

Disparities in diseases of the liver and pancreas: race and lifestyles



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Outline

- Multiethnic Cohort Study (MEC) background
- Trends in liver and pancreatic cancer rates in the United States
- Liver cancer & chronic liver disease findings
- Pancreatic cancer & pancreatitis findings
- Ongoing studies and future plans

The Multiethnic Cohort Study



- A prospective cohort study of men and women from Hawaii and California (Los Angeles County) established in 1993-1996
- >215,000 African Americans, Native Hawaiians, Japanese Americans, Latinos, and whites (aged 45-75 at recruitment)
- Demographic and exposure data were obtained from self-administered questionnaires
 - Baseline 1993-1996; 26 pages
 - Follow up every 5 years (1999-2001, 2003-2008, 2011-2013, 2014-2017)
- Biological specimen collected in 2001-2006 (N ~70,000)

The Multiethnic Cohort Study

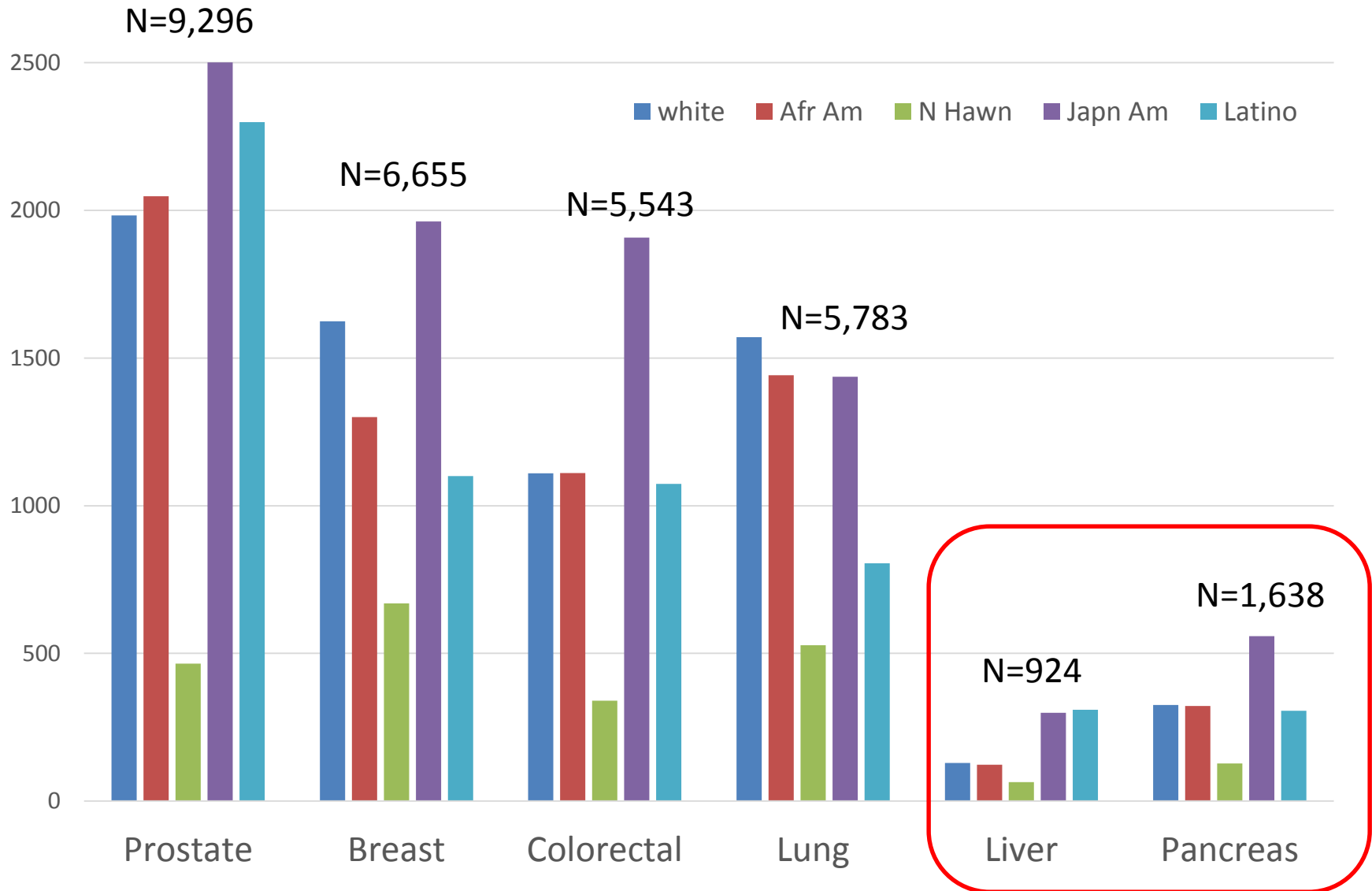
- Incident cancers are identified via annual linkage to SEER cancer registries
 - Tumor characteristics and initial treatment information
- Deaths are identified via annual linkage to state death certificate files and periodically to NDI
- CMS Medicare claim files and CA Hospital Discharge Data
 - Comorbid condition and follow-up treatment
 - Non cancer phenotypes

Distribution of the Cohort by Sex and Ethnicity

Ethnicity	Males	Females	Total
Latino	22,818	24,620	47,438
African American	12,851	22,256	35,107
Japanese	26,964	29,957	56,921
White	22,857	26,502	49,359
Native Hawaiian	6,120	7,851	13,971
Other	5,200	7,255	12,455
Total	96,810	118,441	215,251




No. of Incident Cases in the MEC (12/31/2014)




Ten Leading Cancer Types for the Estimated New Cases & Deaths by Sex United States, 2016

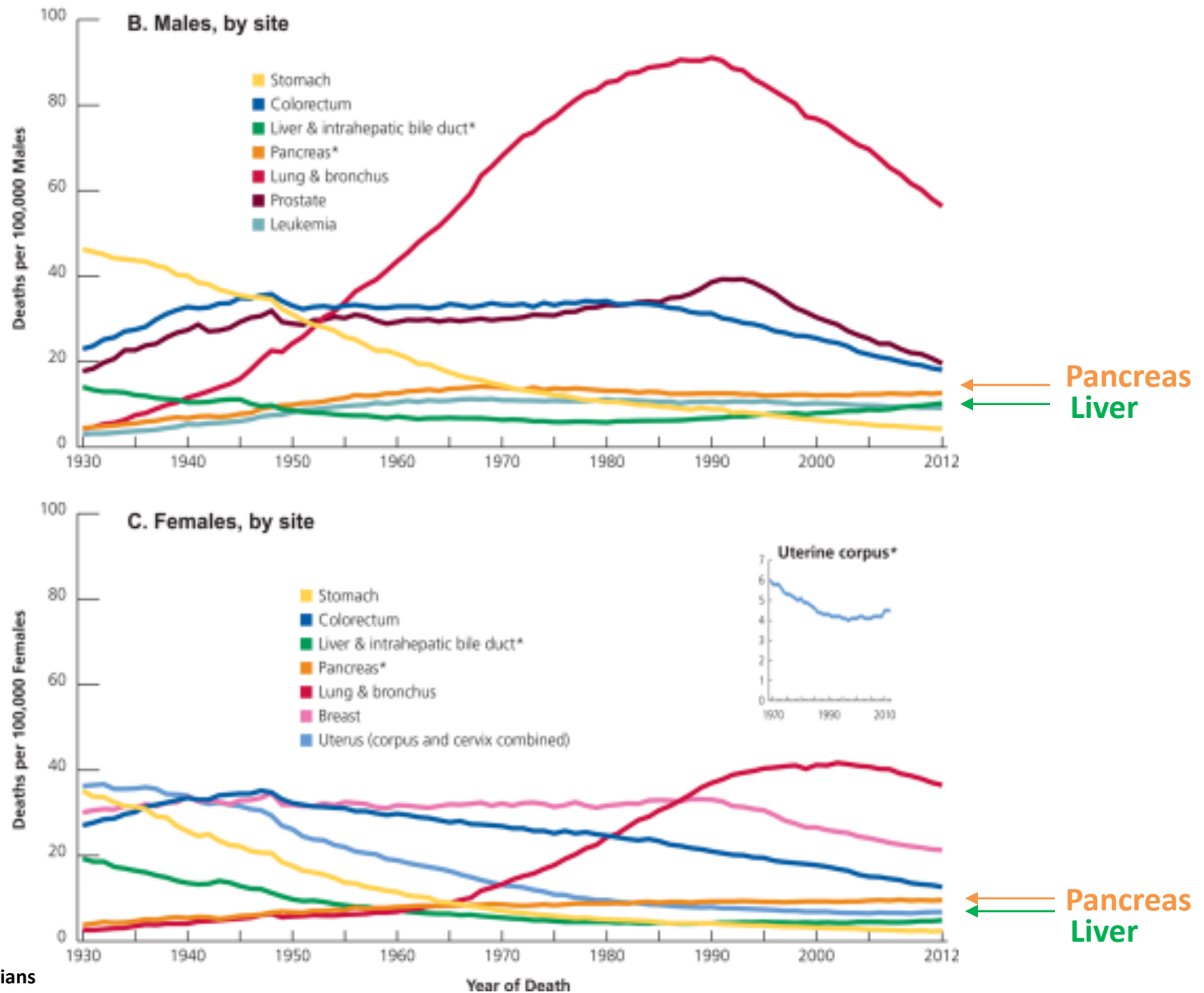
Estimated New Cases

				Males	Females				
Prostate	180,890	21%			Breast	246,660	29%		
Lung & bronchus	117,920	14%			Lung & bronchus	106,470	13%		
Colon & rectum	70,820	8%			Colon & rectum	63,670	8%		
Urinary bladder	58,950	7%			Uterine corpus	60,050	7%		
Melanoma of the skin	46,870	6%			Thyroid	49,350	6%		
Non-Hodgkin lymphoma	40,170	5%			Non-Hodgkin lymphoma	32,410	4%		
Kidney & renal pelvis	39,650	5%			Melanoma of the skin	29,510	3%		
Oral cavity & pharynx	34,780	4%			Leukemia	26,050	3%		
Leukemia	34,090	4%			Pancreas	25,400	3%		
Liver & intrahepatic bile duct	28,410	3%			Kidney & renal pelvis	23,050	3%		
All Sites	841,390	100%		All Sites	843,820	100%			

Estimated Deaths

				Males	Females				
Lung & bronchus	85,920	27%			Lung & bronchus	72,160	26%		
Prostate	26,120	8%			Breast	40,450	14%		
Colon & rectum	26,020	8%			Colon & rectum	23,170	8%		
Pancreas	21,450	7%			Pancreas	20,330	7%		
Liver & intrahepatic bile duct	18,280	6%			Ovary	14,240	5%		
Leukemia	14,130	4%			Uterine corpus	10,470	4%		
Esophagus	12,720	4%			Leukemia	10,270	4%		
Urinary bladder	11,820	4%			Liver & intrahepatic bile duct	8,890	3%		
Non-Hodgkin lymphoma	11,520	4%			Non-Hodgkin lymphoma	8,630	3%		
Brain & other nervous system	9,440	3%			Brain & other nervous system	6,610	2%		
All Sites	314,290	100%		All Sites	281,400	100%			

Trends in Death Rates for Selected Sites by Sex, United States, 1930-2012



Pancreatic and liver cancers are projected to be top cancer killers by 2030

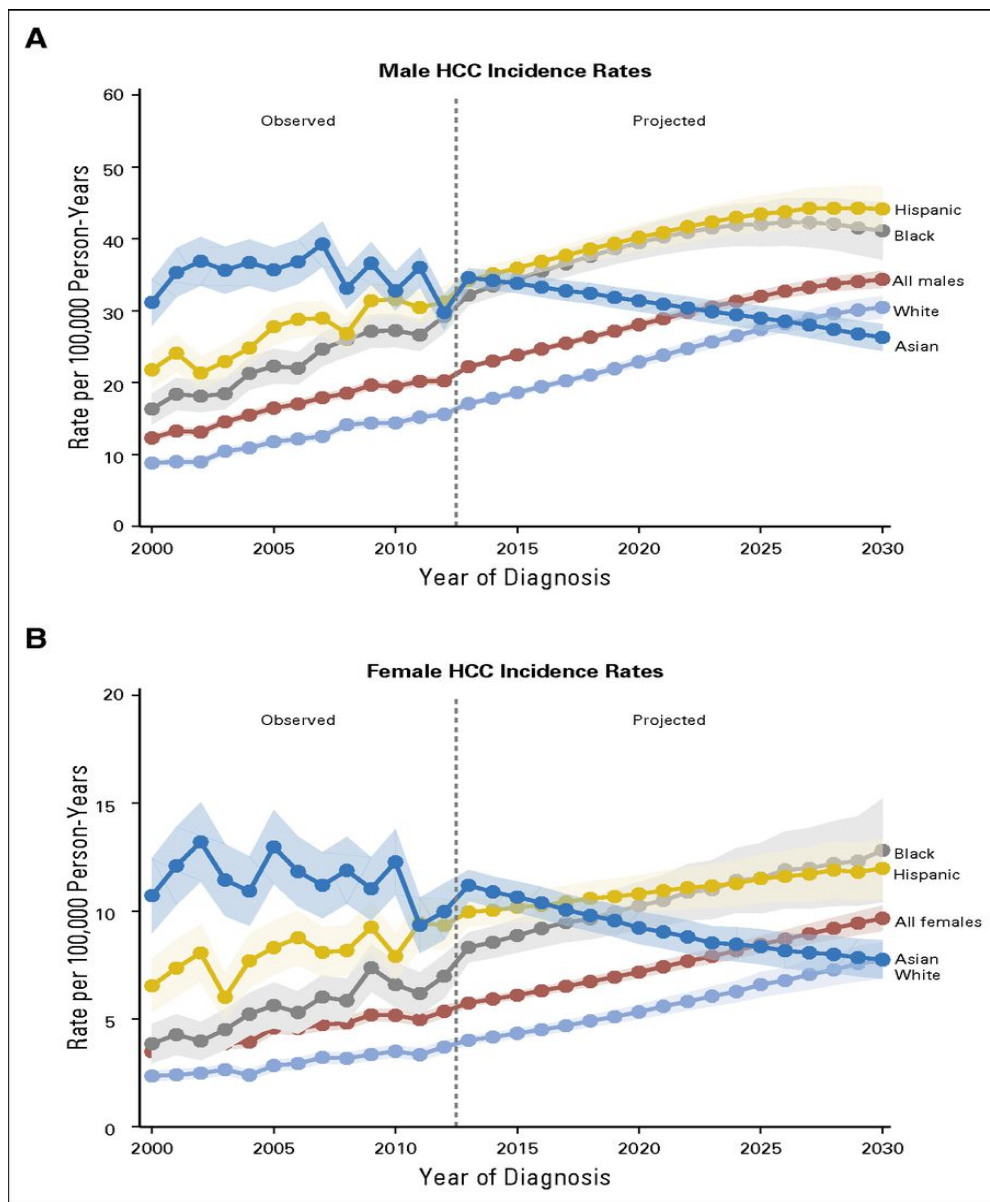
Commentary

Annual Report to the Nation on the Status of Cancer, 1975-2012, Featuring the Increasing Incidence of Liver Cancer

