
2021
NCSCG
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DDW 2021

DDW 2021 Hepatology Update

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CALIFORNIA PACIFIC MEDICAL CENTER, SAN FRANCISCO, CA
JUNE 27, 2021

Topics

- COVID-19 and alcoholic liver disease
- Non-alcoholic steatohepatitis (NASH)
- Hepatocellular carcinoma (HCC)
- Cholestatic liver disease
- Healthcare disparities in liver diseases

COVID-19

Trends in Alcohol Related Liver Disease During the SARS-COV2 Pandemic: Real-Time Analysis of Systemwide Data Trends Using Epic SlicerDicer™

Travis Roark[1], MD

Julio Gutierrez[2], MD

Catherine Frenette[2], MD, FAST, AGAF, FAASLD

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[2] Scripps Center for Organ and Cell Transplant, Division of Gastroenterology & Hepatology, La Jolla, CA

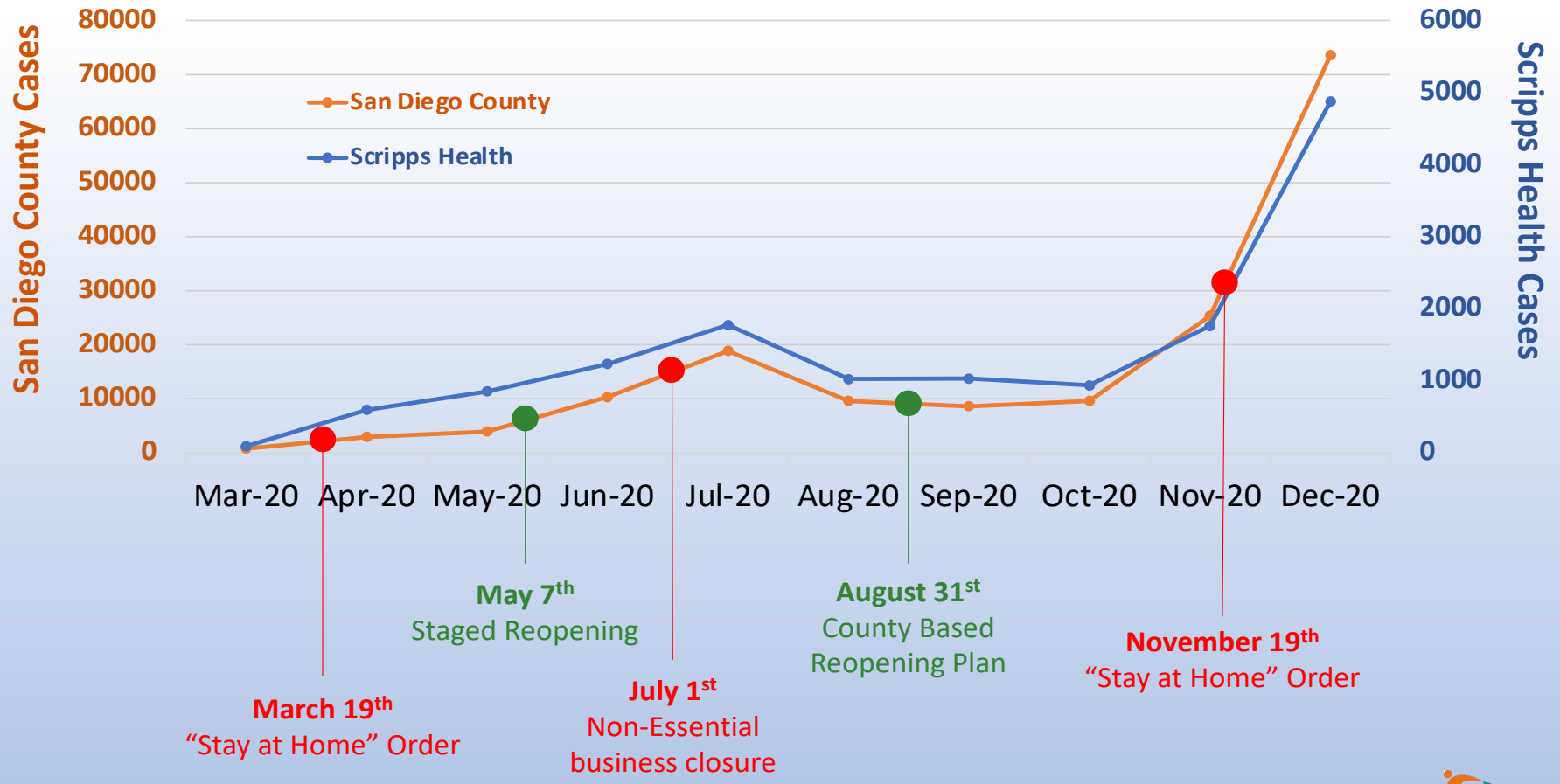
DDW 2021 Abstract #11

Methods

- Performed retrospective analysis of diagnosis and hospitalization trends using the Scripps Health electronic
- They included primary alcohol related diagnoses and alcohol related diseases specifically alcohol pancreatitis and alcohol hepatitis by searching various ICD- 10 codes from January 2019 through December 2020.
- They used publicly available government data of San Diego County SARS-CoV 2 cases to compare trends with internal cases.
- Gathered national alcohol sales data from the Federal Reserve Bank Economic Research website to compare 2020 sales with the prior three years.
- They analyzed trend significance using Z-score analysis.

Results

COVID-19 Cases with Milestones

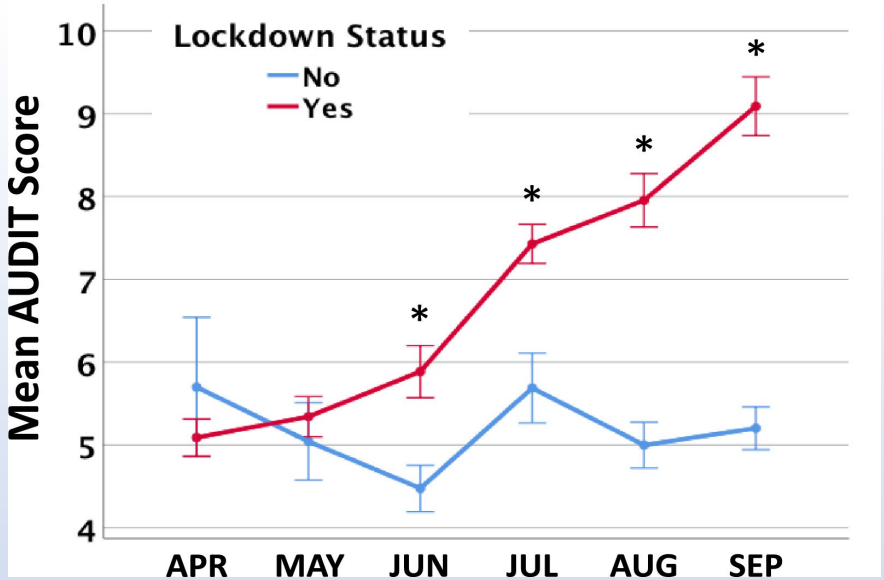


Scripps

Courtesy of Dr. Catherine Frenette

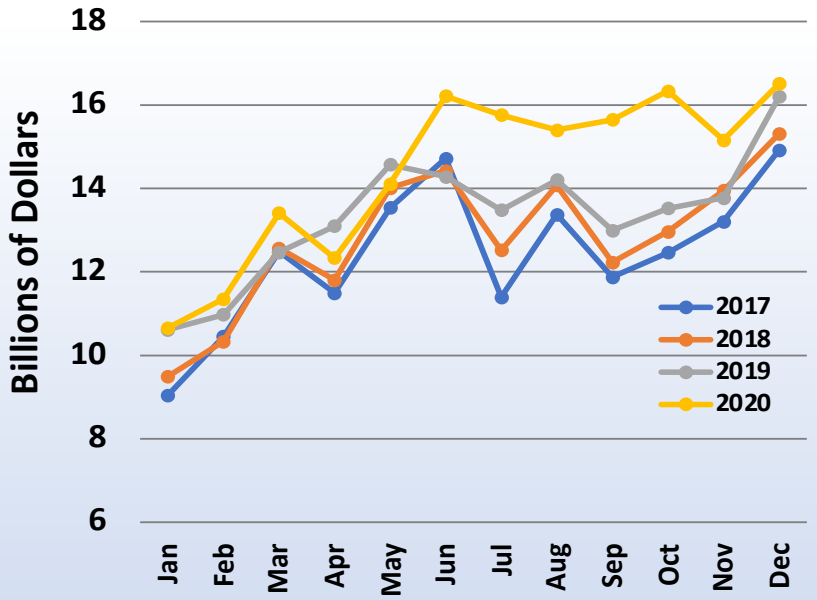
Alcohol Dependence During COVID-19 Lockdowns

