



Texas Collaborative Center for Hepatocellular Cancer (TeCH)

FUNDED BY CANCER PREVENTION AND RESEARCH INSTITUTE OF TEXAS (CPRIT)

RP190641
AUGUST 31ST, 2019 – AUGUST 30TH, 2024

The goal of TeCH is to reduce HCC mortality in Texas by reducing the number of people who develop cancer or detecting it early when it is curable.



To support and enhance research collaborations among CAP researchers by providing multiple levels of connectivity and necessary research support

To setup the framework to educate healthcare providers, researchers, and the public on best practices and to engage private and public entities in policy considerations

To engage all stakeholders and solicit strategies to improve HCC-related prevention and care and to best disseminate those improvements

To begin disseminating results on best practices and new opportunities that will impact HCC in Texas

Organizational Structure of TeCH

Oversight, Evaluation, and Coordination	Research Support and Synergy	Dissemination and Implementation
Steering Committee	Scientific Committee	Clinical Network Committee
Administrative Core	Data and Biospecimen Core	Community Outreach Committee
External Advisory Committee		Annual Symposium Committee



Changing HCC Epidemiology in the United States and Texas

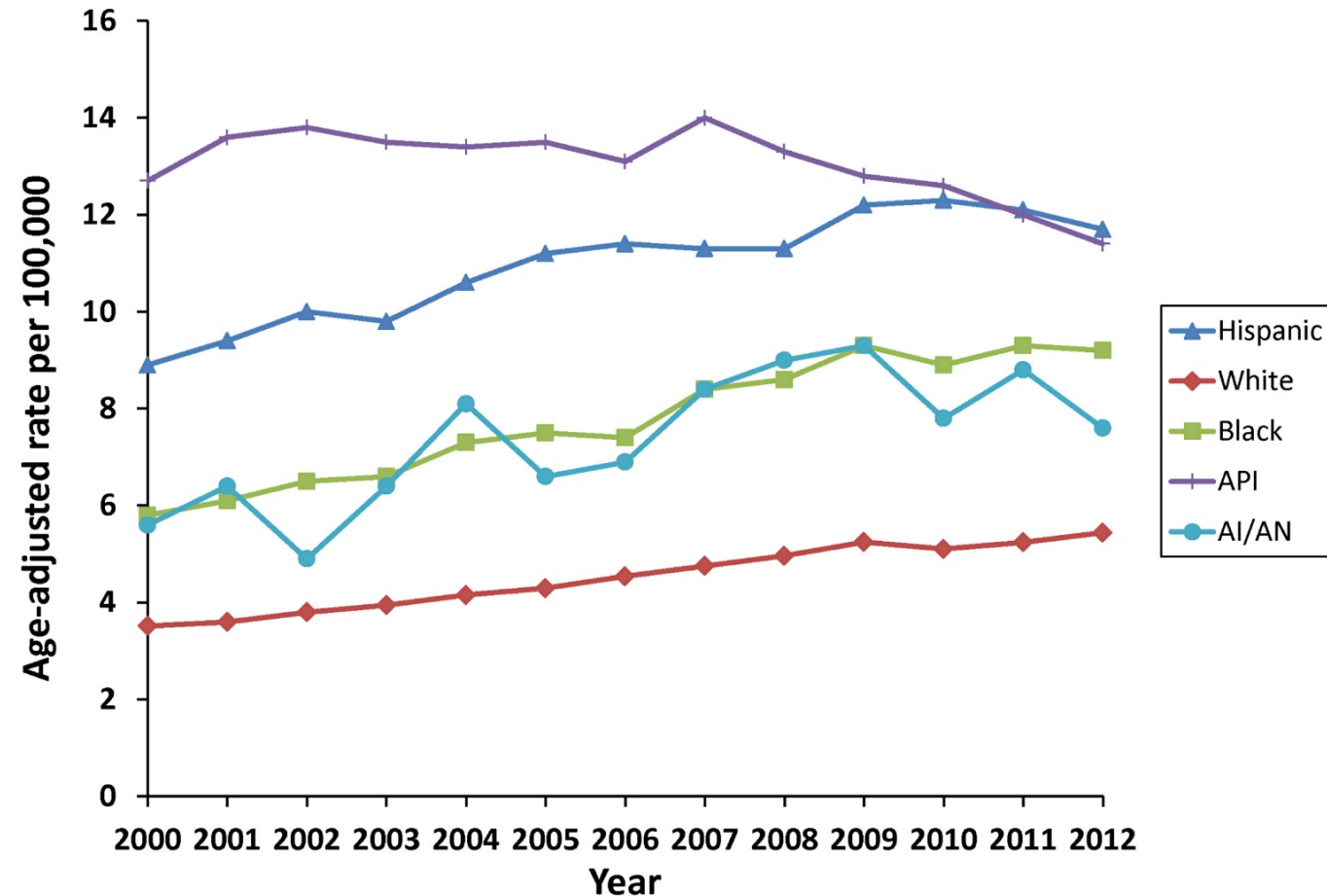
HASHEM B EL-SERAG, M.D., M.P.H.