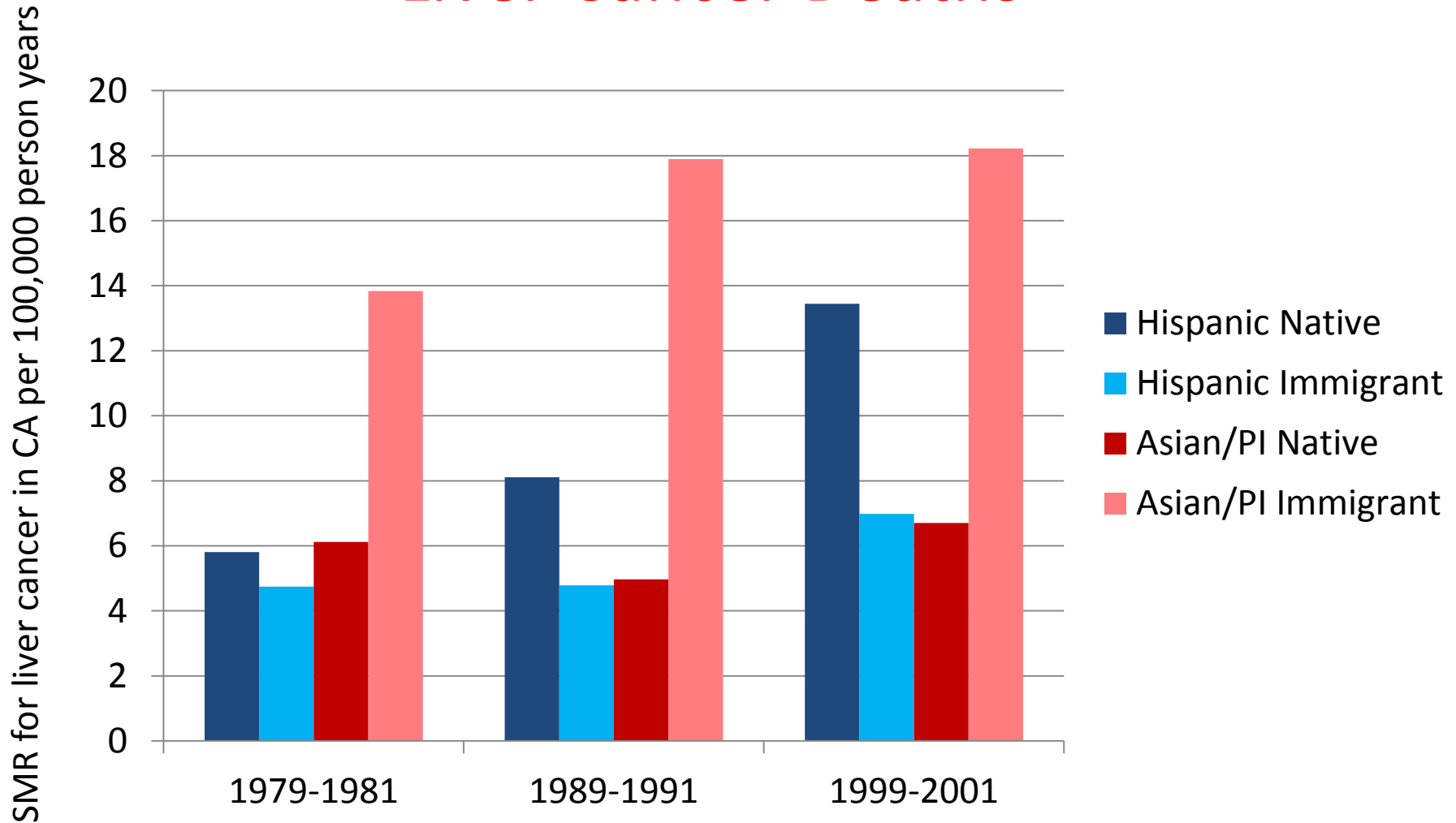
A. Blythe Ryerson, PhD, MPH¹; Christie R. Ehemann, PhD, MSHP¹; Sean F. Altekruze, DVM, MPH, PhD²; John W. Ward, MD³; Ahmedin Jemal, DVM, PhD⁴; Recinda L. Sherman, MPH, PhD, CTR⁵; S. Jane Henley, MSPH¹; Deborah Holtzman, PhD³; Andrew Lake, BS⁶; Anne-Michelle Noone, MS²; Robert N. Anderson, PhD⁷; Jiemin Ma, PhD, MHS⁴; Kathleen N. Ly, MPH³; Kathleen A. Cronin, PhD, MPH²; Lynne Penberthy, MD, MPH²; and Betsy A. Kohler, MPH⁵

Cancer. 2016 May 1;122(9):1312-37.

Observed and projected incidence of hepatocellular carcinoma (per 100,000 person-years) overall and by race in (A) males and (B) females



Immigrant vs. US Native Comparison for Liver Cancer Deaths



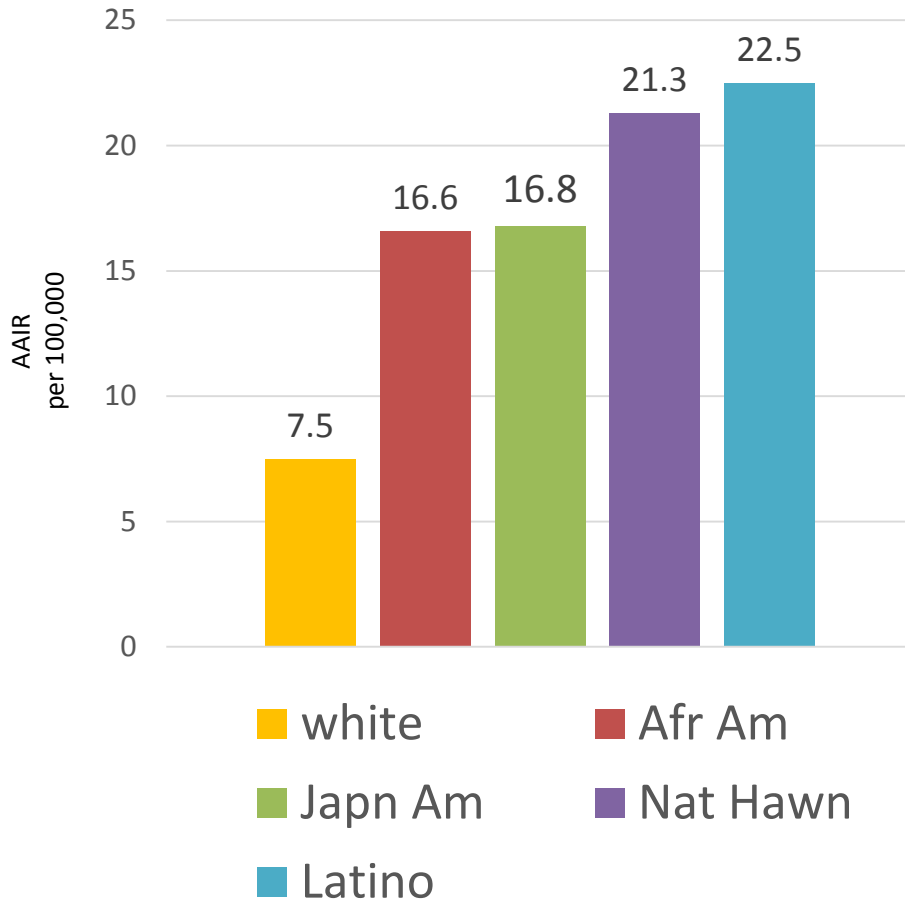
Major HCC Risk Factors in the US

- Chronic HCV and HBV infections
- Alcohol abuse
- Cirrhosis
- Metabolic syndrome: obesity, diabetes mellitus, hyperlipidemia, NAFLD

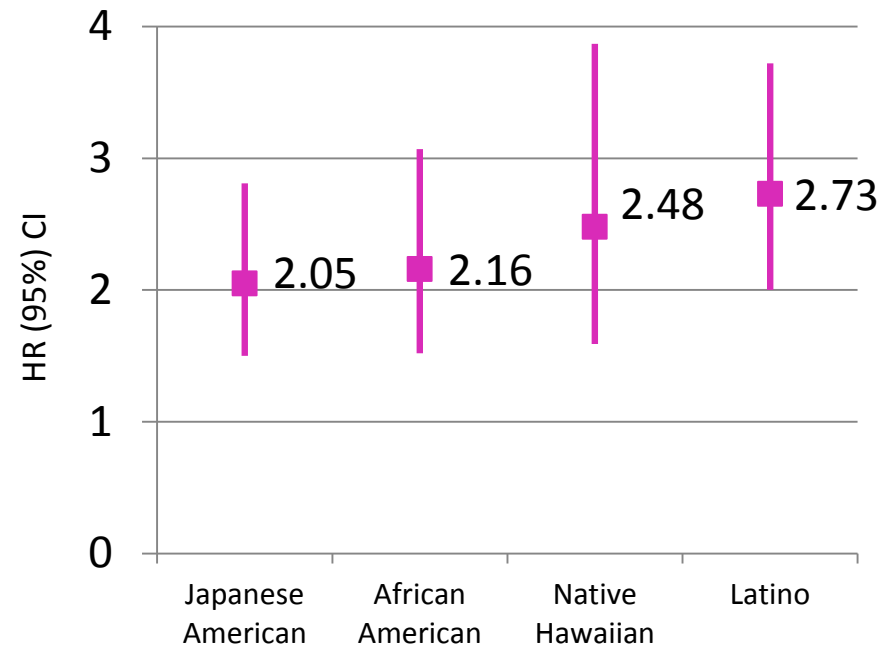
Burden of the main HCC risk factors in the United States

	Risk estimate of HCC	Prevalence in general US population	Population Attributable fraction
HBV	20-25	0.5-1%	5-10%
HCV	20-25	1-2%	20-25%
Alcoholic liver disease	2-3	10-15%	20-30%
Metabolic syndrome	1.5-2.5	30-40%	30-40%