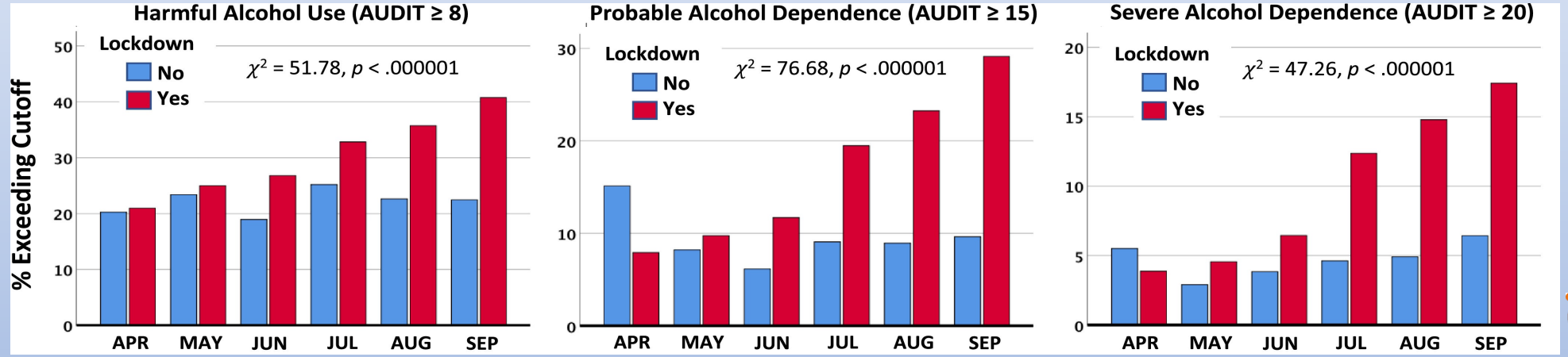
Journal of Psychiatry Research



AUDIT:
Alcohol
Use
Disorder
Identification
Test

National Alcohol Sales (Federal Reserve Data)





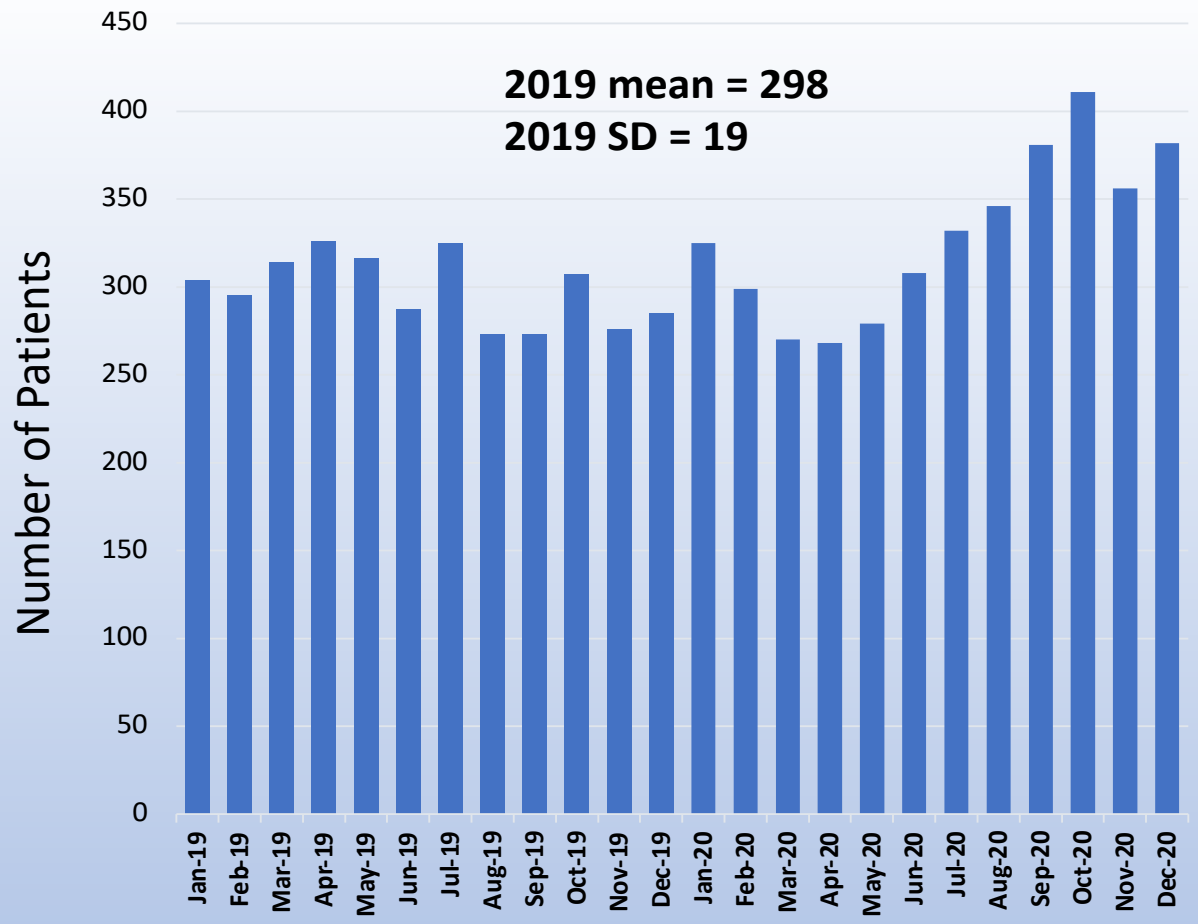
Scripps

William D.S. Killgore, Sara A. Cloonan, Emily C. Taylor, Daniel A. Lucas, Natalie S. Dailey. "Alcohol dependence during COVID-19 lockdowns" Psychiatry Research, Vol. 296, 2021.

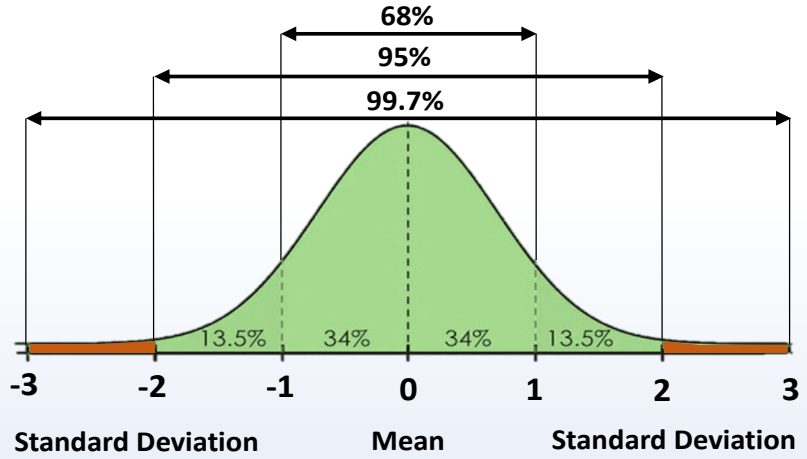
Courtesy of Dr. Catherine Frenette

Cases of Alcohol Related Liver Disease

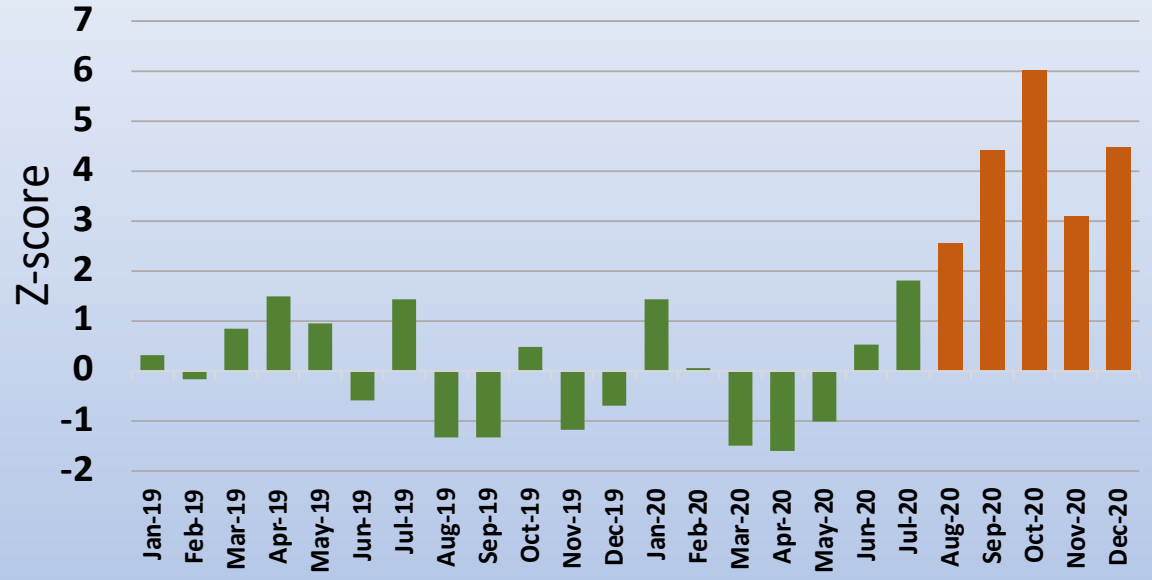
(Inpatient + Outpatient Encounters)