PROFESSOR AND CHAIR OF MEDICINE

BAYLOR COLLEGE OF MEDICINE

HOUSTON TEXAS

Age-adjusted HCC Incidence Rates in the United States between 2000 and 2012

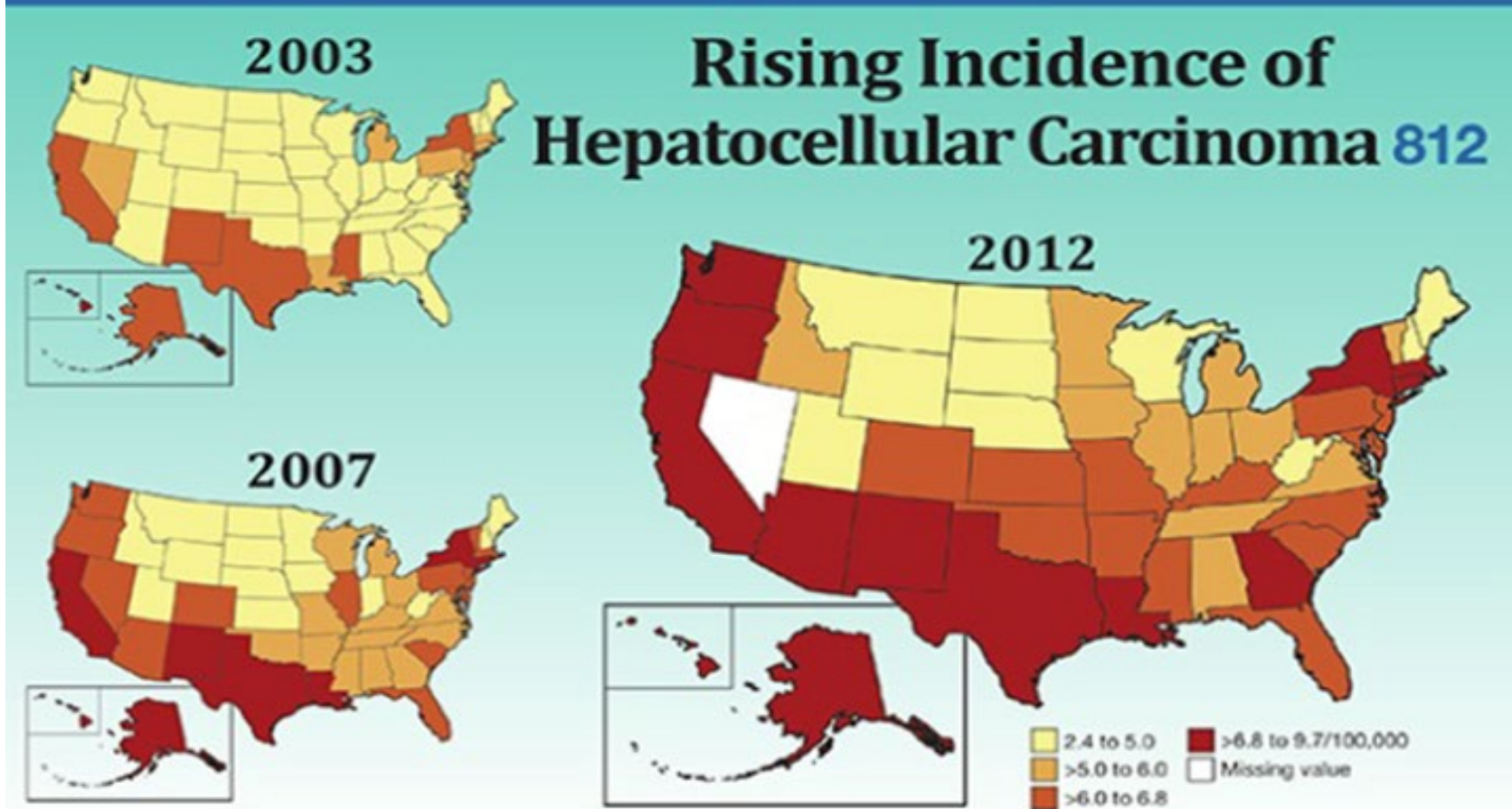


Gastroenterology

www.gastrojournal.org

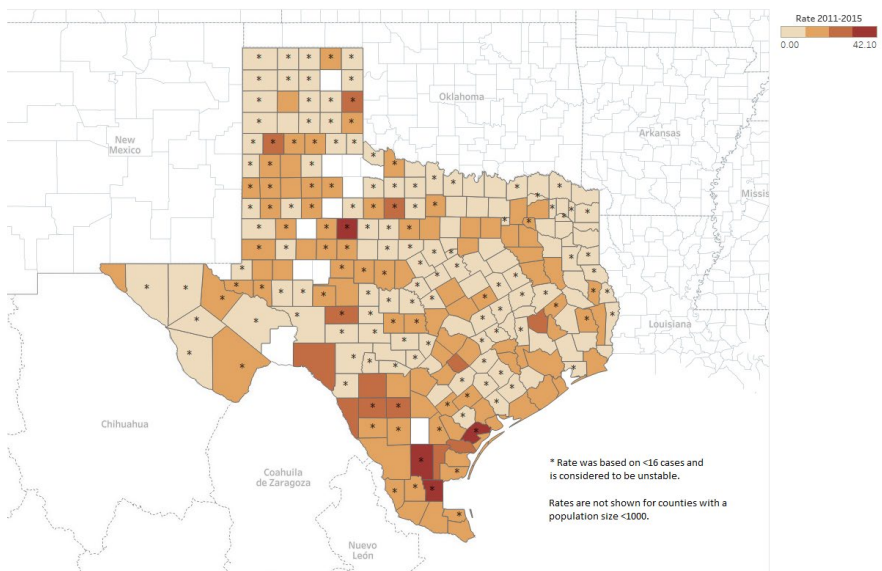
Volume 152 Number 4

March 2017

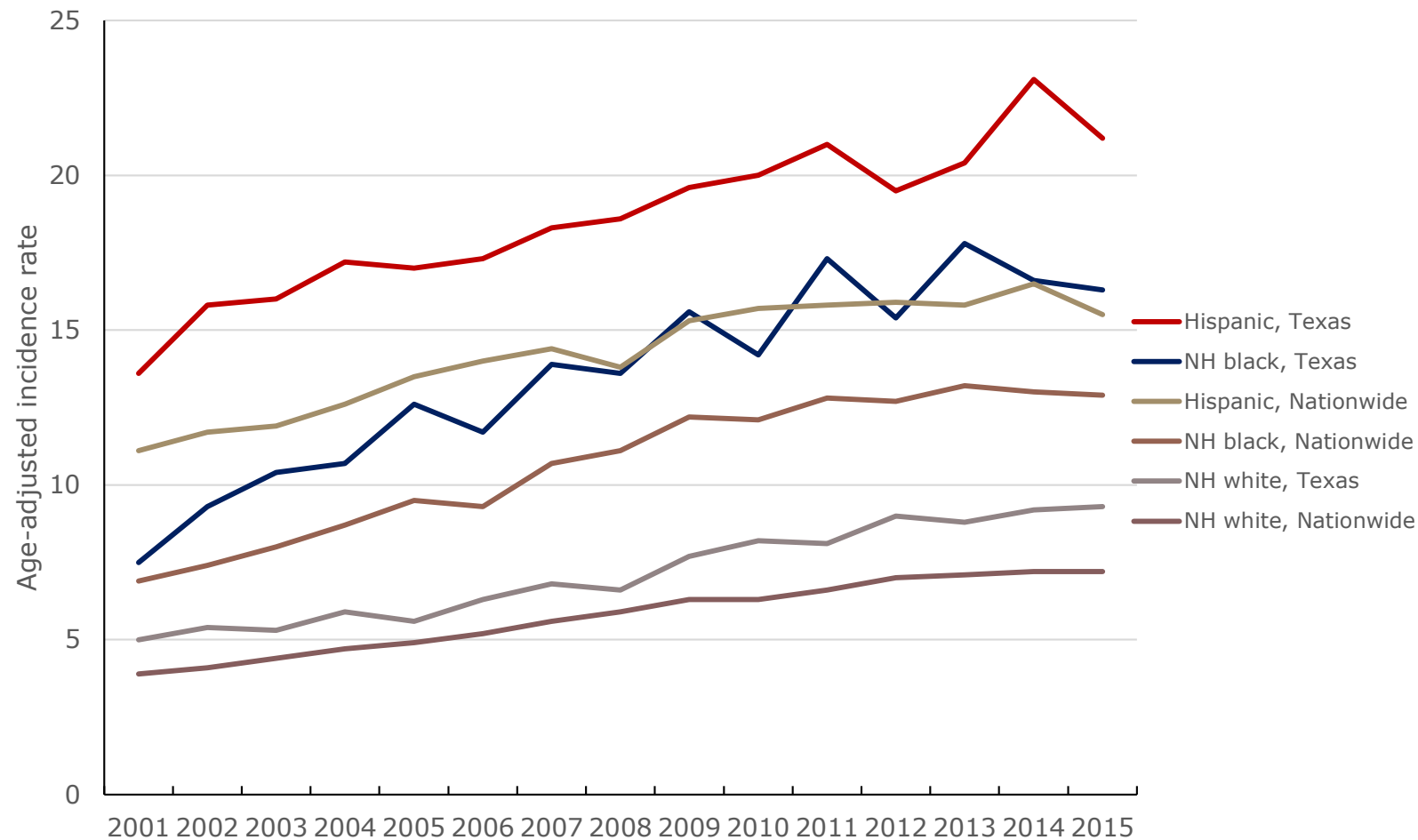


White et al, 2017.

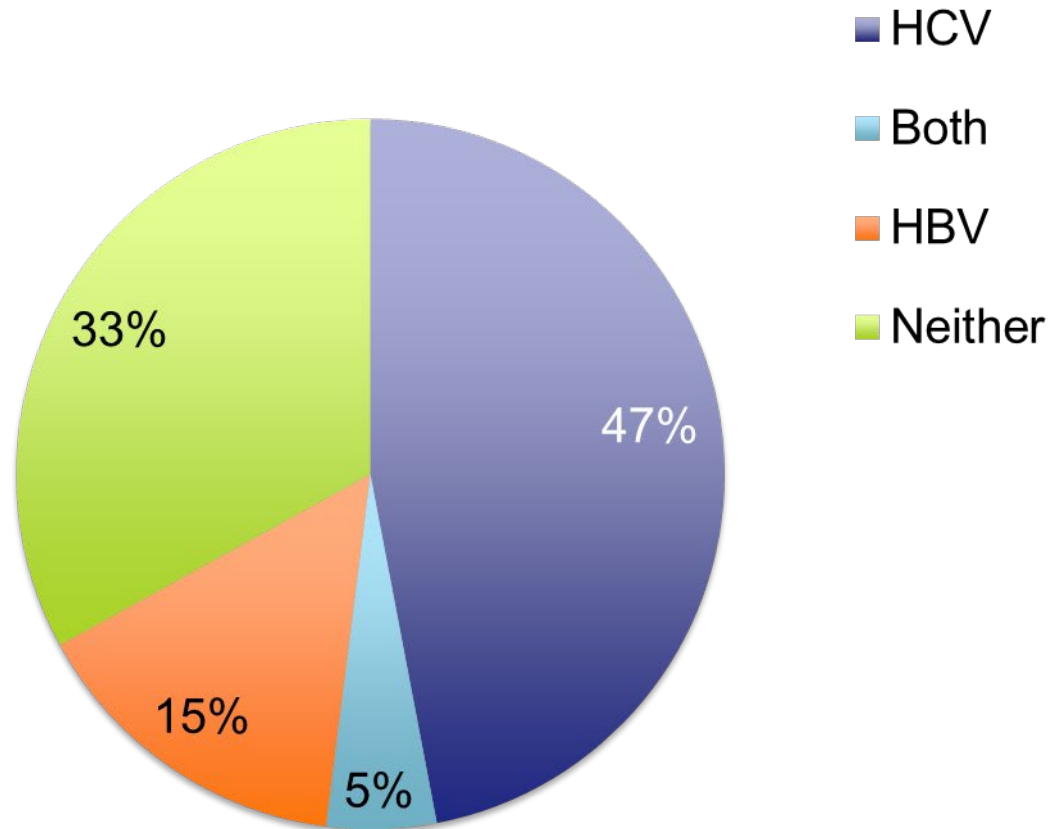
HCC Incidence Rates in Texas



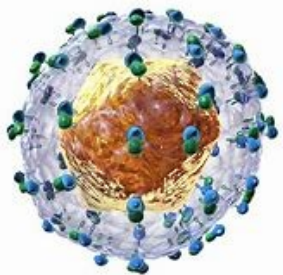
El-Serag et al 2019



HCV **was** the Dominant Risk Factor for HCC in the United States **(1999)**



(N=691)