HCC Incidence Rates* in the MEC

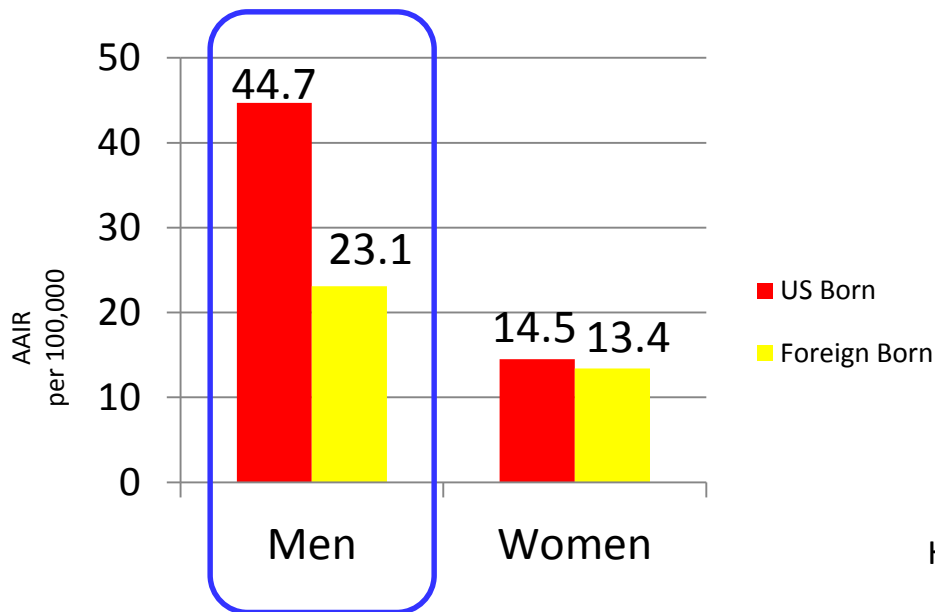


HR for HCC Incidence comparing each ethnic group to whites

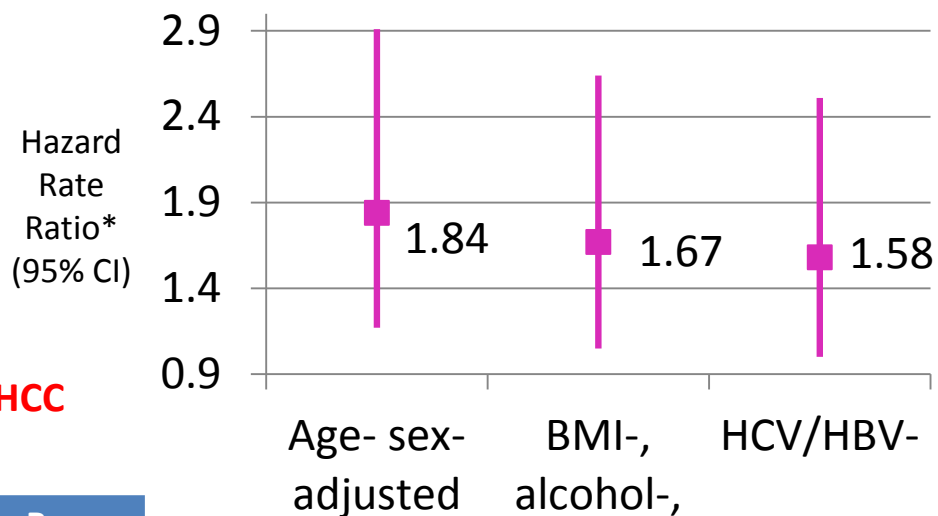


*truncated at age 45

HCC Incidence rates in Latinos by birth place



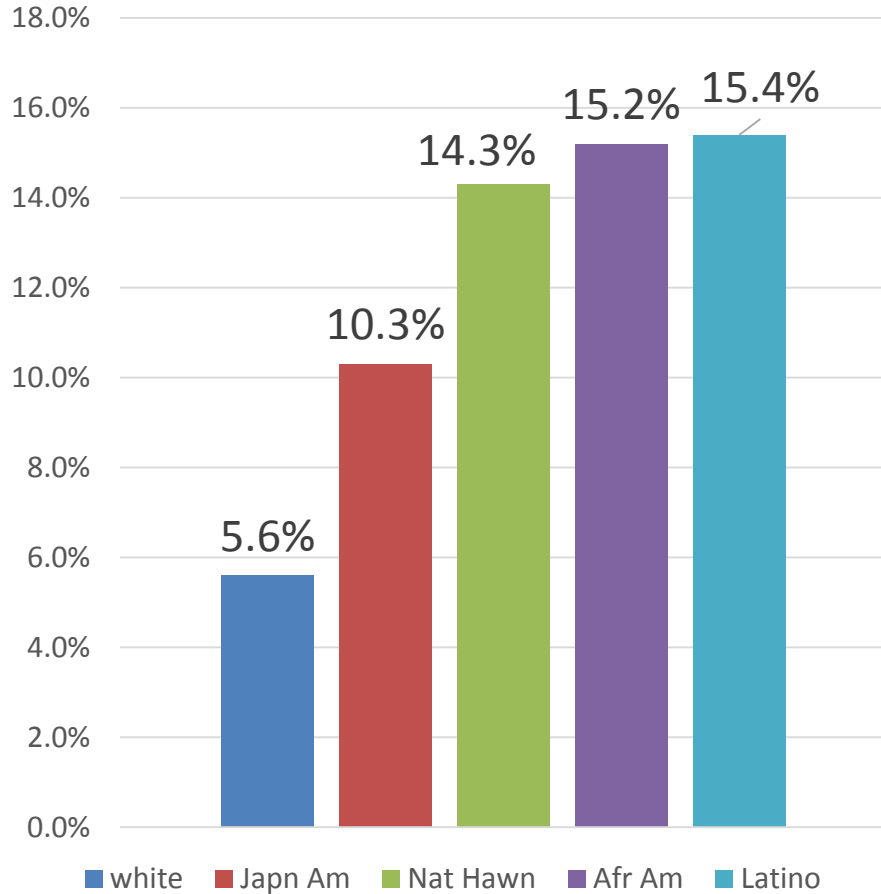
HRs for HCC Incidence Comparing US-Born with Foreign-Born Latinos



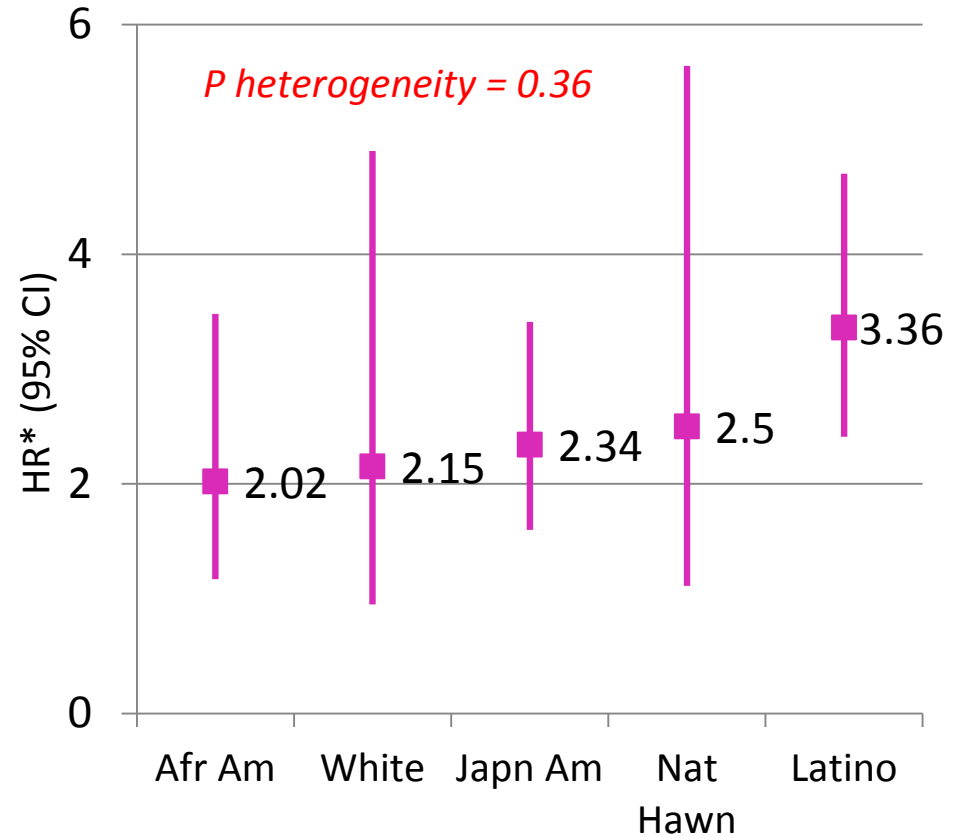
Association between known risk factors and HCC incidence in Latinos by Nativity

	US Born	Foreign Born
Alcohol 2+ drinks/day	1.49 (0.89, 2.50)	2.98 (1.44, 6.06)
Current Smoking	2.91 (1.75, 4.85)	2.10 (1.13, 3.90)
Diabetes	3.32 (2.26, 4.90)	3.38 (2.03, 5.62)
BMI 30+	1.90 (1.07, 3.39)	1.89 (0.99, 3.63)
HBV/HCV	16.1 (8.73, 29.8)	19.9 (9.44, 42.1)

Prevalence of Diabetes in the MEC



Association Between Diabetes and HCC Incidence

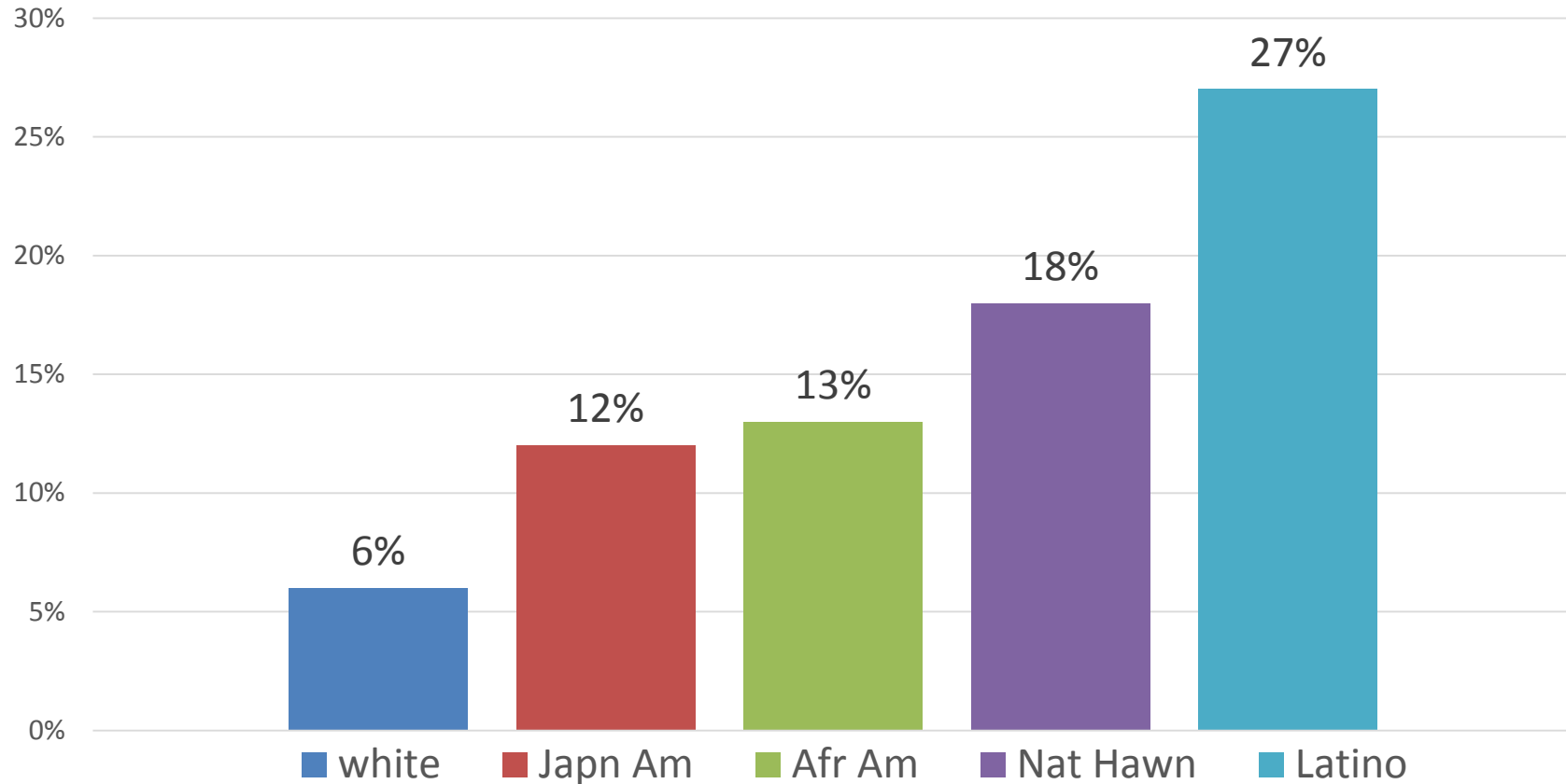


Diabetes-HCC association

	RR* (95% CI)
BMI <25 kg/m ²	3.05 (2.03, 4.58)
Non-drinkers	2.35 (1.78, 3.13)
Non-smokers	3.68 (2.47, 5.48)
Hep B/C negative	2.03 (1.04, 3.95)

*Adjusted for ethnicity, age, sex, education, BMI, alcohol intake, smoking status.

Population Attributable Risk – Diabetes & HCC

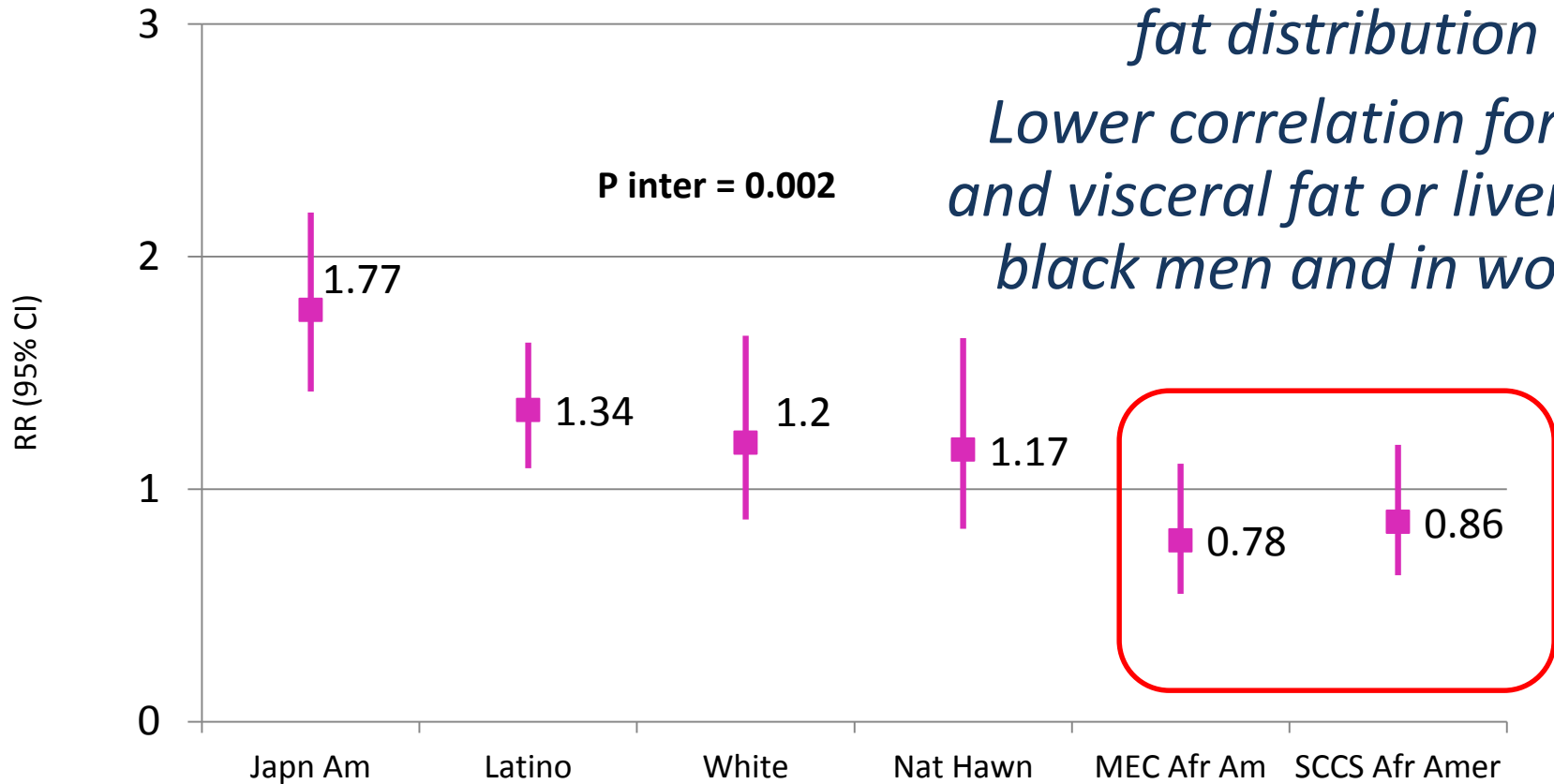


Association of BMI with HCC incidence by sex

BMI (kg/m ²)	HR* (95% CI)		P inter
	MEN	WOMEN	
<25	1.00 (ref.)	1.00 (ref.)	0.036
25-<30	1.50 (1.16, 1.95)	0.98 (0.65, 1.48)	
30+	1.82 (1.31, 2.52) P trend=0.0002	1.32 (0.83, 2.11) P trend=0.29	
Per 5 kg/m ²	1.26 (1.12, 1.42)	1.06 (0.90, 1.25)	0.009

*Adjusted for age, race/ethnicity, education, diabetes, alcohol intake, and smoking status.