Search Criteria:
ICD-10 Code K70 (Alcohol Related Liver Disease)



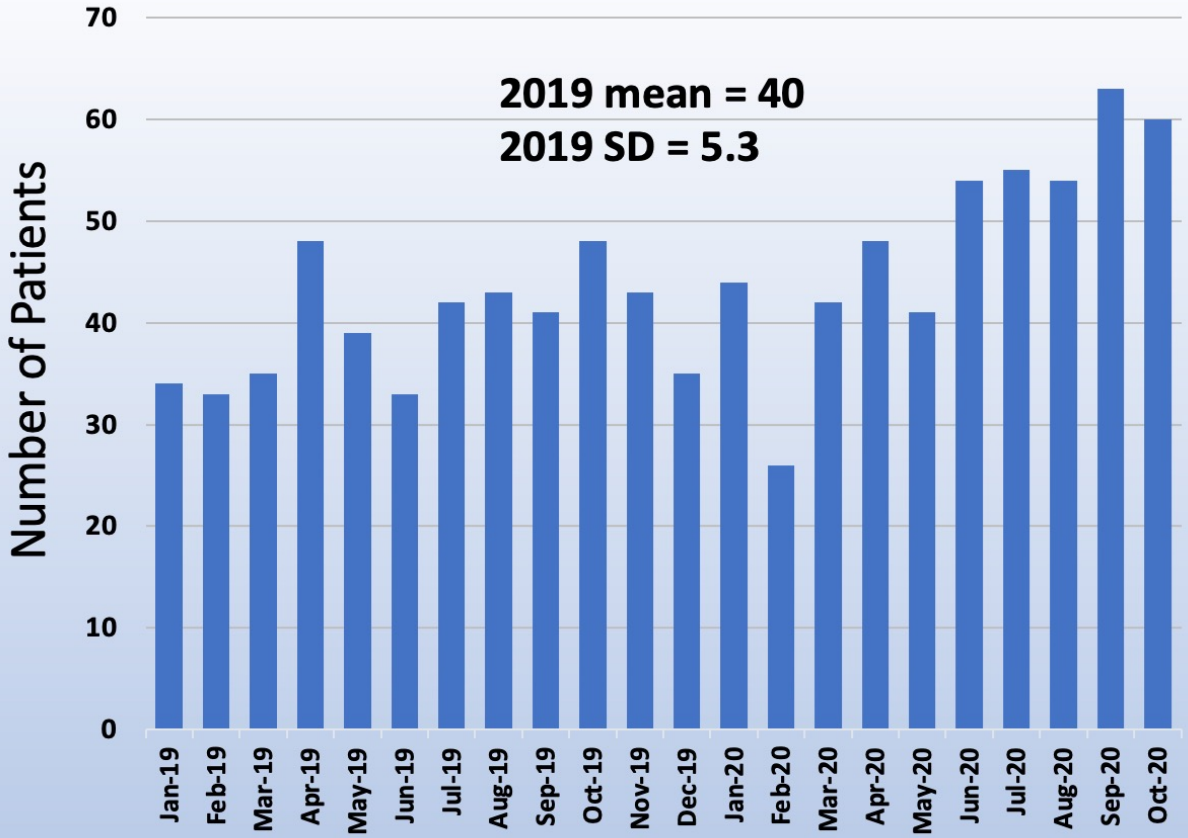
↑ 32.7% (1876/1414)

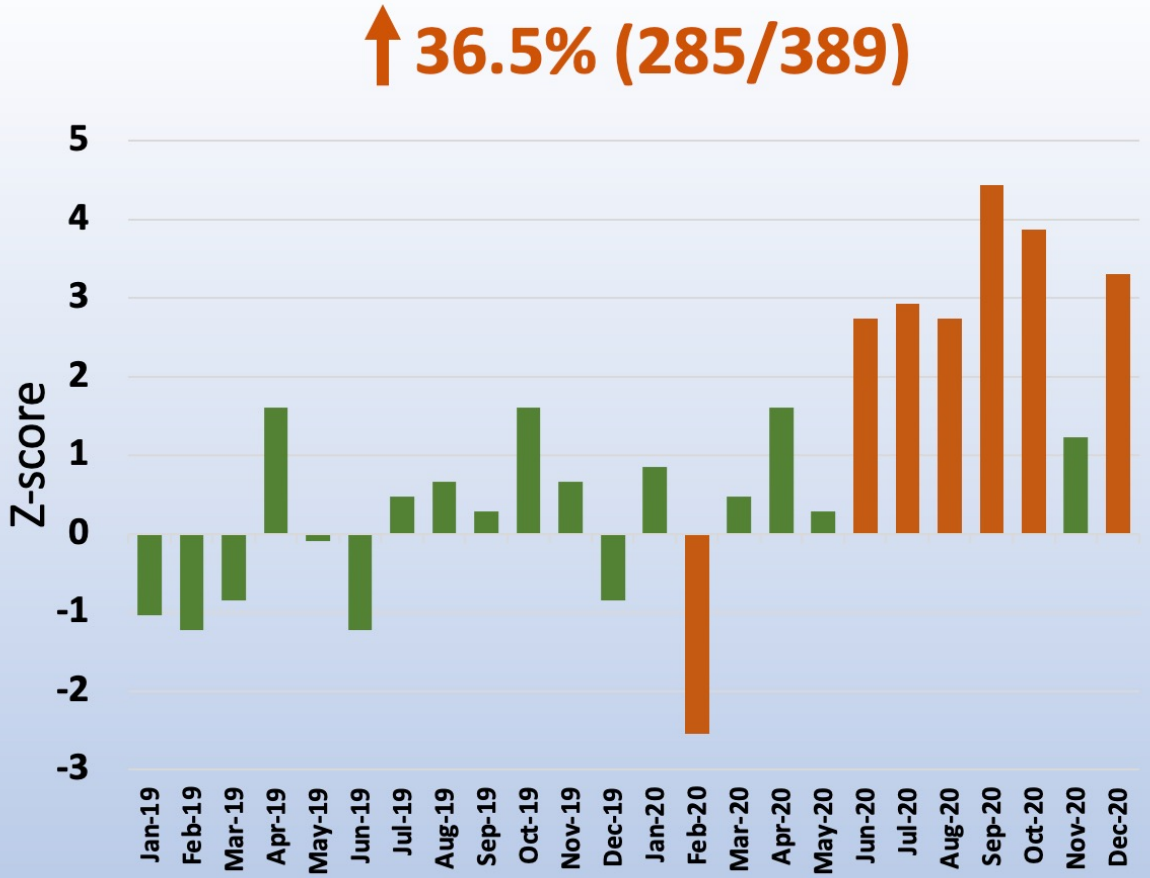


Scripps

Courtesy of Dr. Catherine Frenette

Alcohol Related Pancreatitis





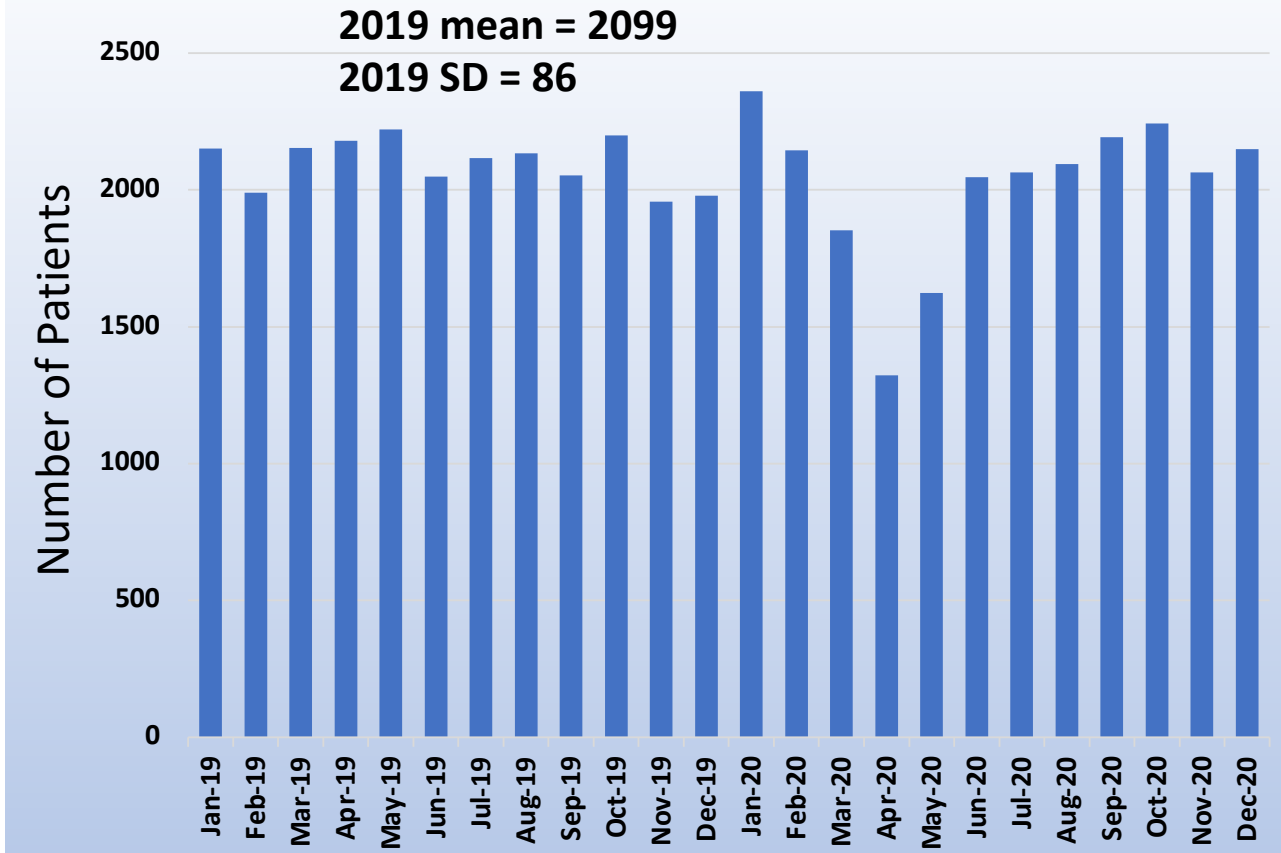
Search Criteria:
ICD-10 Codes: K85.20, K85.21, K85.22

