



# Disparities in Disease Severity and Progressiveness of NAFLD/NASH Across Ethnic Groups in the United States

## 2022 Liver Connect Conference

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# Disclosures

- Advisory Board – Novo Nordisk
- Consultant – Pfizer
- Principal Investigator Study Drug Trial – Pfizer and Galmed
- Principal Investigator Trial – Target Pharma

# Learning Objectives

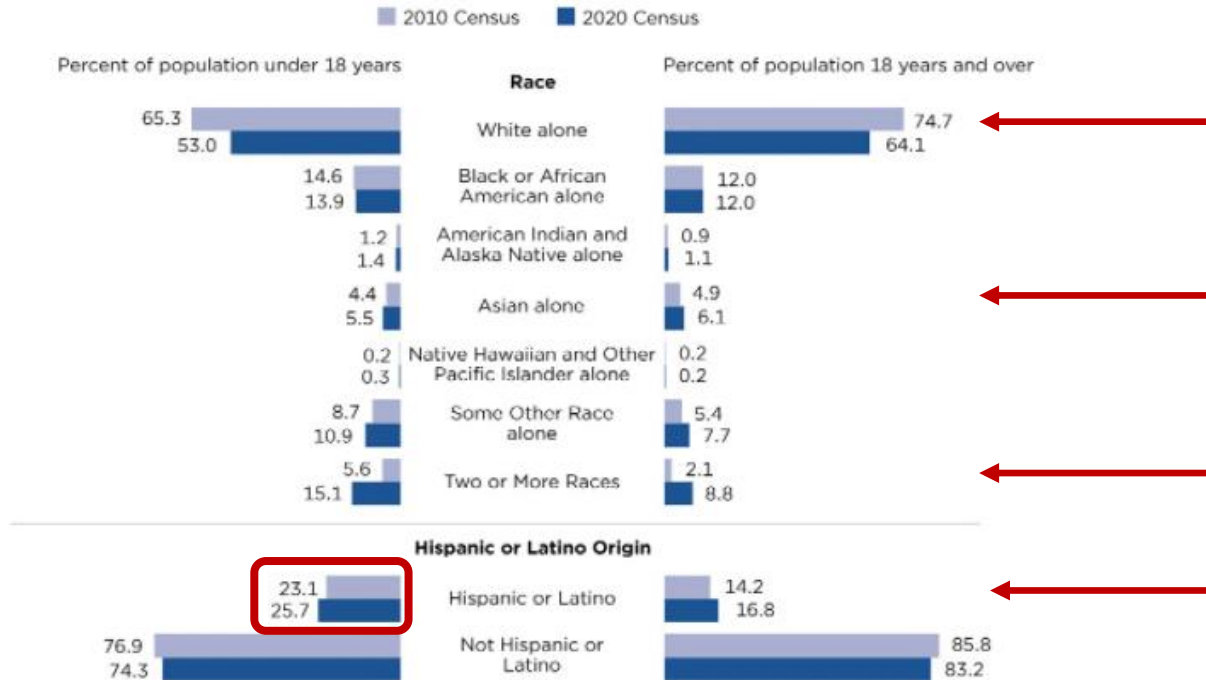
- Review the changing racial and ethnic **landscape** in the US
- Compare NAFLD **prevalence** by race/ethnicity
- Examine disparities in NAFLD **outcomes** by race/ethnicity
- Discuss **reasons** for disparities in NAFLD among racial/ethnic groups

# Review the Changing Racial and Ethnic Landscape in the US



# Race and Ethnicity Changes Over the Last Decade in the US

Figure 5.  
**Percentage Distribution of Race and Hispanic Origin by Age Group:  
 2010 and 2020**



# Race and Ethnicity in the United States: 2010 Census and 2020 Census

Pick a topic. →

Race by Ethnicity

Hispanic Origin

Select a question:

What percentage was each group in 2020?

How has each group changed since 2010?

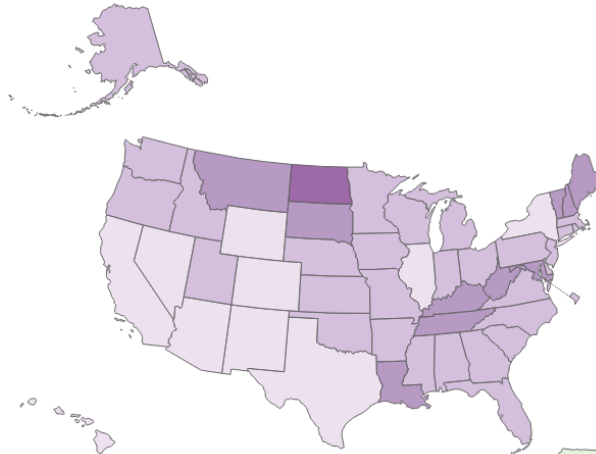
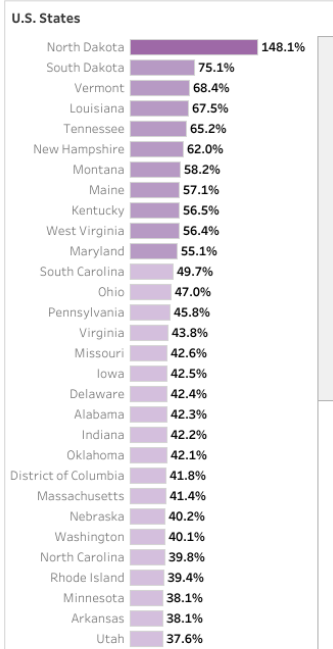
What are facts for my state or county?

To view specific groups: (1) Use the drop-down filter to select Hispanic or Latino or Not Hispanic or Latino, and (2) Hover over the map to view statistics for each state. The list on the left shows states (or state equivalents) ranked by percent change in the population for the selected group. Use the filter to the right of the map to view county-level statistics for your state.

Group: Hispanic or Latino

## Percent Change Hispanic or Latino Population by State: 2010 to 2020

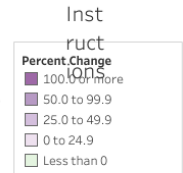
United States: 23.0%



Interested in viewing counties?  
Use the filter to select a state then click the arrow to view counties.