Association of BMI (per 5 kg/m² increase) with HCC Incidence in men



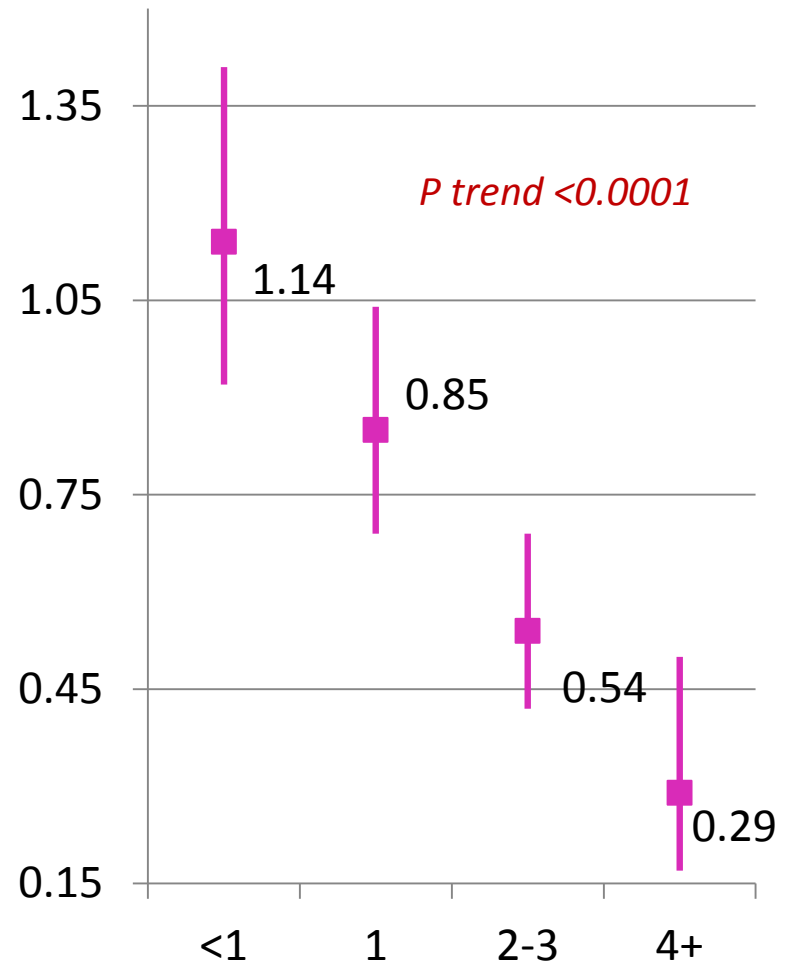
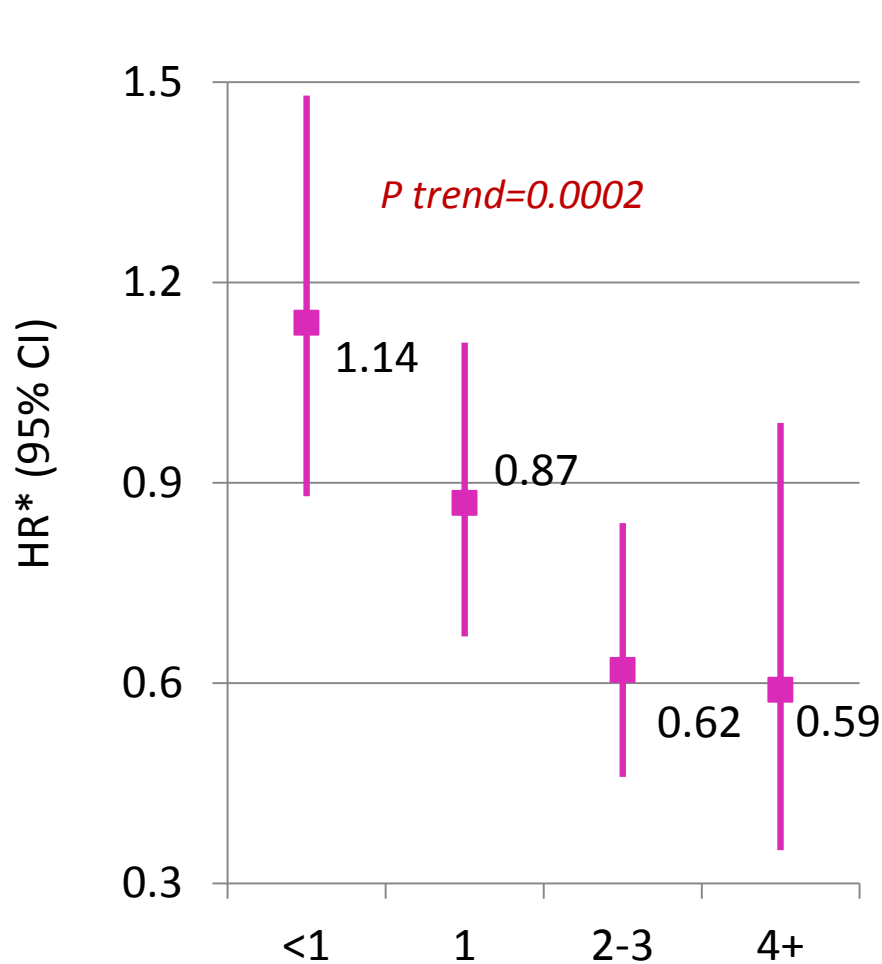
*Adjusted for age, education, diabetes, alcohol intake, and smoking status.



Coffee Intake and HCC and CLD

- Coffee drinking may have beneficial effects on the liver
 - Increasing consumption has been associated with reduced liver enzymes
 - Lower severity of liver diseases and slower liver disease progression
- Coffee drinking is associated with lower risk of diabetes

Coffee Intake - HCC Incidence & CLD deaths



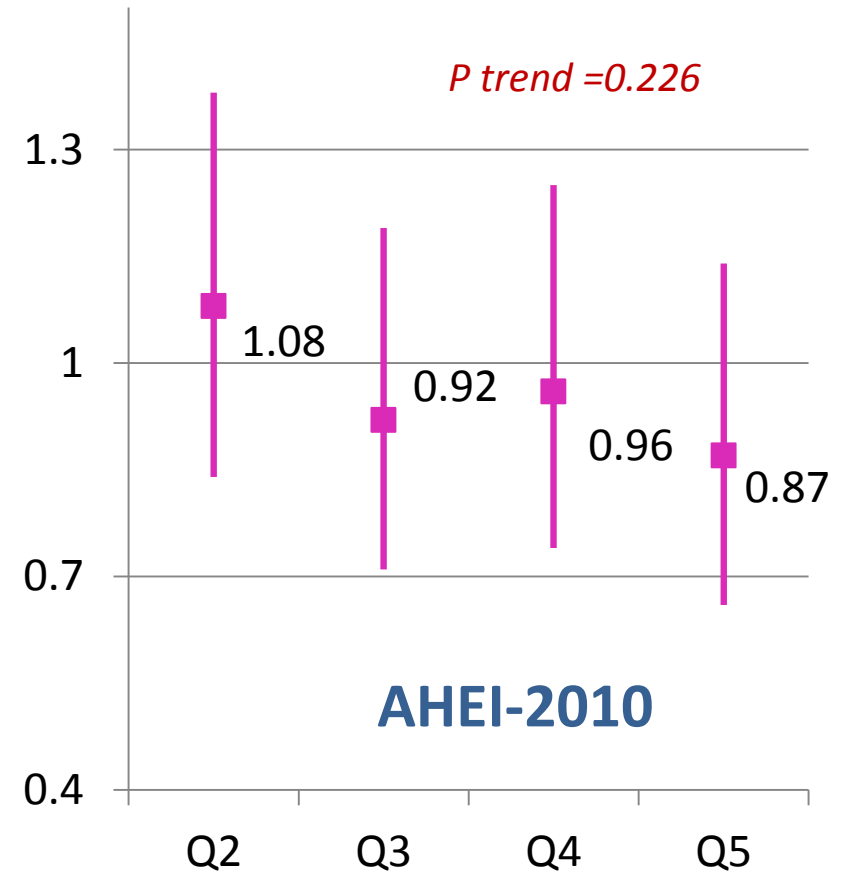
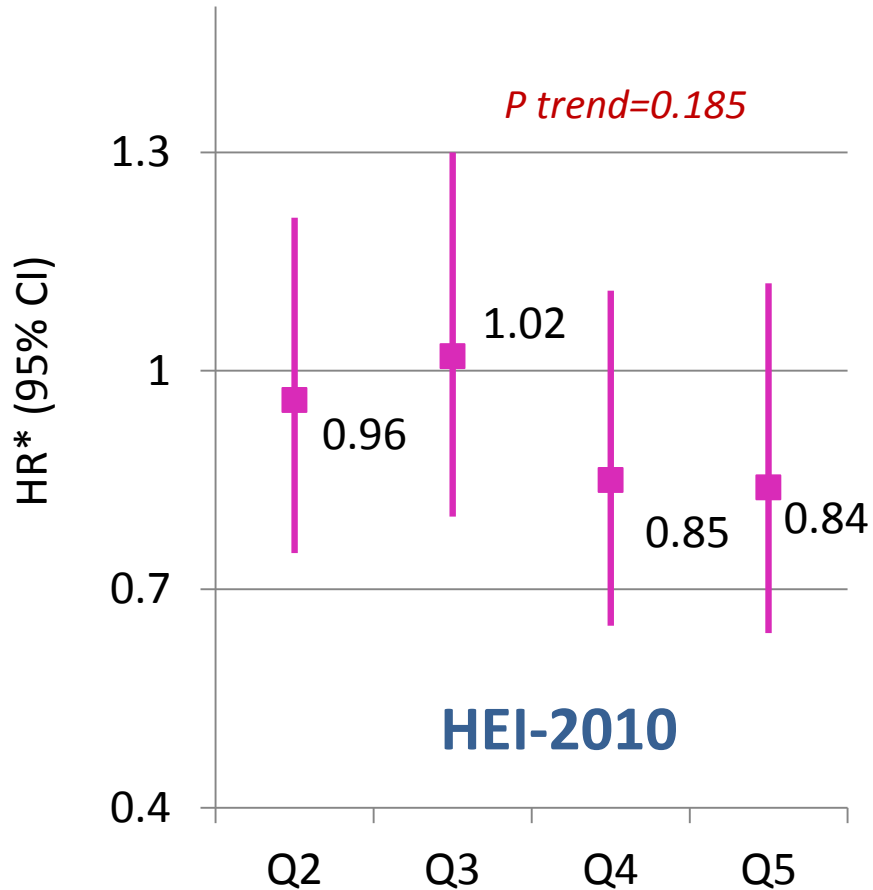
*Adjusted for age, sex, education, BMI, alcohol intake, smoking status, & diabetes.