Factors Associated With Increased HCC Risk in Patients with Active HCV Infection



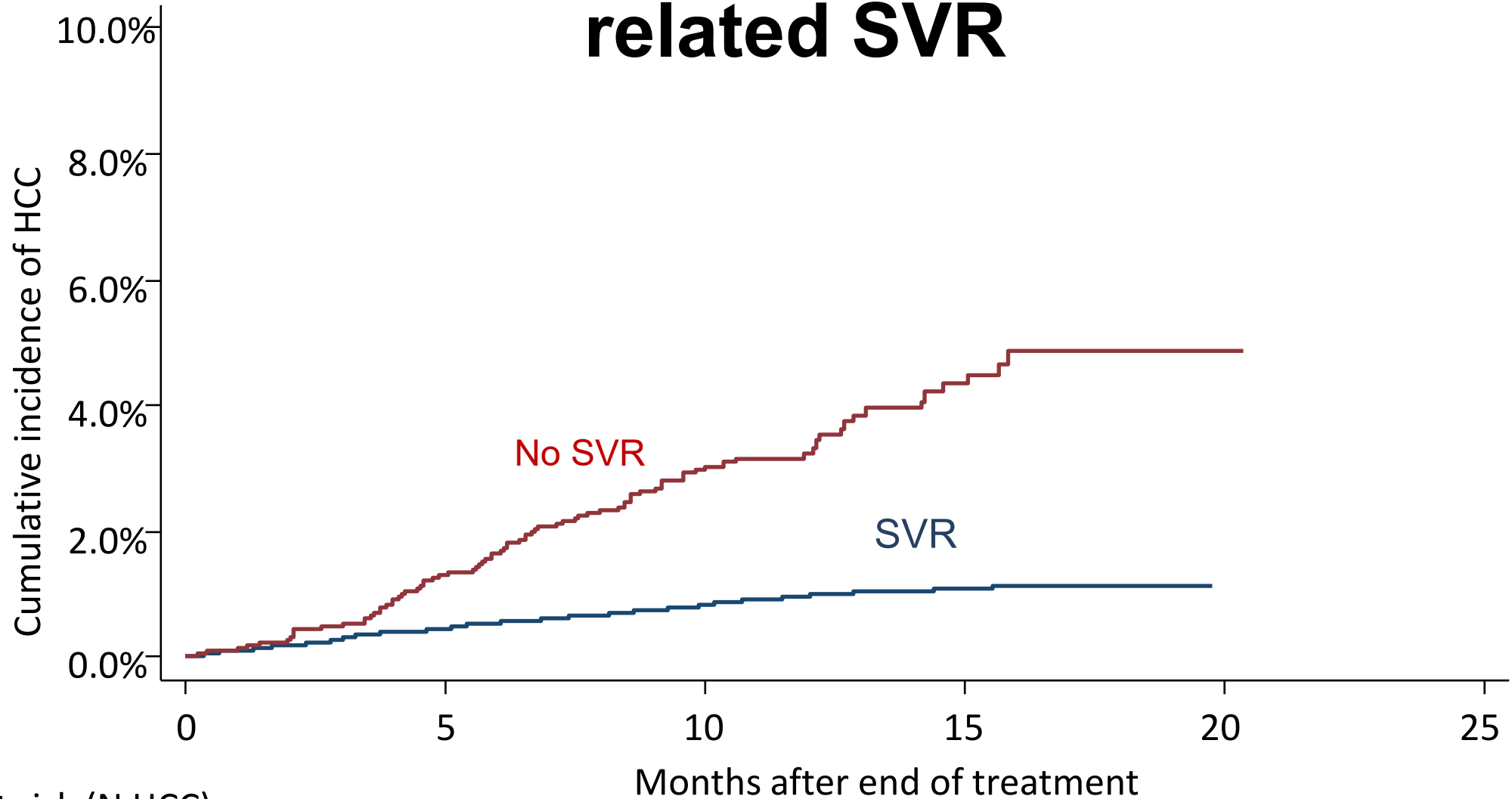
Modifiable

- Alcohol consumption
- Nonalcoholic fatty liver disease
- Obesity
- Diabetes

Antiviral Treatment with SVR

genotype 3
coinfection with HBV or HIV

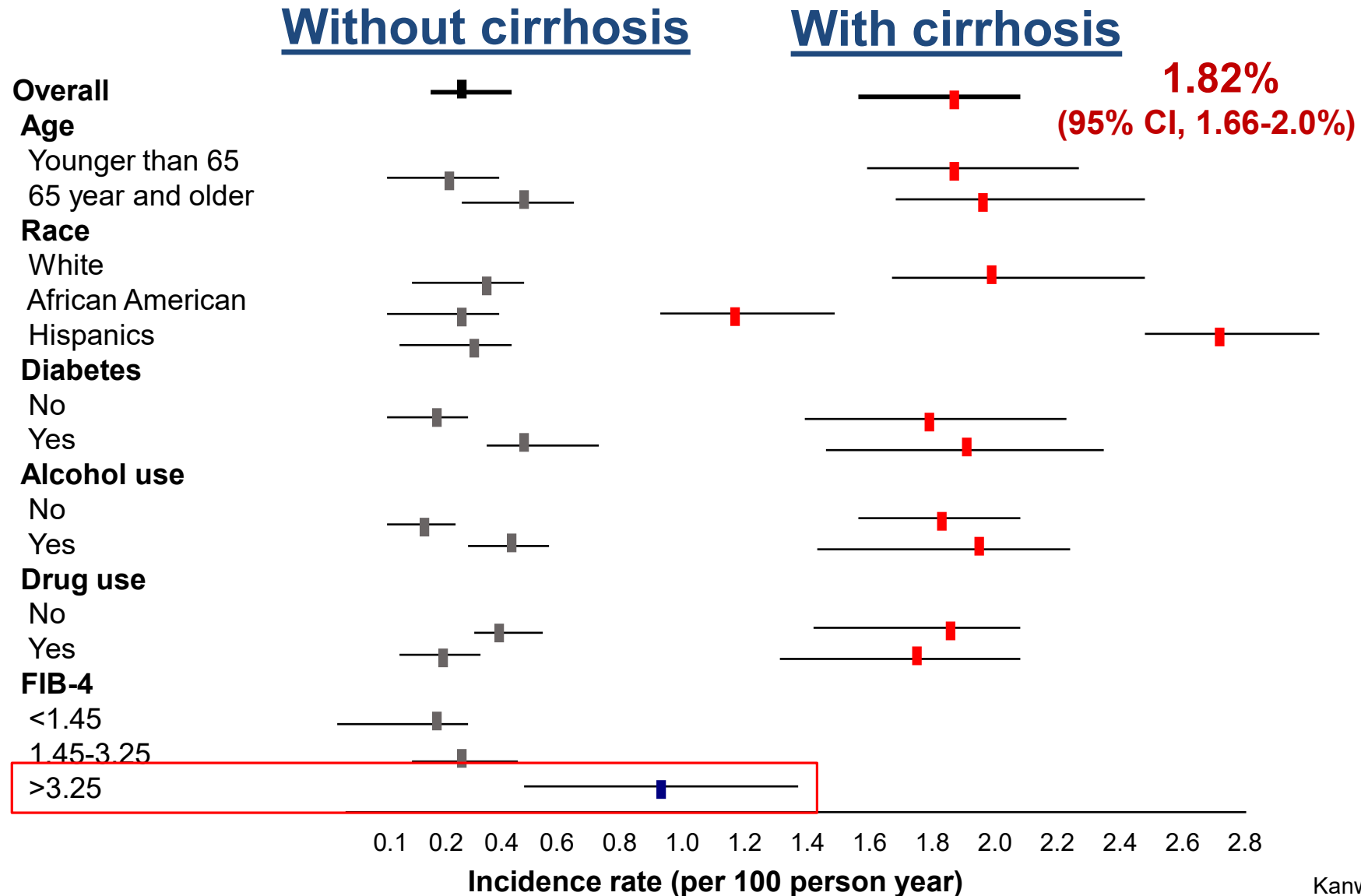
Cumulative HCC incidence rates by DAA-related SVR



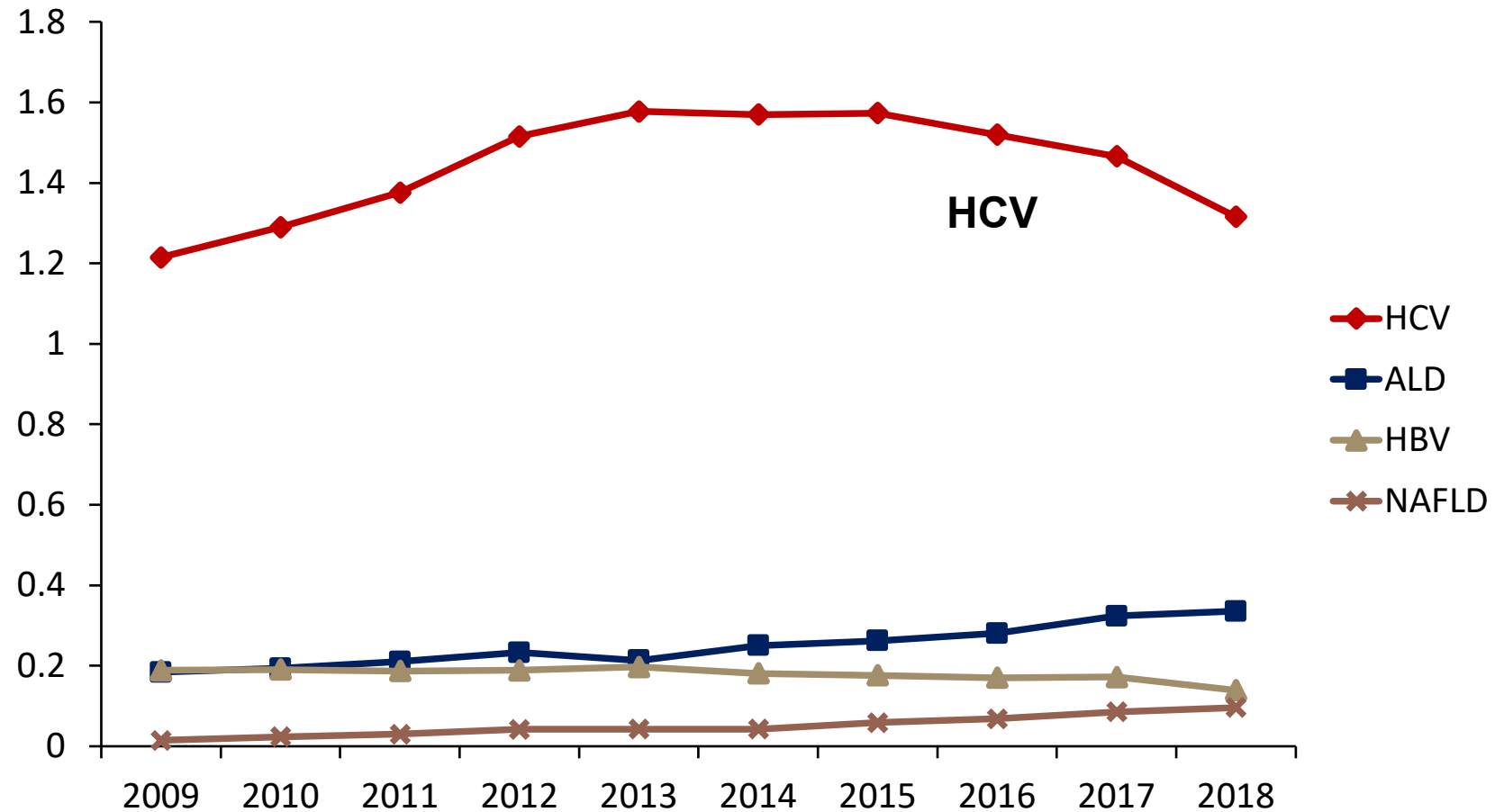
N at risk (N HCC)

