of HCC: A Western Perspective
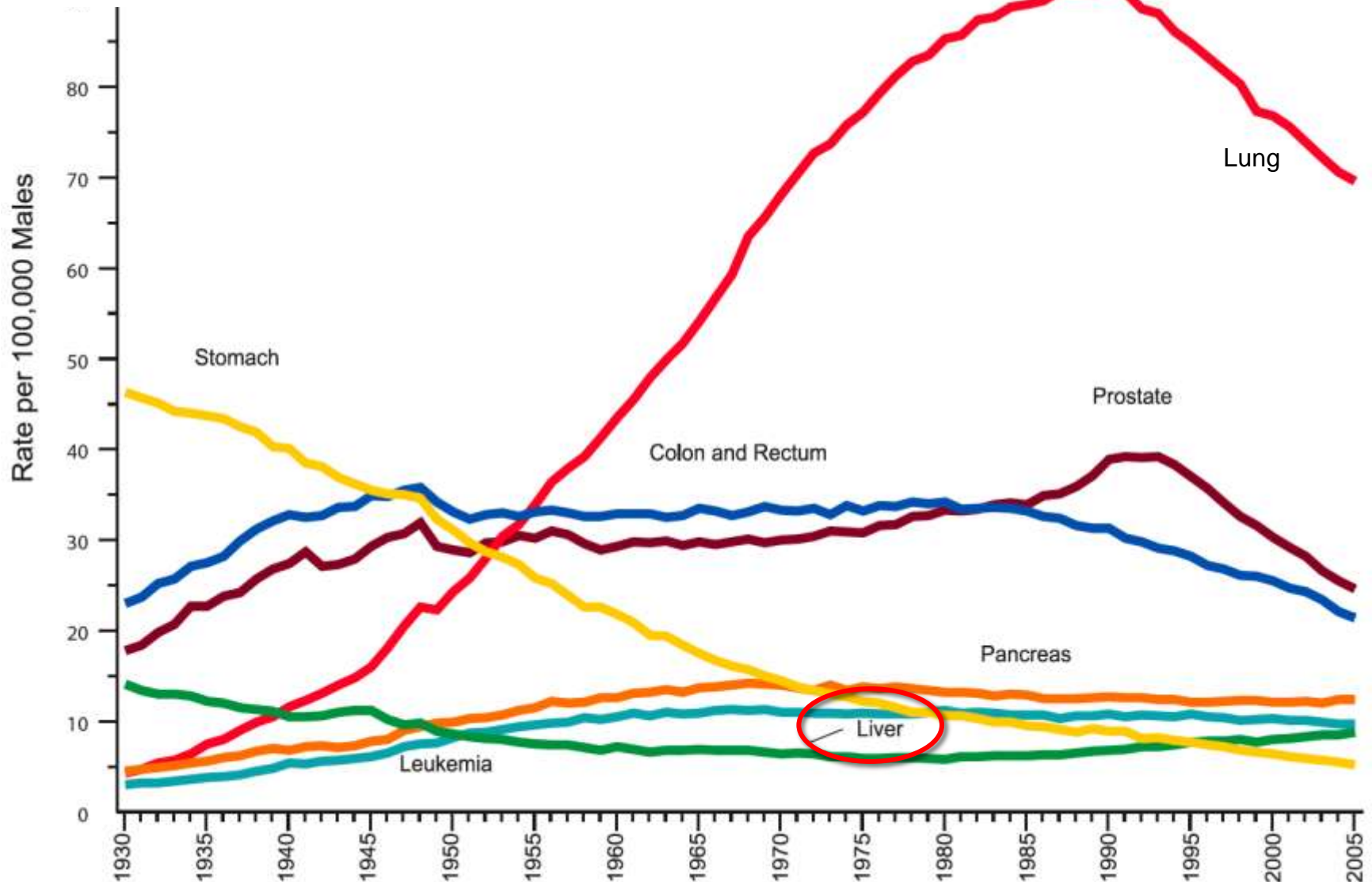
W. Ray Kim, MD

Professor and Chief

Gastroenterology and Hepatology

Stanford University School of Medicine

Mortality from Malignancies in US

Changing Epidemiology of HCC

Olmsted County data

	1976-1990	1991-2000	2001-2008
Incidence*	3.5	3.5	6.8
Age	63.5	60.7	69.4
White	93%	85%	75%
HCV	0%	23%	45%
HBV	10%	4%	4%
EtOH	43%	35%	36%
Unknown cause	33%	42%	17%

*per 100,000 per year

Yang. Mayo Clin Proc. 2012;87(1):9

Super-sizing of America

Autopsy in decedents of non-natural causes (1981-2010, n=465)

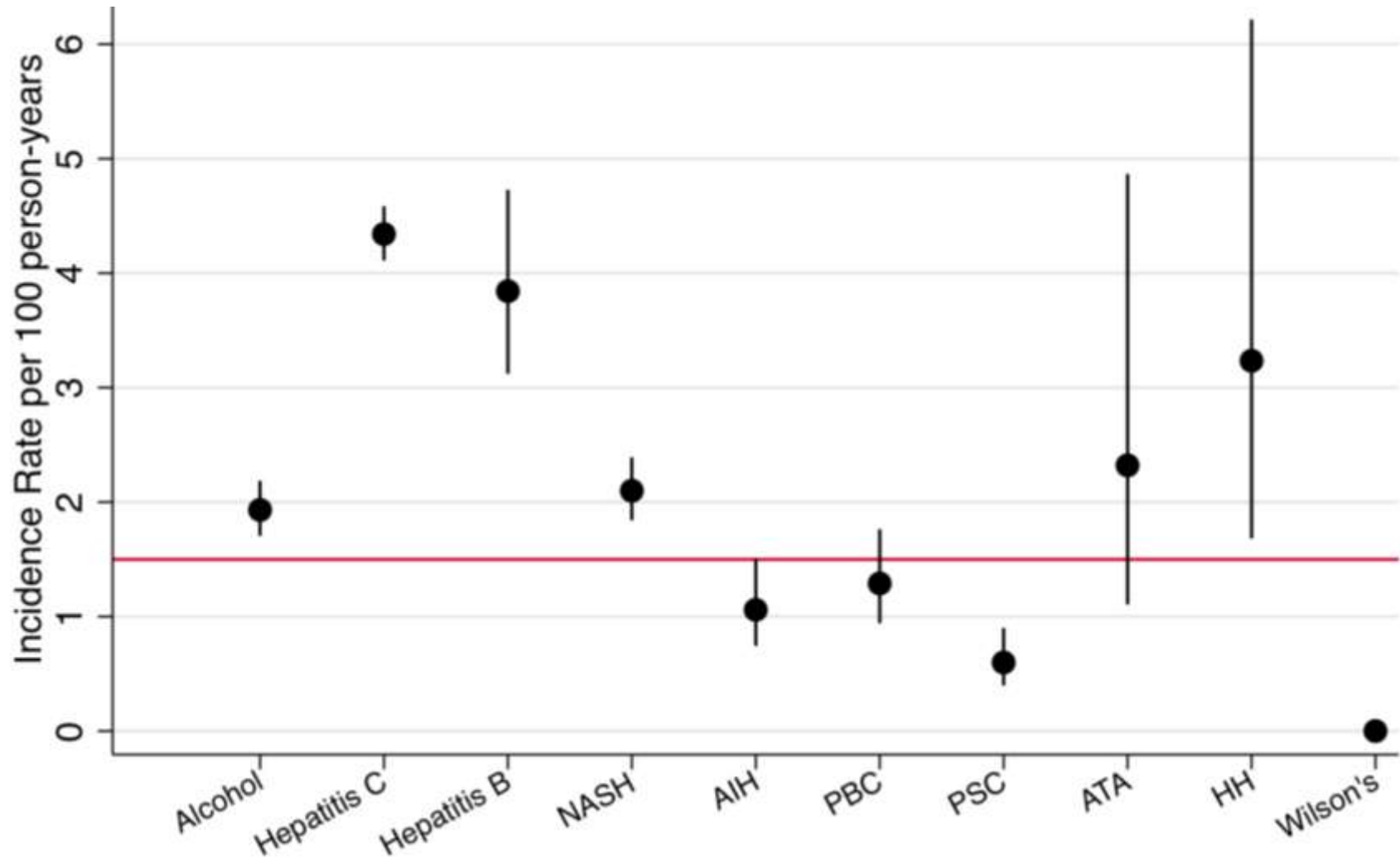|	1981-1990	1991-2000	2001-2010
Mean Age (Yrs)	37.2	37.3	37.3
Male	71%	74%	75%
Mean BMI	23.9	26.5	27.8
Obesity	11%	26%	29%
Fatty liver	15.0%	33.2%	44.3%
NASH	1.6%	2.9%	4.1%