Dietary Quality Index (DQI) and HCC

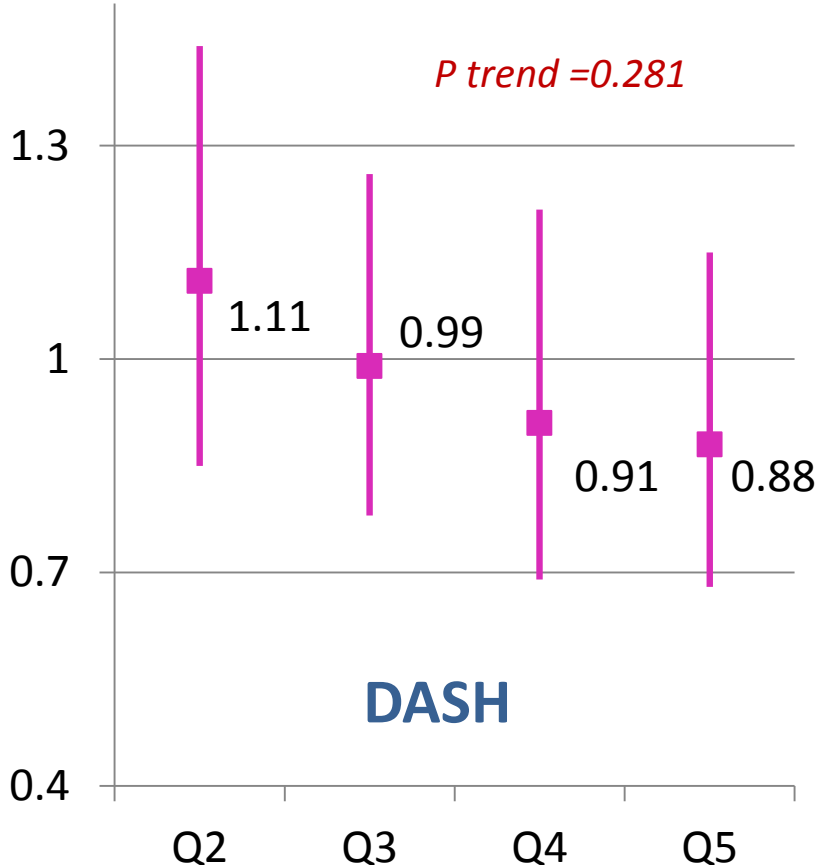
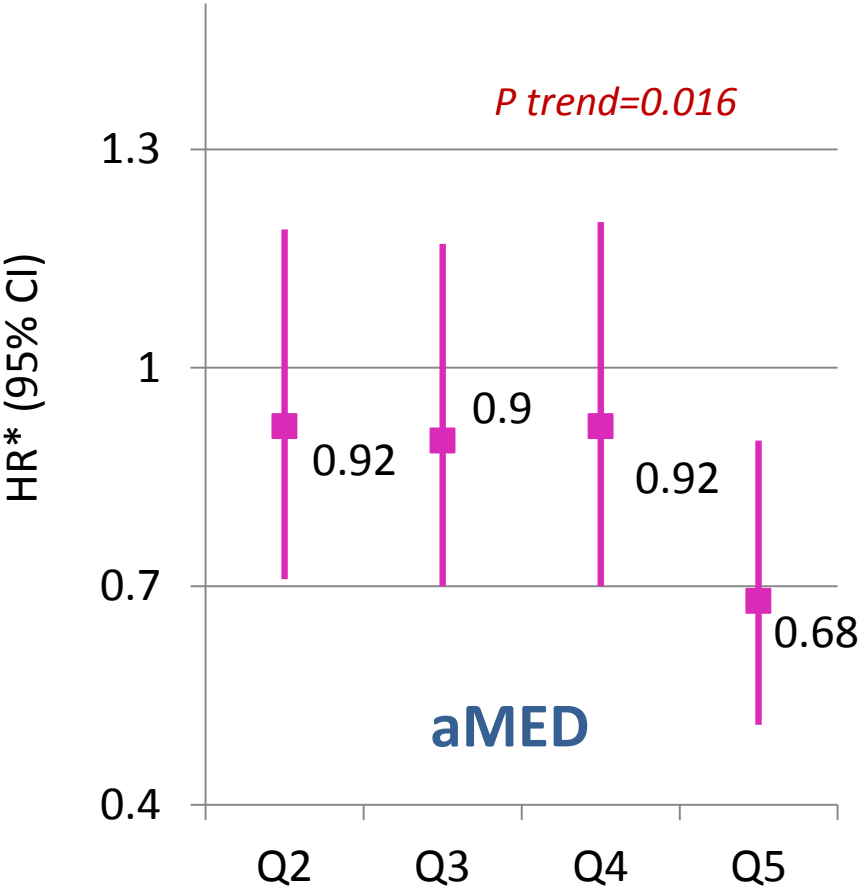
- The role of diet in HCC etiology is poorly understood
- The Dietary Patterns Methods Project* selected 4 DQIs
 - Healthy Eating Index-2010 (HEI-2010)
 - Alternative Healthy Eating Index-2010 (AHEI-2010)
 - Alternate Mediterranean diet score (aMED)
 - Dietary Approaches to Stop Hypertension (DASH) index
- DQIs address the complexity of diet, multicollinearity between dietary components, and can be readily translated into dietary recommendations

Association between DQIs and HCC Incidence



*Adjusted for age, race, sex, education, total energy, BMI, smoking status, & diabetes. For HEI-2010, the model was further adjusted for alcohol consumption.

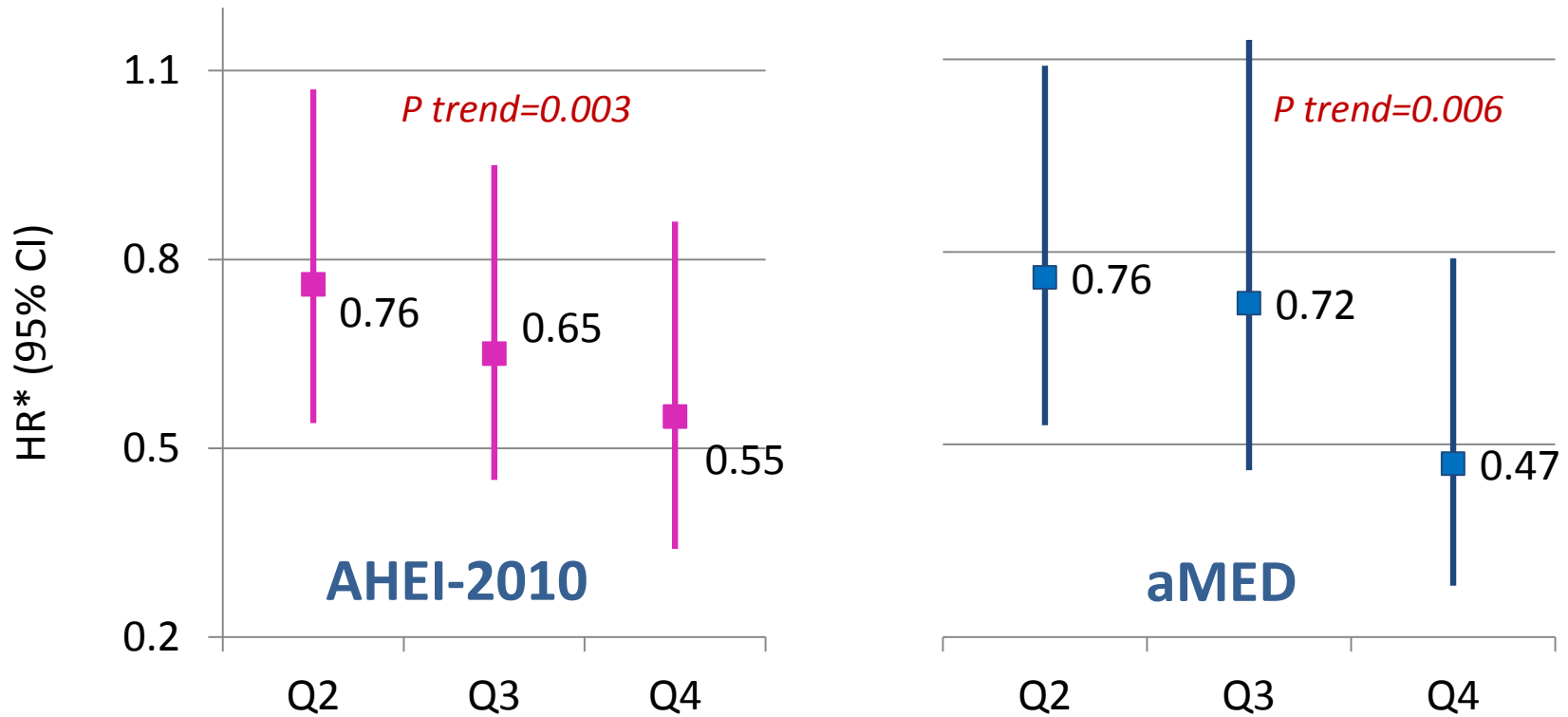
Association between DQIs and HCC Incidence



*Adjusted for age, race, sex, education, total energy, BMI, smoking status, & diabetes. For DASH, the model was further adjusted for alcohol consumption.



Association between DQIs and HCC Incidence in Latinos



*Adjusted for age, sex, education, total energy, BMI, smoking status, & diabetes. These DQIs include alcohol intake.

Expanding epidemiologic research in
the MEC to non-cancer endpoints:
Medicare Linkage

MEC-Medicare Linkage Process and Results

215,722 MEC participants



23,205 aged <65 by Dec 31, 2011
6,424 died before 65
1,845 had no or invalid SSN

184,299 (85%) unique identifiers
(SSN, gender, DOB) sent to CMS



5,171 false or no link

179,128 (97%) matched and assigned Bene ID
(vital status)



97 duplicates/overlap HI/LA
8,265 no match to Medicare enrollment
data

170,766 (93%) successfully linked to
Medicare Enrollment Data

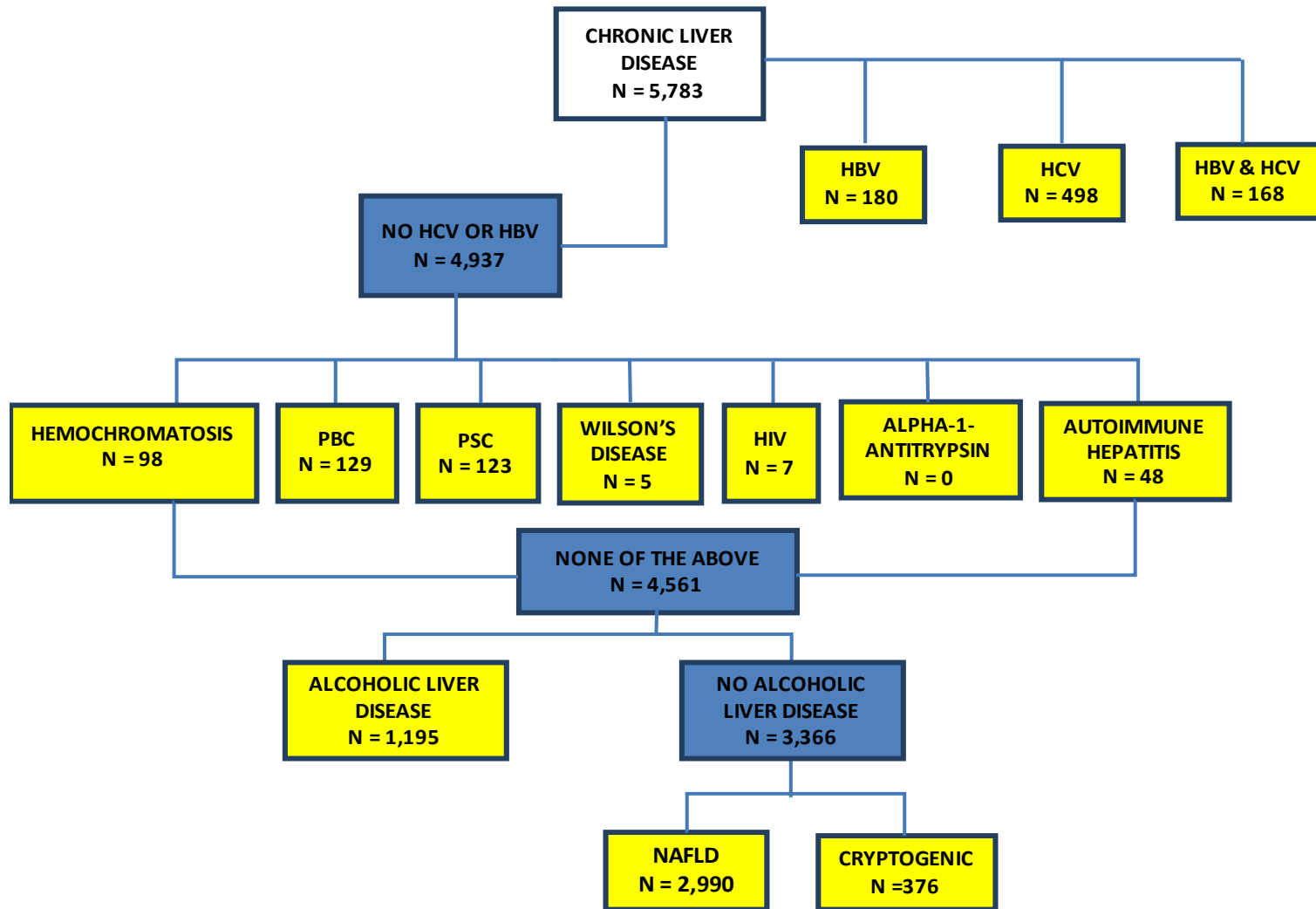


107,031 (63%) enrolled in fee-for-service (FFS) for at least 1 month
63,735 (37%) enrolled in HMO the entire time