Alabama

→



# Race and Ethnicity in the United States: 2010 Census and 2020 Census

Pick a topic. →

Race by Ethnicity

Hispanic Origin

Select a question:

What percentage was each group in 2020?

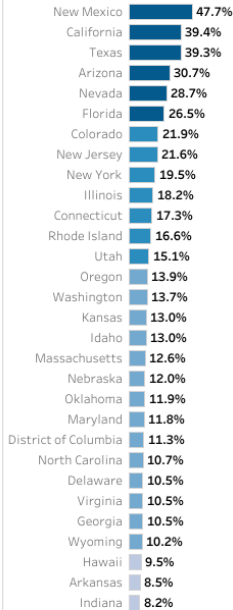
How has each group changed since 2010?

What are facts for my state or county?

To view specific groups: (1) Use the drop-down filter to select Hispanic or Latino or Not Hispanic or Latino, and (2) Hover over the map to view statistics for each state. The list on the left shows states (or state equivalents) ranked by percentage of the total population for the selected group. Use the filter to the right of the map to view county-level statistics for your state.

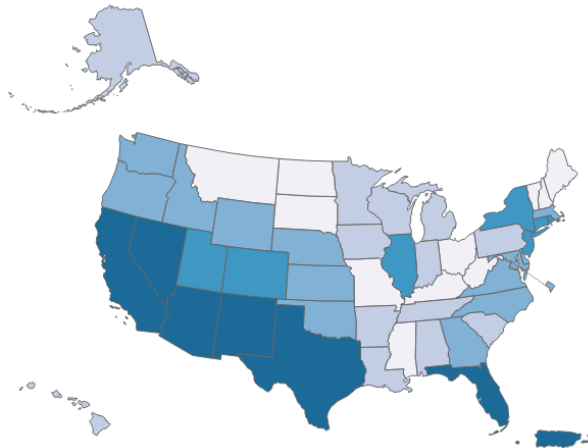
Group: Hispanic or Latino

## U.S. States



## Percent Hispanic or Latino by State: 2020

United States: 18.7%



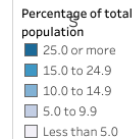
### Interested in viewing counties?

Use the filter to select a state then click the arrow to view ...