Incident HCC on Transplant Waitlist

- UNOS data (2002-2011)
  - Incidence of de novo HCC on UNOS waitlist
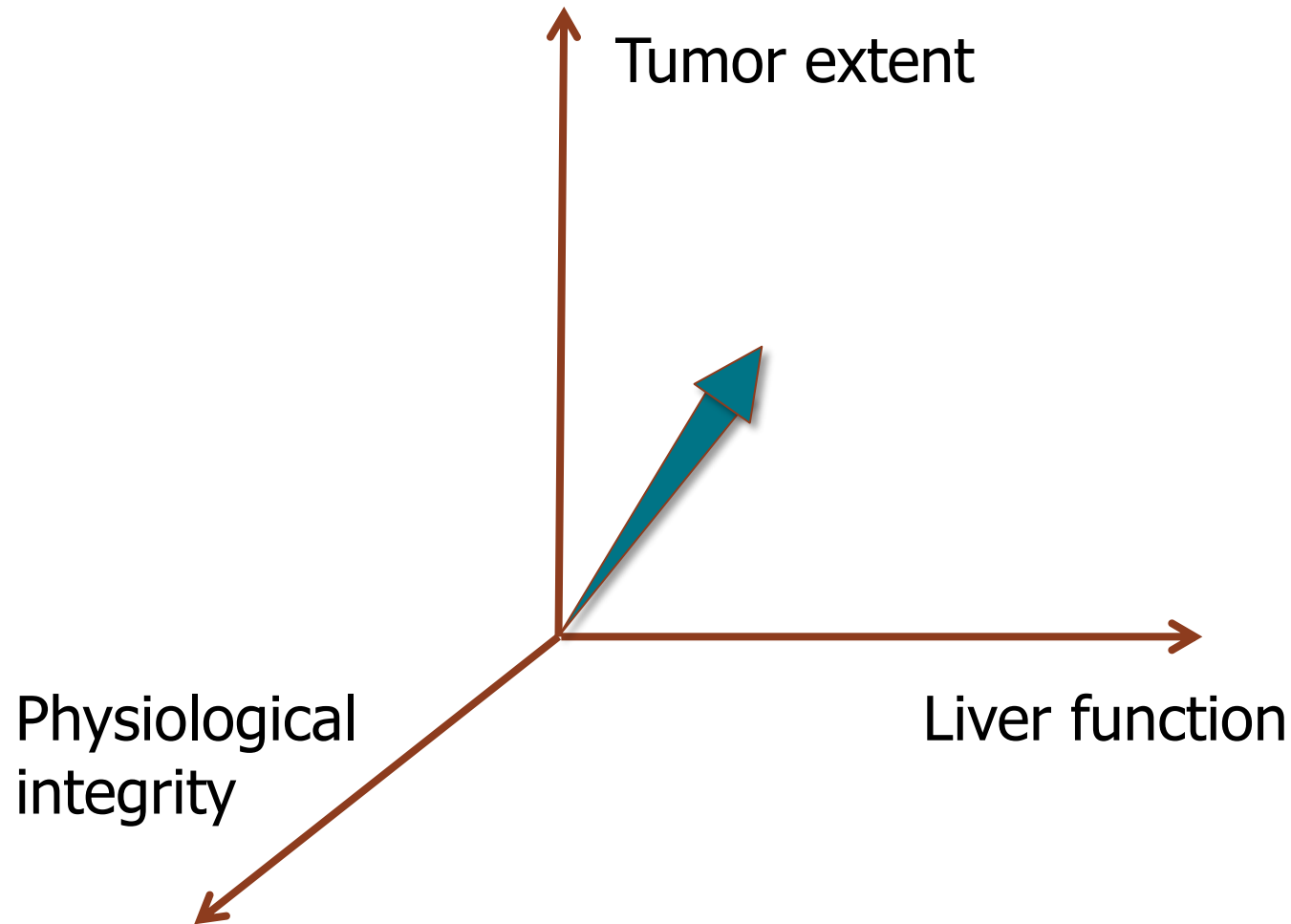 - 1,960 new HCCs in 34,932 waitlist registrants
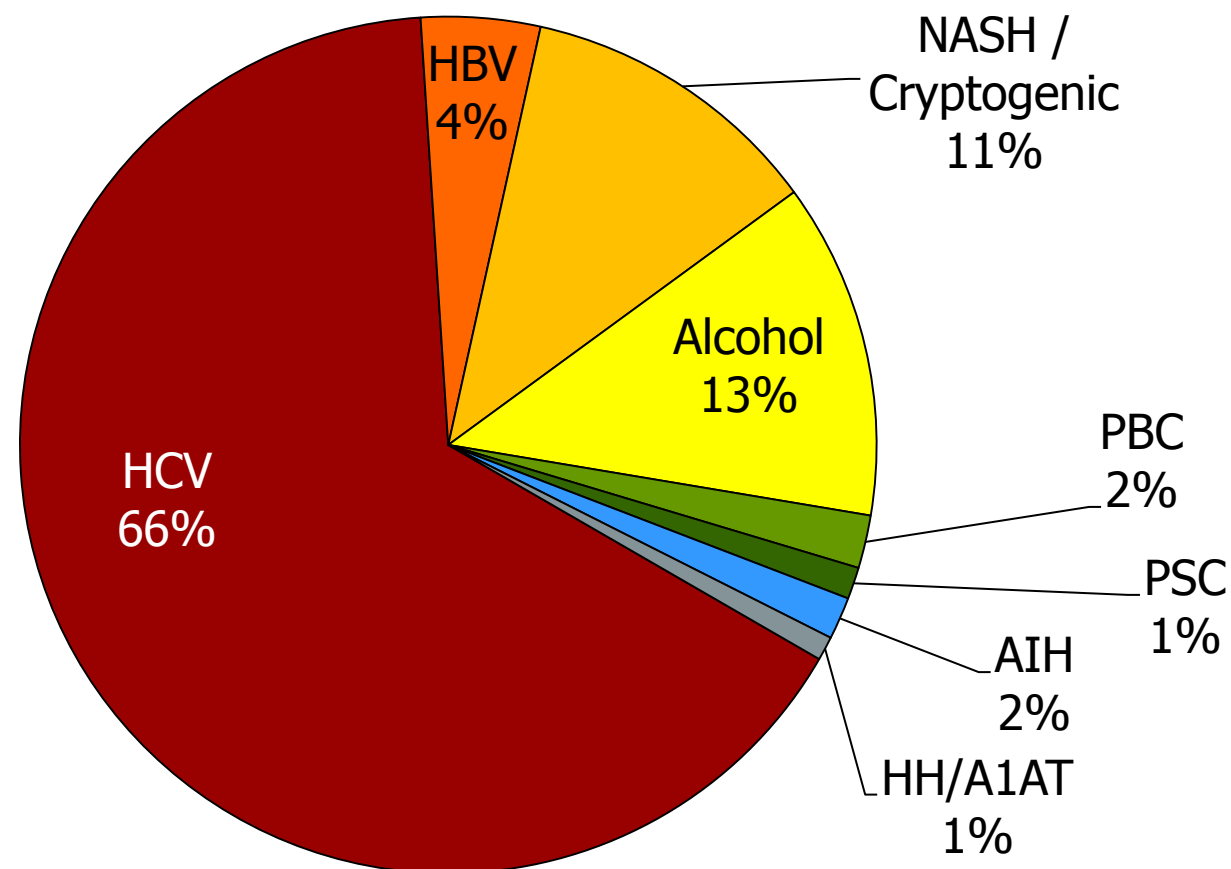
Incidence of HCC by Etiology