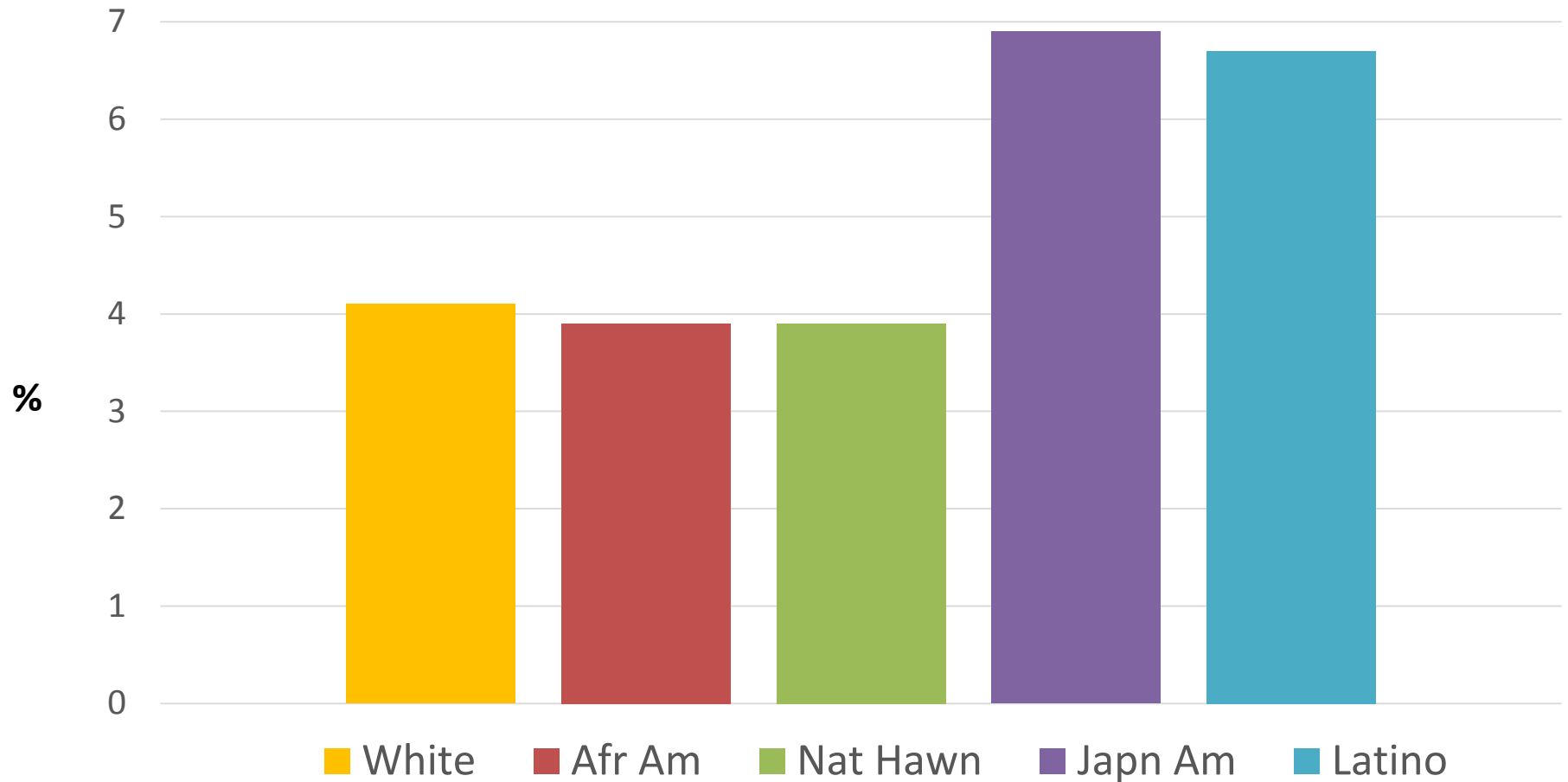
Chronic Liver Disease (CLD)

- CLD is a major health problem in the US
- ALD and HCV/HBV are major causes of CLD, but NALFD has become the most common cause
- Data on ethnic differences in the CLD prevalence are limited and restricted to a few ethnic populations
- Aim: to examine the prevalence of CLD and cirrhosis by underlying etiology in AA, JA, LA, NH, and WH in the MEC

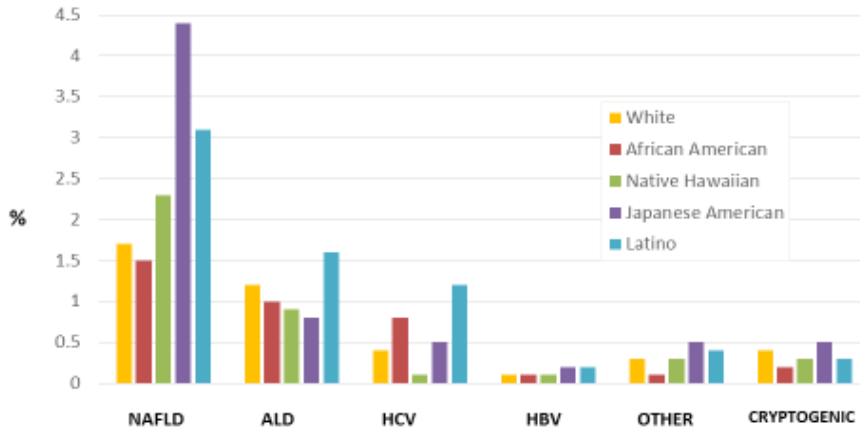
Chronic Liver Disease by Etiology



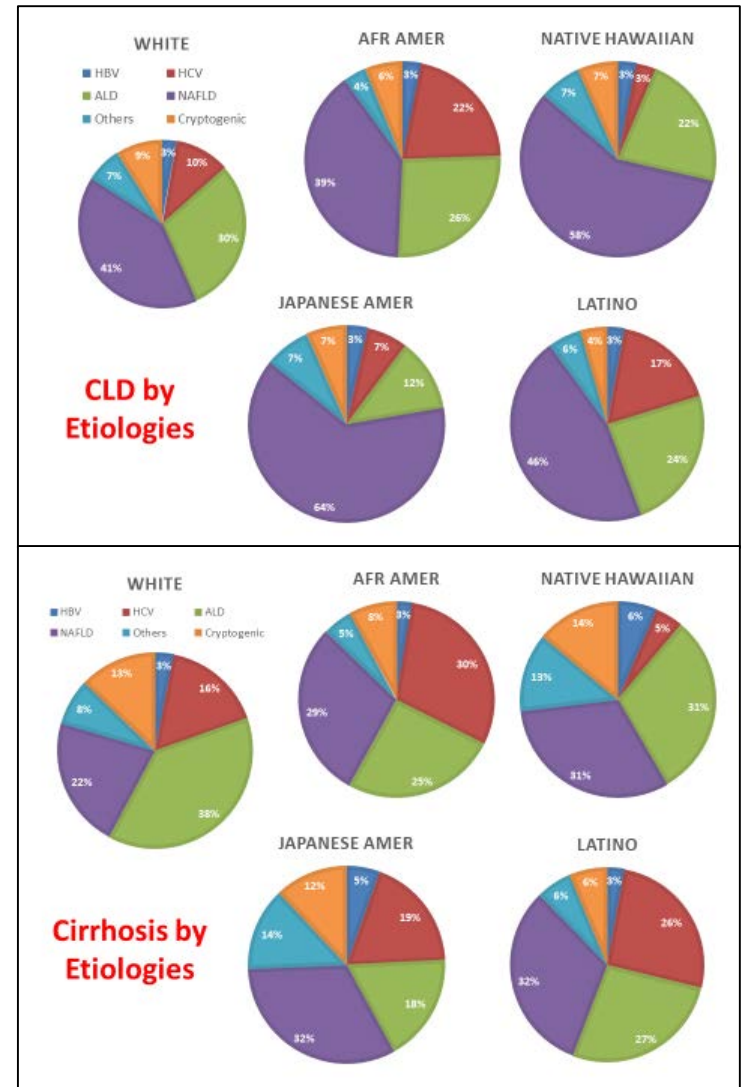
Prevalence of CLD in the FFS participants (1999-2012)



Prevalence of CLD by etiology in the MEC (1999-2012)



- Racial/ethnic variations in the prevalence of CLD and cirrhosis by underlying etiology
- NAFLD is the most common cause of CLD and cirrhosis in all ethnic groups combined
 - NAFLD is the most common cause of cirrhosis in JA, LA and NH; HCV and ALD the most common cause of cirrhosis in AA and WH, respectively
- While the prevalence of NAFLD is low in AA, it is the most common cause of CLD and second most common cause of cirrhosis in AA
- The prevalence of NAFLD in JA is higher than in LA and other ethnic groups

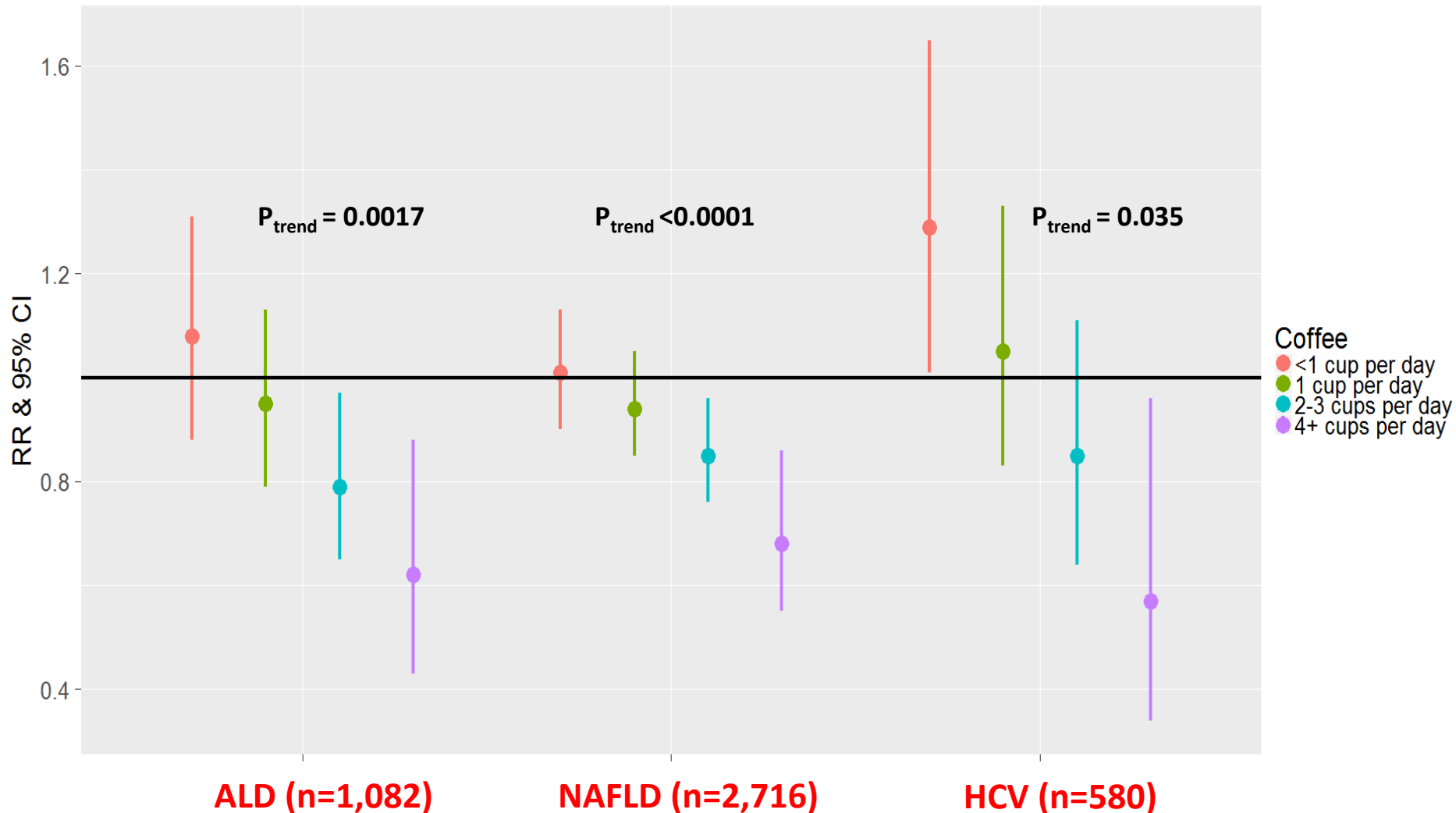




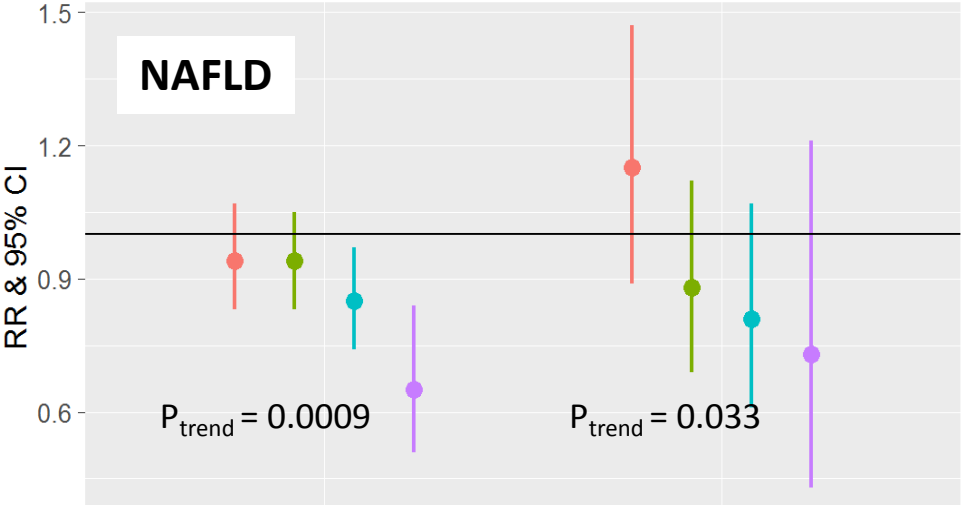
Coffee Drinking and CLD -- Background

- Coffee drinking has been inversely associated with
 - HCC incidence & CLD deaths
 - Progression of fibrosis
 - Cirrhosis incidence
- Data are limited with regard to coffee association with specific CLD etiologic types
 - We examined whether the association of coffee drinking with CLD differs by underlying etiology

Coffee Intake and CLD by etiology

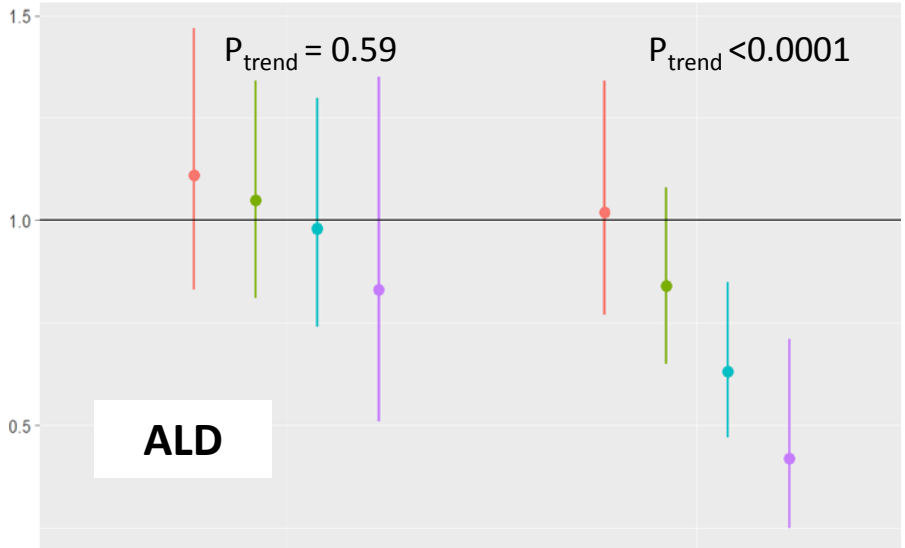


RR stratified by risk set and adjusted for education, BMI, diabetes, smoking status and alcohol intake.