Alabama



Percentage of total population

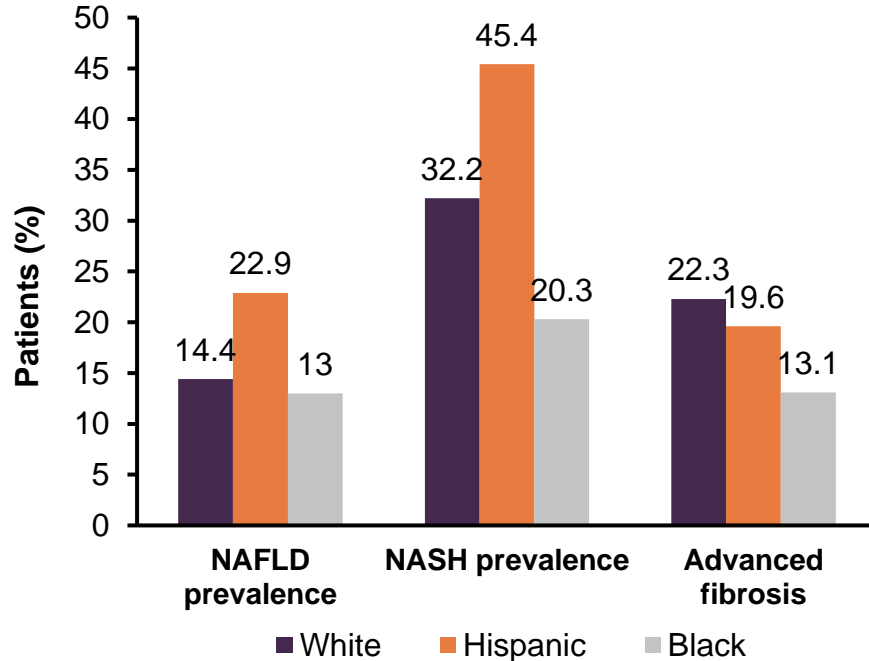


# Compare NAFLD Prevalence by Race/Ethnicity





# Racial and Ethnic Disparities in NAFLD

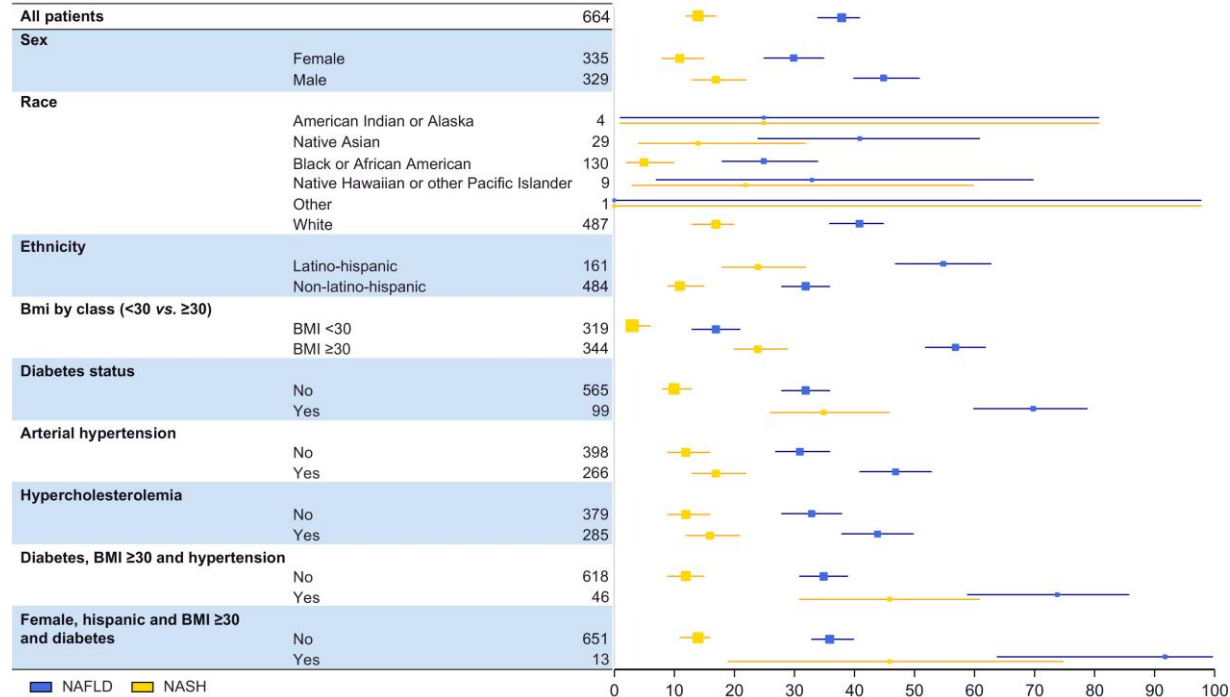


Systematic review and metaanalysis of 34 studies

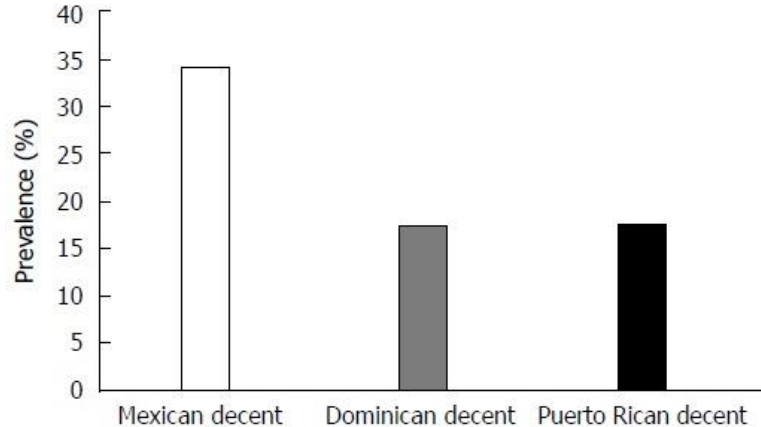
- In reference to Whites:
  - Hispanics have RR=1.47 for NAFLD
  - Blacks have RR=0.74 for NAFLD
- Liver-related outcomes and mortality were not amenable to pooling due to heterogeneity of results
- Limitations: cross-sectional, heterogeneity in method of NAFLD diagnosis

# The Prevalence of NAFLD and NASH in Texas

- **Prospective cohort**
- Overall NAFLD prevalence 38%
- Highest in Latino/Hispanic
- Lowest in Black Americans



# NAFLD Prevalence by Hispanic Subgroups



- Multi-Ethnic Study of Atherosclerosis (MESA) >6000 people from 6 US Universities
- NAFLD defined by CT

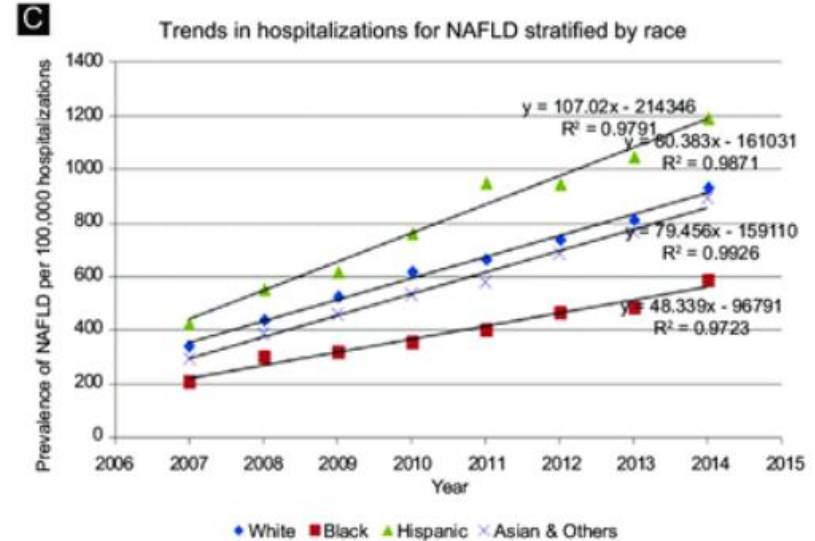
# Examine Disparities in NAFLD Outcomes



# Cirrhosis and Decompensation

- Very few studies, discordant results
- *Suggest* higher odds of cirrhosis and hepatocellular carcinoma in Hispanic people than non-Hispanic White
- Highest rates of hospitalization in Hispanic people

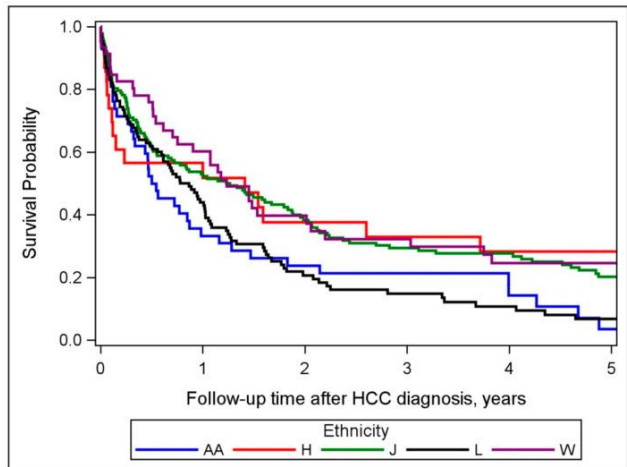
**NEED MORE DATA**



# Hepatocellular carcinoma

Multiethnic cohort study: large prospective cohort with >215,000 adults in HI and CA 1993-1996  
HCC from SEER, followed for >20 years

