STRIVING TOWARDS ENERGY-BALANCE IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

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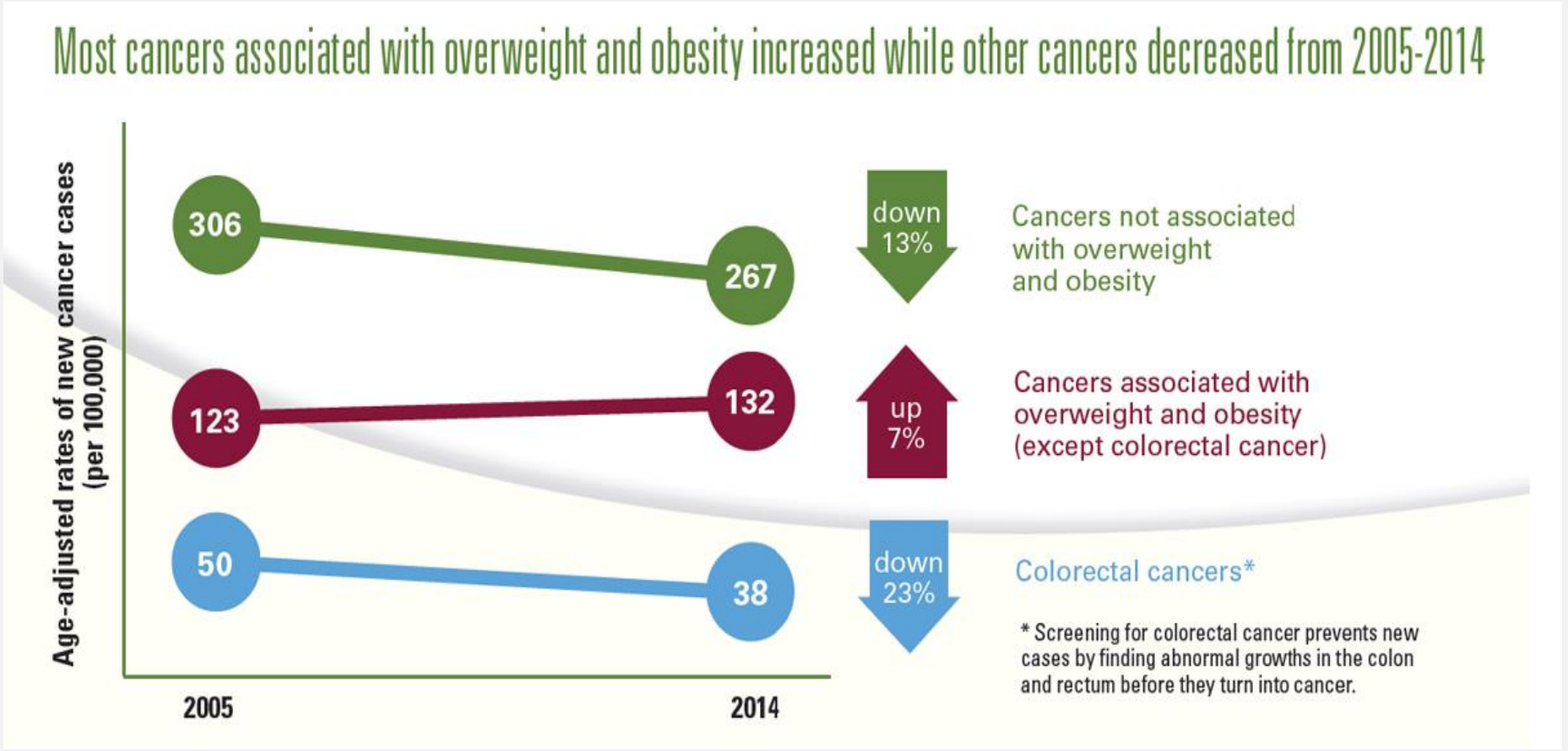


Source: US Cancer Statistics, 2017.

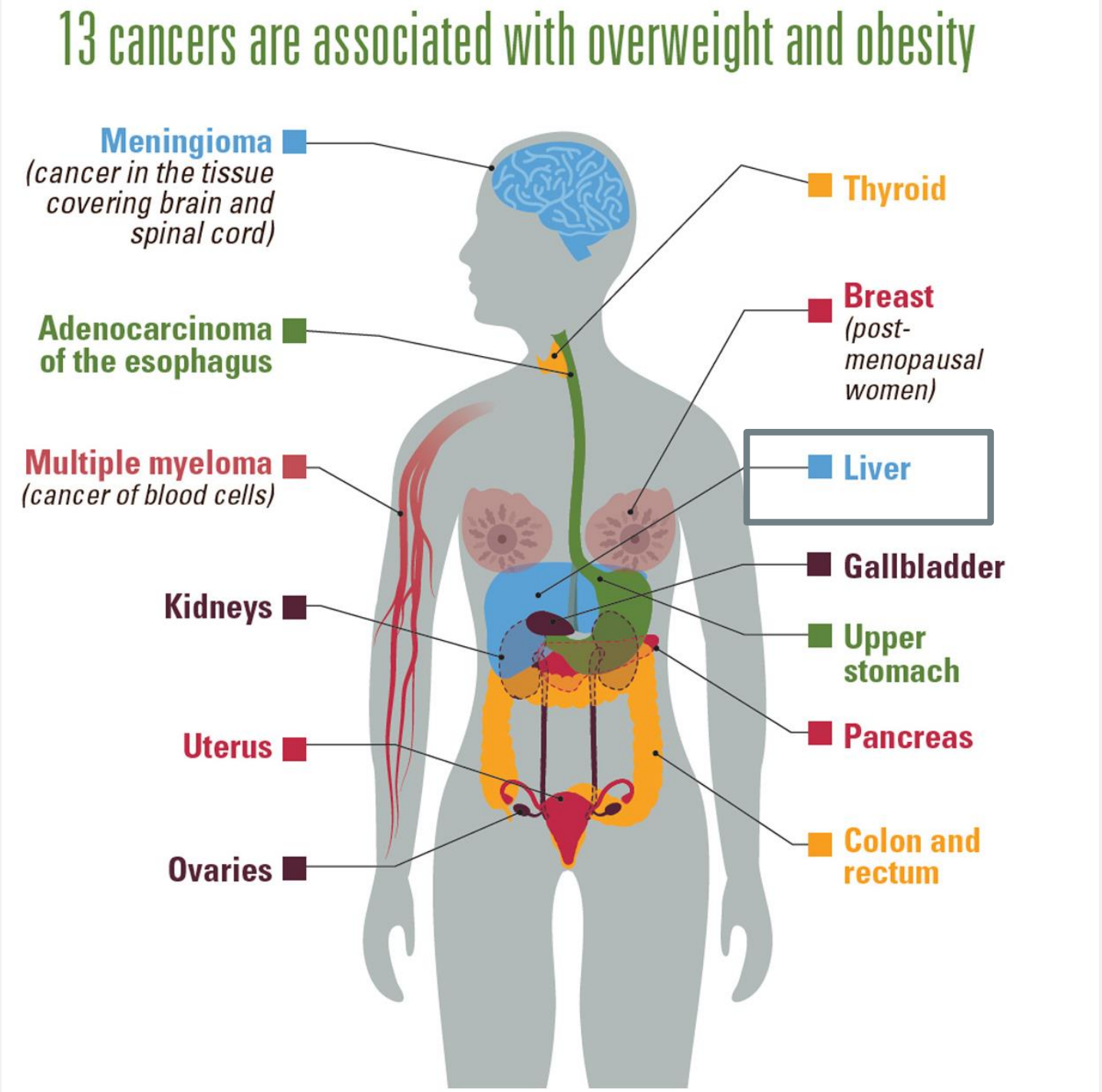
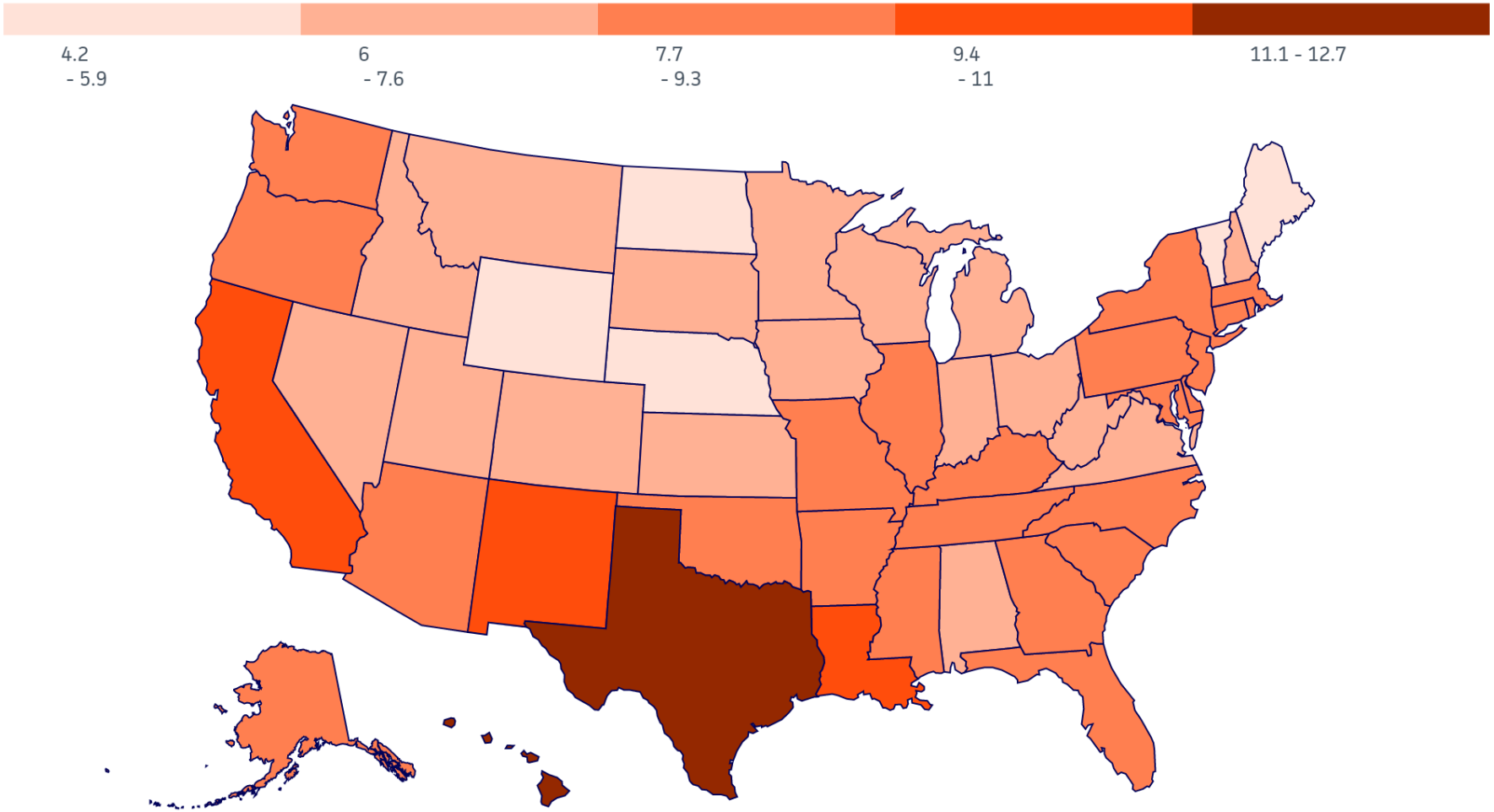