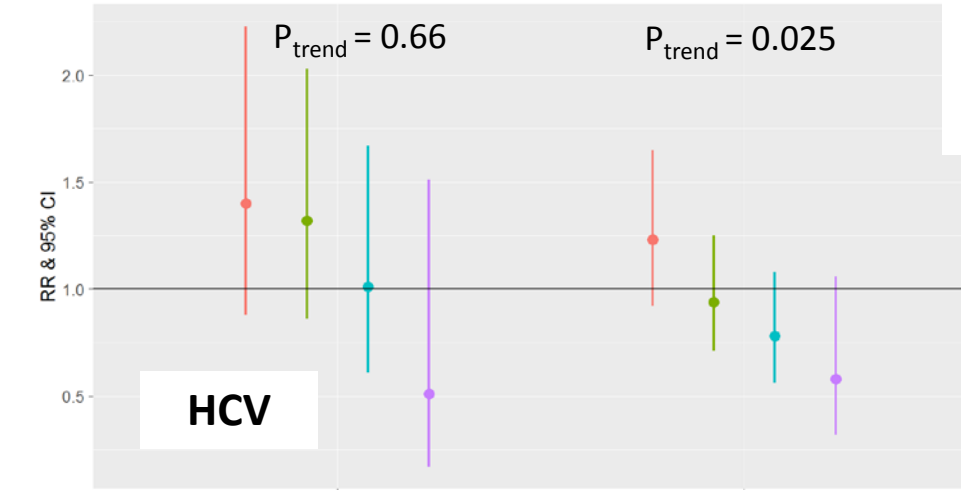
No cirrhosis
n=2,146

Cirrhosis
n=570



No cirrhosis
n=539

Cirrhosis
n=495



No cirrhosis
n=168

Cirrhosis
n=412

Coffee

- <1 cup per day
- 1 cup per day
- 2-3 cups per day
- 4+ cups per day

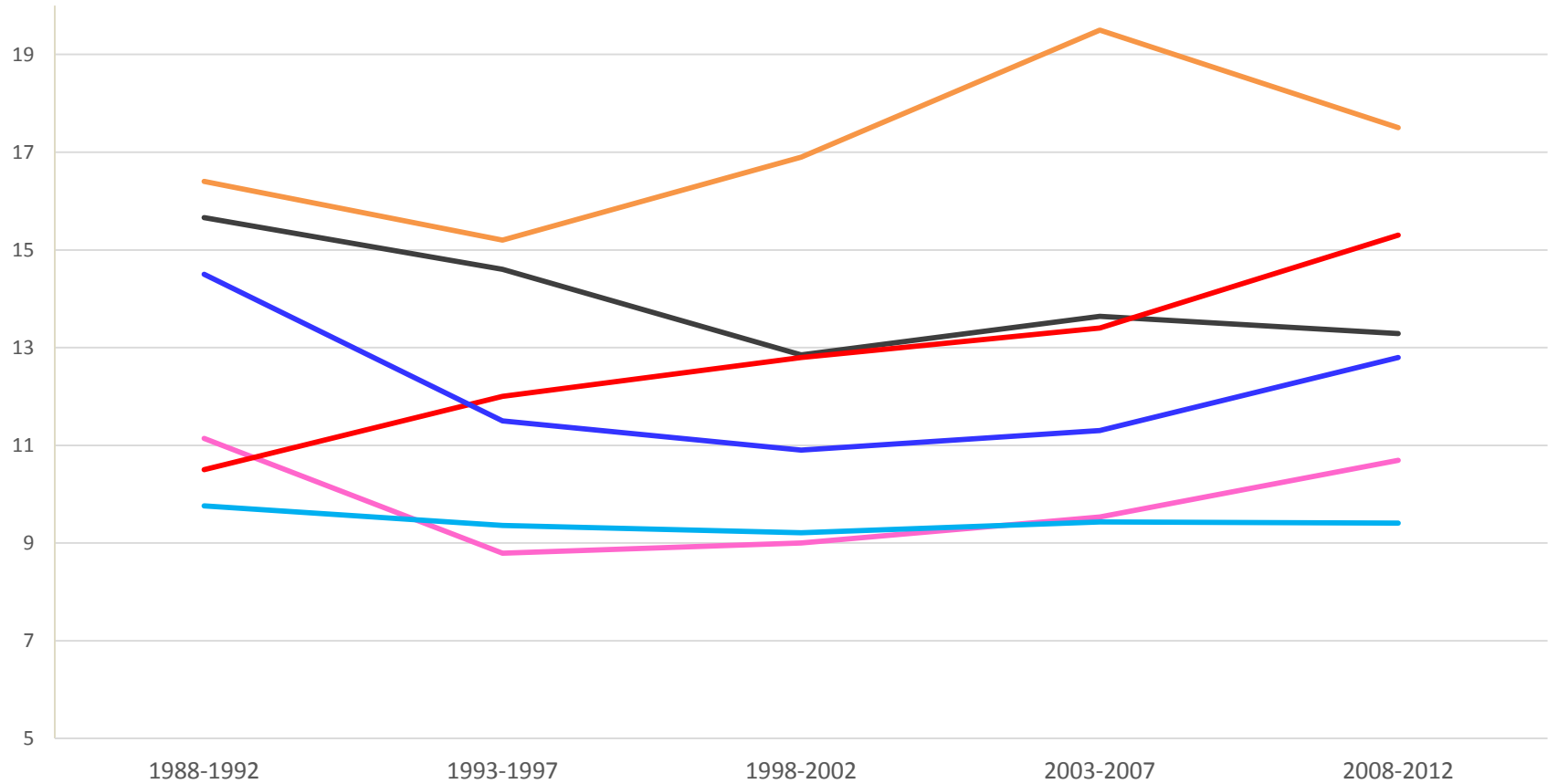
RR stratified by risk set and adjusted for education, BMI, diabetes, smoking status and alcohol intake.

Coffee Drinking & CLD – Summary

- Coffee was associated with reduced risks of NAFLD- ALD-, HCV-related CLD with dose dependent manners
 - Associations were stronger in advanced CLD (cirrhosis) for ALD and HCV
 - Protective association with 2+ cups/day

Diseases of the Pancreas: Pancreatic Cancer & Pancreatitis

Age-adjusted Incidence Rates of Pancreatic Cancer in California and Hawaii 1988-2012



CA Japanese

CA Caucasian

CA African American

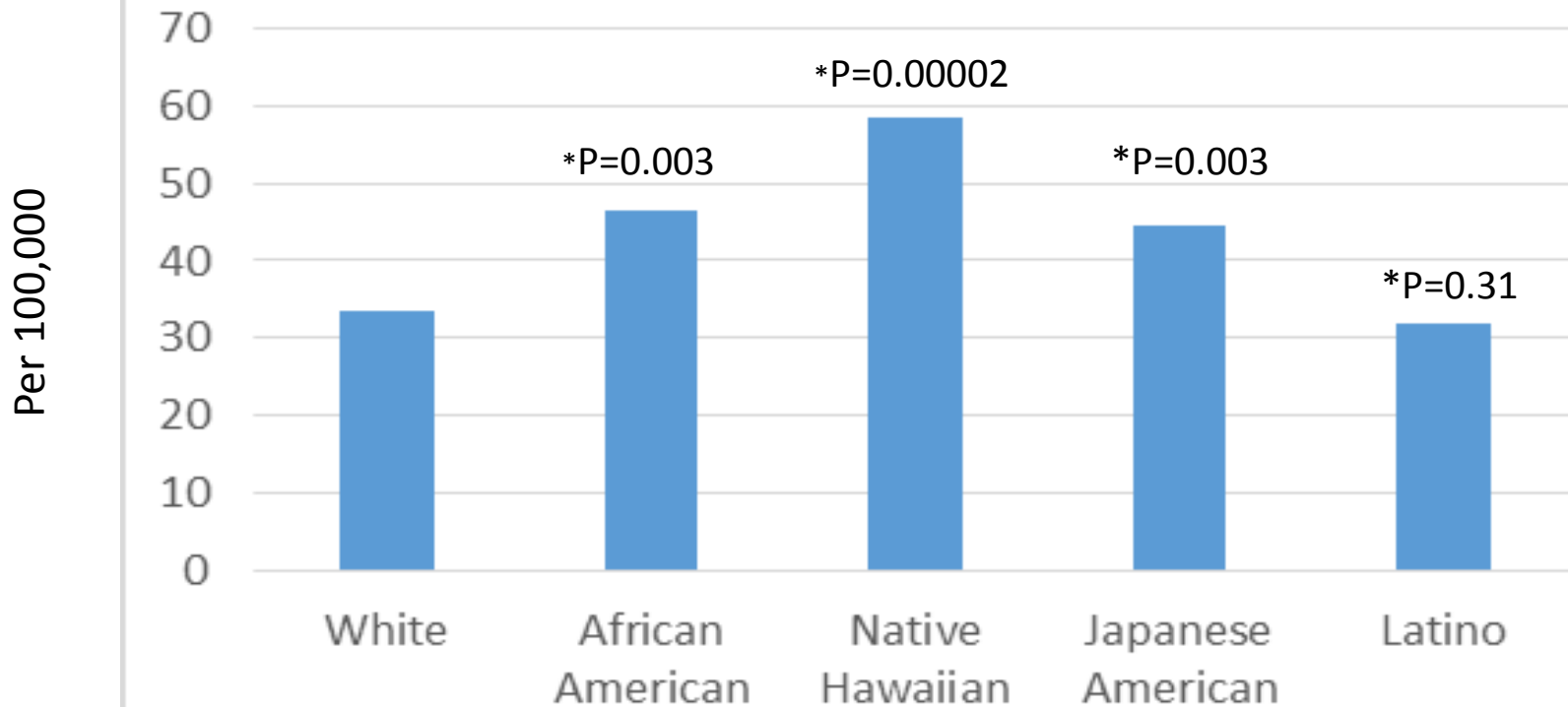
HI Japanese

HI Caucasian

HI Native Hawaiian

Pancreatic Cancer in the MEC

Figure 1. Age-adjusted Incidence Rates of Pancreatic Cancer in the MEC (1993-2012)



*P value comparing pancreatic cancer rate to whites

Associations of risk factors with PC incidence

Risk factors	HR* (95% CI)
Smoking	
Never	1.00
Past <20 pack years	0.96 (0.84, 1.10)
Past ≥ 20 pack years	0.97 (0.80, 1.17)
Current <20 pack years	1.40 (1.15, 1.71)
Current ≥ 20 pack years	1.72 (1.42, 2.09)
Body mass index (kg/m²)	
<25	1.00
25-<30	1.08 (0.96, 1.22)
≥ 30	1.26 (1.08, 1.47)
Diabetes mellitus	
No	1.00
Yes	1.38 (1.18, 1.60)
Alcohol intake (ethanol g/day)	
0	1.00
>0-≤24	0.97 (0.86, 1.10)
>24-≤48	1.00 (0.80, 1.24)
>48	0.94 (0.71, 1.25)
Family history of pancreatic cancer	
No	1.00
Yes	1.91 (1.44, 2.54)
Red meat intake	
Q1	1.00
Q2	1.27 (1.10, 1.48)
Q3	1.14 (0.97, 1.33)
Q4	1.26 (1.08, 1.48)