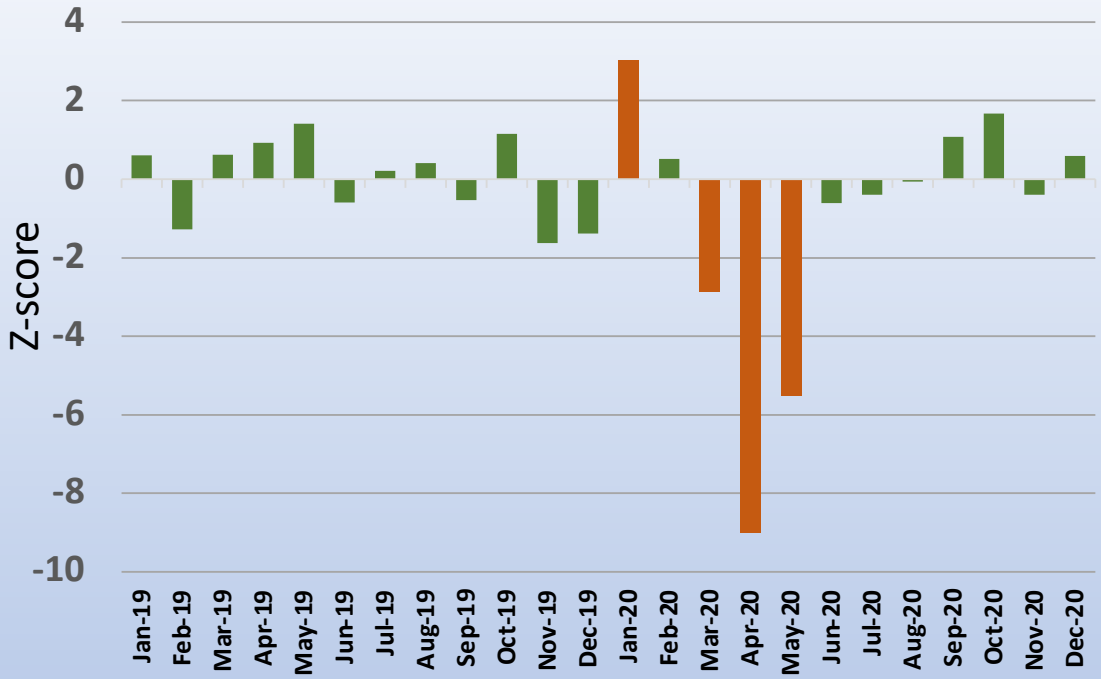
Scripps

Courtesy of Dr. Catherine Frenette

Non-Alcohol Related Liver Disease

(Inpatient + Outpatient Encounters)





Search Criteria:
ICD-10 Codes: K72, K73, K74, K76

Scripps

Courtesy of Dr. Catherine Frenette

COVID-19

INCREASED BURDEN OF ALCOHOL-RELATED GASTROINTESTINAL AND LIVER DISEASES DURING THE COVID-19 PANDEMIC:

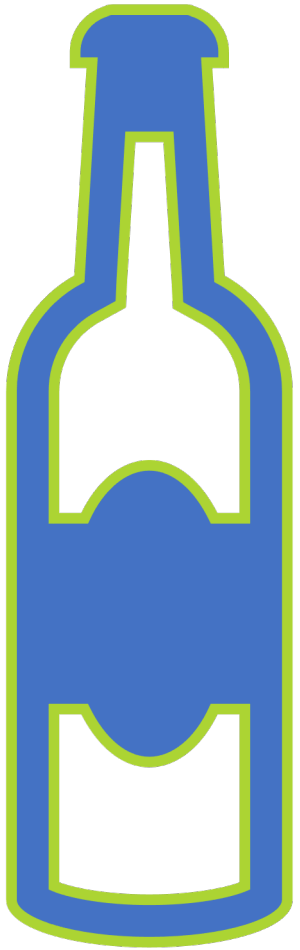
A HOSPITAL SYSTEM-WIDE AUDIT

W. Chung, M. Min, S. Kothadia, F. Saeed, J. Scharfen, F. Habr.
Gastroenterology, Lifespan/ Warren Alpert Brown Medical School, Providence, RI

DDW 2021 Abstract #436, Clinical Science Plenary

Conclusion

- COVID-19 pandemic is associated with increased harmful alcohol use, contributing to increased health complications.
- Social Isolation was likely the cause of increased harmful alcohol use.
- All medical providers should proactively screen for and aggressively address alcohol use disorder.
- Work is needed to identify other health cost/consequences of the pandemic.



NASH/HCC

CHEMOPREVENTIVE EFFECT OF STATIN ON HEPATOCELLULAR CARCINOMA IN NON- ALCOHOLIC STEATOHEPATITIS PATIENTS WITH CIRRHOSIS

W. A. Al-Yaman1, K. Pinyopornpanish1, 2, R. Butler1, W. Carey1, A. McCullough1, C. Romero-Marrero1.

1Digestive Disease and Surgery Institute, Cleveland Clinic, Cleveland, OH; 2Chiang Mai University Faculty of Medicine, Chiang Mai, Thailand

DDW 2021 Abstract #13

Methods

- They conducted a retrospective study at two US tertiary academic centers of patients with NASH-related cirrhosis followed between July 2009 and June 2016.
- Patients were followed from date of diagnosis to the time of last abdominal imaging, liver transplantation or HCC diagnosis.
- HCC was defined by histological diagnosis of HCC or radiological diagnosis of Liver Imaging Reporting and Data System (LI- RADS) 5 criteria.
- **Multivariable Cox regression analysis was performed to evaluate the risk factors associated with HCC development.**
- Statin user was defined as a patient who was on statin with cumulative defined daily dose (cDDD) of at least 28 days.

Result

- A total of 950 patients with NASH cirrhosis were identified,
  - 506 patients (53.3%) with histologic confirmation of NASH cirrhosis
  - 444 patients (46.7%) with clinical diagnosis of NASH cirrhosis.

- **HCC developed in 82 patients with NASH cirrhosis** during 4,326 person-year follow-up
  - Annual incidence rate of 1.90 per 100 person-year (95% CI, 1.53-2.35 / 100 person-year).
  - Mean follow up time was 4.6 ± 3.3 years.

- Multivariable analysis demonstrated that HCC development was associated with
  - **Male gender (HR 4.00; 2.56-6.25, p<0.001), older age (HR 1.06; 1.03-1.08, p<0.001), and albumin level (HR 0.38; 0.28-0.51, p<0.001**).

Result

- **Statin use was associated with lower risk of HCC (HR 0.49; 0.30-0.80, p=0.003).**

- After adjusting for age, gender, race, decompensation status, smoking history, alcohol use, diabetes mellitus, BMI, and MELD- Na score demonstrated that:
  - **Patients who used lipophilic statin were associated with significant HCC risk reduction (adj. HR 0.31, 95%CI 0.17-0.56, P<0.001), while**
  - Patients who used hydrophilic statin were not associated with statistically significant reduction (adj. HR 0.85, 95%CI 0.42-1.72, p=0.648).

- Each 365 increment in cDDD of statin use reduced HCC risk by 23.6%.

Conclusion

- **Statin use reduced HCC risk significantly in cirrhotic NASH patients after adjusting for multiple variables.**
- Lipophilic statins were associated with HCC risk reduction.
- We need to change the habit of "stopping" statins in patients with cirrhosis.
- Though we have not started routine use of statins in patients with liver diseases without indications, data showing reduction of HCC and other complications of cirrhosis is compelling.