Figure: Centers for Disease Control and Prevention. (2017). Cancers Associated with Overweight and Obesity Make up 40 percent of Cancers Diagnosed in the United States.

Incidence rates, 2012-2016

by state, for liver and intrahepatic bile duct

Average annual rate per 100,000, age adjusted to the 2000 US standard population.



Data Sources: North American Association of Central Cancer Registries (NAACCR), 2019

Estimated Deaths

Males		
Lung & bronchus	3,500	16%
Liver & intrahepatic bile duct	2,700	12%
Colon & rectum	2,400	11%
Prostate	2,000	9%
Pancreas	1,700	8%
Stomach	1,100	5%
Leukemia	1,000	5%
Non-Hodgkin lymphoma	1,000	4%
Kidney & renal pelvis	900	4%
Brain & other nervous system	700	3%
All sites	22,300	100%

Females		
Breast	3,200	16%
Lung & bronchus	2,600	13%
Colon & rectum	1,800	9%
Pancreas	1,600	8%
Liver & intrahepatic bile duct	1,300	6%
Ovary	1,100	5%
Uterine corpus	1,000	5%
Leukemia	900	4%
Stomach	800	4%
Non-Hodgkin lymphoma	700	3%
All sites	20,400	100%

Miller KD, Goding Sauer A, Ortiz AP, Fedewa SA, Pinheiro PS, Tortolero-Luna G, Martinez-Tyson D, Jemal A, Siegel RL. Cancer statistics for hispanics/latinos, 2018. CA: A Cancer Journal for Clinicians. 2018 Nov;68(6):425-45.

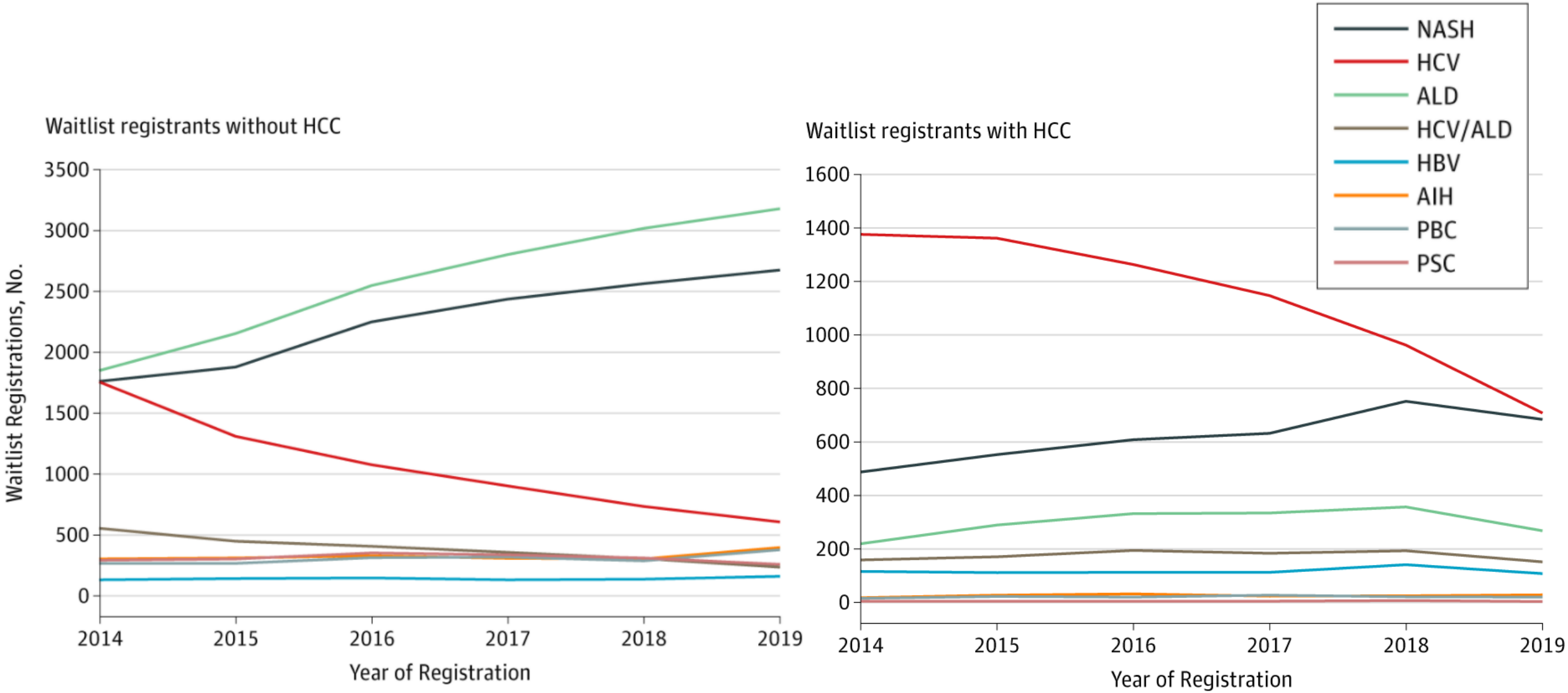
INCREASING IMPORTANCE OF METABOLIC DISORDERS AND NAFLD

TABLE 7. Race and Ethnicity-Specific Hepatocellular Carcinoma Population Attributable Fractions, Surveillance, Epidemiology, and End Results-Medicare, 2000–2011