**African American: lowest survival**

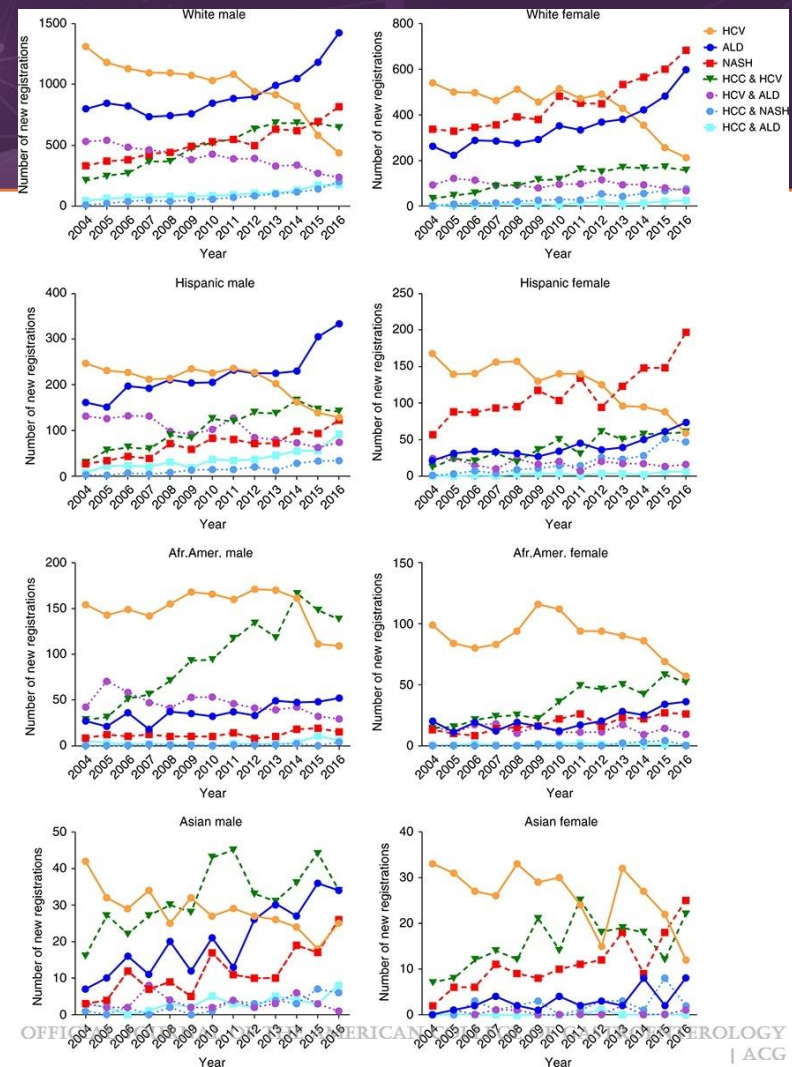


Association of race/ethnicity and other factors with overall mortality.

	No. Deaths	Univariate HR (95% CI) <sup>a</sup>	p-Value	Multivariate HR (95% CI) <sup>b</sup>	p-Value
Race/ethnicity					
White	35	1.00		1.00	
African American	38	1.73 (1.08–2.78)		1.87 (1.06–3.28)	
Japanese American	111	0.96 (0.65–1.41)	<0.0001	1.02 (0.66–1.57)	0.0067
Latino	93	1.92 (1.29–2.85)		1.47 (0.91–2.38)	
Native Hawaiian	18	0.75 (0.42–1.34)		0.65 (0.34–1.23)	

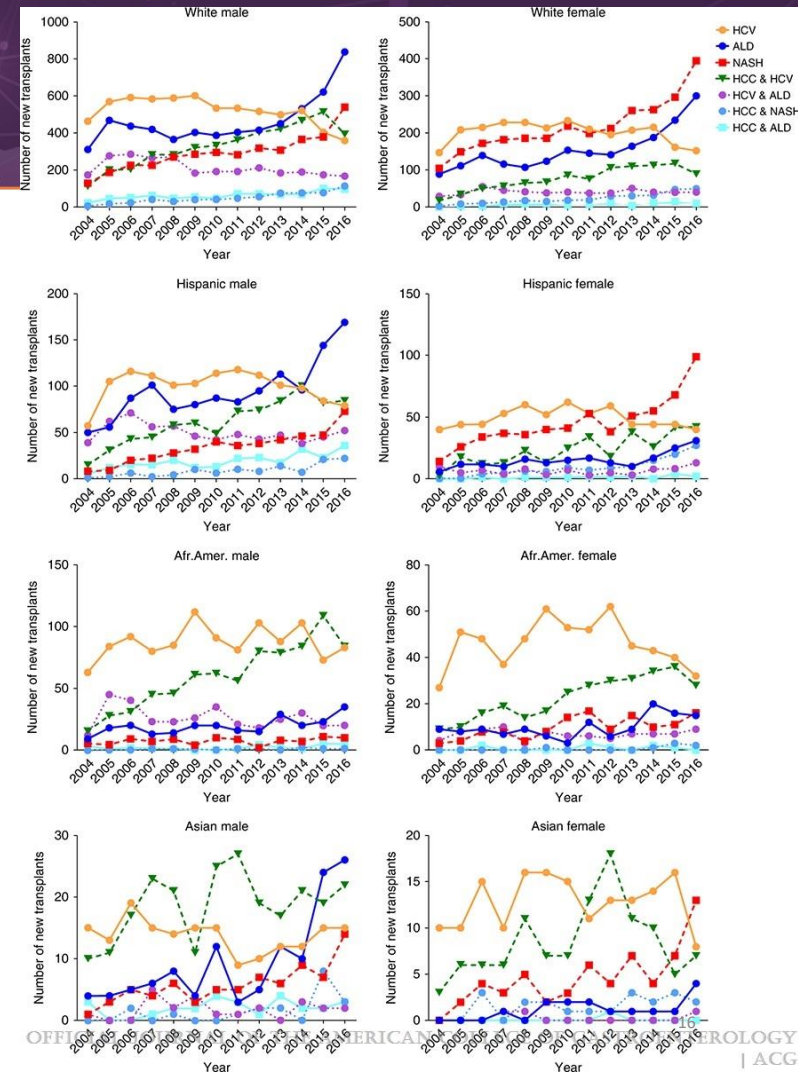
# OPTN Waitlist Registrants

- NASH (red lines) increasing as indication for liver transplantation in
  - Women of any race/ethnicity
  - Most pronounced in Hispanic and Asian
- NASH is the #1 indication for LT in women (except AA)



# Liver Transplantation

- NASH (red lines) increasing as indication for liver transplantation in
  - Women of any race/ethnicity
  - Most pronounced in Hispanic and Asian
- NASH is the #1 indication for LT in women (except AA)





# Outcomes After Liver Transplantation

- Hispanics have a decreased risk of death when transplanted for NASH (HR 0.84, 95% CI 0.71–0.99;  $p = 0.04$ ).
- Hispanics have similar or better long-term post-LT outcomes compared to non-Hispanic whites despite a worse pretransplant risk factor profile.

