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ADVANCES IN RISK FACTORS FOR HEPATOCELLULAR CARCINOMA

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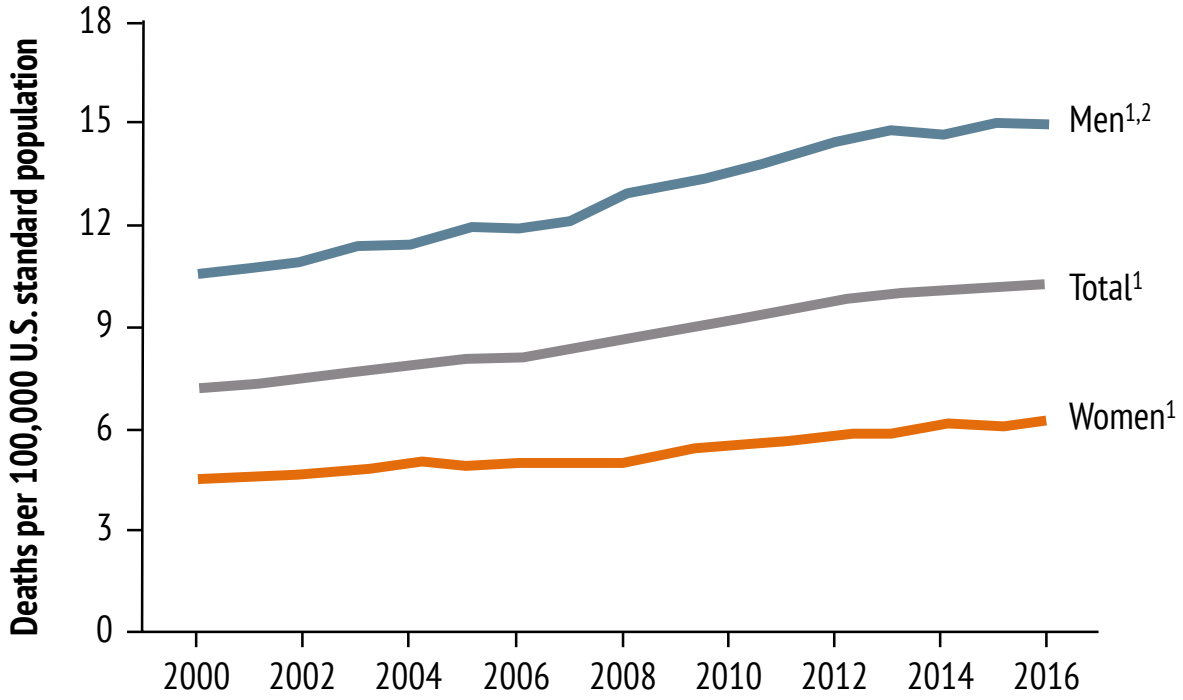
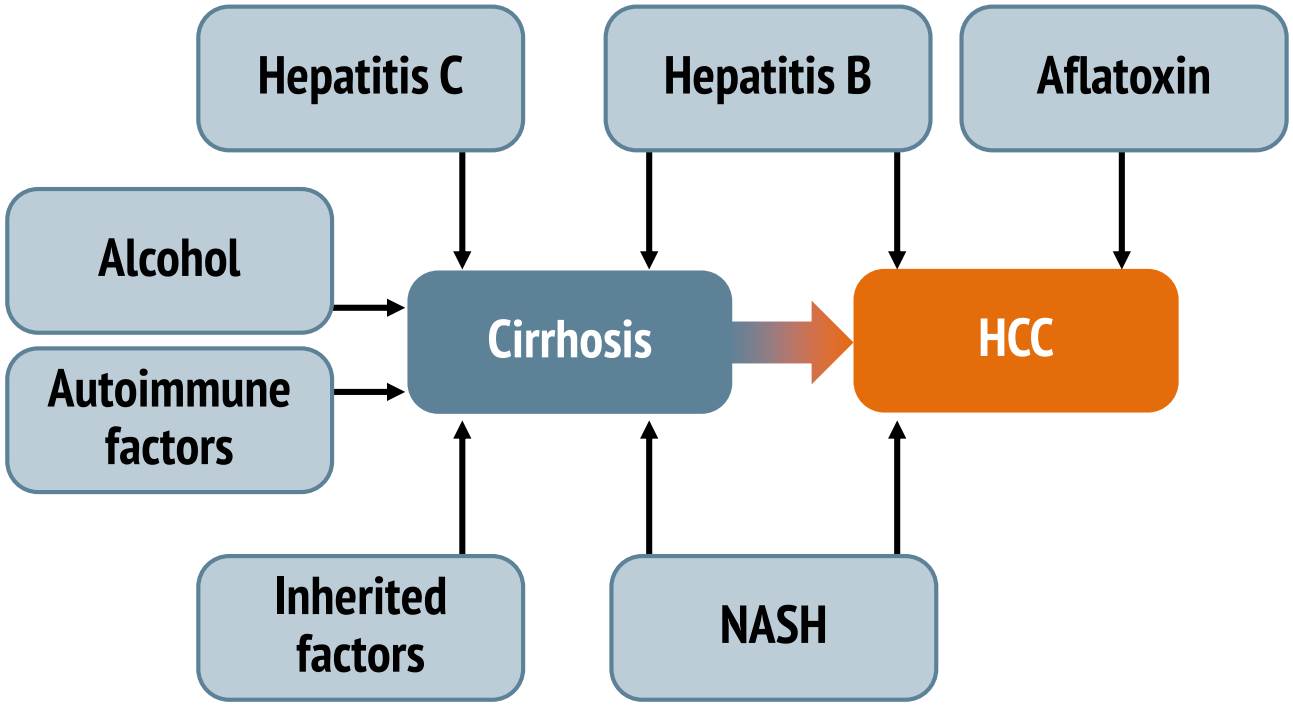
AGE-ADJUSTED DEATH RATES FOR LIVER CANCER AMONG ADULTS AGED 25 AND OVER, BY SEX: UNITED STATES, 2000–2016