SVR	19518	(85)	19372	(68)	14364	(29)	6128	(1)	0	(0)	0
No SVR	2982	(35)	2453	(36)	1617	(14)	636	(3)	5	(0)	0

Annual Incidence of HCC after SVR Stratified by Cirrhosis



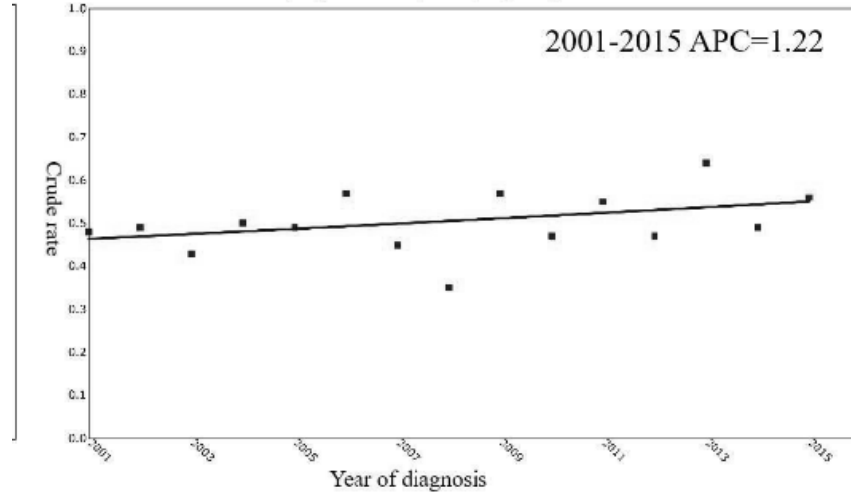
HCV-related HCC Has Started to Decline



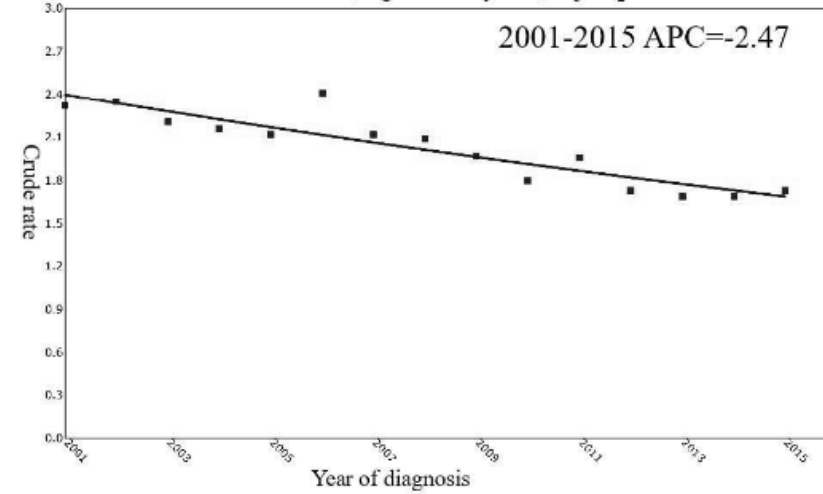
National Vital Statistics System
2009-2018

HCC is Declining in Young Men

Female, age 40-44 years, 0 joinpoint

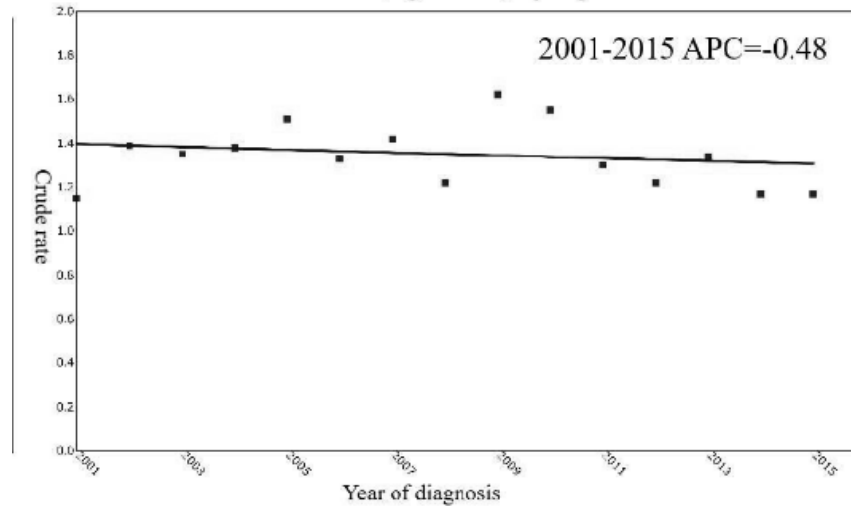


Male, age 40-44 years, 0 joinpoint

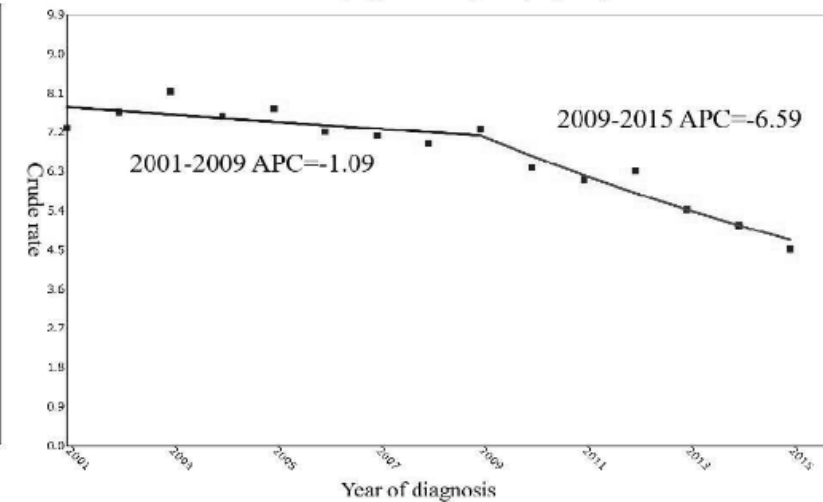


Females

Female, age 45-49 years, 0 joinpoint



Male, age 45-49 years, 1 joinpoint



Males

HBV: Risk Factors for Progression to HCC

Viral factors

Persistently elevated HBV DNA levels

HBV CP variants

HBV genotype (C > B)

Host factors

Age

Sex

Alcohol

Antiviral Treatment

Family history of HCC

HBV Vaccination and HCC: Taiwan Experience



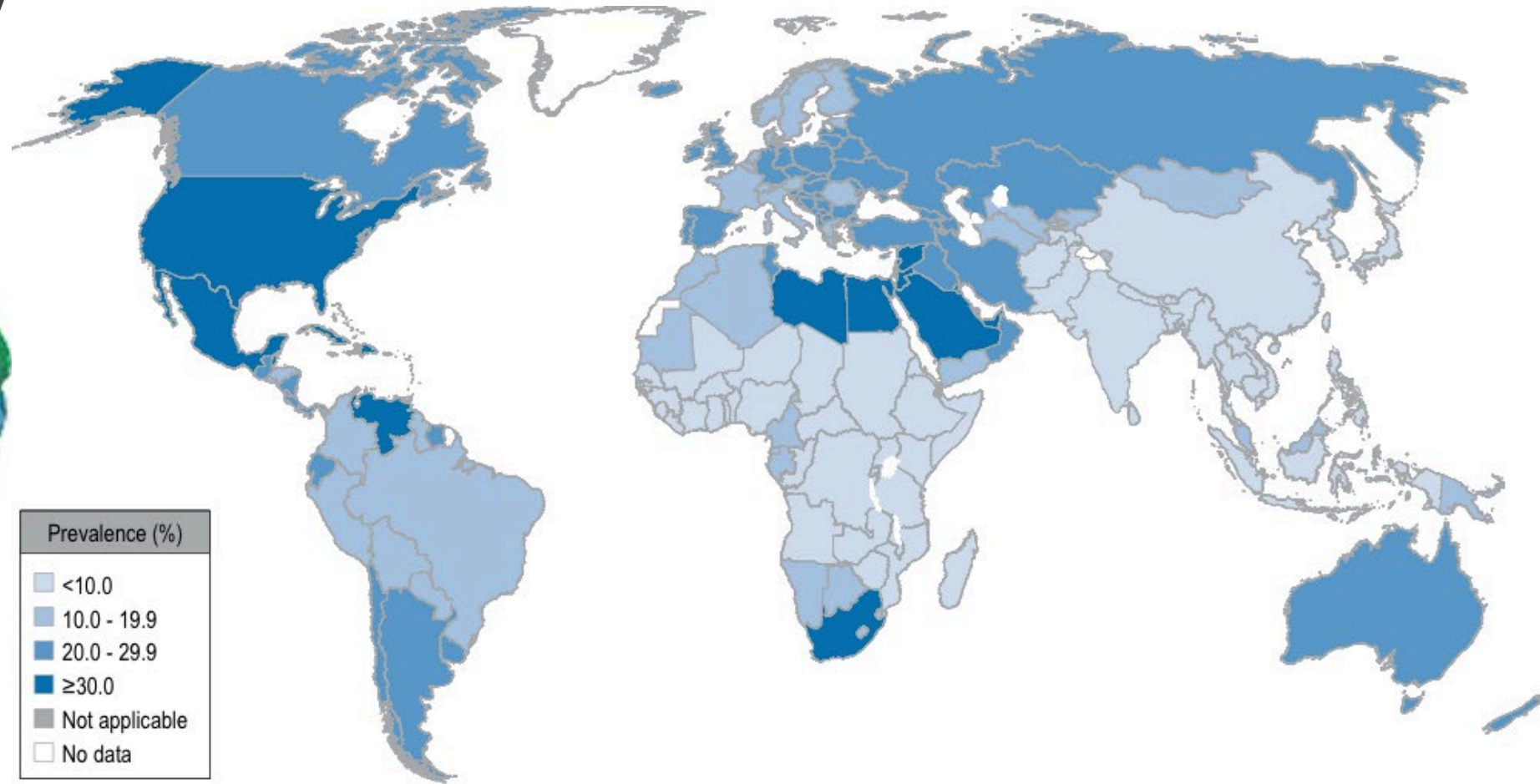
ARTICLE

Decreased Incidence of Hepatocellular Carcinoma in Hepatitis B Vaccinees: A 20-Year Follow-up Study