Cholestatic Liver Disease

OBETICHOLIC ACID EXPOSURE IS ASSOCIATED WITH HEPATIC DECOMPENSATION IN SUBJECTS WITH PRIMARY BILIARY CHOLANGITIS AND CIRRHOSIS

B. V. John1, K. Schwartz1, C. Levy2, B. Dahman3, Y. Deng3, P. Martin2, T. H. Taddei4, D. E. Kaplan5.

1Miami VA Healthcare System, Miami, FL; 2University Of Miami Hospital, Miami, FL; 3Virginia Commonwealth University, Richmond, VA; 4Yale University School of Medicine, New Haven, CT; 5Penn Medicine, Philadelphia, PA

DDW 2021 Abstract #237

Background

- Obeticholic acid (OCA) is approved for the treatment of patients with primary biliary cholangitis (PBC) who are incomplete responders or intolerant to ursodeoxycholic acid (UDCA) since 2016.

- Recently, the FDA reported severe adverse events of using OCA in patients with advanced liver disease using data from it's serious adverse event reporting system
  - 25 cases of liver failure (2016-2021)
    - 18/25 – had compensated cirrhosis
      - 10/18 – clinical evidence of portal hypertension
    - Median time to liver failure after OCA initiated (2 weeks to 10 months)
    - 4 needed liver transplant and 1 died of liver failure

US Food and Drug Administration
https://www.accessdata.fda.gov

Background

- Though the FDA report highlighted individual cases with severe drug-induced liver toxicity, quantification of increased risk of decompensation related to OCA **requires a comparator group of OCA unexposed PBC patients at similar baseline risk.**

Methods

- This study investigated the impact of OCA use on hepatic decompensation and liver-related death or transplantation, **in a cohort of patients with PBC and well-compensated cirrhosis and compared outcomes with a propensity-matched cohort of patients without OCA exposure.**

- This was a retrospective cohort study utilizing national data of US Veterans with PBC and cirrhosis.

Result

- They identified 509 subjects with compensated PBC cirrhosis.
  - **21 OCA users were matched with 84 non-users**
- The initial and maintenance dose of OCA was 5 mg daily in 90%, 10 mg daily in 5% and 5 mg per week in 5% of subjects.
- Over 569 and 3847 person-months respectively of follow-up, **5 (23.8%) OCA users, and 22 (26.2%) OCA non-users decompensated.**
- On multivariable analysis, after adjusting for potential confounders, **OCA use was associated with an increased risk of hepatic decompensation**
  - **aHR 3.3, 95% CI 1.01-10.77, p=0.048.**
- **There was no association between OCA use and liver-related mortality or transplantation (aHR 2.09, 95% CI 0.50-8.68, p=0.31**

Conclusion

- This data suggest that exposure to OCA in patients with PBC cirrhosis is associated with a 3.3-fold higher risk of hepatic decompensation but not liver-related mortality or transplantation.
- The mechanism of liver injury has not been well described yet.
- Note these are male VA patients and different from the majority of PBC patients, mostly female.
- More comparison studies are needed to assess outcomes of patients with PBC or other liver diseases treated with OCA.
- OCA remains beneficiary and safe in PBC patients with no advanced fibrosis (majority of our patients with PBC).

Key Obeticholic Acid Label Change Boxed Warning

Previous Label (2018)

OCALIVA® (obeticholic acid) tablets, for oral use
Initial U.S. Approval: 2016

WARNING: HEPATIC DECOMPENSATION AND FAILURE IN INCORRECTLY DOSED PBC PATIENTS WITH CHILD-PUGH CLASS B OR C OR DECOMPENSATED CIRRHOSIS
See full prescribing information for complete boxed warning

- **In postmarketing reports, hepatic decompensation and failure, in some cases fatal, have been reported in patients with primary biliary cholangitis (PBC) with decompensated cirrhosis or Child-Pugh Class B or C hepatic impairment when OCALIVA was dosed more frequently than recommended. (5.1)**
- **The recommended starting dosage of OCALIVA is 5 mg once weekly for patients with Child-Pugh Class B or C hepatic impairment or a prior decompensation event. (2.2)**

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See full prescribing information for complete boxed warning

- **Hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, have been reported with OCALIVA treatment in primary biliary cholangitis (PBC) patients with either compensated or decompensated cirrhosis. (5.1)**
- **OCALIVA is contraindicated in PBC patients with decompensated cirrhosis, a prior decompensation event, or with compensated cirrhosis who have evidence of portal hypertension. (4)**
- **Permanently discontinue OCALIVA in patients who develop laboratory or clinical evidence of hepatic decompensation, have compensated cirrhosis and develop evidence of portal hypertension, or experience clinically significant hepatic adverse reactions while on treatment. (2.3, 5.1)**

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Disparities in HCC Care

RACIAL AND ETHNIC DISPARITIES IN SURVIVAL AMONG PATIENTS WITH HEPATOCELLULAR CARCINOMA IN THE UNITED STATES: A SYSTEMATIC REVIEW AND META-ANALYSIS

N. E. Rich, C. Carr, A. Yopp, J. A. Marrero, A. G. Singal.
Internal Medicine, Division of Digestive and Liver Diseases , UT Southwestern Medical Center, Dallas, TX

DDW 2021 Liver & Biliary Distinguished Abstract Plenary, Abstract #356

Background/Aim

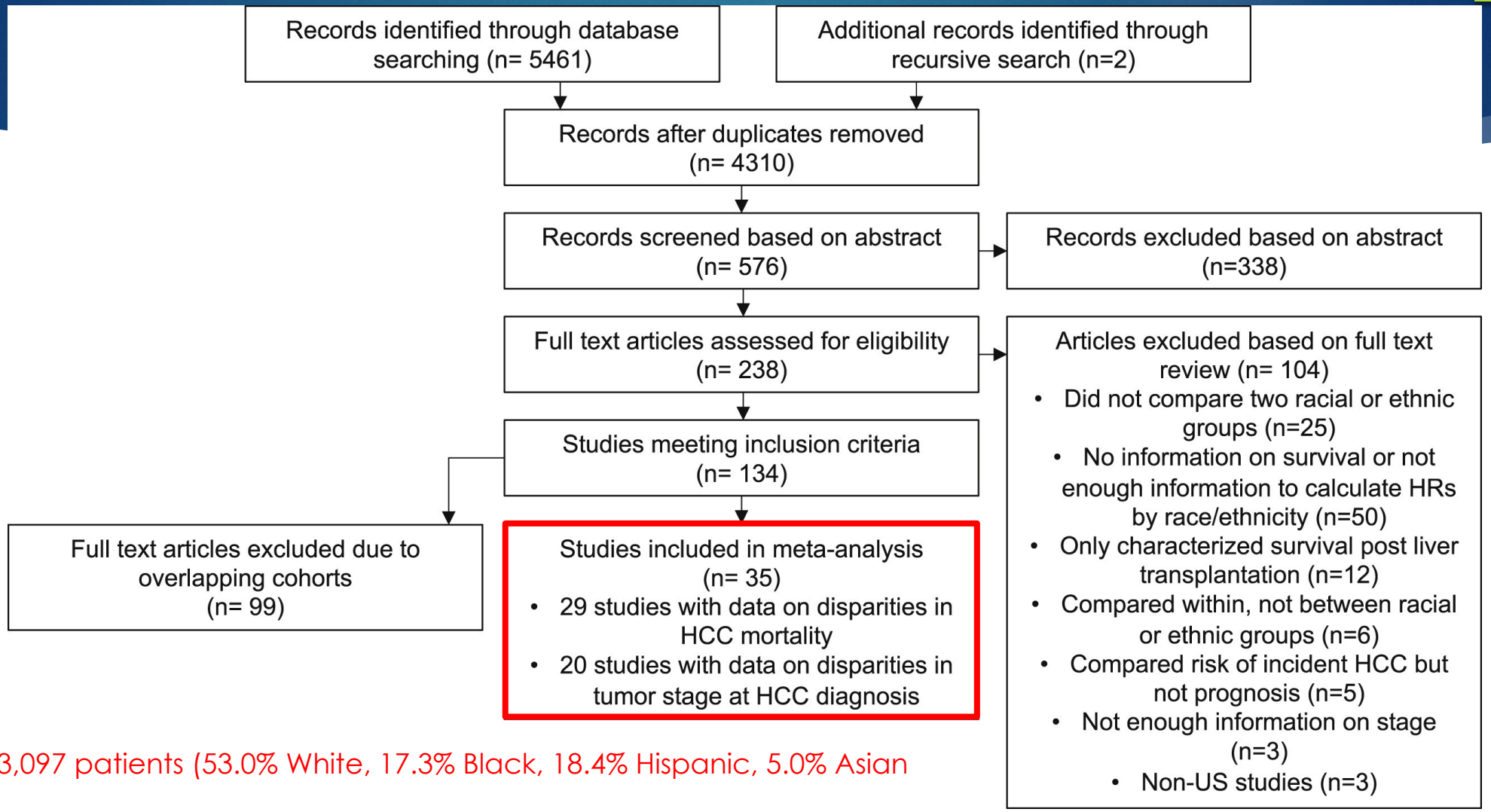
- HCC is the fastest rising cause of cancer-related death in the United States; however, HCC incidence and mortality are not equally distributed among racial/ethnic groups.