[1]Significant increasing trend from 2000 to 2016 ($p < 0.05$).
[2]Significantly higher than women throughout the period ($p < 0.05$).
NOTES: Liver cancer deaths are identified with International Classification of Diseases, 10th Revision, using underlying cause-of-death code C22. Access data table for Figure 1 at: https://www.cdc.gov/nchs/data/databriefs/db314_table.pdf#1.
SOURCE: NCHS, National Vital Statistics System, Mortality.

INSULTS CONTRIBUTING TO HCC



HCC, hepatocellular carcinoma
Shariff MI, et al. Expert Rev Gastroenterol Hepatol. 2009;3:353-367

THE #1 RISK FACTOR FOR HCC IS VIRAL HEPATITIS

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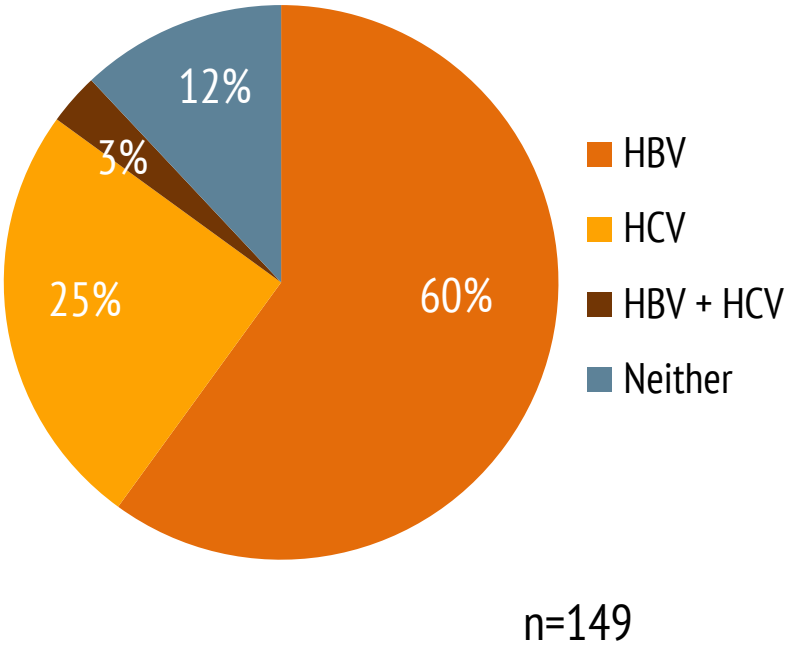
HCC Incidence by Etiology: Overall in the U.S.[1]

Cause	Percentage
HBV	15-17%
HCV	47-55%
HCV + alcohol	27% of above
Alcohol	9%
Cryptogenic	7%
Other	6%
No cirrhosis or virus	4%

HCC Incidence by Etiology: U.S. Urban Setting[2]



HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus.