Mei-Hwei Chang, San-Lin You, Chien-Jen Chen, Chun-Jen Liu, Chuan-Mo Lee, Shi-Ming Lin,
Heng-Cheng Chu, Tzee-Chung Wu, Sheng-Shun Yang, Hsu-Sung Kuo, Ding-Shinn Chen,
the Taiwan Hepatoma Study Group

- HCC prevention extended from childhood to early adulthood
- Failures: incomplete vaccination, maternal HBsAg or HBeAg

Globesity

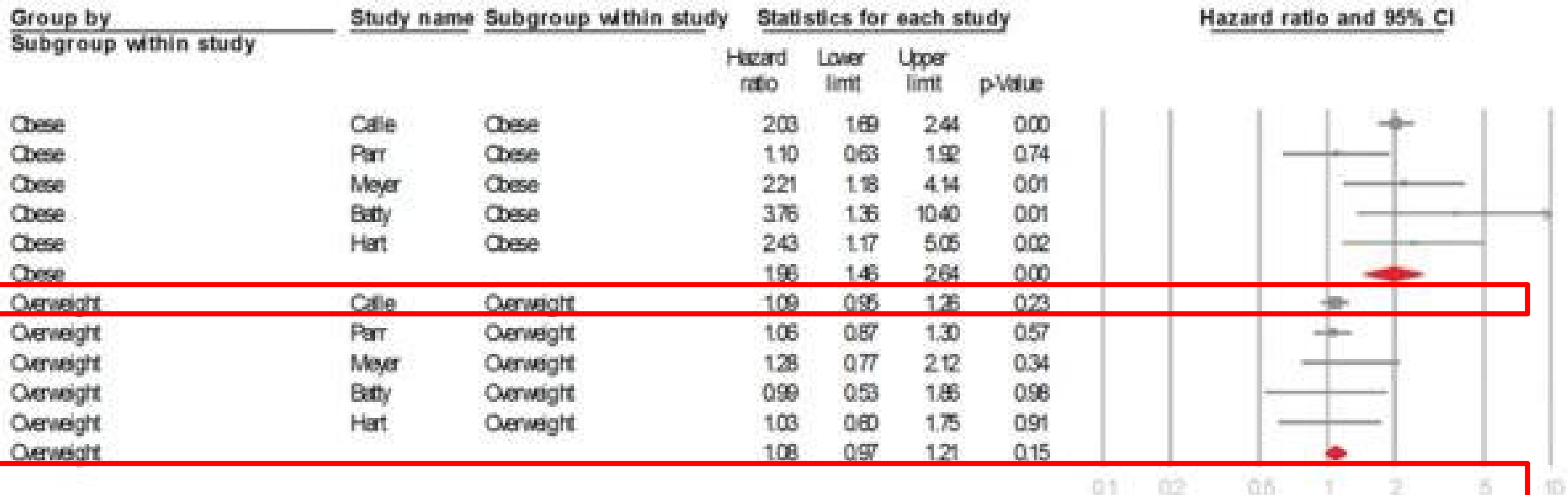


Source: BofA Merrill Lynch Global Research, WHO

Obesity and Risk of HCC

Most—but not all—studies suggest a modest increase in the relative risk of HCC in obese persons

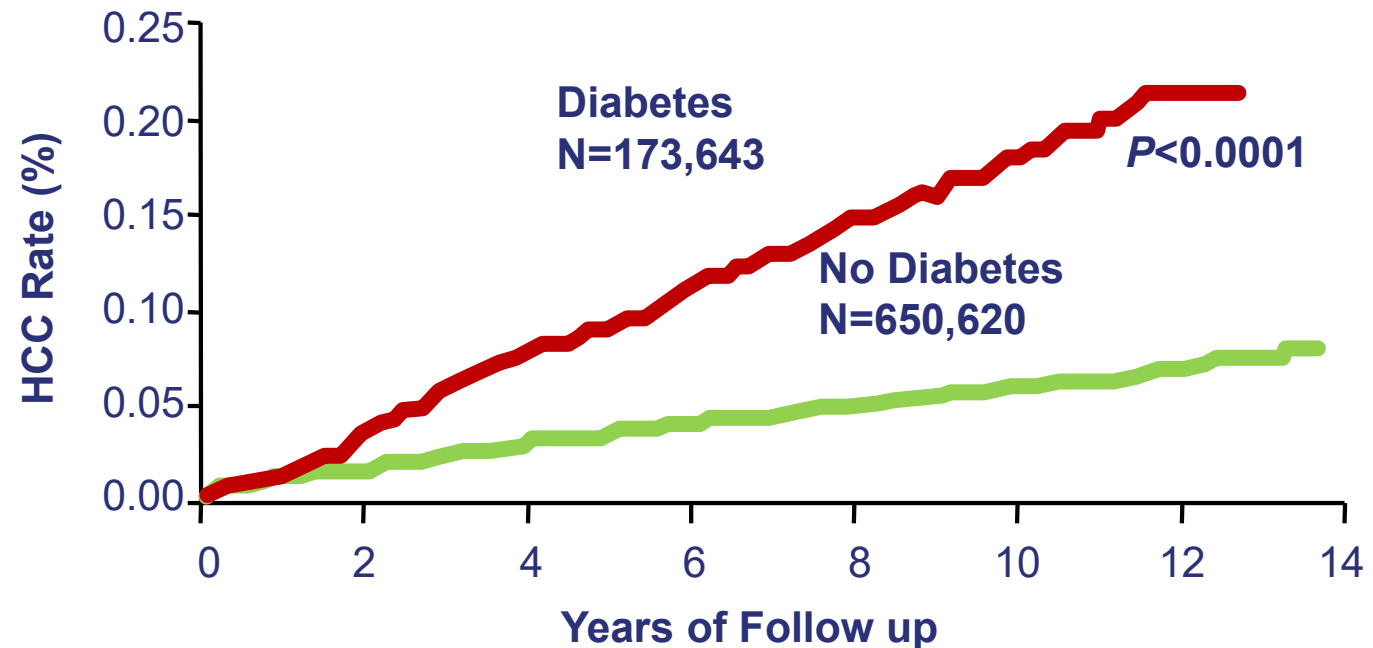
Pre-morbid Obesity and Hepatocellular Cancer-related Mortality



Diabetes Is Associated with a Two-fold Increase in Risk of HCC



- A total of 25 cohort studies
- 18 studies showed that DM was associated with an increased incidence of HCC
- SRRs = 2.01, 95% CI: 1.61-2.51