- The aim of this study was to characterize the direction and magnitude of racial/ethnic disparities among patients with HCC
  - **Overall survival**
  - **Early tumor detection**

Method

- They searched MEDLINE, EMBASE and Cochrane databases from inception through August 2020 for studies reporting HCC outcomes (early-stage presentation and overall survival) by race and ethnicity.
- The primary outcome of interest was overall survival; the secondary outcome of interest was detection of HCC at an early stage.
- They calculated pooled hazard ratios (HRs) and odds ratios (ORs) for each racial/ethnic group (White, Black, Hispanic, Asian).
- They performed pre-planned subgroup analyses by cohort type (i.e., academic or hospital-based vs population-based).

Study Selection

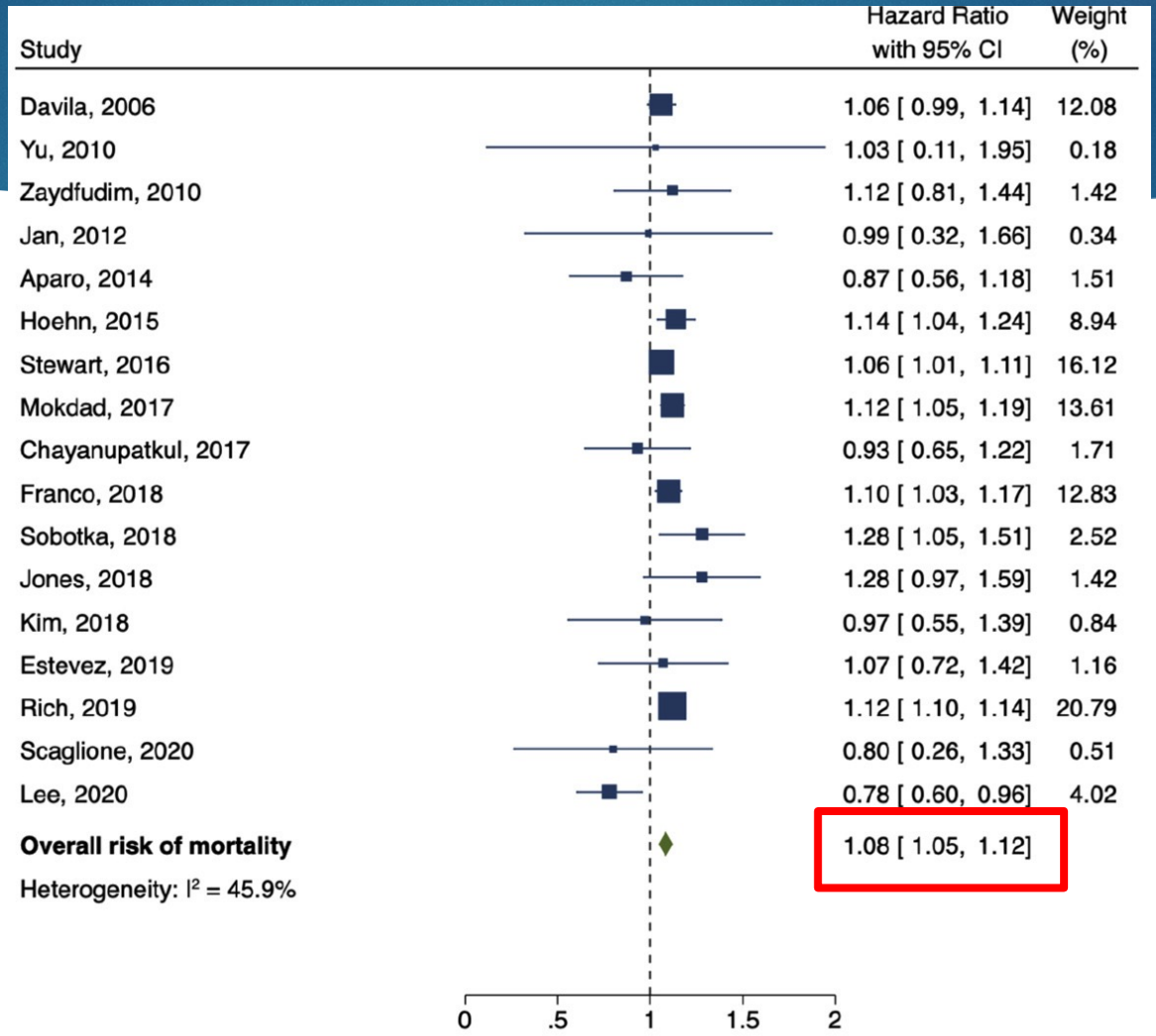


563,097 patients (53.0% White, 17.3% Black, 18.4% Hispanic, 5.0% Asian

Rich NE et al, *CGH* (in press)

Courtesy of Dr. Nicole Rich

Black patients with HCC had worse overall survival compared to White patients

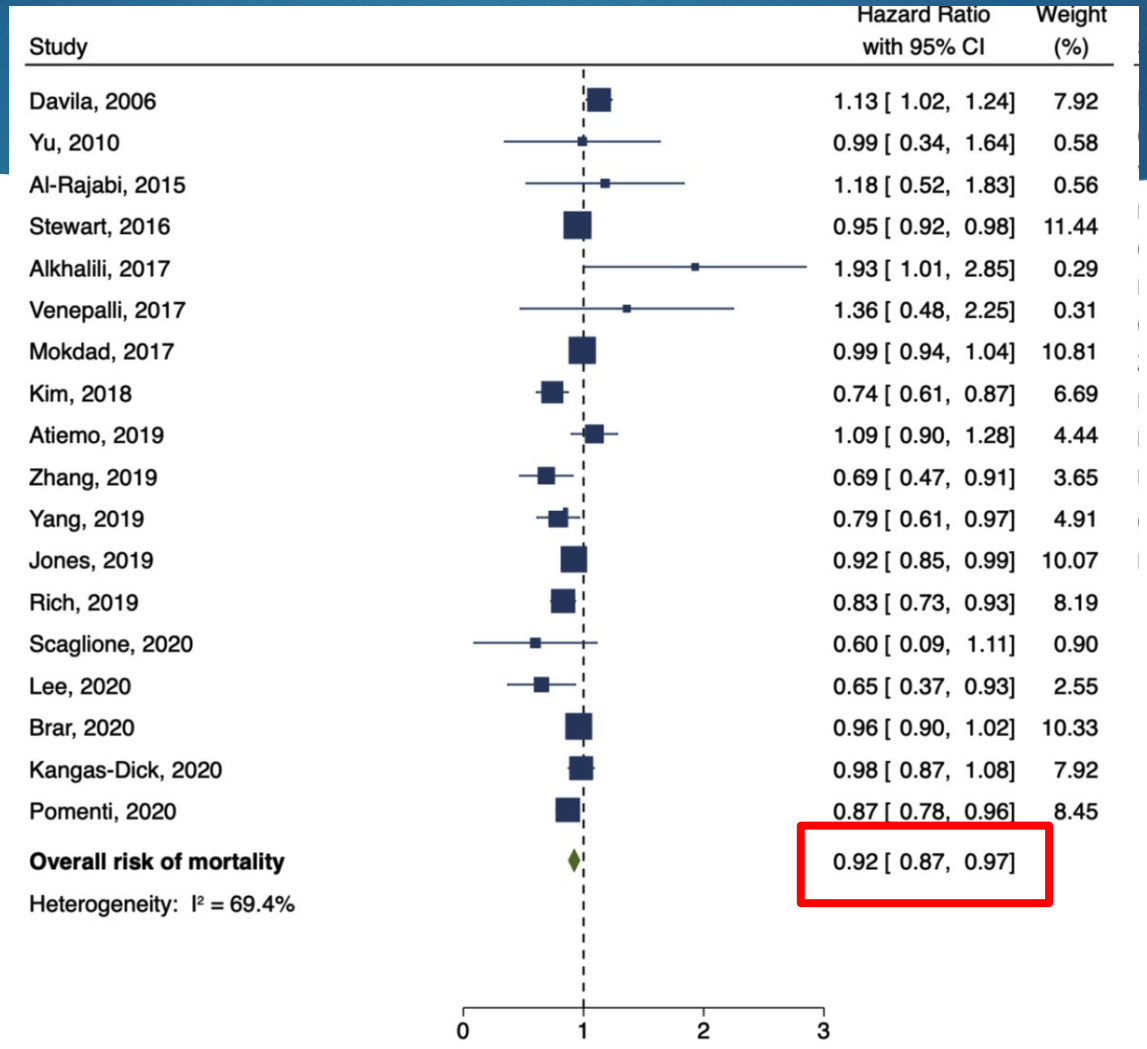


Rich NE et al, *CGH* (in press)