1. Davis GL, et al. Proc (Bayl Univ Med Cent). 2008;21:266-280; 2. Hiotis SP, et al. BMC Gastroenterol. 2012;12:64.

MAJOR GUIDELINES RECOGNIZE THE IMPORTANCE OF ROUTINE SURVEILLANCE IN HIGH-RISK POPULATIONS

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Society/Institution	Guidelines
AASLD[1] American Association for the Study of Liver Diseases	US every 4-8 months
EASL[2] European Association for the Study of the Liver	US every 6 months
APASL[3] Asian-Pacific Association for the Study of the Liver	US + AFP every 6 months
NCCN[4] National Comprehensive Cancer Network	US +/- AFP every 6-12 months
VA[5] United States Department of Veterans Affairs	US +/- AFP every 6 months
JSH-HCC[6] Japan Society of Hepatology	High risk: US every 6 months + AFP/DCP/AFP-L3 every 6 months Very high risk: US every 3-4 months + AFP/DCP/AFP-L3 every 3-4 months + CT/MRI (optional) every 6-12 months

AFP, alpha-fetoprotein; AFP-L3, *Lens culinaris* agglutinin-reactive fraction of AFP; CT, computerized tomography; DCP, des-γ-carboxyprothrombin; HCC, hepatocellular carcinoma; MRI, magnetic resonance imaging; US, ultrasound.

1. Heimbach J, et al. Hepatology. 2018;67:358-380. 2. EASL, EORTC. J Hepatol. 2018;69:182-236. 3. Omata M, et al. Hepatol Int. 2017;11:317-370.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatobiliary Cancers v1.2019. © National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed January 7, 2019. 5. US Dept of Veterans Affairs. Available at: https://www.hepatitis.va.gov/pdf/HCC-multidisciplinary-management-best-practices.pdf. Accessed Accessed January 7, 2019. 6. Kokudo N, et al. Hepatol Res. 2015;45

IN MEDICARE PATIENTS WITH HEPATOCELLULAR CARCINOMA (HCC), NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) IS AMONG THE TOP CAUSES FOR MORTALITY AND RESOURCE UTILIZATION

Shahab O, et al.
AASLD 2018, Abstract #273.

METHODS

- Aim: to assess the recent trends in mortality and healthcare utilization of HCC among Medicare population in the U.S.
  - Random 5% sample of Medicare beneficiary from 2005-2014 with a diagnosis of HCC, HCV, HBV, ALD, NAFLD and presence of cirrhosis, based on ICD-9 codes
- Temporal trends in HCC rates, demographic, clinical, and utilization parameters were analyzed by Join Point Regression (JPR) model
- Independent predictors of outcomes were evaluated in multiple generalized linear or logistic regression models

ALD, alcoholic liver disease; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; ICD-9, International Classification of Diseases, 9th Revision; NAFLD, non-alcoholic fatty liver disease

Shahab O, et al. AASLD 2018. Abstract 273

RESULTS

- 13,648 patients with HCC who sought inpatient or outpatient care
  - Mean age 70.0 years
  - 63% male
  - 76% white

	Results
1-year mortality, %	45.0
Inpatient setting	64.4
Outpatient setting	40.6
Increase in death rates, AAPC, % (95% CI)	
Males	4.4 (3.1-5.6)
Females	2.2 (0.9-3.5)
Length of stay, days	From 9.23 to 8.81
AAPC, % (95% CI)	-0.2 (-1.7-1.3)
Inpatient setting, days	8.5
Number of outpatient visits	From 1.86 to 3.18
AAPC, % (95% CI)	5.5 (4.3-6.7)

AAPC, Average Annual Percentage Change; CI, confidence interval; HCC, hepatocellular carcinoma
Shahab O, et al. AASLD 2018. Abstract 273

RESULTS

- Total charges increased
  - For inpatients: from $67,679 to $98,902
    - AAPC 5.1% (95% CI 3.3-6.8%)
  - For outpatients: from $11,933 to $32,084
    - AAPC 5.1% (95% CI 3.3-6.8)
- In the inpatient HCC cohort, compared with patients with HCV alone patients with both HCV and ALD had a higher risk of mortality (OR: 2.08, 95% CI 1.23-3.50, followed by NAFLD (OR: 1.37, 95% CI 1.10-1.71, all $p < 0.05$)
- Similarly, compared to patients with HCV alone, coexistence of HCV and ALD followed by ALD and NAFLD had higher charges: (beta value $32,892, $20,931 and $17,123; respectively

AAPC, Average Annual Percentage Change; ALD, alcoholic liver disease; CI, confidence interval; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; NAFLD, non-alcoholic fatty liver disease; OR, odds ratio

Shahab O, et al. AASLD 2018. Abstract 273

CONCLUSION

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- There is an increasing number of HCC hospitalizations and mortality among Medicare recipients
- Coexistence of ALD and HCV and NAFLD are associated with higher mortality and charges

ALD, alcoholic liver disease; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; NAFLD, non-alcoholic fatty liver disease
Shahab O, et al. AASLD 2018. Abstract 273

DIFFERENCES IN HEPATOCELLULAR CARCINOMA RISK, PREDICTORS AND TRENDS OVER TIME ACCORDING TO ETIOLOGY OF CIRRHOSIS: A COHORT OF 116,404 PATIENTS WITH CIRRHOSIS INCLUDING 10,042 WHO DEVELOPED HCC

Ionnou G, et al.
AASLD 2018, Abstract #274.