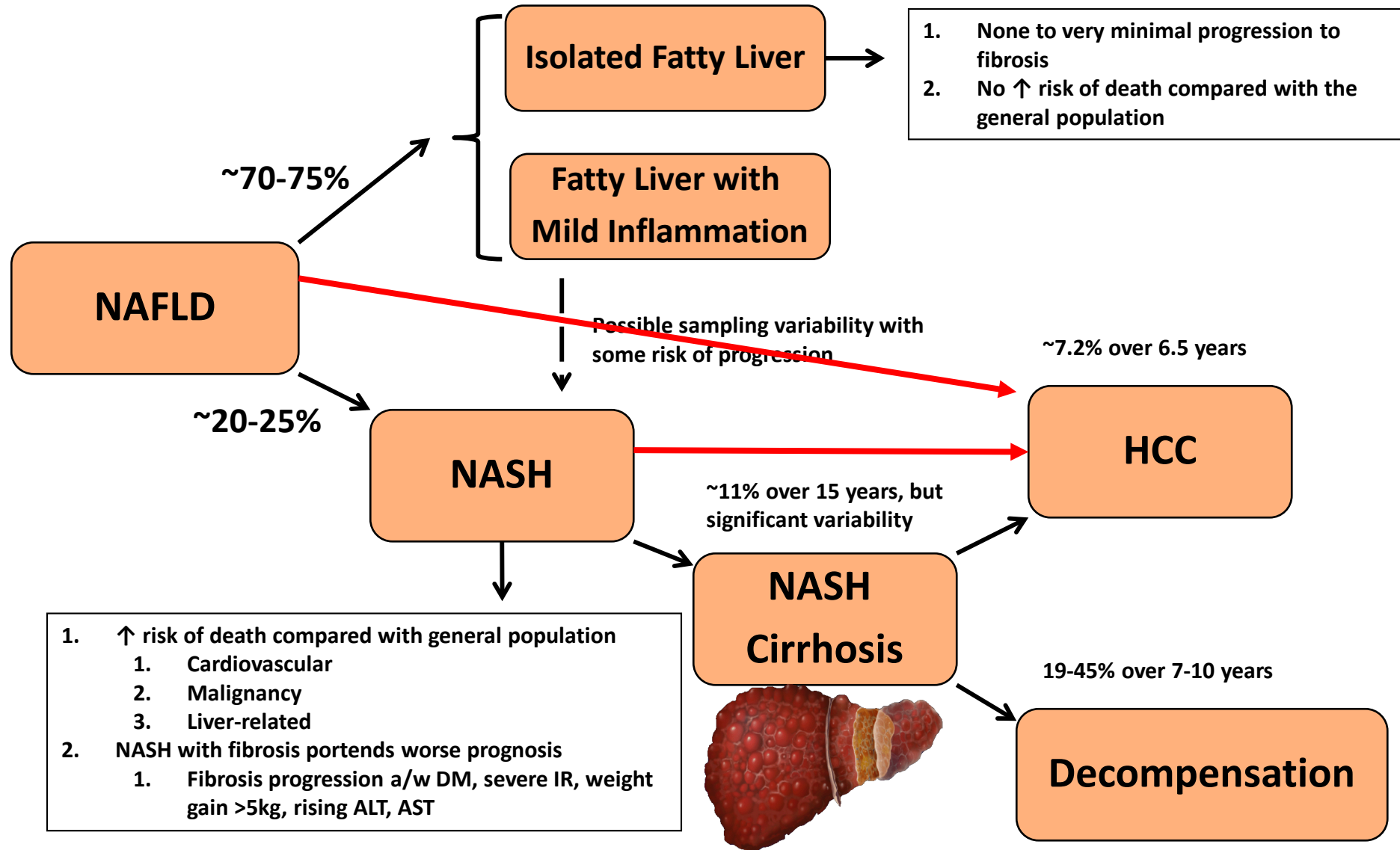


Obesity/Diabetes and HCC

Distal vs. Proximal Associations



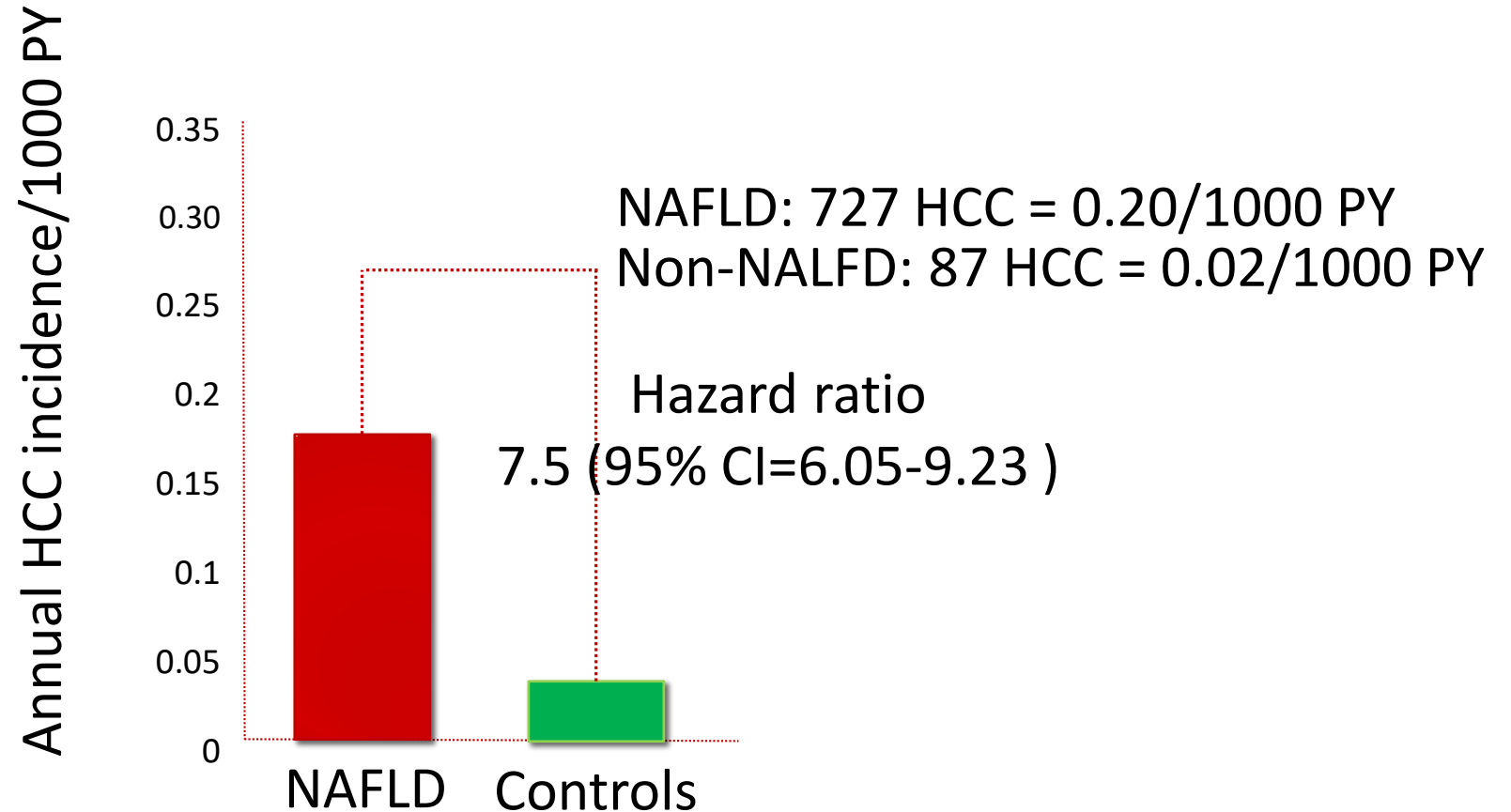
Natural History of NAFLD



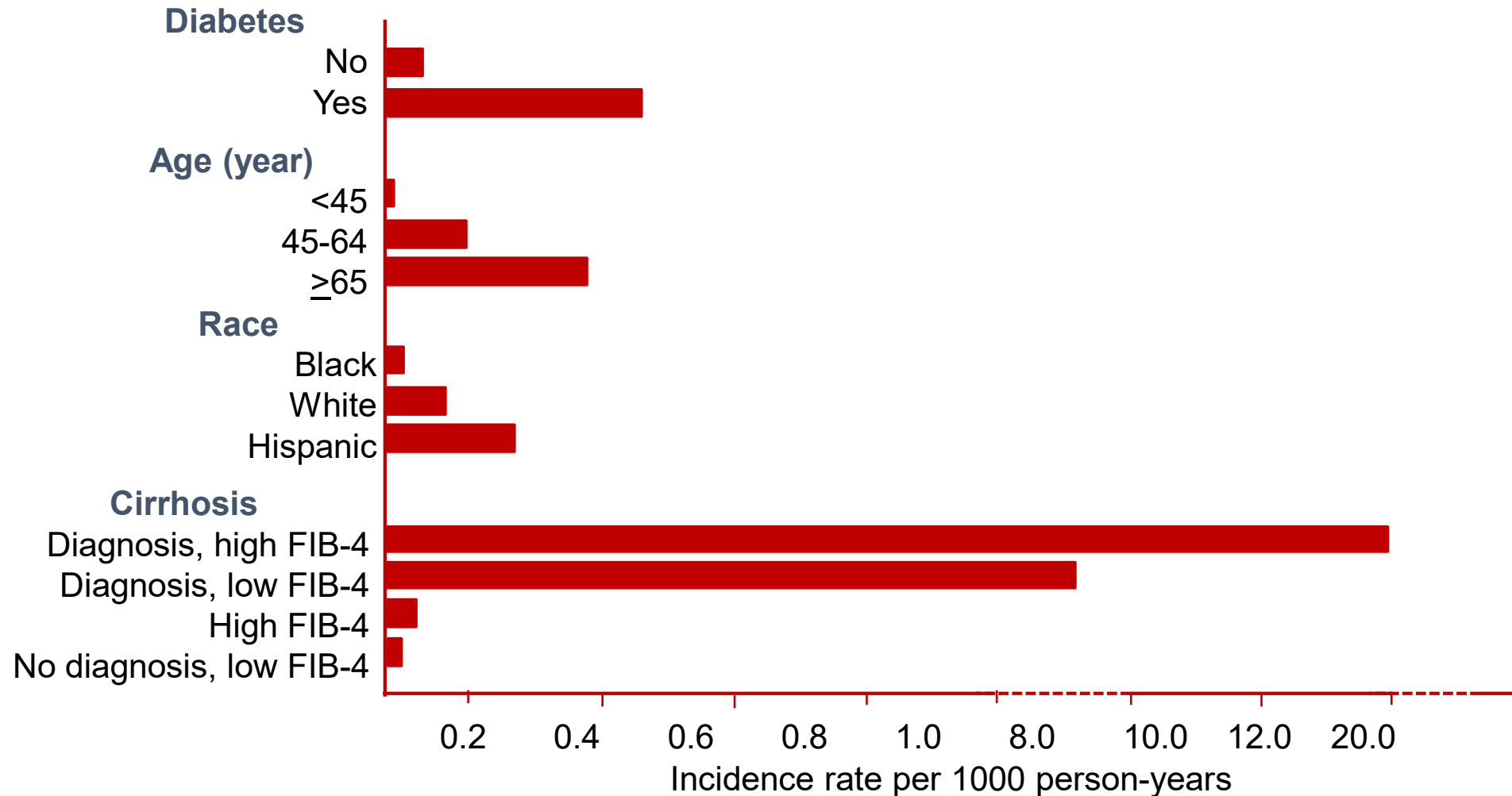
HCC in Patients with (Biochemical) NAFLD