Courtesy of Dr. Nicole Rich

UTSouthwestern Medical Center

Hispanic patients with HCC had better survival than non-Hispanic White patients

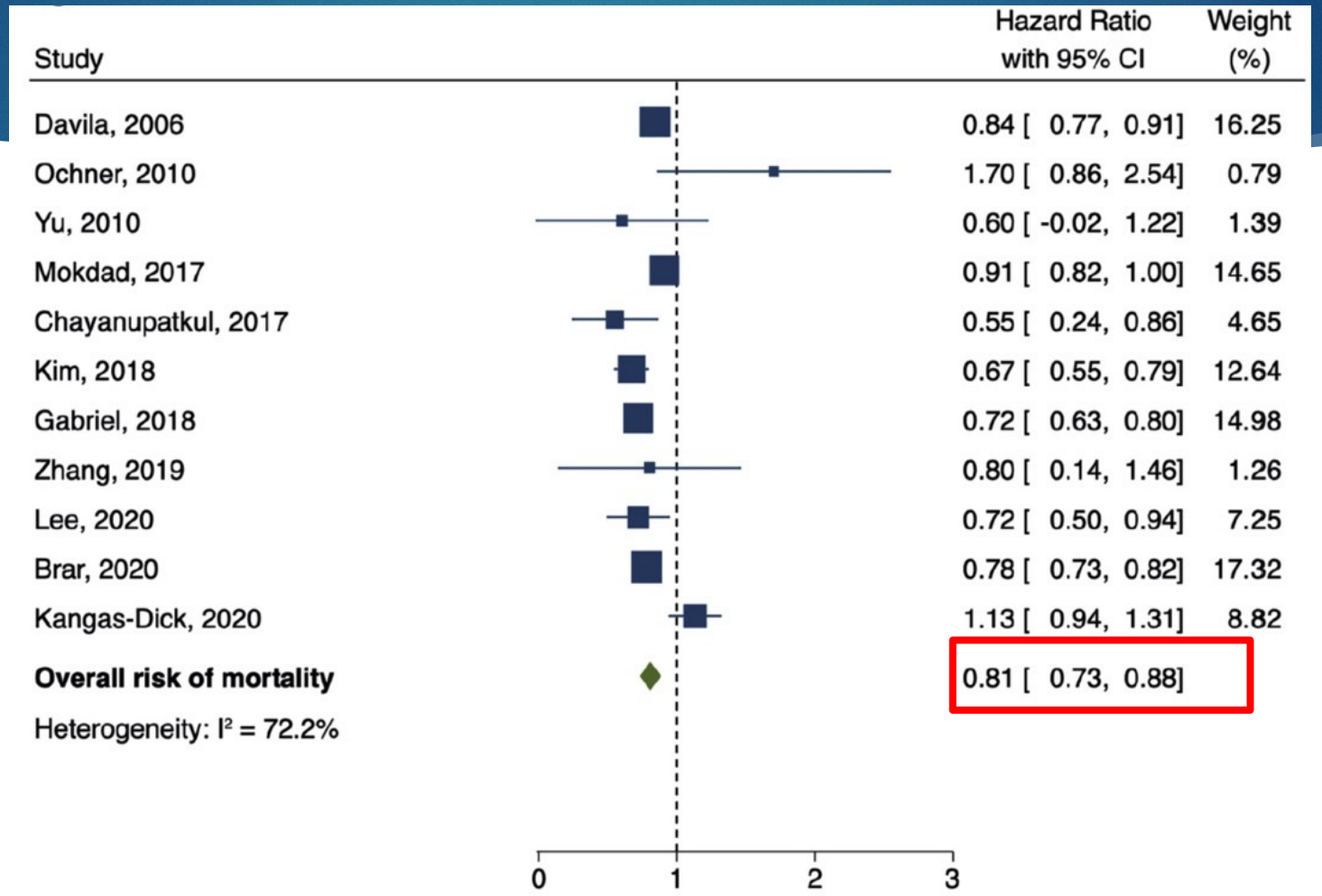


Rich NE et al, *CGH* (in press)

Courtesy of Dr. Nicole Rich

UT Southwestern Medical Center

Asian patients with HCC had better survival than White patients

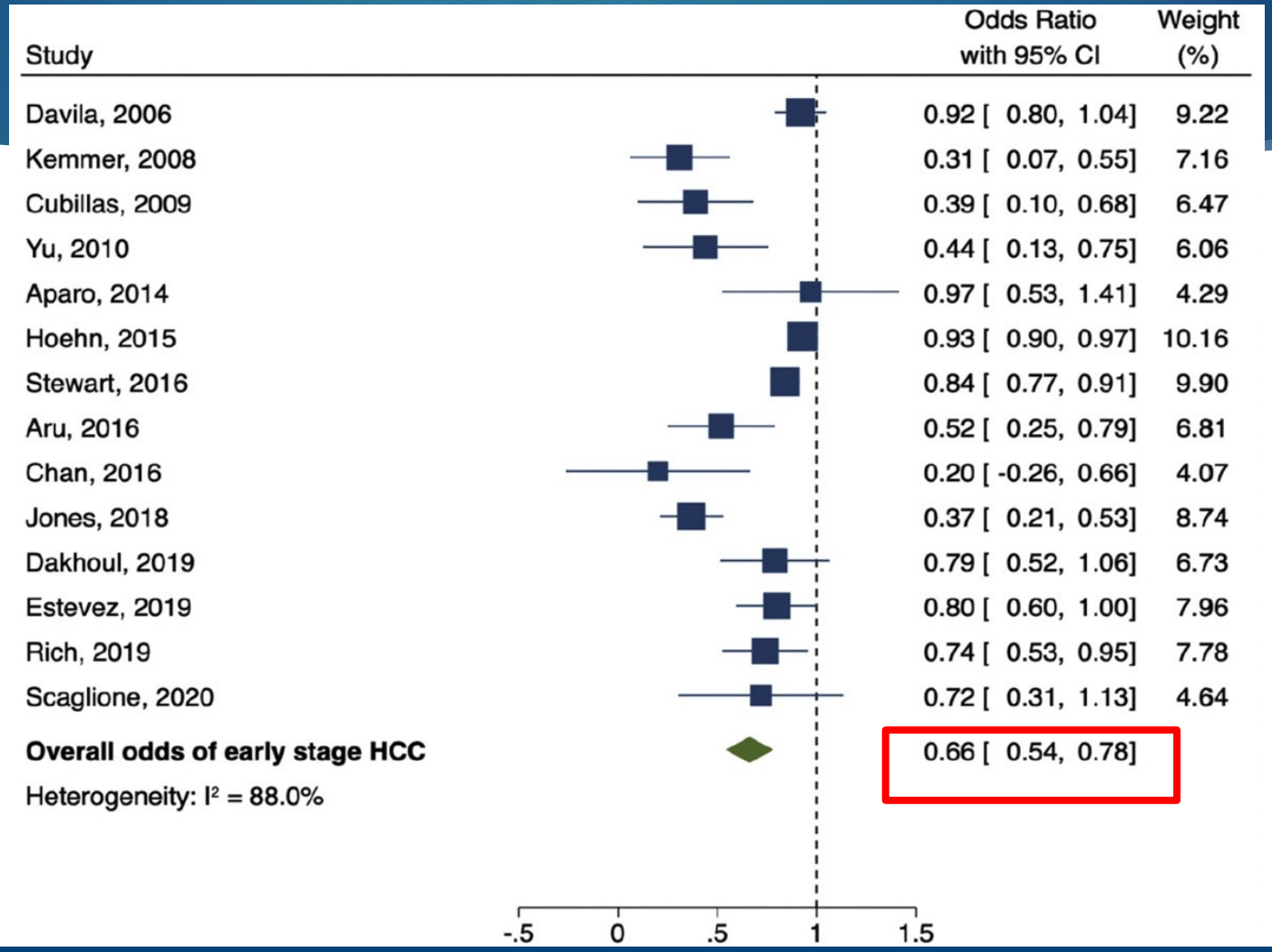


Rich NE et al, *CGH* (in press)

Courtesy of Dr. Nicole Rich

UTSouthwestern Medical Center

Black patients less likely than White patients to be diagnosed with early-stage HCC