Pancreatic Cancer in the MEC

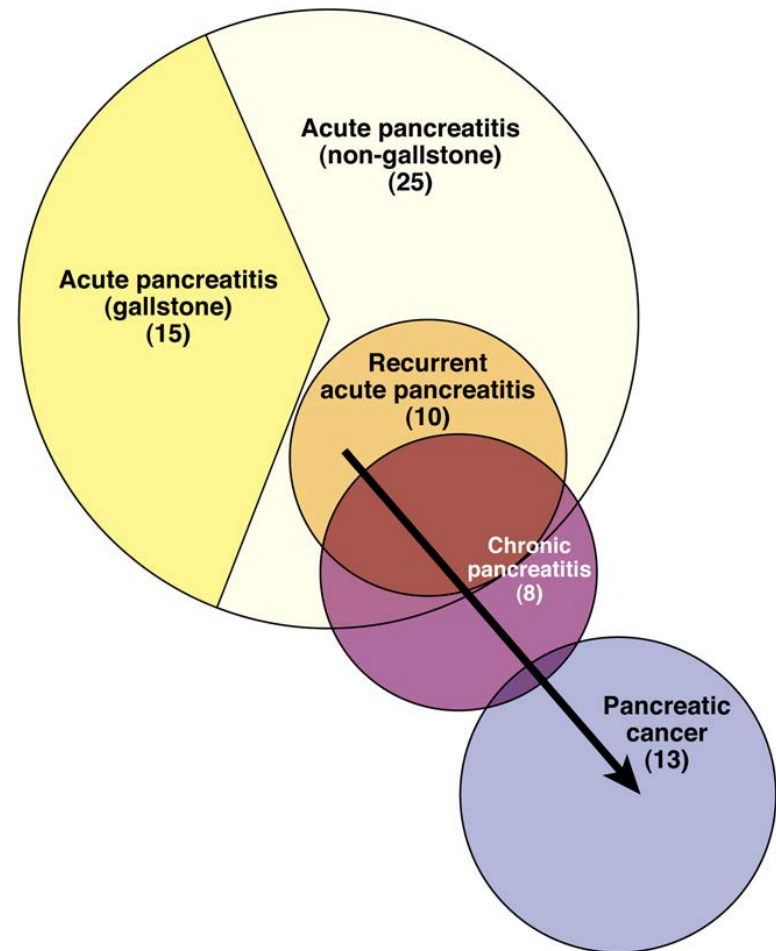
	HR* (95% CI)	HR** (95% CI)
Afr Am	1.34 (1.13, 1.58)	1.20 (1.01, 1.43)
Nat Hawn	1.76 (1.42, 2.18)	1.56 (1.26, 1.95)
Japn Am	1.28 (1.11, 1.48)	1.29 (1.10, 1.50)
Latino	0.93 (0.79, 1.11)	0.87 (0.73, 1.04)

*Age- sex- adjusted

**Further adjusted for BMI, smoking, alcohol, diabetes, red meat, family history of pancreatic cancer

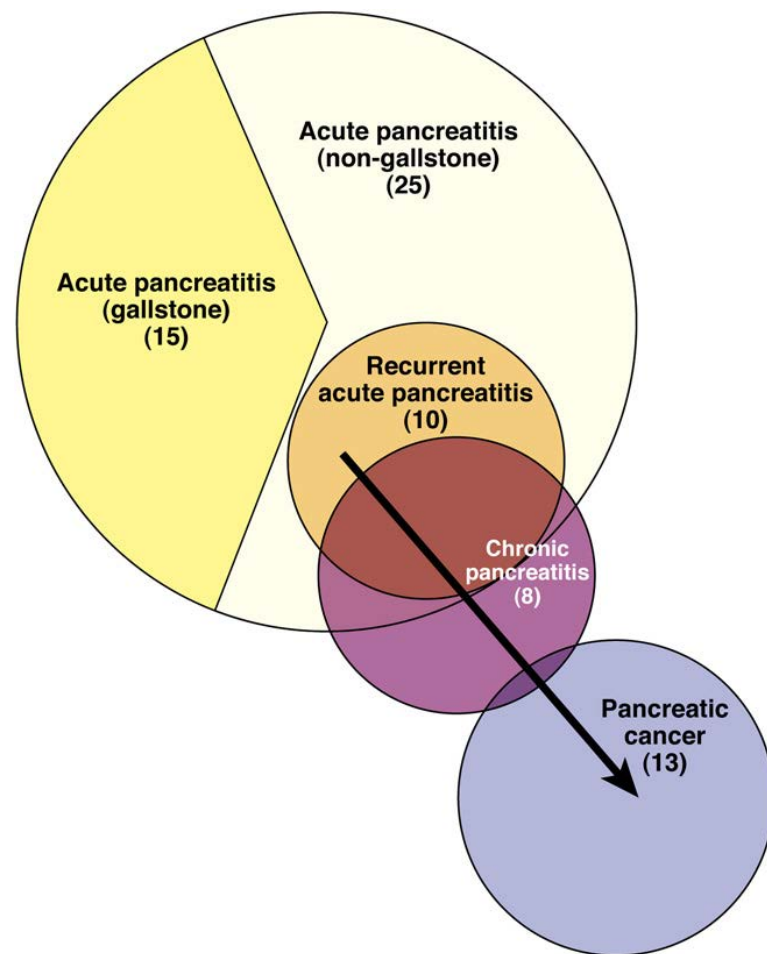
Pancreatitis

- Pancreatitis is a significant medical and financial problem in the US
- RAP can lead to CP, a serious condition which severely impacts quality of life and can lead to serious complications including diabetes and pancreatic cancer
- There is no available treatment for pancreatitis and no therapy to prevent recurrent episodes
- Racial disparity in pancreatitis incidence is striking
 - The risk is 2- to 3-fold higher among AA than Whites
 - AA aged 35-65 are nearly 10 times more likely to develop pancreatitis compared to other ethnic populations in the same age group
 - Whether the increased incidence in AA is related to genetics or to dietary or other lifestyle factors is unclear



Pancreatitis

- Acute, recurrent acute, chronic pancreatitis
 - Gallstone & non gallstone related
- Case identification using hospitalization claim (1999-2012) principal dx
 - AP: 1 claim (ICD-9: 577.0)
 - RAP: 1+ AP claims, >30 days apart
 - CP: 2+ claims (ICD-9: 577.1), ≥60 days apart
- 1,065 GS AP, 1,222 non GS AP, 523 RAP/CP



Smoking & non-GS pancreatitis

MEN	NON GS AP (n=508)	RAP/CP (n=206)
Smoking		
Never	1.00 (ref.)	1.00 (ref.)
Past	1.21 (0.97-1.51)	1.25 (0.89-1.78)
Current	1.87 (1.44-2.43)	1.72 (1.12-2.66)
Smoking-pack years		
Never	1.00 (ref.)	1.00 (ref.)
Past, <20	1.25 (0.99-1.57)	1.28 (0.89-1.85)
Past, 20+	1.10 (0.80-1.50)	1.17 (0.72-1.90)
Current, <20	1.87 (1.37-2.56)	1.96 (1.18-3.24)
Current, 20+	1.87 (1.34-2.60)	1.47 (0.84-2.60)
WOMEN	NON GS AP (n=714)	RAP/CP (n=317)
Smoking		
Never	1.00 (ref.)	1.00 (ref.)
Past	1.35 (1.13-1.61)	1.28 (0.97-1.68)
Current	1.63 (1.30-2.04)	2.31 (1.70-3.14)
Smoking-pack years		
Never	1.00 (ref.)	1.00 (ref.)
Past, <20	1.27 (1.05-1.53)	1.20 (0.89-1.61)
Past, 20+	1.83 (1.34-2.50)	1.75 (1.07-2.85)
Current, <20	1.45 (1.11-1.91)	1.89 (1.29-2.75)
Current, 20+	2.01 (1.45-2.80)	3.22 (2.12-4.87)

RR stratified by risk set adjusted for education, BMI, diabetes, vigorous activity and alcohol intake.

Alcohol Intake & non-GS Pancreatitis

MEN	NON GS AP (n=508)	RAP/CP (n=206)
Alcohol Intake (g/day)		
0	1.00 (ref.)	1.00 (ref.)
< 24	0.85 (0.69-1.03)	0.57 (0.41-0.79)
24-≤ 48	0.70 (0.49-1.00)	0.59 (0.34-1.02)
> 48	1.06 (0.75-1.50)	1.50 (0.94-2.39)
WOMEN	NON GS AP (n=714)	RAP/CP (n=317)
Alcohol Intake (g/day)		
0	1.00 (ref.)	1.00 (ref.)
< 12	0.81 (0.67-0.97)	0.66 (0.49-0.87)
12-≤ 24	0.69 (0.44-1.08)	0.73 (0.39-1.35)
> 24	0.86 (0.58-1.27)	0.58 (0.30-1.11)

RR stratified by risk set adjusted for education, BMI, diabetes, vigorous activity and smoking.

Joint Effect Smoking & Alcohol for non GS Pancreatitis

MEN		WOMEN	
Never smoker		Never smoker	
Non-drinker	1.00 (ref.)	Non-drinker	1.00 (ref.)
≤ 48g daily	0.70 (0.51-0.96)	< 24g daily	0.81 (0.66-1.01)
> 48g daily	1.59 (0.87-2.87)	≥ 24g daily	0.65 (0.30-1.38)
Past smoker		Past smoker	
Non-drinker	1.28 (0.98-1.68)	Non-drinker	1.39 (1.16-1.66)
≤ 48g daily	0.86 (0.65-1.12)	< 24g daily	0.97 (0.77-1.23)
> 48g daily	1.30 (0.85-1.99)	≥ 24g daily	1.04 (0.61-1.76)
Current smoker		Current smoker	
Non-drinker	1.48 (1.03-2.12)	Non-drinker	1.88 (1.50-2.37)
≤ 48g daily	1.54 (1.13-2.09)	< 24g daily	1.32 (0.99-1.75)
> 48g daily	2.06 (1.28-3.30)	≥ 24g daily	1.67 (1.03-2.71)

BMI, Diabetes & Pancreatitis

MEN	GS AP	NON GS AP	RAP/CP
BMI (kg/m²)			
< 25	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
25 – < 30	1.40 (1.10-1.77)	1.11 (0.90-1.37)	0.75 (0.54-1.04)
≥ 30	1.99 (1.49-2.65)	1.35 (1.03-1.75)	1.05 (0.70-1.57)
	<.0001	0.0325	0.9045
Diabetes	1.67 (1.30-2.14)	1.49 (1.16-1.89)	1.65 (1.15-2.38)
WOMEN	GS AP	NON GS AP	RAP/CP
BMI (kg/m²)			
< 25	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
25 – < 30	1.31 (1.06-1.63)	1.09 (0.90-1.32)	1.00 (0.74-1.34)
≥ 30	2.02 (1.61-2.53)	1.13 (0.91-1.40)	1.29 (0.95-1.76)
	<.0001	0.2578	0.1002
Diabetes	1.43 (1.13-1.81)	1.91 (1.56-2.34)	1.98 (1.48-2.65)

RR stratified by risk set adjusted for education, BMI, diabetes, vigorous activity and smoking.

Diet & Pancreatitis

	GS AP	NON GS AP	RAP/CP
Total Red Meat (g/kcal/day)			
≤ 14.4	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
> 14.4 – ≤ 24.5	1.22 (1.03-1.46)	1.12 (0.95-1.33)	1.04 (0.75-1.44)
> 24.5 – ≤ 36.3	1.26 (1.06-1.51)	1.03 (0.87-1.23)	1.37 (1.01-1.87)
> 36.3	1.46 (1.22-1.74)	1.04 (0.87-1.24)	1.36 (0.99-1.87)
p for trend	<0.0001	0.9182	0.0202
Eggs (g/kcal/day)			
≤ 2.9	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
> 2.9 – ≤ 5.1	1.03 (0.87-1.22)	0.94 (0.79-1.11)	1.02 (0.75-1.38)
> 5.1 – ≤ 9.0	1.15 (0.97-1.36)	1.05 (0.89-1.23)	1.07 (0.79-1.44)
> 9.0	1.24 (1.05-1.47)	0.99 (0.84-1.17)	0.97 (0.71-1.31)
p for trend	0.0052	0.8094	0.9032
% of calories from saturated fat			
≤ 7.2	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
> 7.2 – ≤ 9.1	1.13 (0.95-1.36)	0.89 (0.75-1.06)	0.88 (0.64-1.21)
> 9.1 – ≤ 10.9	1.21 (1.01-1.45)	0.94 (0.79-1.12)	0.99 (0.72-1.35)
> 10.9	1.35 (1.12-1.62)	1.00 (0.83-1.19)	1.06 (0.77-1.46)
p for trend	0.0011	0.8082	0.5242

Diet & Pancreatitis

	GS AP	NON GS AP	RAP/CP
Cholesterol (mg/kcal/day)			
≤ 79.0	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
> 79.0 – ≤ 103.2	1.18 (0.99-1.40)	0.98 (0.83-1.17)	0.94 (0.69-1.28)
> 103.2 – ≤ 130.6	1.32 (1.11-1.57)	1.03 (0.86-1.22)	0.90 (0.66-1.23)
> 130.6	1.33 (1.12-1.59)	1.03 (0.87-1.23)	1.02 (0.75-1.39)
p for trend	0.0008	0.6272	0.9393
Total dietary fiber (g/kcal/day)			
≤ 6.7	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
> 6.7 – ≤ 8.6	0.99 (0.83-1.16)	0.79 (0.67-0.94)	0.98 (0.72-1.33)
> 8.6 – ≤ 11.0	0.88 (0.74-1.05)	0.74 (0.62-0.87)	0.98 (0.71-1.33)
> 11.0	0.74 (0.62-0.89)	0.77 (0.65-0.92)	1.00 (0.72-1.38)
p for trend	0.0005	0.0035	0.9907

Ongoing Analyses/Studies

- **Liver Cancer/CLD**

- Comprehensive diet analyses; physical activity; medication use
- Ethnic differences in HCC underlying etiology and secular changes
- Pending R01MD012581 (PI: Setiawan) *Understanding the Determinants of Racial/Ethnic Disparities in Liver Cancer and Chronic Liver Disease in Understudied and High-Risk Populations*

- **Pancreatic Cancer/Pancreatitis**

- ACS RSG CPHPS 130010: *Determinants of racial/ethnic disparities in pancreatic cancer incidence in the MEC*
- R01CA209798: *Investigating the cause of racial/ethnic disparity in pancreatic cancer incidence*
- Pending R01CA227133 (MPI: Setiawan/Shu): *Use of Circulating MicroRNAs for Early Detection and Risk Assessment Pancreatic Cancer*
- Comprehensive diet analyses; physical activity; medical conditions; timing of diabetes onset; medication use
- Genetic analysis for known loci

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Thank you!

Questions?

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Chronic Conditions Summary

n = 120,607

Original Medicare Plan Blood Samples