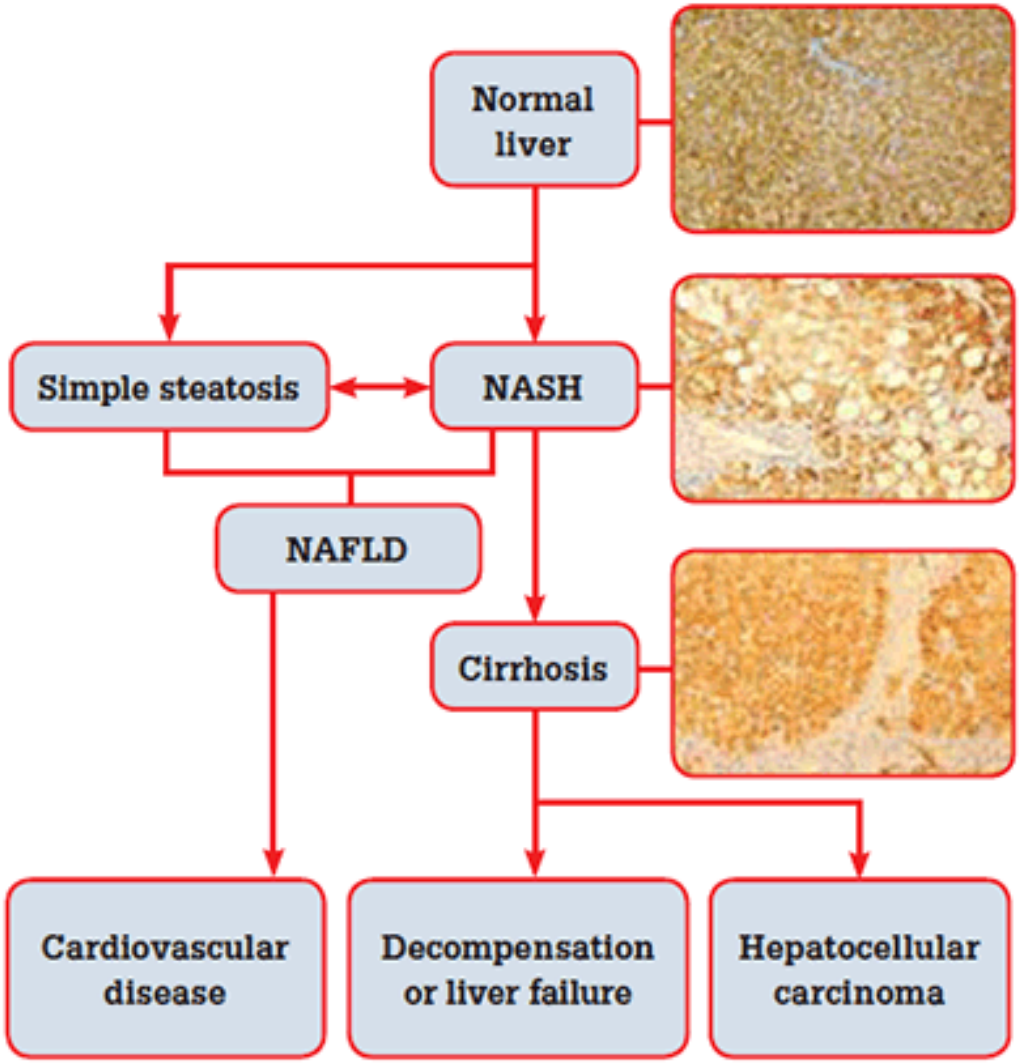
	White		Black		Asian		Hispanic	
Risk Factor	PAF[a]	95% CI	PAF[a]	95% CI	PAF	95% CI	PAF[a]	95% CI
Metabolic disorders	34.8	33.1–36.5	14.4	6.4–22.3	21.8	16.5–27.1	39.3	31.9–46.7
Hepatitis C virus	16.9	15.1–18.8	36.1	31.8–40.4	29.7	25.9–33.4	21.1	14–28.3
Alcohol	14.9	13–16.8	12.4	6.2–18.5	5	−0.1, 10.1	20	12.7–27.3
Smoking	10.5	8–13	10.6	2.8–18.5	5.2	−0.7, 11.1	1.1	−11, 13.2
Hepatitis B virus	1.7	−0.5, 3.9	2.7	−3.9, 9.3	17.8	13.4–22.2	1.1	−8.3, 10.5
Genetic disorders	1.9	−0.3, 4.1	0.4	−6.3, 7.1	0.1	−5.3, 5.5	0.3	−8.8, 9.3
Total	59.8	58.7–61	56.2	52.1–60.4	58.8	55.9–61.6	63.1	58.3–68

Abbreviations: CI, confidence interval; PAF, population attributable fraction.
[a] Analyses were adjusted for sex, socioeconomic status, age at diagnosis, and other risk factors.

Makarova-Rusher OV et al. Population attributable fractions of risk factors for hepatocellular carcinoma in the United States. *Cancer.* 2016;122(11):1757-1765.