UNOS DATA (2002-2011)

Dimensions in HCC Prognosis

Tumor extent

Liver function

Physiological
integrity

HCC Staging Systems

Author (year)	n	Tumor Stage	Liver Function	Health Status
			Prognostic Variables	
Primack (1975)[8]	72	—	Ascites, bilirubin, portal hypertension	Weight loss
Chlebowski (1984)[9]	121	Metastases	Bilirubin	Age
Attali (1987)[10]	127	—	Encephalopathy, alcohol bilirubin, AST, BUN	—
Falkson (1988)[11]	432	—	Jaundice	Male sex, PS, appetite, age
Calvet (1990)[12]	206	Tumor size Metastases	Bilirubin, serum sodium BUN, GGT, ascites	Constitutional syndrome age
Stuart (1996)[13]	314	Portal vein invasion AFP	Albumin	—
CLIP (1998)[14]	435	Tumor morphology AFP, portal vein invasion	Child-Pugh	—
Chevret (1999)[18]	761	Portal vein invasion AFP	Bilirubin Alkaline phosphatase	Karnofsky
Llovet (1999)[15]	102	Portal vein invasion, metastases	—	PS
Villa (2000)[16]	96	Estrogen receptor status	Bilirubin	—
CUPI (2002)[19]	926	TNM AFP	Bilirubin, ascites Alkaline phosphatase	Symptoms
JIS (2003)[20]	722	TNM by LCSGJ	Child-Pugh	—
SLiDe (2004)[21]	177	TNM by LCSGJ	Liver damage by LCSGJ, PIVKA	—
Tateishi (2005)[22]	403	Size and number	Albumin Bilirubin	—

Sala. Sem Liver Dis 2005;171

CLIP Score

Variable	0	1	2
CTP Class	A	B	C
Tumor morphology	Uninodular and <50% of liver volume	Multinodular and <50% of liver volume	Massive or >50% of liver volume
AFP	<400	$\geq$ 400	-
Portal vein invasion	No	Yes	-

Cancer of the Liver Italian Program. Hepatology 1998;751

BCLC Classification
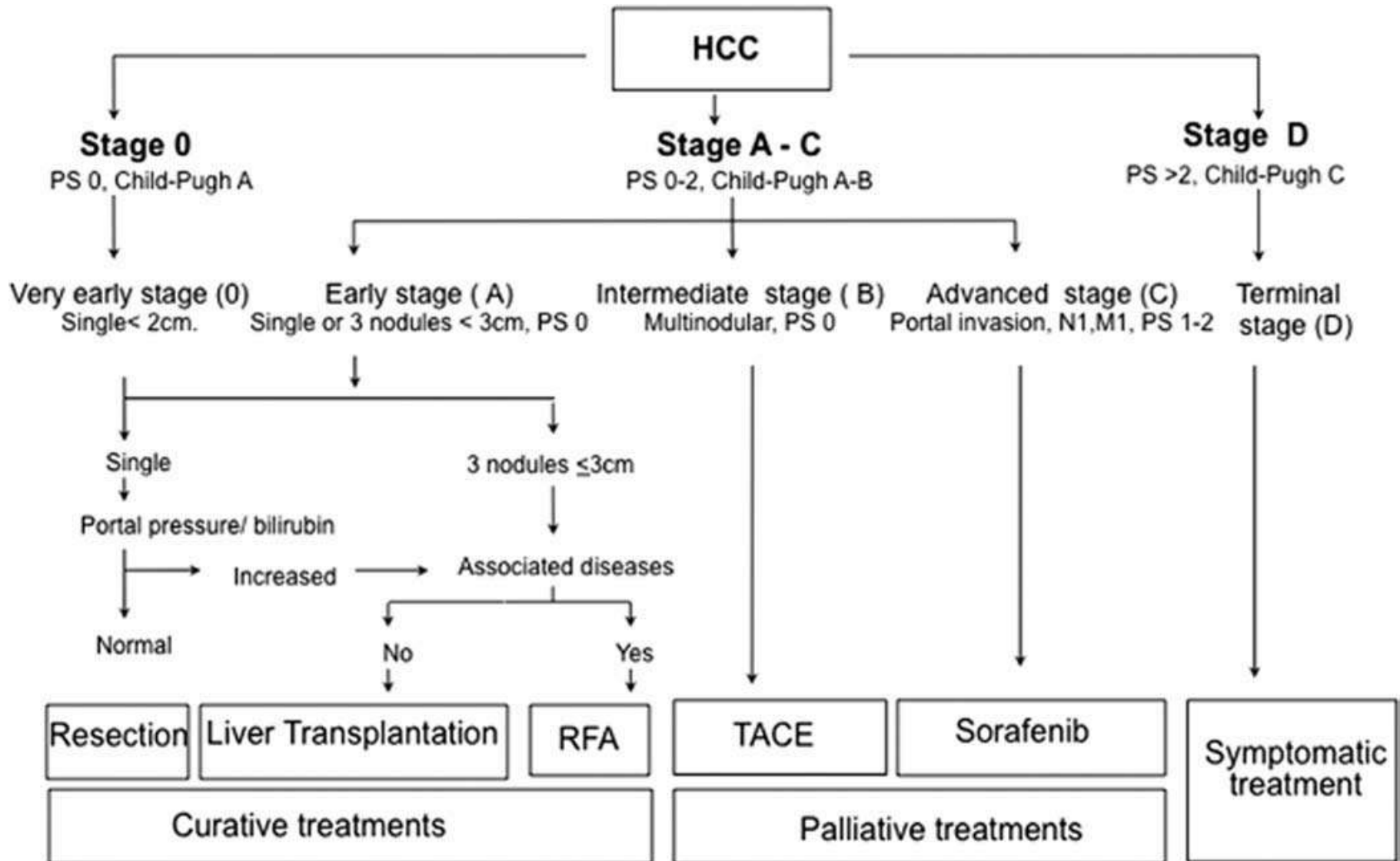
MESIAH
Model to Estimate Survival in Ambulatory HCC Patients