# Mortality

- NHANES study 1988-94
- Follow-up to 2006
- Higher risk of death in Black Americans

Factors	Overall	HR (95% CI)
Person-years		25,398
Number of deaths		377
Age		1.08 (1.06–1.09)
Diagnosis of having NAFLD with metabolic syndrome		2.22 (1.26–3.91)
Race,		
<i>Black</i>		1.36 (1.03–1.78)
<i>Other, including American–Mexican</i>		0.65 (0.43–0.96)
Smoking status,		
<i>Never</i>		Reference
<i>Current</i>		43.24 (21.88–85.41)
<i>Former</i>		1.32 (0.83–2.09)

# Independent Predictors of Overall, Cardiac and Liver-Related Mortality in NAFLD

- 2 centers, biopsy-based registry, median f/u 13 years
- Race was not an independent predictor of death

Risk factor	Overall mortality	Liver-related mortality	Cardiac mortality
	aHR (95 % CI)	aHR (95 % CI)	aHR (95 % CI)
NASH	1.13 (0.74–1.71)	<b>9.16 (2.10–9.88)</b>	0.51 (0.23–1.10)
Age	<b>1.07 (1.05–1.10)</b>	<b>1.06 (1.02–1.10)</b>	<b>1.12 (1.08–1.18)</b>
Male gender	0.95 (0.62–1.47)	1.44 (0.62–3.34)	0.83 (0.36–1.90)
Caucasian race	1.67 (0.92–3.06)	1.85 (0.62–5.47)	1.37 (0.39–4.83)
Obesity	0.91 (0.60–1.40)	0.88 (0.38–2.04)	1.56 (0.70–3.47)
Type II diabetes	<b>2.09 (1.39–3.14)</b>	<b>2.19 (1.00–4.81)</b>	1.71 (0.75–3.86)
Hyperlipidemia	1.01 (0.68–1.52)	0.48 (0.19–1.23)	1.68 (0.78–3.61)

# Why Are There Disparities Among Race and Ethnic Groups in NAFLD?



# Why Are There Disparities?

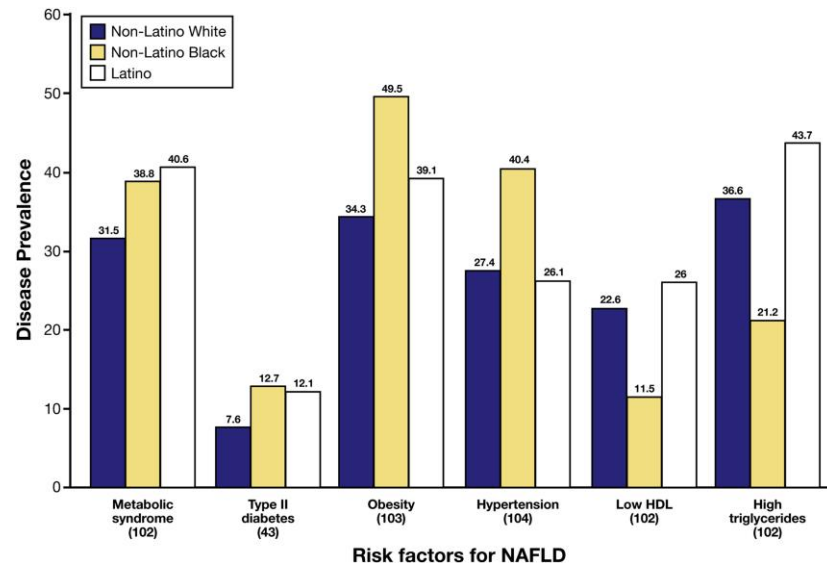
- Metabolic risk factors, such as obesity, diabetes, and dyslipidemia
- Genetic factors: PNPLA3
- Cultural and socioeconomic factors: dietary and exercise habits, access to health care, socioeconomic status (employment, housing, food insecurity)

**Complex, multilevel interactions between these factors**

# Disparities in Metabolic risk factors

- Blacks have high rates of
  - Metabolic syndrome
  - Diabetes
  - Obesity
  - HTN