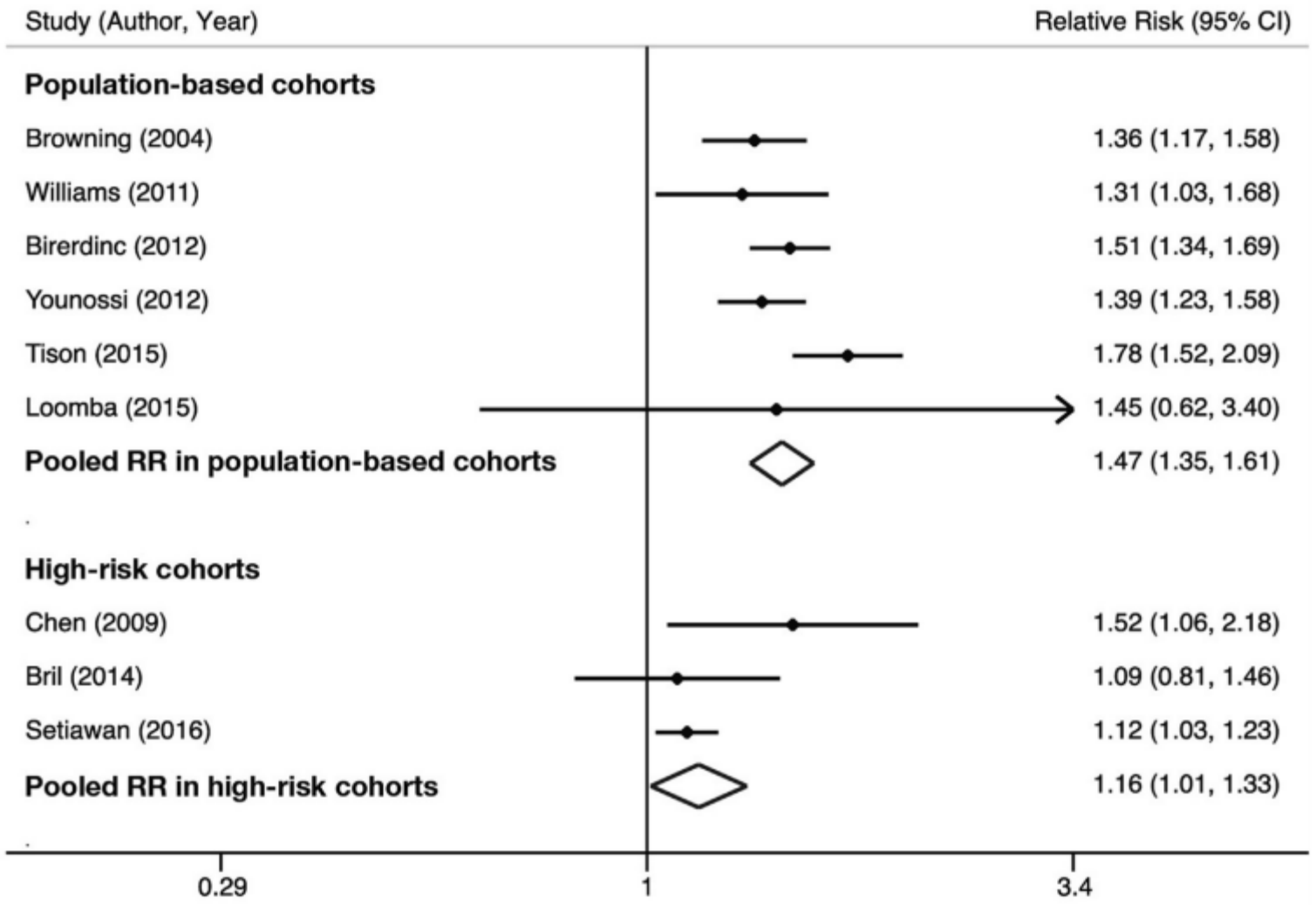


Wong RJ, Singal AK. Trends in Liver Disease Etiology Among Adults Awaiting Liver Transplantation in the United States, 2014-2019. JAMA Network Open. 2020 Feb 5;3(2):e1920294-.



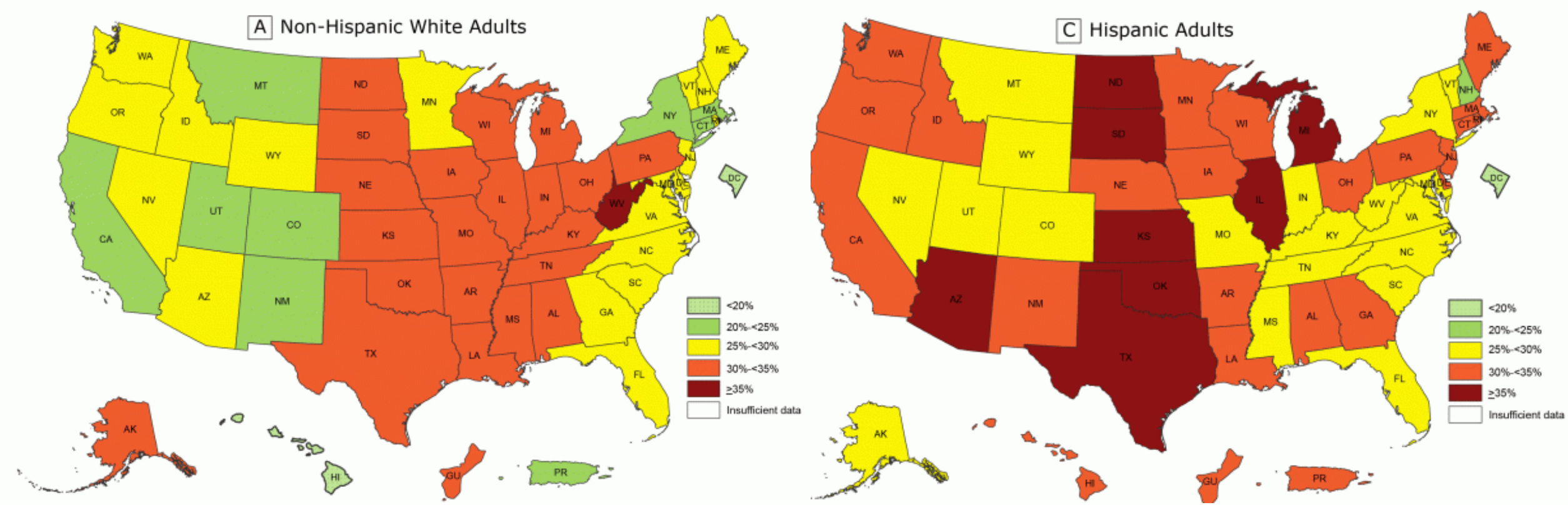
Iser D, Ryan M. Fatty liver disease: a practical guide for GPs. Australian family physician. 2013 Jul;42(7):444.

NAFLD prevalence among Hispanic versus Non-Hispanic white persons in population-based and high-risk cohorts.



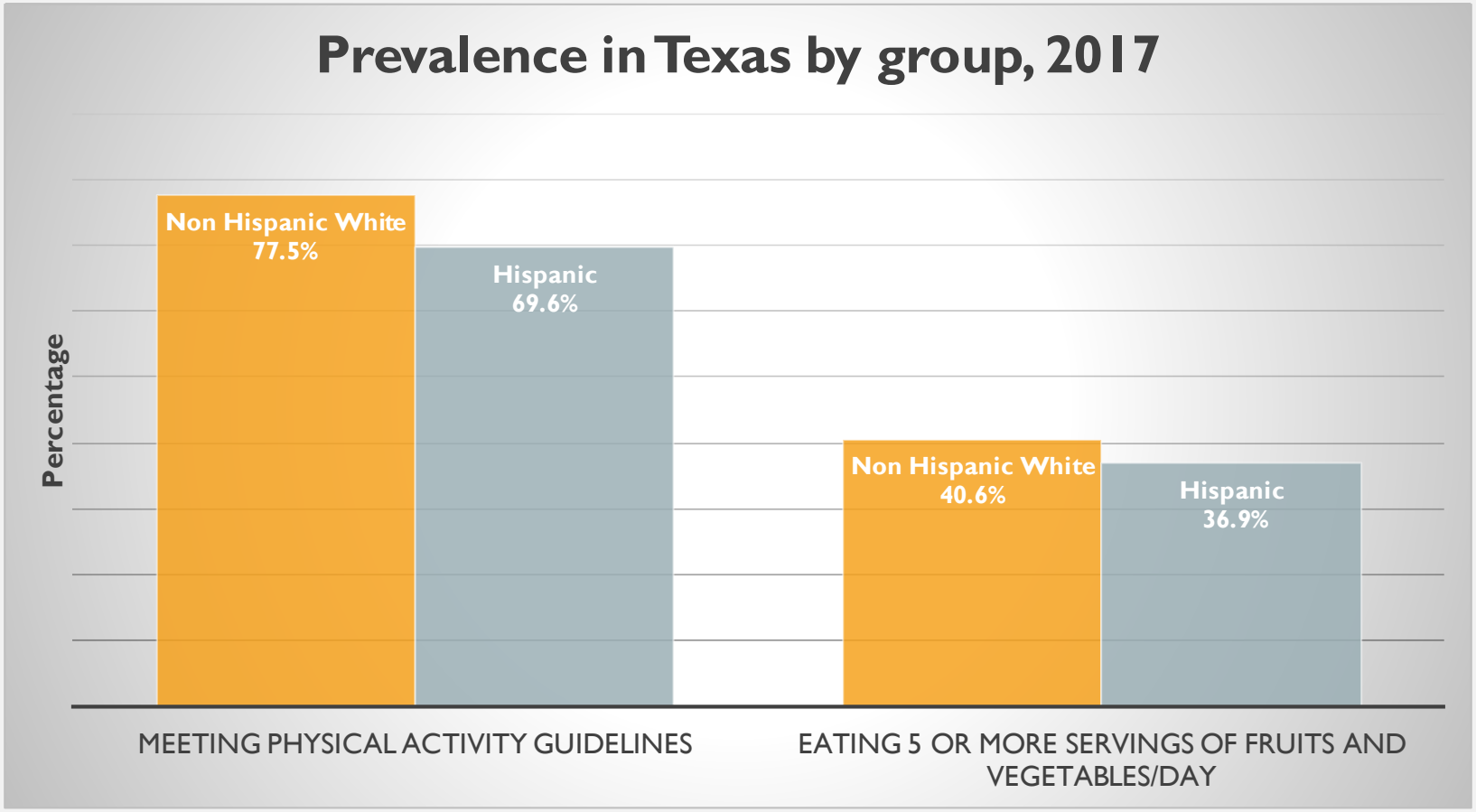
Rich et al. Racial and ethnic disparities in nonalcoholic fatty liver disease prevalence, severity, and outcomes in the United States: a systematic review and meta-analysis. Clinical Gastroenterology and Hepatology. 2018 Feb 1;16(2):198-210.