HCC with viral etiology seen at Mayo Clinic (1994-2008, n=477)

HCV (82%) Cirrhosis (HCV) White (85%)

Variable	Data	Variable	Data
Age	56 [51-67]	MELD	9.2 [6.5-12.7]
Albumin	3.4 [2.9-3.8]	AFP	47.9 [8.8-588.0]
Size of the largest nodule		Number of nodules	
<=1cm	14 (3%)	1	249 (53%)
1-2cm	82 (18%)	2	81 (17%)
2-3cm	109 (24%)	3	43 (9%)
3-5cm	122 (26%)	4	29 (6%)
5-10cm	104 (23%)	>=5	72 (15%)
10-15cm	21 (5%)	Vascular invasion	103 (22%)
15-20cm	9 (2%)	Distant metastasis	32 (7%)

Yang. Hepatology 2012;56:614

Multivariable Analysis

Variable	Hazard Ratio	P value
Age (in decades)	1.262 (1.128, 1.412)	<0.01
MELD[†]	1.104 (1.064, 1.147)	<0.01
Albumin	0.676 (0.538, 0.851)	<0.01
Number of Nodules	1.166 (1.062, 1.280)	<0.01
Size of Largest Nodule	1.336 (1.182, 1.511)	<0.01
AFP	1.086 (1.028, 1.146)	<0.01
Extrahepatic Metastasis	3.095 (1.865, 5.137)	<0.01
Vascular invasion	3.070 (2.177, 4.328)	<0.01

Yang. Hepatology 2012;56:614

Application of MESIAH

MESIAH Score =   0.232 * (Age in Decades)
                 + 0.099 * (MELD)
                 - 0.391 * (Albumin)
                 + 0.290 * (Tumor size)
                 + 0.153 * (Tumor number)
                 + 1.122 * (Vascular invasion)
                 + 1.130 * (Metastasis)
                 + 0.082 * (AFP) + 1

Case	Age	MELD	# Nodules	Size	Vascular Invasion	Metastasis	Albumin	AFP	Risk Score
1	50.0	6.0	1	4.0	0	0	4.2	5.0	2.97
2	56.5	6.8	4	4.0	0	0	3.5	5.2	4.44
3	70.0	15.0	4	5.5	1	0	3.0	50.0	6.45

Yang. Hepatology 2012;56:614

Application of MESIAH

Case	Age	MELD	# Nodules	Size	Vascular Invasion	Metastasis	Albumin	AFP	Risk Score
1	50.0	6.0	1	4.0	0	0	4.2	5.0	2.97
2	56.5	6.8	4	4.0	0	0	3.5	5.2	4.44
3	70.0	15.0	4	5.5	1	0	3.0	50.0	6.45

Yang. Hepatology 2012;56:614
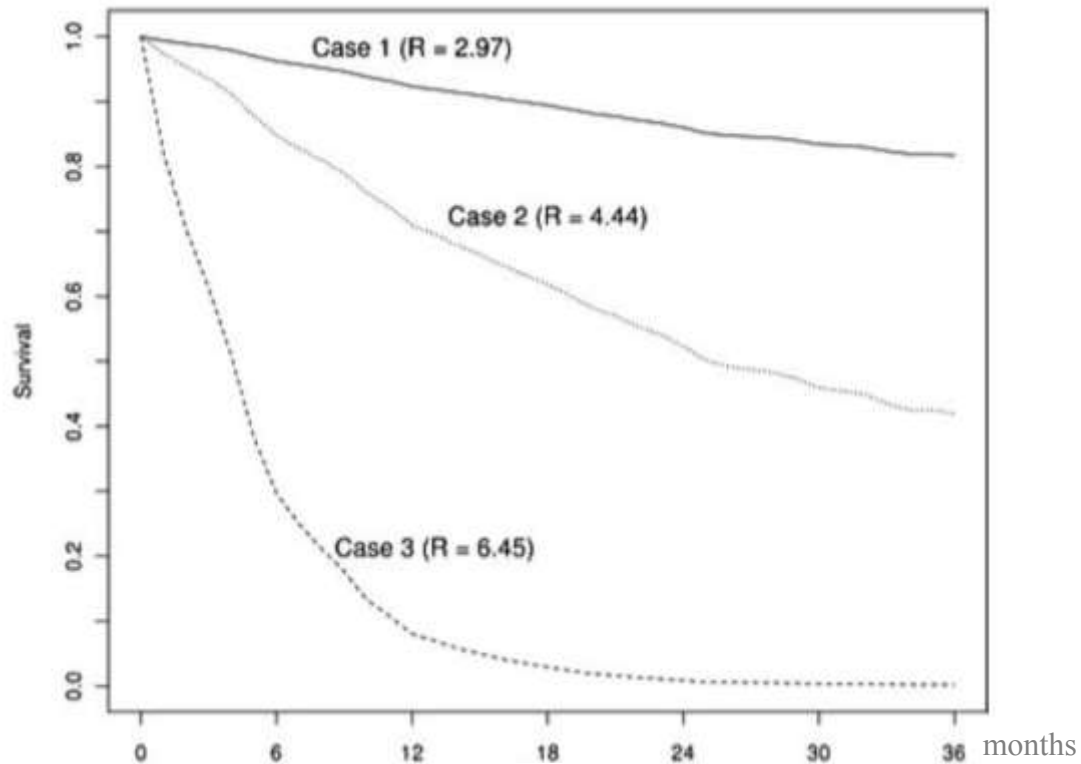
Application of MESIAH

Grand Rounds

Clinical Updates

Publications

Sign up for email newsletters

The Model to Estimate Survival In Ambulatory HCC Patients (MESIAH)

To estimate survival of ambulatory patients with hepatocellular carcinoma, please enter the following variables:

TOP RANKED MORE OFTEN

Mayo Clinic is highly ranked for quality more often than any other academic medical center in the nation.