452,767 with NAFLD and 450,627 w/o NAFLD

Mean 9.1 (SD 2.9) year follow-up

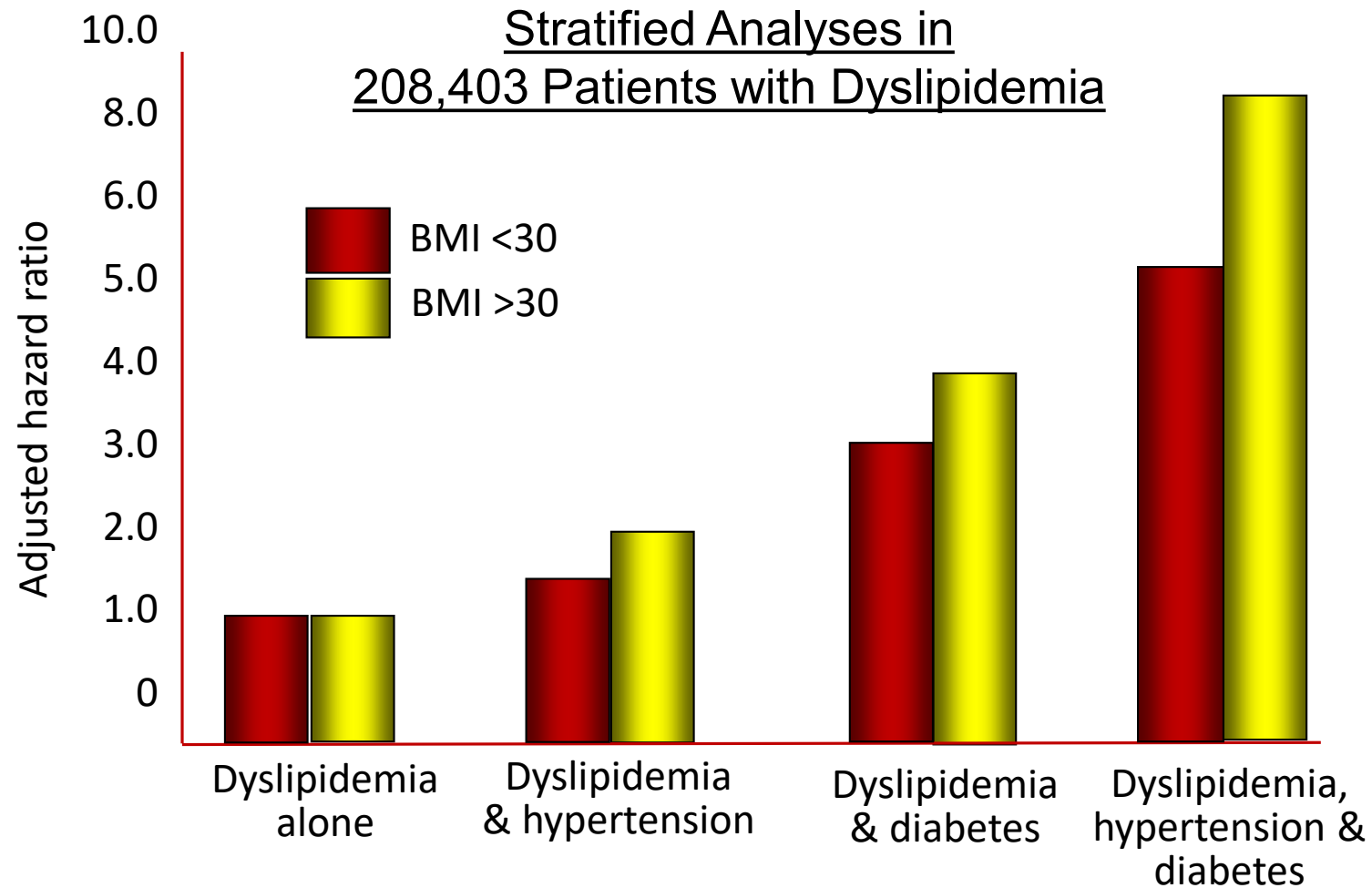


HCC Incidence in Subgroups Of Patients with NAFLD



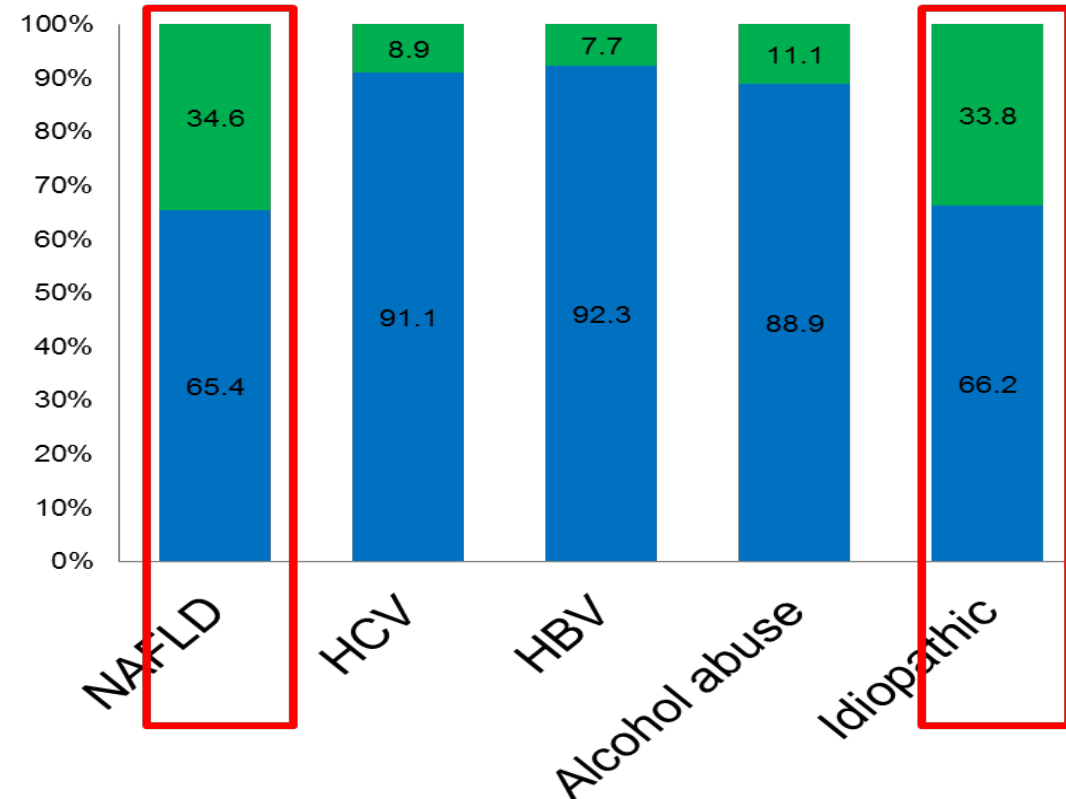
Factors Associated with Risk of NAFLD Progression to Cirrhosis or HCC

Multivariate Analyses (Joint Effects)



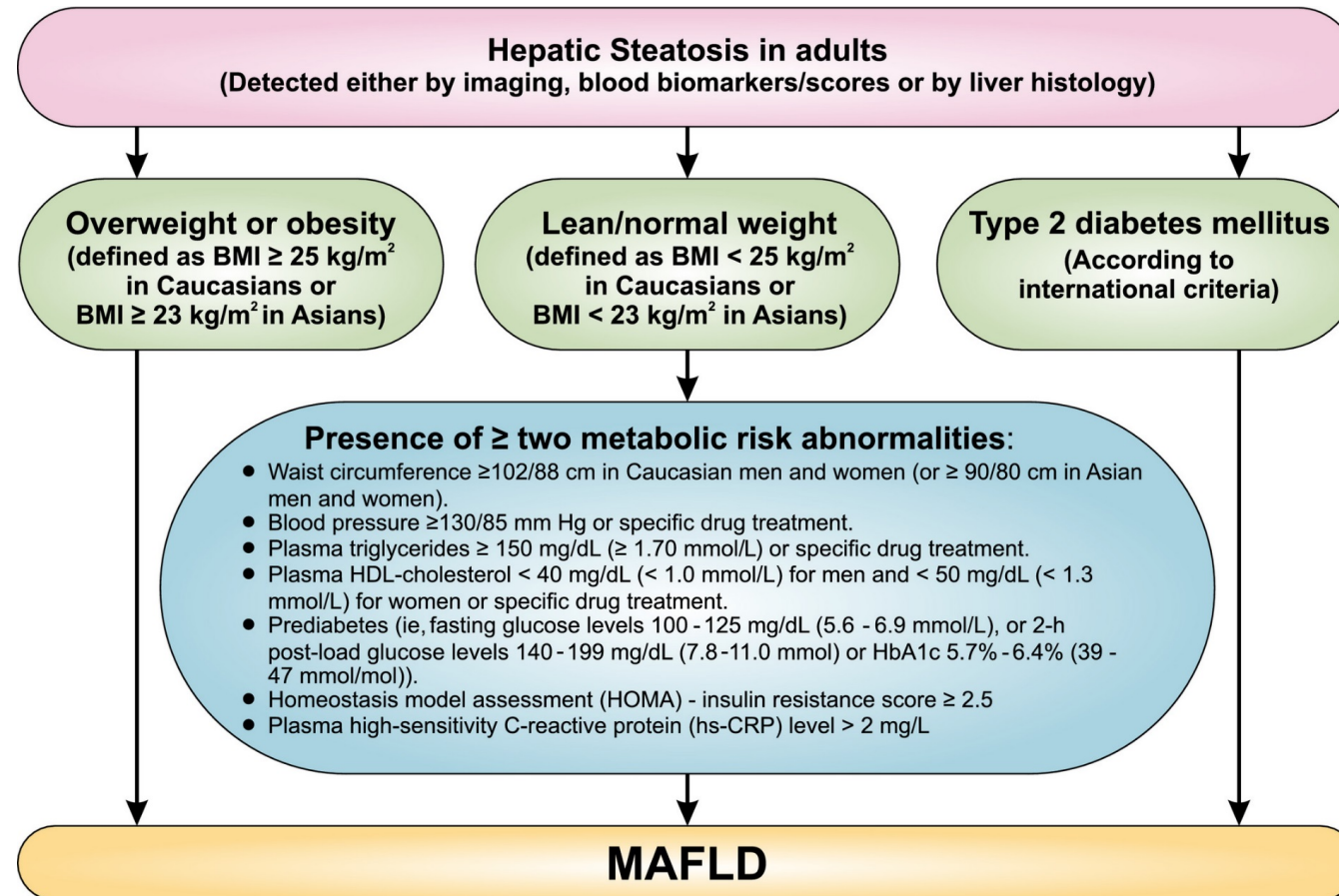
HCC in the Absence of Cirrhosis

- 1500 VA patients & HCC (2005- 2010)
- Patients without cirrhosis 13%
- Risk of HCC in absence of cirrhosis
 - NAFLD:
 - OR: 5.4; 95% CI (3.4–8.5)
 - Metabolic Syndrome:
 - OR: 5.0; 95% CI (3.1–7.8)



- NAFLD and Metabolic Syndrome are main risk factors for HCC in the absence of cirrhosis

Metabolic Associated Fatty Liver Disease (MAFLD)