OBESITY DISPARITIES



Petersen R, Pan L, Blanck HM. Racial and Ethnic Disparities in Adult Obesity in the United States: CDC's Tracking to Inform State and Local Action. Prev Chronic Dis 2019;16:180579

LOWER PREVALENCE OF ENERGY-BALANCE BEHAVIORS AMONG HISPANIC/LATINO ADULTS



Overview

Study 1: Perceptions of Weight Status and Energy-Balance Behaviors Among Patients with NAFLD

Study 2: Primary care physicians perspectives' on NAFLD

STUDY 1: PURPOSE

Inaccurate identification of weight status among those who are overweight or obese associated with fewer weight loss attempts and less physical activity (Dorsey et al, 2010).

1. Characterize energy-balance perceptions and behaviors in patients with NAFLD
2. Assess concordance between these perceptions and behaviors
3. Identify predictors of concordance

Heredia NI, Gaba R, Liu Y, Jain S, Rungta M, Gunta M, El-Serag HB, Kanwal F, Thrift AP, Balakrishnan M**.** Perceptions of weight status and energy-balance behaviors in patients with non-alcoholic fatty liver disease. *Under review.*

METHODS

- Harris County NAFLD Cohort (HCNC)
  - Prospective cohort study of adult patients with NAFLD referred to a multidisciplinary clinic within the Harris Health system, staffed by both a hepatologist and an endocrinologist within
- At the initial visit, all consented patients completed self-administered questionnaires
- Patients then underwent clinical evaluation

NAFLD DIAGNOSIS

- Presence of hepatic steatosis detected on liver imaging, in the absence of:
  - excessive alcohol consumption, viral hepatitis, hemochromatosis, Wilsons disease, cholestatic or autoimmune disease, drug induced liver injury, or medications associated with hepatic steatosis.
- All patients offered a liver biopsy as part of clinical care except for:
  - age>70 years
  - liver biopsy performed <5 years prior to baseline visit
  - ≥5% weight loss within the prior 6 months
  - serious competing medical condition(s)
  - life expectancy <2 years and ongoing use of an anticoagulant

QUESTIONNAIRE

- **Body mass index (BMI):** measured height and weight from at initial visit
- **Physical activity:** Rapid Assessment of Physical Activity Scale (RAPA)
  - Classified as active or insufficiently active.
- **Diet:** National Cancer Institute's FLASHE dietary screener (26 items) commonly consumed foods, including fruit and vegetable (FV) intake.
  - Classified as meeting and not meeting FV intake guidelines
- **Demographics and covariates**: age, sex, race/ethnicity, education, primary language, country of birth, age moved to the U.S. , alcohol use and smoking status.

QUESTIONNAIRE

- Self-perceptions of body weight, diet, and physical activity
  - Do you consider yourself to be overweight, underweight or about right?
  - Do you feel you need to lose weight?
  - Do you consider yourself to be physically active?
  - Do you want to be more physically active?
  - Do you think you could eat healthier?
  - Do you think you eat the right amount of fruits and vegetables now, or do you think you should eat more?
  - Do you think you eat the right amount of fat in your diet or do you think you should eat less?
  - Do you think you eat the right amount of sugar in your diet or do you think you should eat less?

DEMOGRAPHIC CHARACTERISTICS

Variable	All Participants
M (SD) or N (%)	**N=458**
Age, M (SD)	46.45 (11.40)
Female	348 (75.98)
Hispanic	412 (89.96)
Primary Language	
Spanish	350 (76.42)
English	76 (16.59)
Both Spanish and English	14 (3.06)
Country of Birth	
United States	69 (15.1)
Mexico	256 (55.9)
Central-America	107 (23.4)
Age moved to the U.S., M (SD)	24.06 (11.60)
Length In US (yr),M (SD)	21.74 (10.60)
Education	
Less than high school	189 (41.27)
Some or equal high schoo	139 (30.35)
Beyond high school	99 (21.62)

Note: missing values not pictured

CLINICAL CHARACTERISTICS

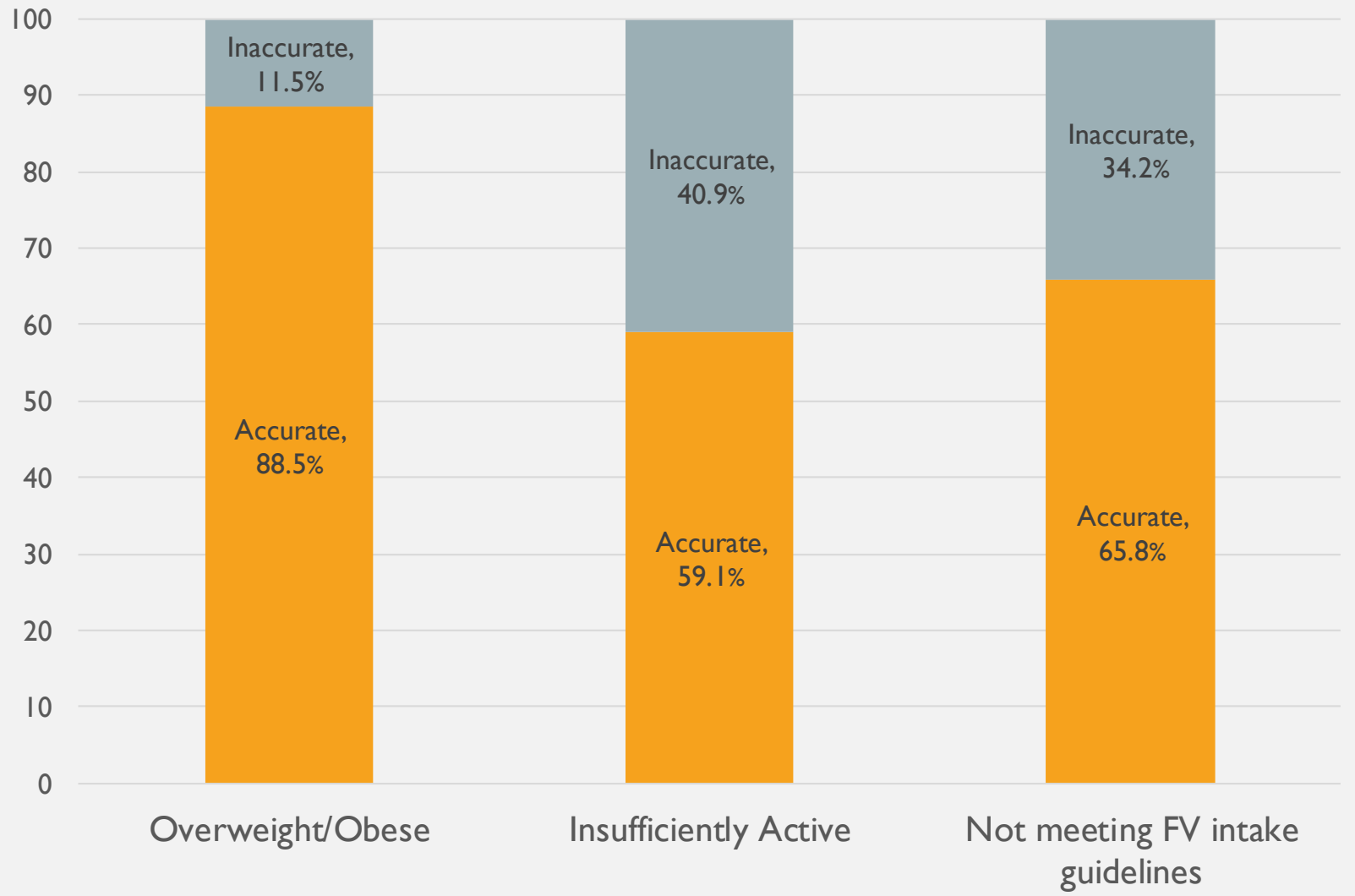
Variable	All Participants
M (SD) or N (%)	**N=458**
Average BMI (Kg/m2)	34.70 (7.22)
Body Mass Index categories	
18.5 to <25 (Normal)	16 (3.49)
25 to <30 (Overweight)	100 (21.83)
≥30 (Obese)	342 (74.67)
Diabetes	
No prediabetes or diabetes	149 (32.53)
Diabetes	245 (53.49)
Prediabetes	64 (13.97)
Fibrosis*	
Early(F0-F2)	211 (78.44)
Advanced(F3-F4)	58 (21.56)