MAYO CLINIC

Learn More

Question	Answer
What is the age(years)?	55
What is the MELD score?	10
What is serum albumin (g/dL)?	3.9
What is the diameter of the largest tumor nodule (cm)?	5
How many tumor nodules?	1
Is there vascular invasion?	○ Yes ● No
Is there extrahepatic metastasis?	○ Yes ● No
What is serum AFP (ng/mL)?	4000

MESIAH score: [   ]

Compute   Reset form

Yang. Hepatology 2012;56:614

Application of MESIAH

The Model to Estimate Survival In Ambulatory HCC Patients (MESIAH)

Grand Rounds

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How many tumor nodules?	1
Is there vascular invasion?	○ Yes ● No
Is there extrahepatic metastasis?	○ Yes ● No
What is serum AFP (ng/mL)?	4000

MESIAH score: 4.01

Compute   Reset form

Yang. Hepatology 2012;56:614

Application of MESIAH

MESIAH score: 4.01

[Compute] [Reset form]

Probability of Survival

1 Month	3 Months	6 Months	12 Months	24 Months	36 Months
0.98	0.96	0.9	0.8	0.66	0.57

This online calculator is based on the following publication:

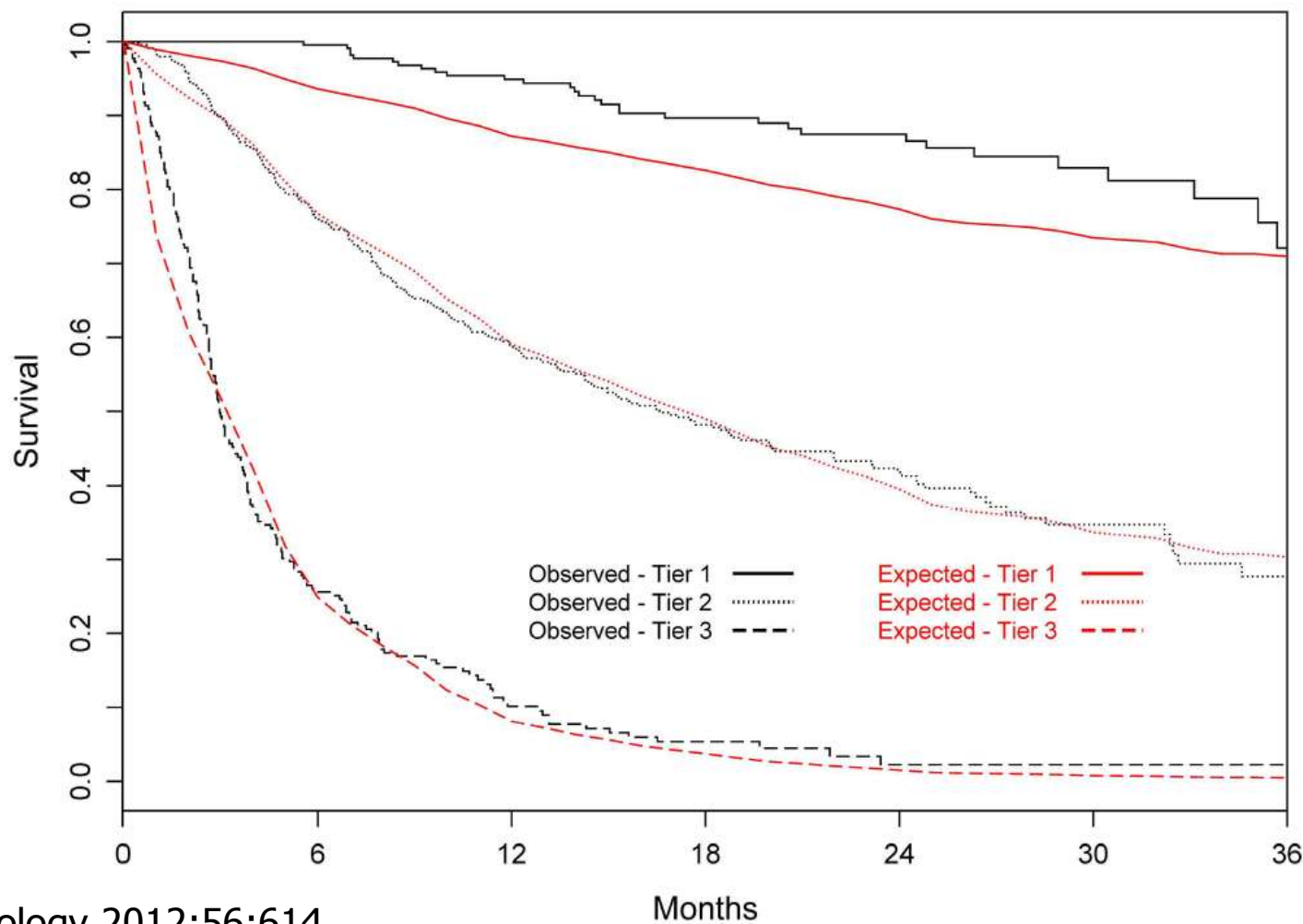Yang, JD. Model to estimate survival in ambulatory patients with hepatocellular carcinoma. Hepatology. 2012; 56: 614.
http://www.ncbi.nlm.nih.gov/pubmed/22370914.

www.mayoclinic.org\MELD

Yang. Hepatology 2012;56:614

Validation

904 patients at Korean National Cancer Center (2000-3)

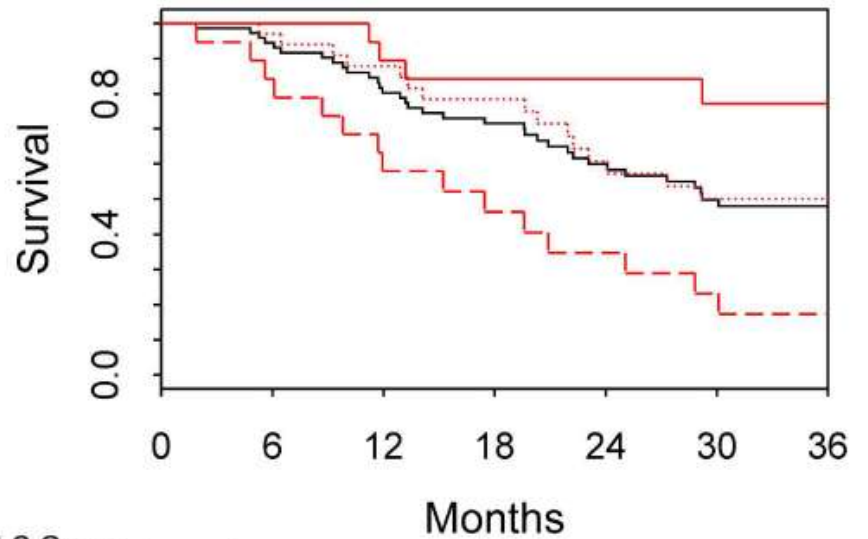HBV (75%) Cirrhosis (73%)