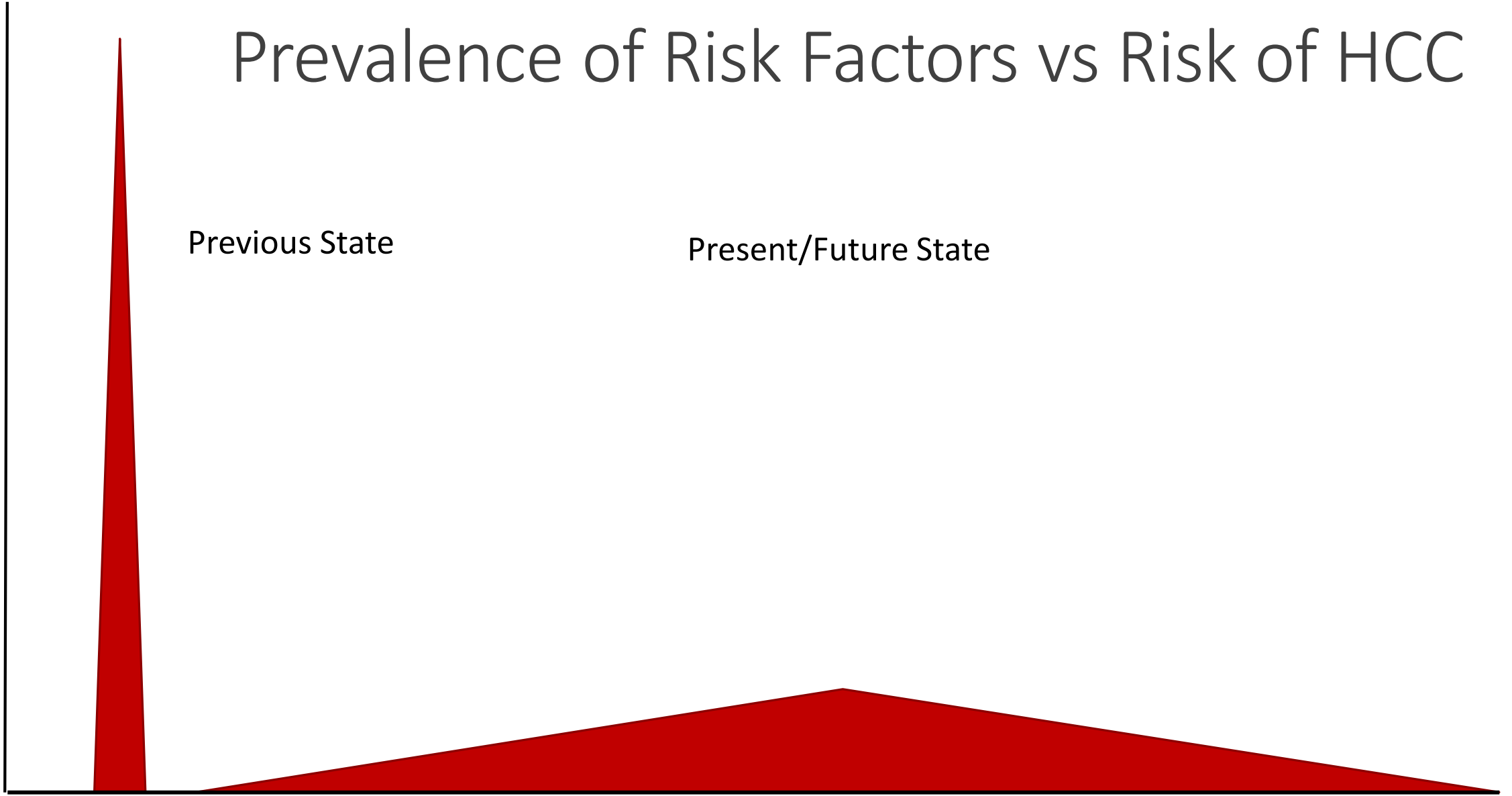
Prevalence of Risk Factors vs Risk of HCC

HCC Risk

Previous State

Present/Future State

Prevalence of Risk Factor



HCC Risk Factors



Prevalence, Relative Risk Estimates, and Population Attributable Fraction

Disease type	Prevalence in general population	Risk estimate of HCC	Population attributable fraction
HBV	Drop	Decline	Drop
HCV			
Alcoholic liver disease	10-15%	2-3	20-30%
Metabolic syndrome	30-40%	1.5-2.5	30-40%
MAFLD	70-80%	1.5	70-80%

Texas HCC Consortium (THCCC) Accrual as of October 12, 2020



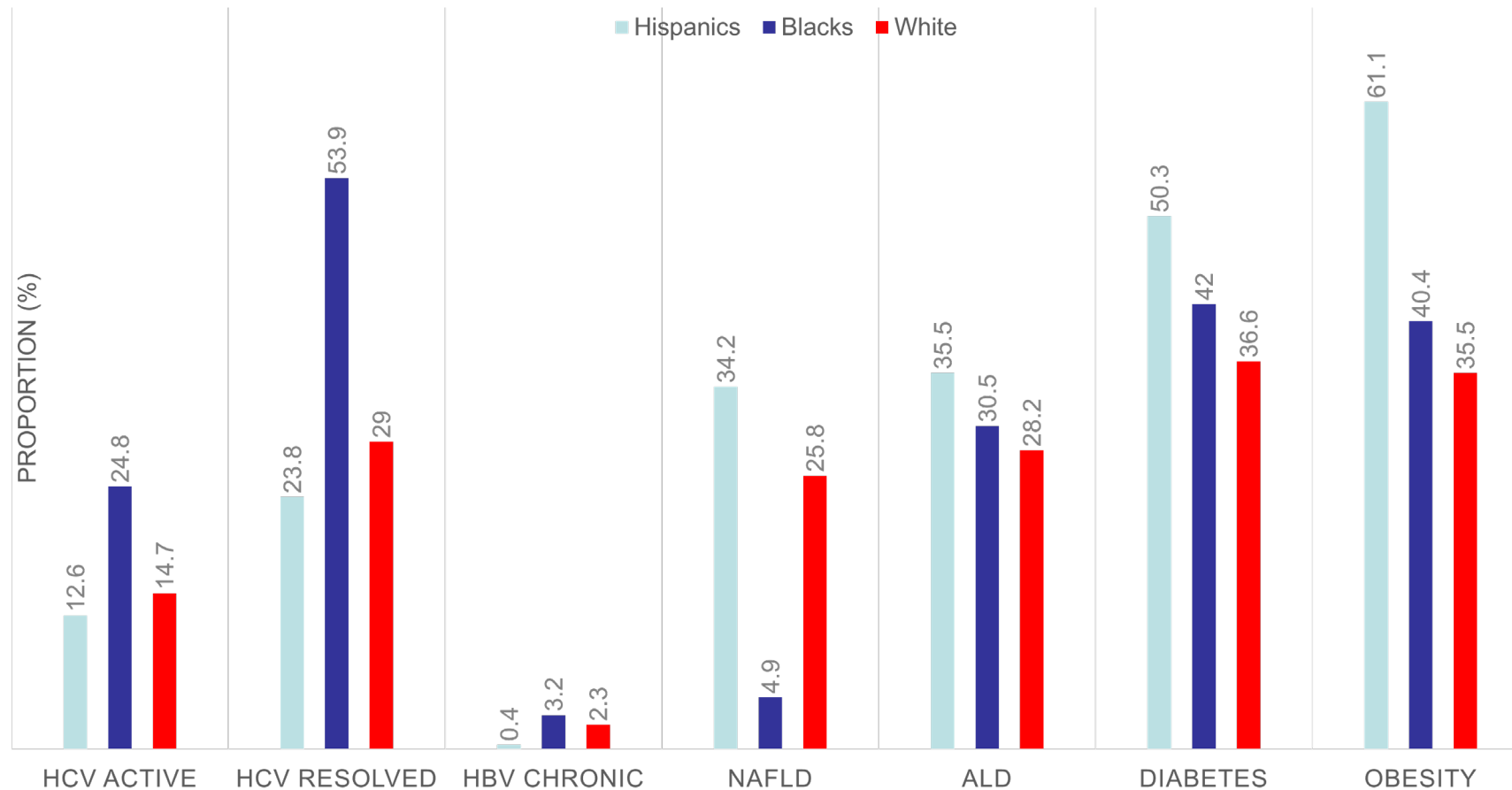
Institution Name	Start Date*	Total Accrual	% of Total Registered
Michael E DeBakey VAMC	Dec. 21, 2016	630	25.1%
UT Southwestern Medical Center at Dallas	Jan. 9, 2017	435	17.4%
Parkland Health and Hospital System	Jan. 10, 2017	493	19.7%
Baylor College of Medicine	Feb. 9, 2017	525	20.9%
The Texas Liver Institute	Apr. 20, 2017	140	5.6%
Baylor Scott & White Research Institute	Jun. 14, 2019	172	6.9%
Doctor's Hospital at Renaissance	Oct. 8, 2019	93	3.7%
Baylor All Saints Medical Center	Jun. 4, 2020	18	0.7%
Total		2506	100%

*Start date is defined as the date that the first subject was enrolled.

THCCC: Cirrhosis Risk Factors in the Main Racial/Ethnic Groups



(El-Serag HB et al. *Gastroenterology*; 2020 accepted)



HCC Incidence Rate as of February 19, 2020



$$\text{HCC Annual Incidence Rate} = \frac{75}{\left(\frac{\text{OSD, DD, HCC, or Current Date}^\dagger - \text{Registration Date}}{365.24} \right)} = 1.93\%$$

Abbreviations:

OSD: Off-study date

DD: Death date

HCC: HCC date

†Whichever occurs first

Summary

Changing HCC Risk Factors

- Less active HCV and HBV
- More Metabolic Syndrome

Changing in HCC Risk

- Lower individual risk but more individuals at risk

Metabolic Syndrome and HCC Risk

- Relative risk of HCC is modestly elevated but absolute risk is low
- Factors influencing HCC risk: abdominal obesity, diabetes, NAFLD, PNPLA3

Knowledge Needed

- Risk stratification
- Mechanisms
- Treating metabolic syndrome

Acknowledgments

Collaborators:

- David Davila, PhD
- Jennifer Kramer, PhD
- Donna White, PhD
- Fasiha Kanwal, MD
- Aaron Thrift, PhD

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