*Reported only among 269 patients with liver biopsy

AIM 1. CHARACTERIZE ENERGY-BALANCE PERCEPTIONS AND BEHAVIORS OF PATIENTS WITH NAFLD

Variable	All Participants
Meeting FV intake guidelines	41 (8.95)
Sufficiently active	168 (36.68)
Perceptions	
Perceived themselves as overweight	357 (77.95)
Perceived Need to Lose Weight	406 (88.65)
Consider themselves Physically Active	233 (50.87)
Want to be more physically active	411 (89.74)
Believe they could eat healthier	421 (91.92)
Believe they should eat more FV	277 (60.48)
Believe they should eat less dietary fat	317 (69.21)
Believe they should eat less sugar	298 (65.07)

AIM 2. ASSESS CONCORDANCE BETWEEN PERCEPTIONS AND BEHAVIORS



AIM 3. PREDICTORS OF CONCORDANCE

Multivariate model for accuracy of perceived weight status

Patient Characteristic	OR (95% CI) (n=414)
Age at baseline (yr)	0.98 (0.95-1.01)
Female	**2.87 (1.43-5.78)**
Hispanic	1.68 (0.43-6.57)
Spanish or Bilingual (ref=English)	0.92 (0.31-2.69)
Education (ref=Less than HS)	
Some or equal HS	1.30 (0.57-2.97)
Higher than HS	0.75 (0.32-1.75)
Diabetes/Prediabetes	1.22 (0.62-2.40)

AIM 3. PREDICTORS OF CONCORDANCE

Multivariate model for accuracy of perceived physical activity

Patient Characteristic	OR (95% CI) (n=421)
Age at baseline (yr)	1.02 (1.00-1.04)
Female	**0.58 (0.34-0.98)**
Hispanic	1.32 (0.49-3.52)
Spanish or Bilingual (ref=English)	**2.38 (1.24-4.59)**
Education (ref=Less than HS)	
Some or equal HS	1.05 (0.62-1.80)
Higher than HS	0.81 (0.44-1.47)
Diabetes/Prediabetes	**0.60 (0.38-0.97)**

AIM 3. PREDICTORS OF CONCORDANCE

Multivariate model for accuracy of perceived FV intake

Patient Characteristic	OR (95% CI) (n=431)
Age at baseline (yr)	0.99 (0.97-1.01)
Female	1.31 (0.75-2.27)
Hispanic	1.32 (0.48-3.62)
Spanish or Bilingual (ref=English)	0.74 (0.37-1.48)
Education (ref=Less than HS)	
Some or equal HS	0.76 (0.44-1.33)
Higher than HS	0.80 (0.43-1.49)
Diabetes/Prediabetes	**3.22 (1.90-5.47)**

DISCUSSION

- There exists the desire in patients with NAFLD to lose weight, do more physical activity, and eat healthier
- While most patients with NAFLD accurately self-recognize their weight status, over a third do not recognize their inadequate diet.
- Need for targeted and detailed counseling regarding specific dietary components in patients with NAFLD.

DISCUSSION

- Women with NAFLD had twice the odds as men to accurately identify their weight status BUT lower odds of accurately identifying their physical activity levels.
- Lower acculturation associated with **higher odds** of accurately self-perceiving physical activity levels.
- Physical activity interventions with highly acculturated and/or female Hispanic patients with NAFLD should emphasize the minimum physical activity recommendations and provide examples to appropriately contextualize how much physical activity is needed.

DISCUSSION

- Patients with pre-diabetes/diabetes had **2.5 times greater odds** of accurately perceiving their fruit and vegetable intake while also having **lower odds** of accurately identifying their physical activity levels.
- Prediabetic/diabetic patients may be more likely to have seen a dietician or have discussed dietary issues with a physician prior to presenting to clinic.
- Additional focus or referrals for exercise or physical activity for those with prediabetes/diabetes.

LIMITATIONS

- Cross-sectional study
- Single item constructs for several variables
- Self-reported dietary and physical activity behavior subject to misclassification, recall, and social desirability biases

CONCLUSION

- To our knowledge, this is the first study to provide insight into the concordance between actual and self-perceived patterns of weight status, physical activity and fruit and vegetable intake among patients with NAFLD.
- It is possible to make the NAFLD diagnosis a moment of behavioral change.
- Our findings provide a starting point for assessing patients' readiness for behavioral change and key areas to target in NAFLD-specific lifestyle behavior change programs.

Overview

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Study 2: Primary care physicians' perspectives on NAFLD

PRIMARY CARE PHYSICIANS PERSPECTIVES ON NAFLD

- In-depth interviews with primary care physicians in Houston area
  - Recruited through professional networks, email and word-of-mouth
  - Practice at clinics with predominately Hispanic patient populations
  - Interviews were 30-45 minutes in length
  - Interviews addressed current clinic practice for diagnosing and managing NAFLD, perceptions of the burden of NAFLD on patients, etc.
  - Two coders used NVivo was used to identify patterns and themes

Heredia NI, John JC, Hwang J, Strong LL, Balakrishnan M, McNeill LH. Primary care physicians' perspectives on the diagnosis and management of non-alcohol fatty liver disease. *In Progress.*

PRELIMINARY RESULTS

- n=16
- Internal Medicine and Family Practice
- Wide range of clinical experience (1.5 to 30 years)
- n=5 males, n=11 females
- 7 institutions, 12 clinic locations

NAFLD OFTEN IDENTIFIED INCIDENTALLY

- Elevated liver enzymes ⟶ liver imaging.
- Mostly identified incidentally.

"I like to have a liver panel on all my patients each year, so if I were to see—sometimes, you know, the lab will be there for other reasons, not necessarily because they're looking at the transaminases in particular, I don't look specifically for NAFLD."

(006, Female, Internal Medicine, Safety-Net clinic)

INSURED VS. UNINSURED PATIENTS

- For patients with abnormal liver imaging with insurance or within a safety-net health system, PCPs sometimes referred to GI.

"because we have so much backlog, we cannot send the patient to GI, but once the liver function test is elevated and it has to be 150% elevated then that's the time they will see the patient."

(010, Female, Internal Medicine, Safety-Net clinic)

INSURED VS. UNINSURED PATIENTS

- For uninsured patients outside of the safety-net health system, PCPs sometimes proceeded with lifestyle modification recommendations, given concerns about ability to access imaging services or see a specialist.

"…I'm also constrained with funding for a lot of my patients and so I have to take into account how much am I going to gain from this ultrasound compared to the hundred bucks they're going to have to shell out for it. Oftentimes, it's going to end up being "Watch what you eat""
(009, Female, Internal Medicine, FQHC)

INSURED VS. UNINSURED PATIENTS

- For uninsured patients outside of the safety-net health system, PCPs sometimes proceeded with lifestyle modification recommendations, given concerns about ability to access imaging services or see a specialist.

"I started referring people all the time, but then I would talk to the patient and be like, "Oh, what did the hepatologist say?" and they are like, "Nothing. They just told me to eat better." I was like, "Oh, then I can do that." So I pulled back a little bit on referrals." (007, Female, Internal Medicine, FQHC)

COMMUNICATION BETWEEN PCPS AND SPECIALISTS

"We try to take some responsibility for monitoring it with liver function testing and then like I said, I tend to refer patients to hepatology as well so we'd be doing it—the monitoring with them—but as primary care physicians, we'd want to make sure that we know what the hepatologist has recommended and that they're adhering to that follow-up plan."

(004, Male, Internal Medicine, Private Clinic)

EVOLVING FIELD

- Several PCPs expressed frustration with the lack knowledge about NAFLD progression.

"Well, I'd say it is frustrating to not know who is at risk or progressing. I haven't looked into the literature lately so maybe more is known than I know about, but the general sense is that it's kind of unclear about who is going to get worse and it's also unclear about how helpful it is to lose weight even though that's what we're talking about here. Those are the two issues that I have or concerns I have with the condition."
(004, Male, Internal Medicine, Private Clinic)

DOES IT MATTER- ON ITS OWN?