Yang. Hepatology 2012;56:614

Concordance
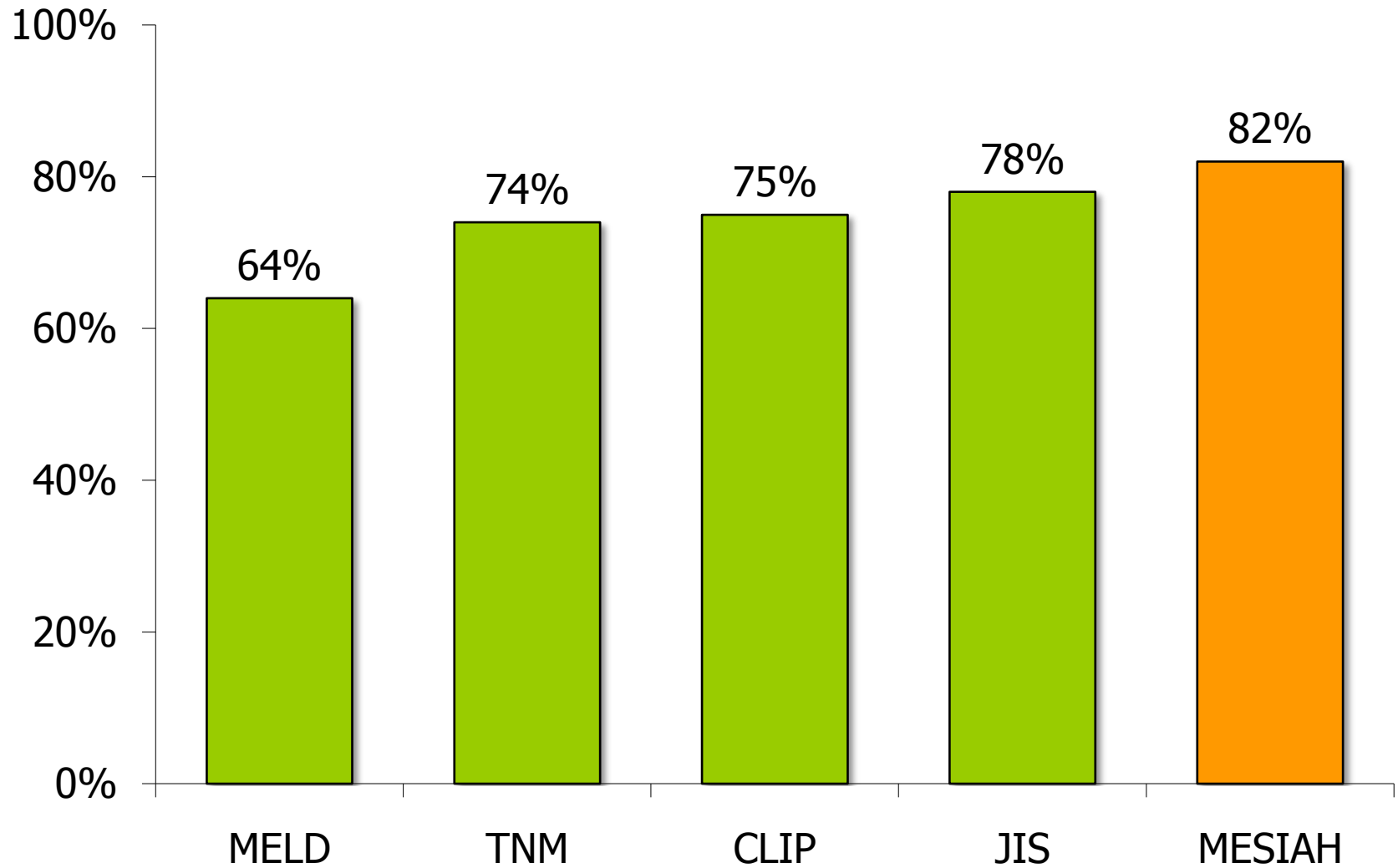
BCLC 0/A   BCLC B   BCLC C   BCLC D
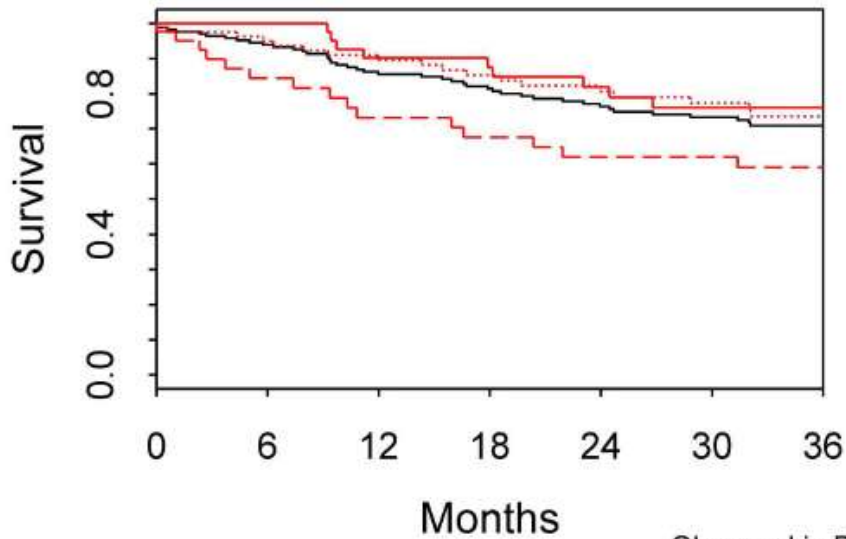