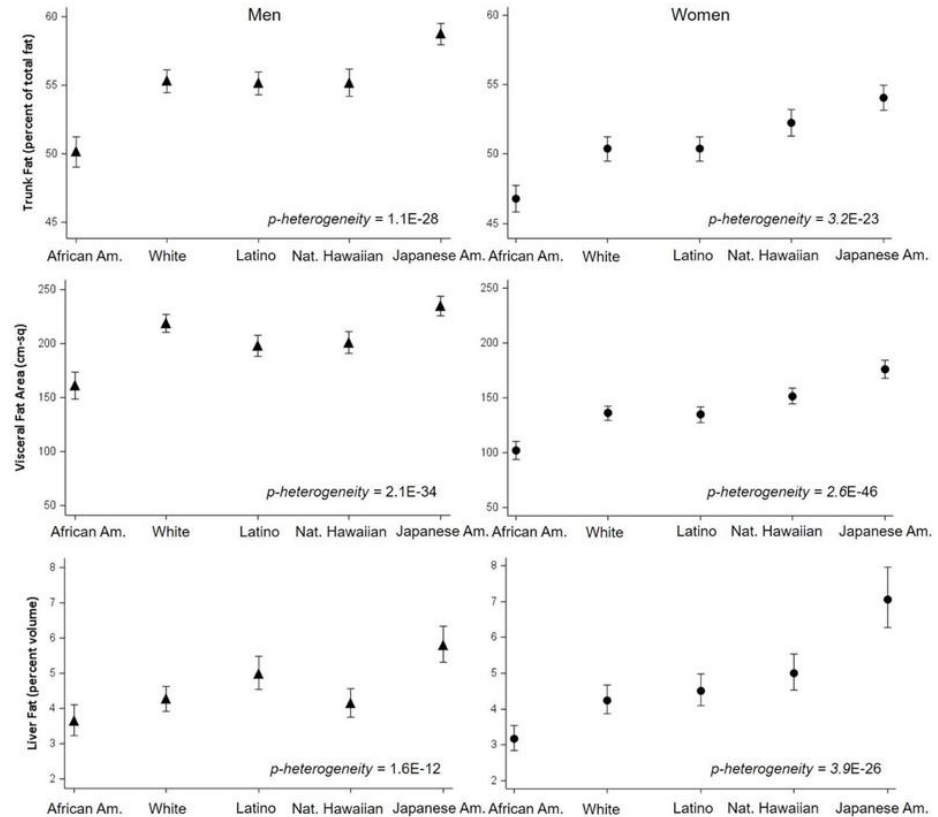
But lowest NAFLD rates



# Fat Distribution Varies Among Ethnic Groups

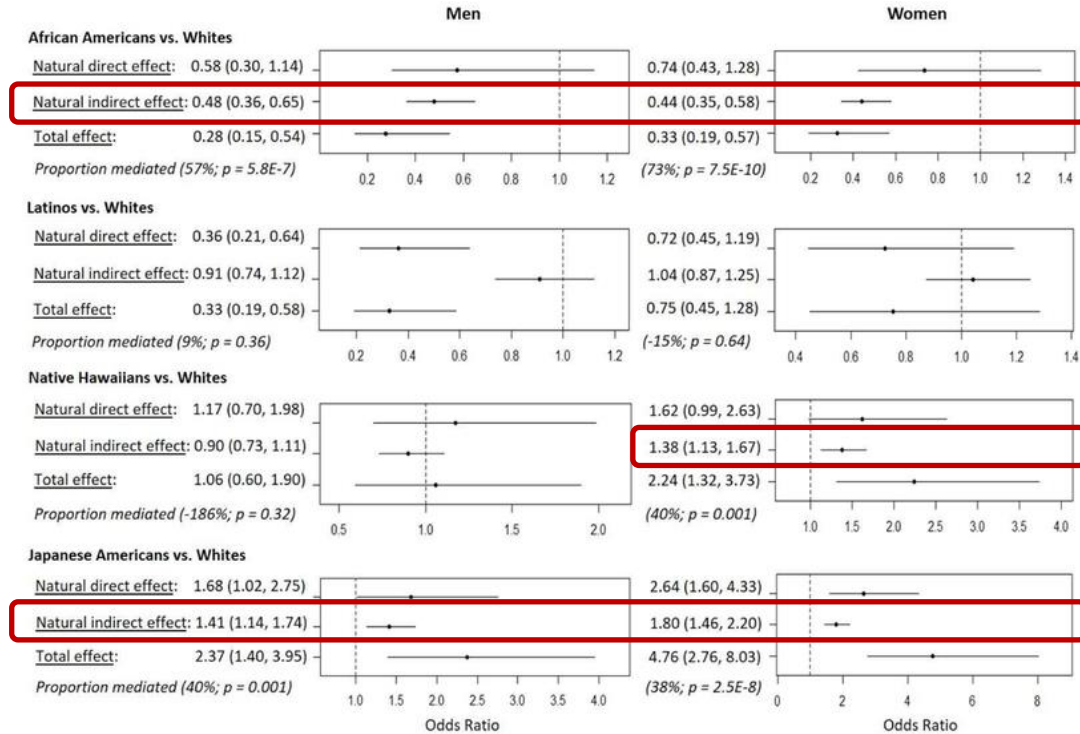
- 1794 participants of the Multiethnic Cohort Study
- 60-77 years old
- BMI 17-46
- DEXA and MRI abdomen

\*adjusted for age, height and total fat mass



# The Impact of Race/Ethnicity on Metabolic Syndrome Is Partly Mediated by Fat Distribution

- Mediation analysis using natural effect modeling
- **Natural indirect effect: through visceral and liver fat**



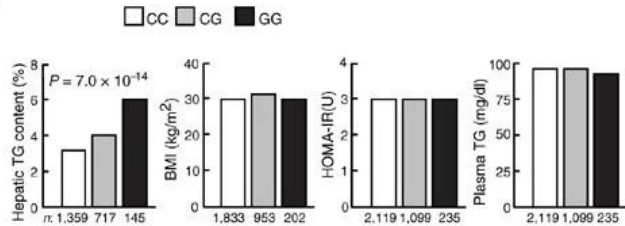


# Disparities in Genetic Risk Factors

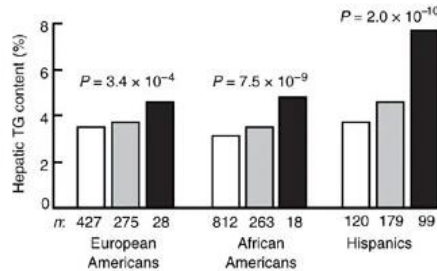
## PNPLA3 rs738409[G] allele

Is associated with a systematic increase in hepatic fat content and abnormal liver enzymes