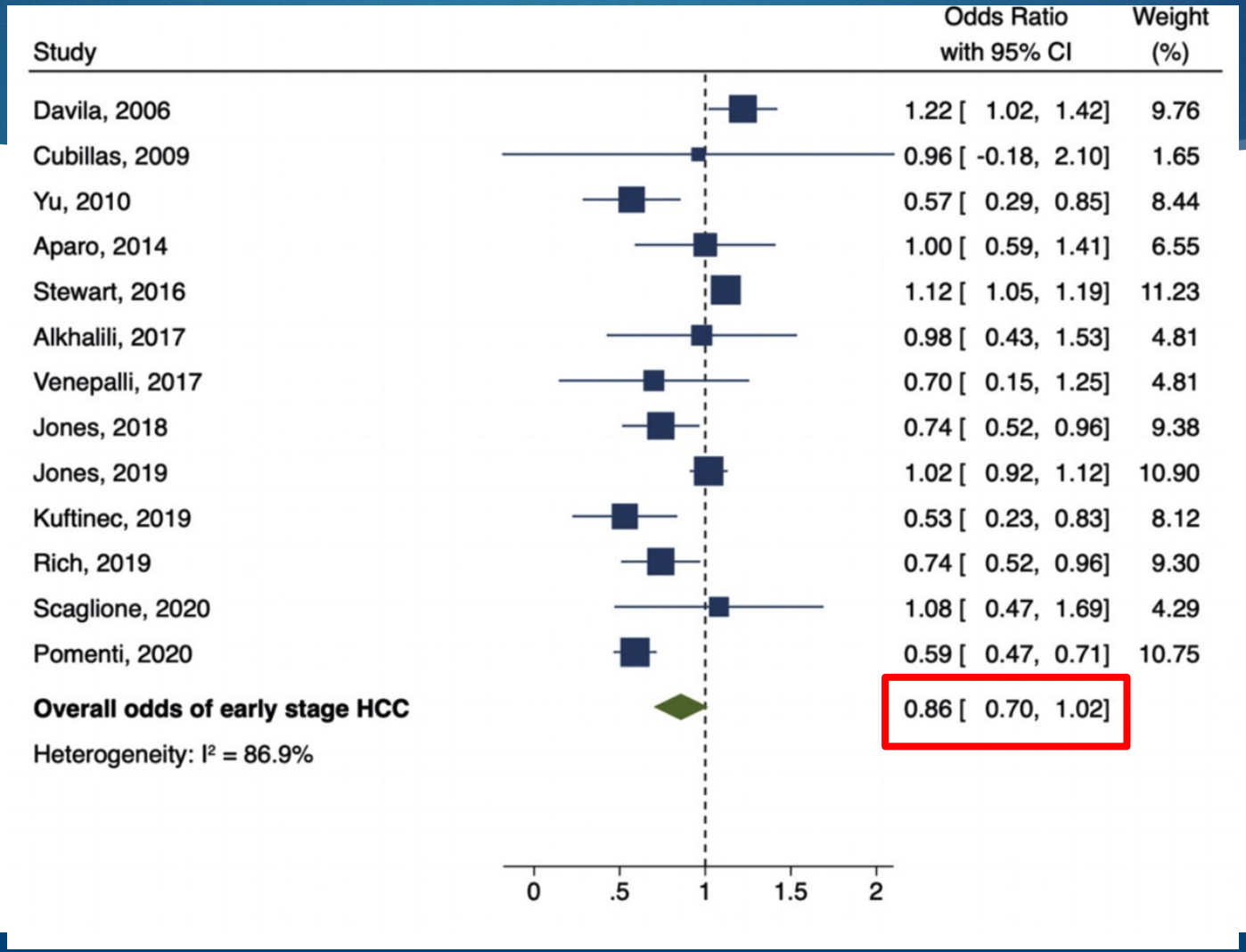


Rich NE et al, *CGH* (in press)

Courtesy of Dr. Nicole Rich

UT Southwestern Medical Center

No difference in early-stage detection between Hispanic patients and non-Hispanic White patients

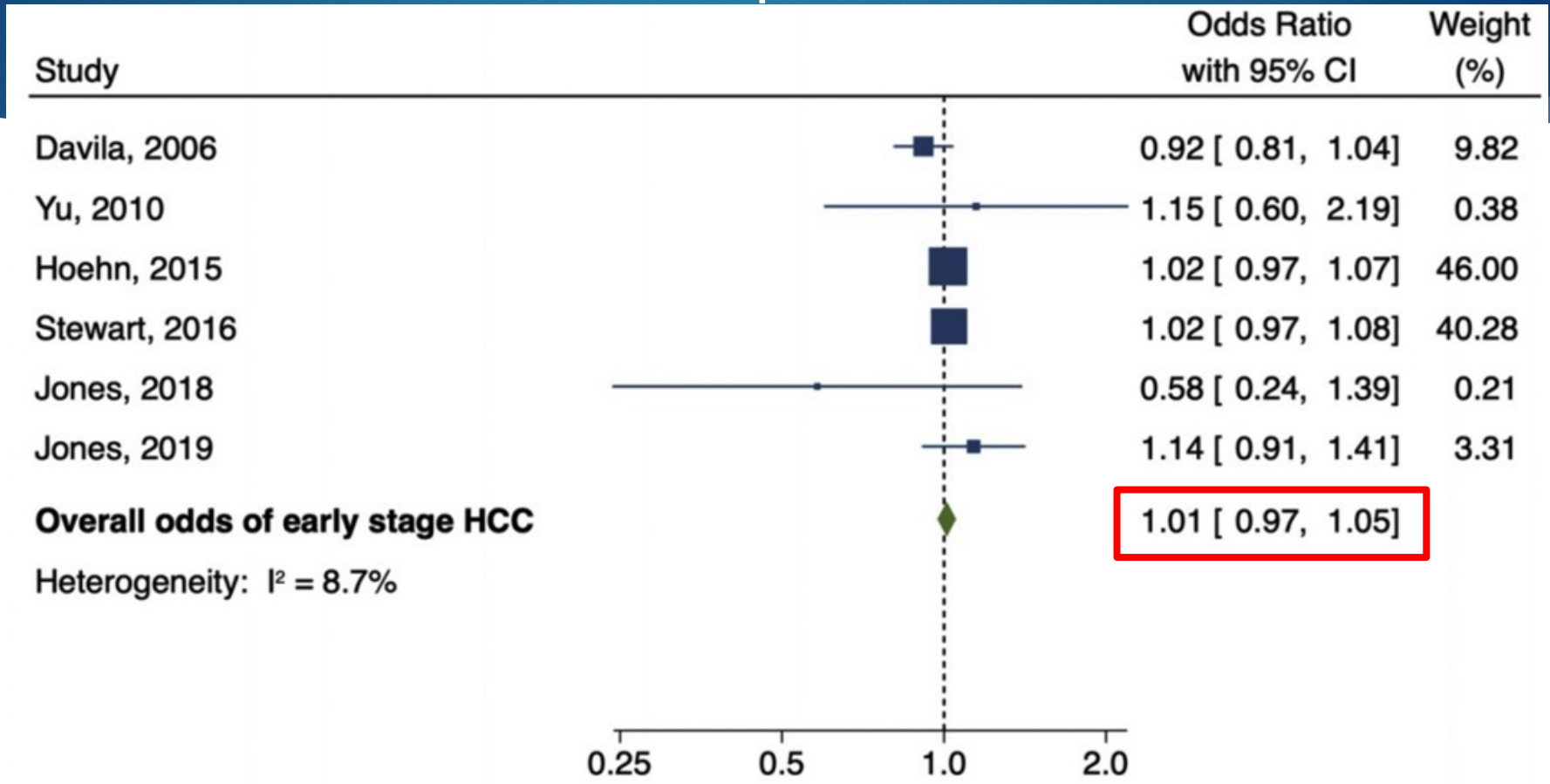


Rich NE et al, *CGH* (in press)

Courtesy of Dr. Nicole Rich

UT Southwestern Medical Center

No difference in early-stage detection between Asian patients and White patients



Rich NE et al, *CGH* (in press)

Courtesy of Dr. Nicole Rich

Subgroup analyses – overall survival

	Population-based cohorts	Academic cohorts
Black vs. White	HR 1.09 (95%CI 1.06 – 1.12)	HR 1.00 (95%CI 0.85 – 1.15)
Hispanic vs. White	HR 0.97 (95%CI 0.93 – 1.02)	HR 0.81 (95% CI 0.75 -0.90)
Asian vs. White	HR 0.83 (95%CI 0.75 – 0.92)	HR 0.73 (95%CI 0.56 – 0.90)

Limitations of Included Studies

- All studies retrospective
  - Missing data, measurement bias
  - Potential misclassification of race/ethnicity
  - Selection bias (n=21 studies at academic centers)

- Lack data on cirrhosis etiology, liver disease severity, treatments beyond 1st HCC treatment

- Most studies controlled for tumor stage or treatment receipt (n=19); fewer adjusted for liver disease severity (n=6) and SES (n=14)

Conclusion

- There are significant racial and ethnic disparities in HCC prognosis in the United States, **with Black patients having worse overall survival and Hispanic and Asian patients having better overall survival compared to White patients.**

- Though considerable progress has been made in describing the magnitude of disparities in HCC, data are still limited on the specific determinants driving these disparities (multifactorial).

- **Future studies are needed to take the critical next steps to determine the root causes of HCC disparities and implement interventions.**

Thank You

DDW 2021