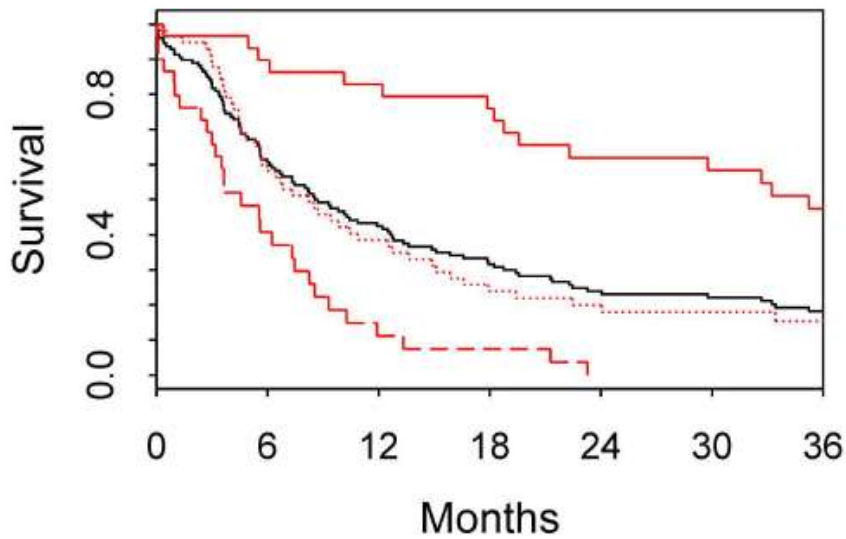
Observed in BCLC Group
Risk - Tier 1
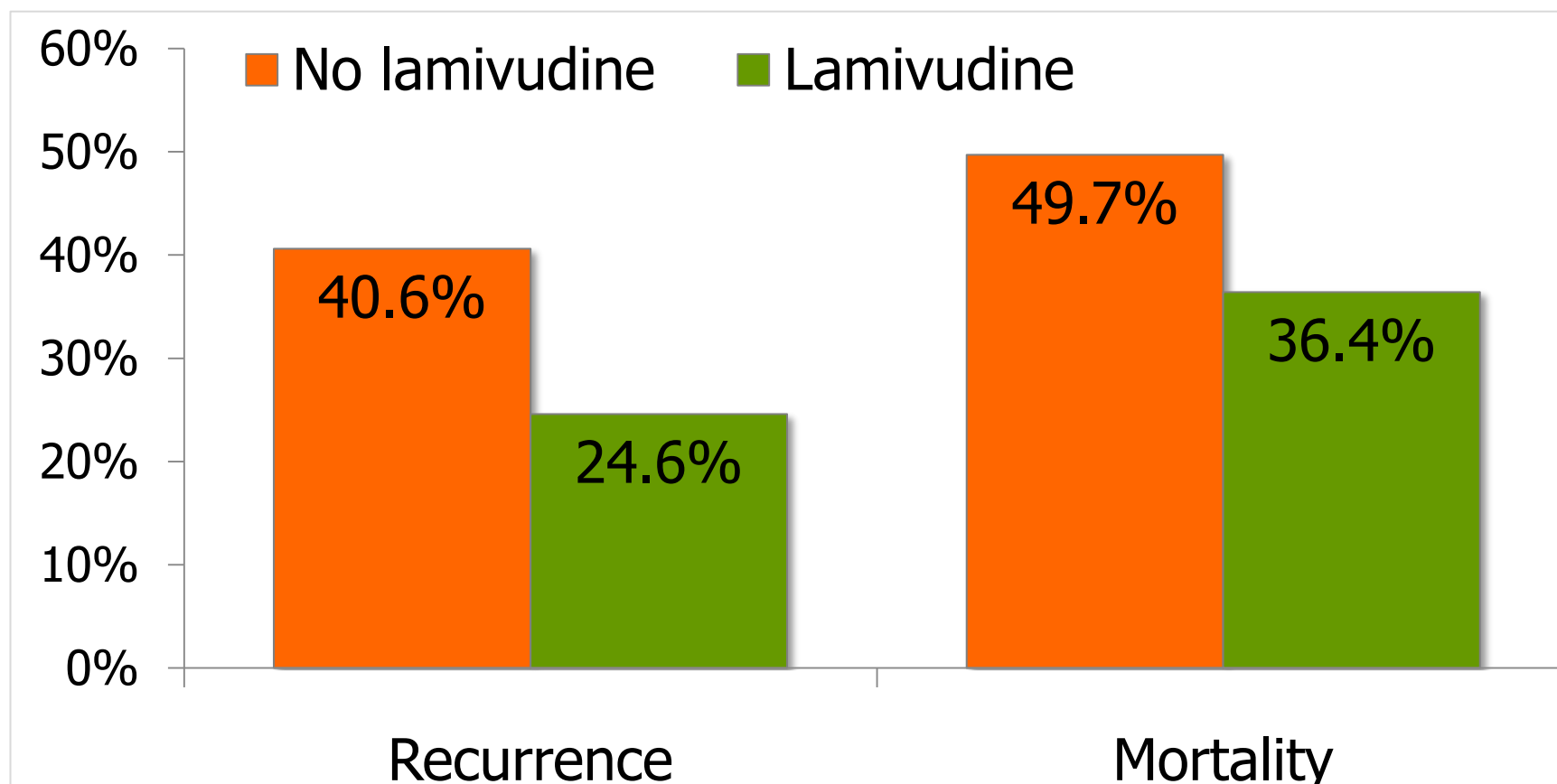Risk - Tier 2
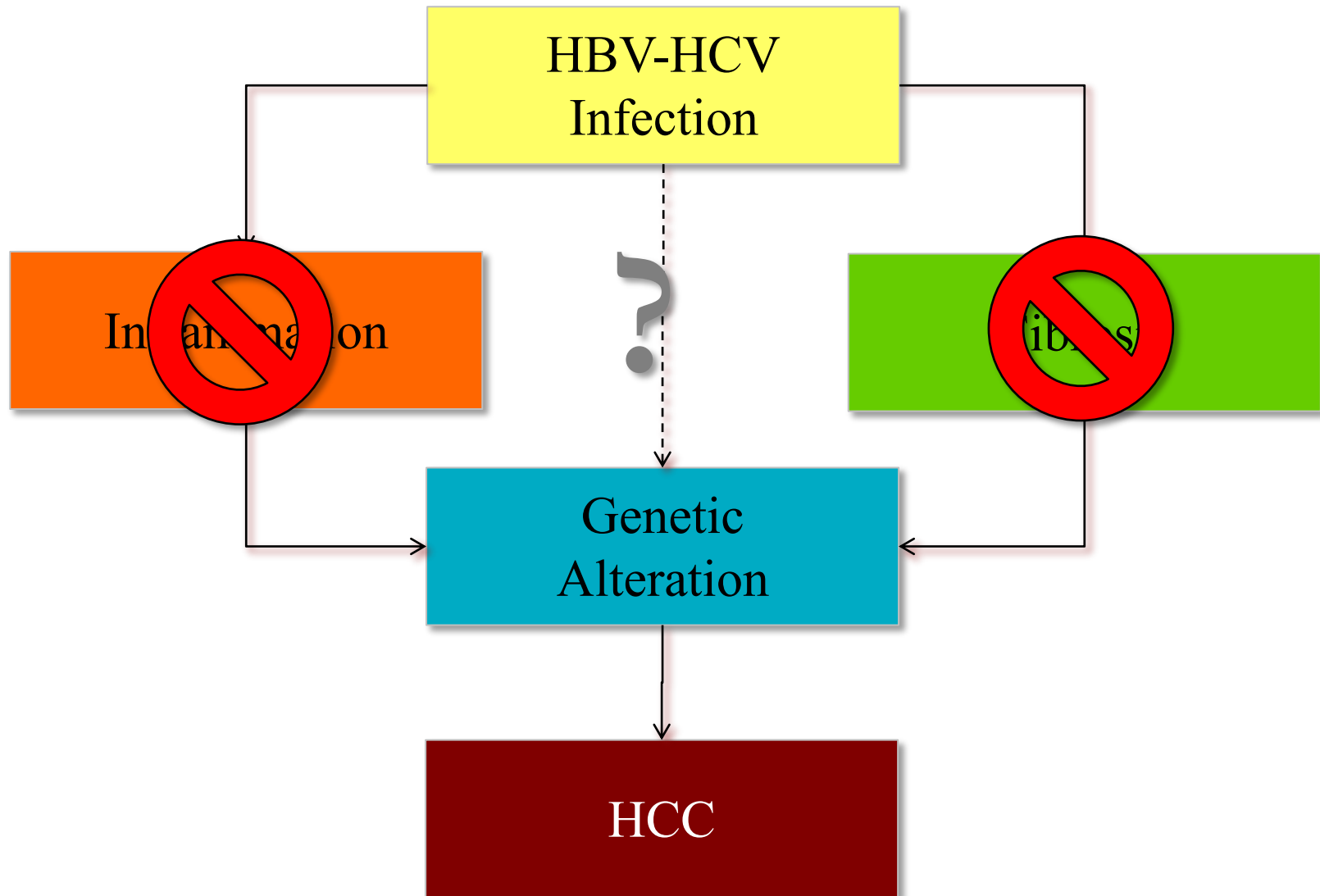Risk - Tier 3