“I really do see it—it's more than just a marker...for things and so I use it to kind of reinforce the importance of working on a healthy lifestyle and weight loss. And then we'll monitor and some people will get better, some people will stay the same, but I guess it's not like—I haven’t seen it yet for me becoming an outcome like diabetes or blood pressure control that we're aiming for this specific outcome. It's more like a marker of things that will affect all of those things.”

(002, Male, Internal Medicine, Private Clinic)

MANAGEMENT OF NAFLD

- There was wide variation in the role PCPs play in the management of NAFLD. Some physicians simply gave verbal recommendations and/or referred on to a dietician.

"Well, we basically—I mean, we just give them—we can refer them to a dietician." (016, Female, Family Medicine, FQHC)

"[I] just to tell the patient to lose 10% of their body weight, avoid all alcohol, take a healthy diet, exercise regularly." So, this is what I tell the patients… I always tell my patients brisk walking five days a week, try to develop that practice. This is for all my patients." (010, Female, Internal Medicine, Safety-net clinic)

- However, others used motivational interviewing and helped patients set dietary and physical activity goals.

MANAGEMENT OF NAFLD

"So usually, when I talk to my patients about lifestyle, I get a sense of what their day to day is like and I try to get them to identify a change that they think is actionable and successful…I usually try to get them to identify one thing that they can change, like, "Okay, I drink three sodas a day. I'm going to try and cut that down."…So I kind of tailor it individually to what they can afford to do, what is within their lifestyle, their day to day. And then, every time I see them, I readdress, "So, last time we talked about doing this, how's that been going?" Some people are super motivated and they give the change talk and you reinforce what they're doing, you come up with another thing that they can change, which is closer to getting that ideal goal."

(006, Female, Internal Medicine, Safety-net system)

TAKE-HOME POINTS

- There is already a desire to lose weight, do more physical activity, and eat healthier in patients with NAFLD
- Need to correct understanding on lifestyle behavior guidelines, potentially targeting Latinas and/or more acculturated Hispanic/Latinos
- Wide variation in PCPs management behaviors

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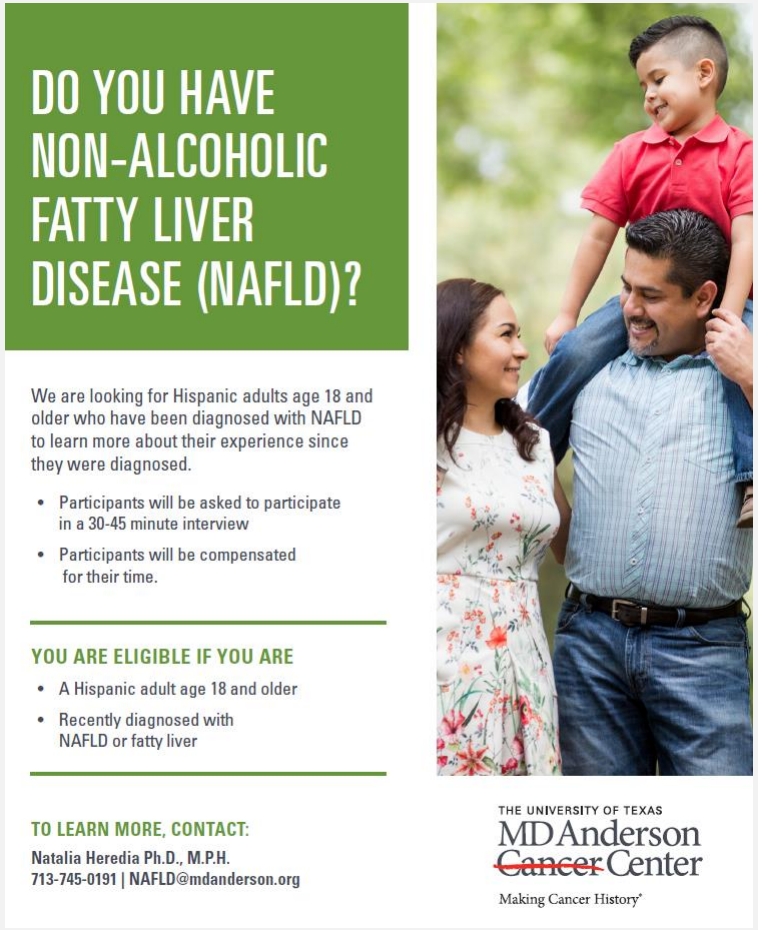
Ongoing: Hispanic/Latino patients' perspectives on NAFLD

HISPANIC/LATINO PATIENTS' PERSPECTIVES ON NAFLD



INTERVIEW GUIDE

- Can you tell me in your own words what non-alcoholic fatty liver disease is?
- How did your doctor explain non-alcoholic fatty liver disease (NAFLD) to you?
- How has NAFLD affected you?
- What do you think caused your non-alcoholic fatty liver disease?
- On a scale of 1-10, with 1 being the lowest and 10 being the highest, how serious do you think your liver disease is? Can you tell me a little bit about why you picked that number?
- What do you think you can do to keep your liver disease from getting worse?
- What research have you done on your own to understand non-alcoholic fatty liver disease, if any?
- Have you told anyone that you have non-alcoholic fatty liver disease? If so, who have you told? What did you tell them?
- Let's talk about your diet, exercise, alcohol, tobacco, medicine use, sleep, before you were diagnosed with liver disease. Most everyone does some things that are healthy and some things that are not so healthy. Tell me about some things that you did that were healthy.
  - Now tell me about some things that you did that were not healthy.
- How, if at all, have any of these behaviors change after your diagnosis of non-alcoholic fatty liver disease?

Study 1: Perceptions of Weight Status and Energy-Balance Behaviors Among Patients with NAFLD

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Ongoing: Hispanic/Latino patients' perspectives on NAFLD

Ongoing: Qualitative exploration of family influences on physical activity in Hispanic households

QUALITATIVE EXPLORATION OF FAMILY INFLUENCES ON PHYSICAL ACTIVITY IN HISPANIC HOUSEHOLDS

- **Challenges to physical activity**
  1. Lack of support
  2. Challenges posed by children
  3. Household sedentary routines
  4. Competing responsibilities
- **Facilitators to physical activity**
  1. Encouragement
  2. Receiving help with responsibilities to be able to exercise
  3. Exercising with a partner
  4. Exercising to appease children

John JC, Heredia NI, McNeill LH, Hoelscher D, Schembre S, Lee MJ, Reininger B, Strong LL. Qualitative exploration of family influences on physical activity in Hispanic households. *In Progress.*

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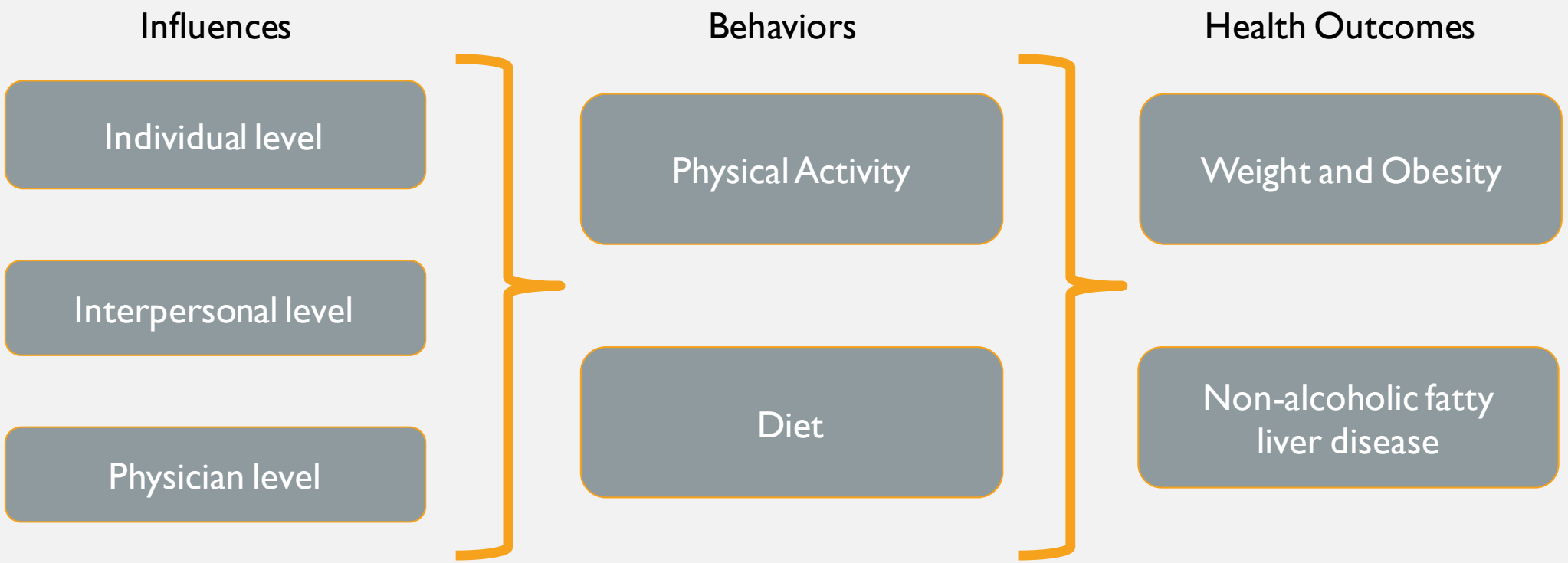
Submission: Culturally-tailored lifestyle intervention for Hispanic NAFLD patients