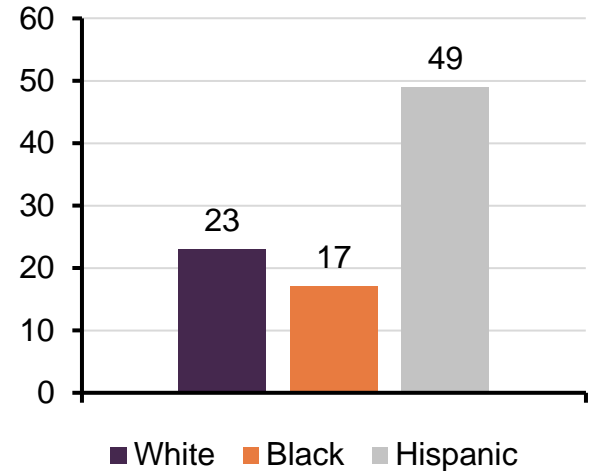
b



c

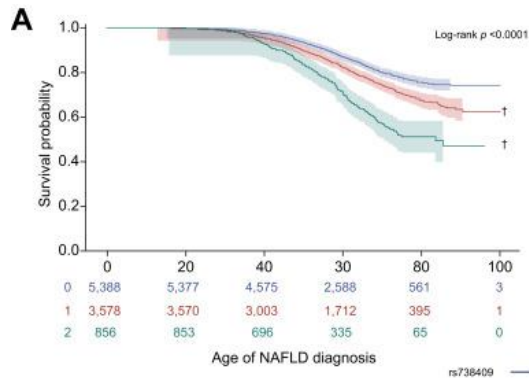


## PNPLA3 rs738409 G frequency

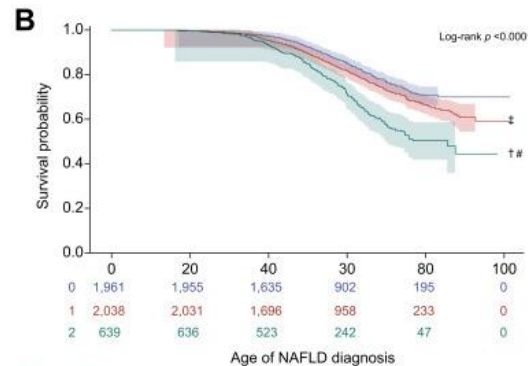


# PNPLA Impacts Age at NAFLD Diagnosis

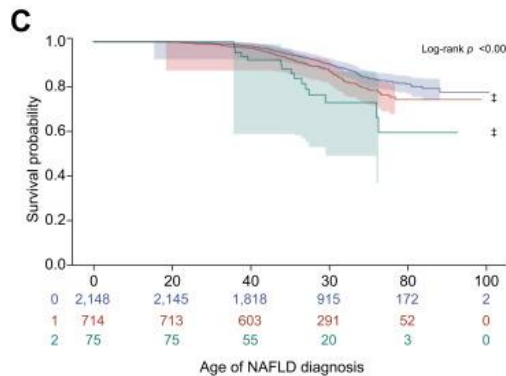
All



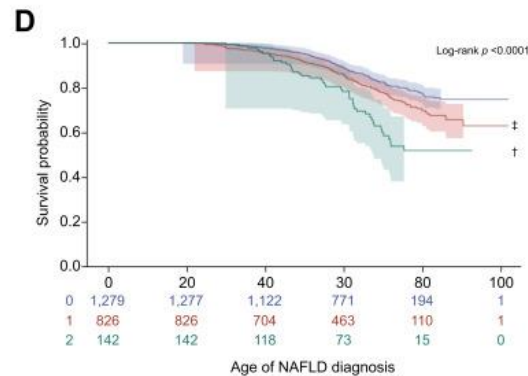
Hispanic



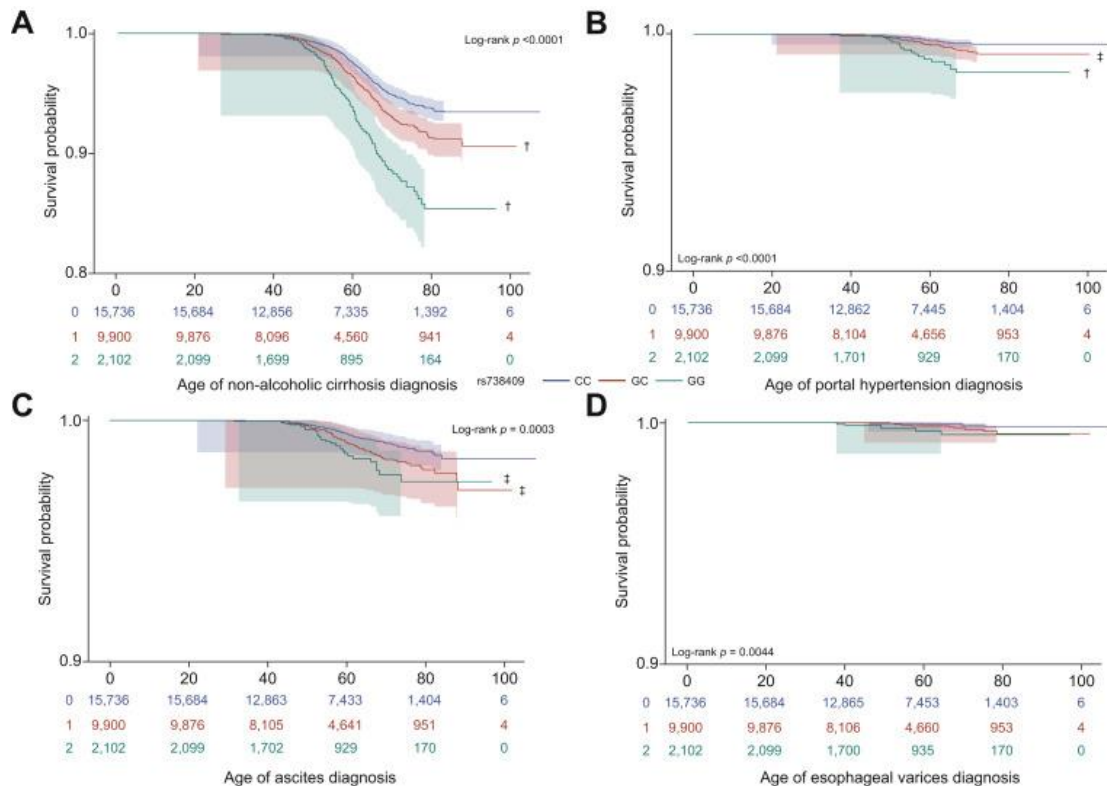
African American



White

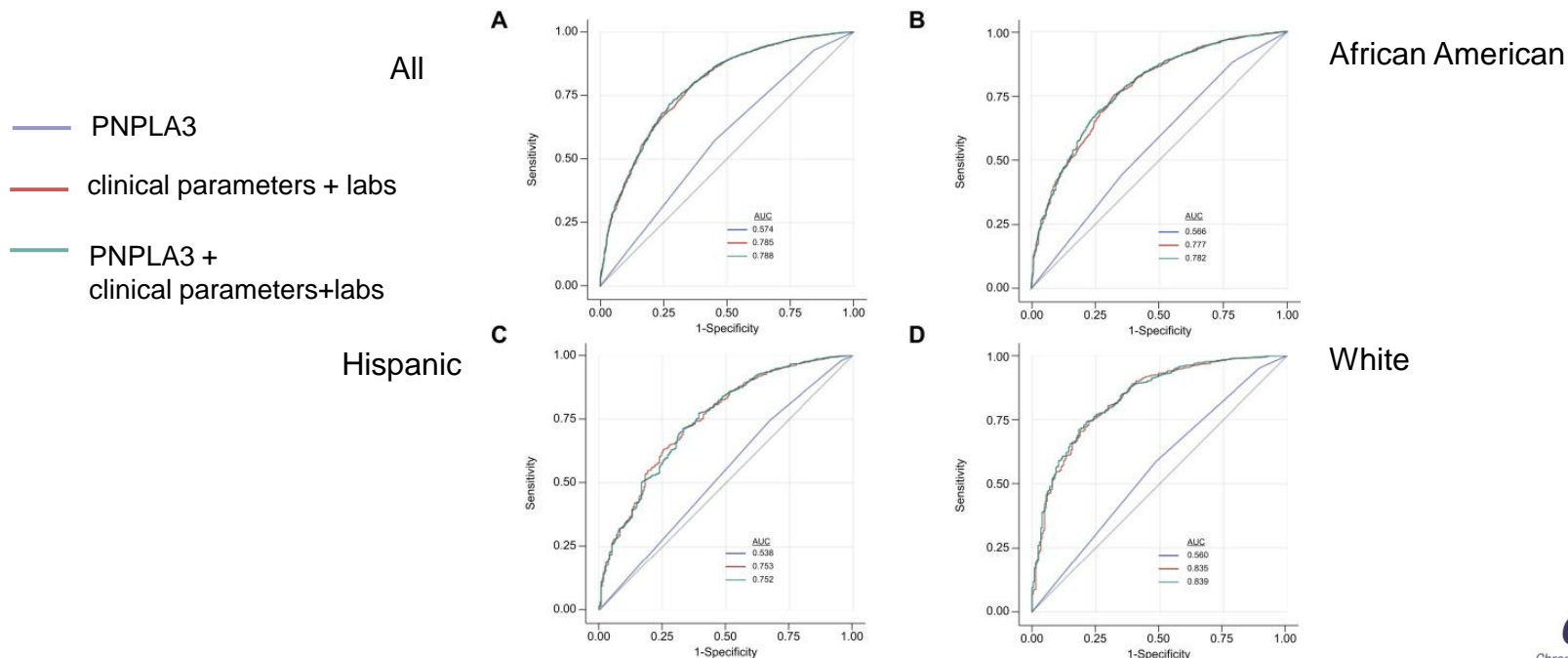


# PNPLA Impacts Age at Diagnosis of Cirrhosis



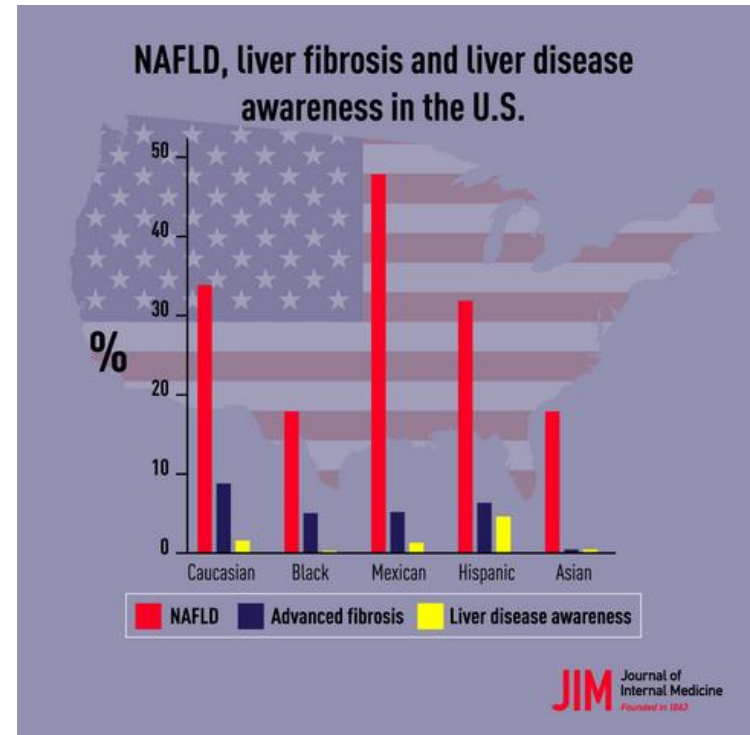
# PNPLA3 has no predictive performance for nafld

- *PNPLA3* did not significantly improve prediction of NAFLD over clinical measures in AA or Whites, nor did it improve the percent of cases correctly classified or improve sensitivity



# Liver Disease Awareness Is Very Low

- NHANES 2011-2016
- NAFLD defined by FLI



# Summary

- Racial/ethnic landscape in the US has changed significantly in the last decade: less white, more multiracial, more Hispanic/Latino
- NAFLD/NASH prevalence: highest in Hispanic/Latino, lowest in Black Americans
- Hispanic: higher progression to cirrhosis and hospitalization rates
- NASH is increasing as indication for LT, especially in Hispanic and Asian people. #1 in women
- Black: worse survival after HCC and higher risk of death in general
- Determinants of disparity are multifactorial (genetics and environment)
- Need for further research in areas of NAFLD severity and prognosis