Yang. Hepatology 2012;56:614
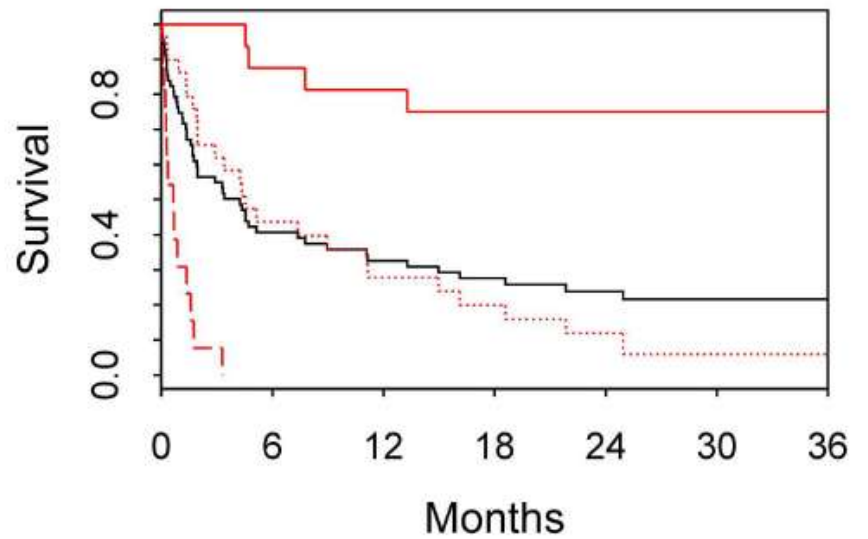
Anti-HBV Tx after HCC Resection

Taiwan National Health Insurance Research Database

- 81,117 newly diagnosed HCC (03-08)
- 3,189 with HBV had curative resection

No lamivudine ■ **Lamivudine** ■

	Recurrence	Mortality
No lamivudine	40.6%	49.7%
Lamivudine	24.6%	36.4%

Wu. JAMA 2013

22

Effect of Antivirals on HCC Risk

Incidence of HCC by Etiology

Flemming. AASLD 2012. Abstract 1931
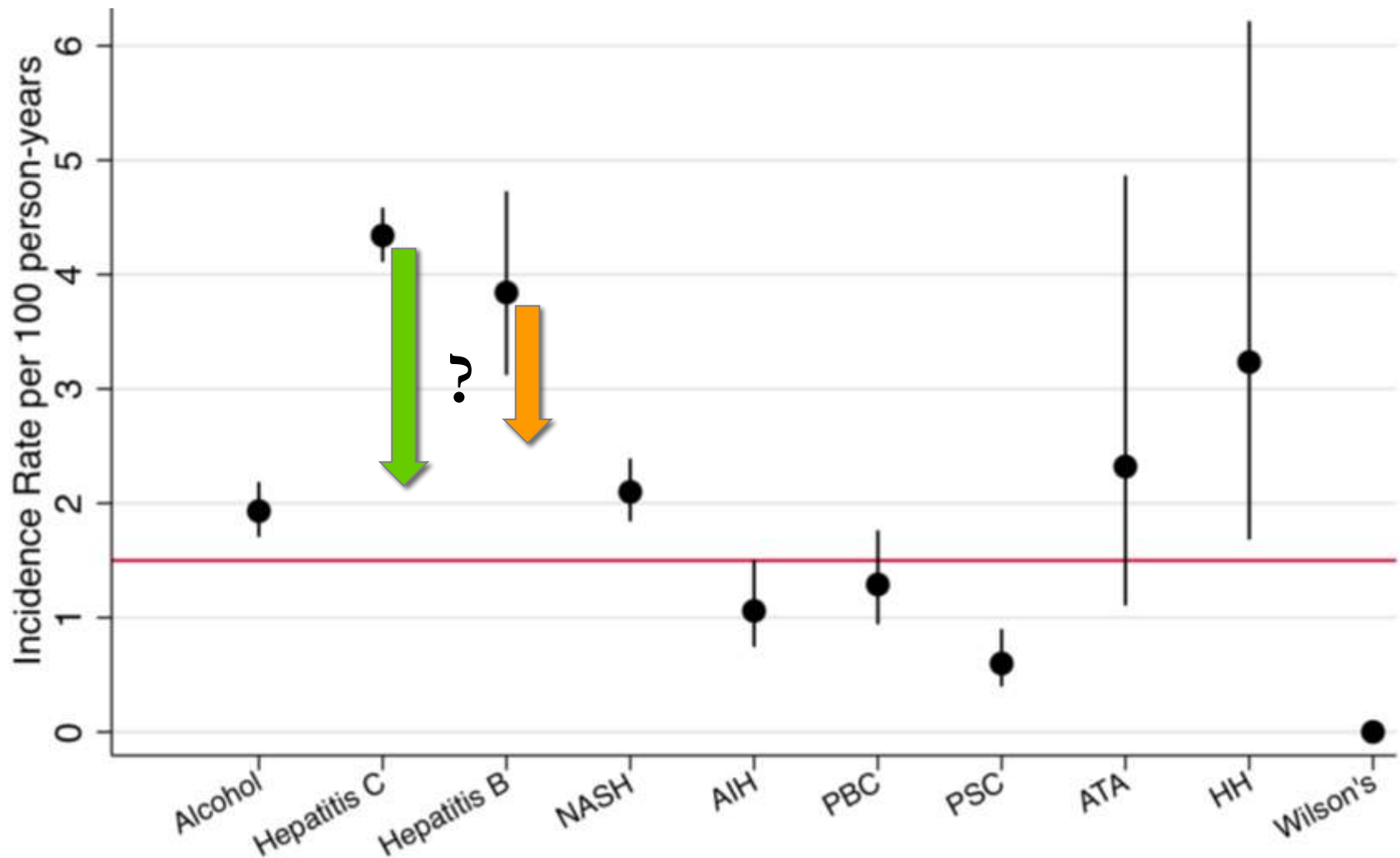
ADRESS-HCC Model

Variable	Score
Age (per year)	1
Diabetes	4
Non-Caucasian **R**ace	4
Etiology - Alcohol/Metabolic* - Viral	7 23
Male **S**ex	10
CTP **S**core	2
Threshold**	88

Example	Case 1	Case 2
Age	50	60
Diabetes	0	4
Non-Caucasian	4	4
Etiology - Alcohol - HBV	7 -	- 23
Male	0	10
CTP Score	10	14
Score	71	115

*Metabolic: NASH, HH, A1ATD, Cryptogenic
** Estimated incidence > 1.5%

Flemming. AASLD 2013

East versus West

The Patient
Race
Comorbidity

The Disease
Etiology
Available treatment

The Environment
Healthcare system
Culture/belief