CAREER DEVELOPMENT AWARD APPLICATION



ACKNOWLEDGEMENTS

Funding support: CPRIT RP170259, PI: Shine Chang

Postdoctoral Mentors:

- Lorna McNeill
- Larkin Strong
- Jessica Hwang

THANK YOU! QUESTIONS?

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AIM 1. CHARACTERIZE NAFLD PATIENTS' ENERGY-BALANCE PERCEPTIONS AND BEHAVIORS

Variable	All Participants
SSB daily intake, mean (SD)	1.32 (1.39)
Sugary food daily intake, mean (SD)	1.09 (1.24)
Fruit servings, daily mean (SD)	2.44 (1.19)
Vegetable servings, daily mean (SD)	2.3 (1.28)
Total FV intake, daily mean (SD)	4.92 (2.25)
Meeting FV intake guidelines	
No	362 (79.04)
Yes	41 (8.95)
Physical activity	
Insufficiently active	254 (55.46)
Active	168 (36.68)

INCIDENCE

Table 3. Incidence and Mortality Rates* for Selected Cancers by Race and Ethnicity, US, 2011-2016

	Hispanic/Latino	Non-Hispanic White	Non-Hispanic Black	Asian and Pacific Islander	American Indian and Alaska Native†
All sites					
Male	377.6	505.5	549.1	298.9	418.4
Female	329.9	438.4	407.0	290.3	386.9
Breast (female)	93.0	130.1	126.5	92.9	100.9
Colon & rectum					
Male	41.7	44.6	55.2	36.1	49.8
Female	28.8	34.2	40.7	26.4	40.1
Gallbladder					
Male	1.2	0.7	1.4	1.1	2.0
Female	2.5	1.1	2.0	1.5	2.9
Kidney & renal pelvis					
Male	21.1	22.5	25.4	11.1	29.9
Female	12.2	11.4	13.1	5.1	17.4
Liver & intrahepatic bile duct					
Male	19.7	10.3	17.6	19.9	20.9
Female	7.8	3.6	5.2	7.4	9.5

DENCE, 2011-2015

Miller KD, Goding Sauer A, Ortiz AP, Fedewa SA, Pinheiro PS, Tortolero-Luna G, Martinez-Tyson D, Jemal A, Siegel RL. Cancer statistics for hispanics/latinos, 2018. CA: A Cancer Journal for Clinicians. 2018 Nov;68(6):425-45.

MORTALITY

	Hispanic/Latino	Non-Hispanic White	Non-Hispanic Black	Asian and Pacific Islander	American Indian and Alaska Native†
All sites					
Male	138.2	197.3	239.8	119.1	178.8
Female	96.4	141.8	160.4	87.0	126.8
Breast (female)	14.3	20.6	28.9	11.3	14.5
Colorectum					
Male	14.4	16.6	24.5	11.7	19.5
Female	8.8	11.9	16.0	8.4	13.1
Gallbladder					
Male	0.6	0.4	0.7	0.6	1.1
Female	1.2	0.6	1.0	0.7	1.6
Kidney & renal pelvis					
Male	5.0	5.7	5.6	2.7	8.2
Female	2.3	2.4	2.3	1.1	3.8
Liver & intrahepatic bile duct					
Male	13.3	8.3	13.6	13.9	14.6
Female	6.0	3.4	4.8	5.8	7.5

Miller KD, Goding Sauer A, Ortiz AP, Fedewa SA, Pinheiro PS, Tortolero-Luna G, Martinez-Tyson D, Jemal A, Siegel RL. Cancer statistics for hispanics/latinos, 2018. CA: A Cancer Journal for Clinicians. 2018 Nov;68(6):425-45.

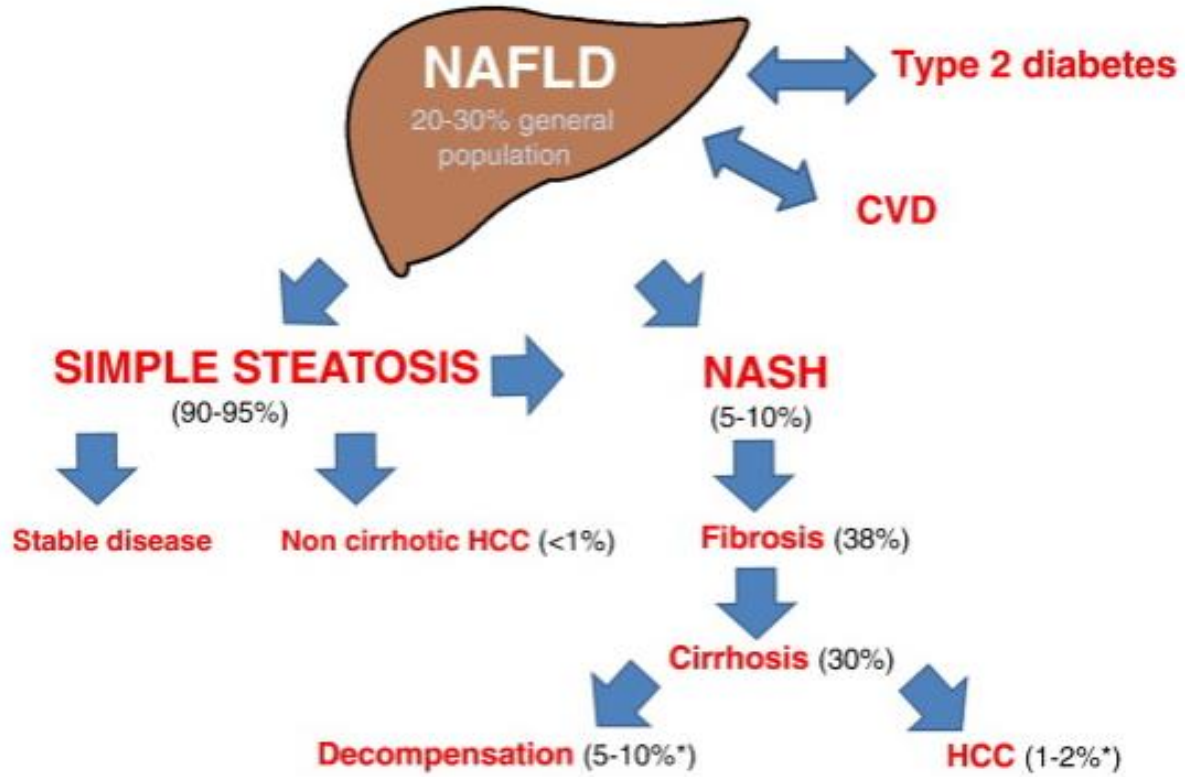

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Fig. 1. Natural history of NAFLD.

Buzzetti E, Pinzani M, Tsochatzis EA. The multiple-hit pathogenesis of non-alcoholic fatty liver disease (NAFLD). Metabolism. 2016 Aug 1;65(8):1038-48.