METHODS

- Aim: to describe differences in HCC risk, predictors and trends over time according to etiology of cirrhosis
- 116,404 patients with cirrhosis diagnosed between 2001-2014 were identified in the Veterans Affairs healthcare system
- Incident HCC cases occurring from the date of cirrhosis diagnosis until 01/31/2017 were determined

- Patients were divided by cirrhosis etiology
  - HCV: n=52,671
  - ALD: n=35,730
  - NAFLD: n=17,354
  - Other: n=10,649

ALD, alcoholic liver disease; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; NAFLD, non-alcoholic fatty liver disease
Ionnou G, et al. AASLD 2018. Abstract 274

RESULTS

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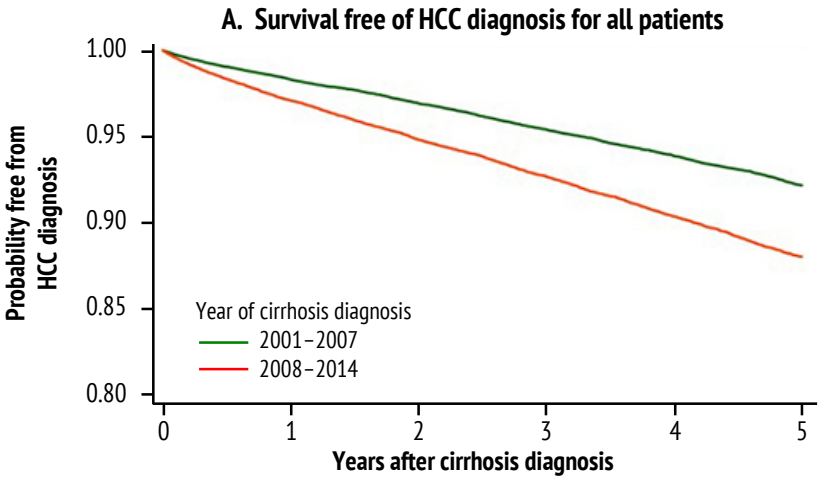
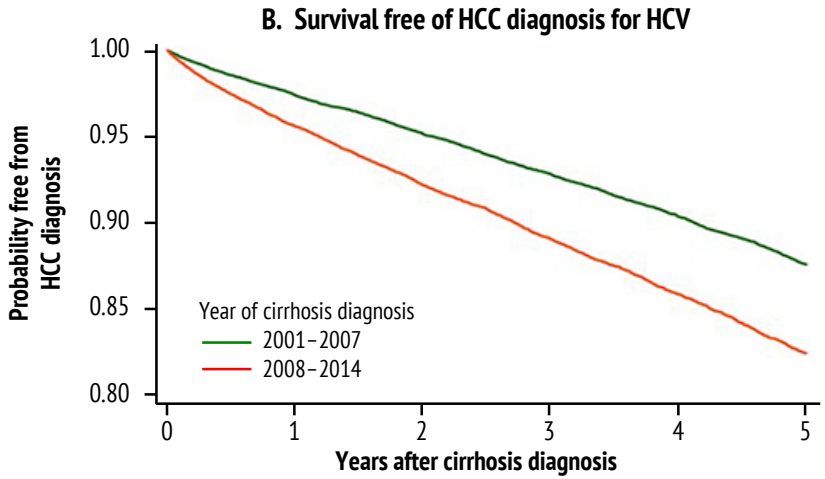
- Mean follow-up of 4.3 years
- 10,042 new HCC cases
- Patients with HCV had > 3 times higher incidence of HCC; this association that after adjusting for baseline characteristics
  - HCV: 3.3/100 py
  - ALD: 0.86/100 py
  - NAFLD: 0.90/100 py
  - Other: 1.0/100 py
- HCC incidence was 1.6 times higher in patients with cirrhosis diagnosed in 2008-2014 (2.47/100 py) than in 2001-2007 (1.55/100 py)
- Independent predictors of HCC among all cirrhosis etiologies
  - Age
  - Male sex
  - Hispanic ethnicity
  - High serum AFP
  - Alkaline phosphatase and AST/ALT ratio
  - Low serum albumin and platelet count
- Diabetes was associated with HCC in ALD-cirrhosis and NAFLD-cirrhosis
- BMI was associated with HCC in ALD-cirrhosis

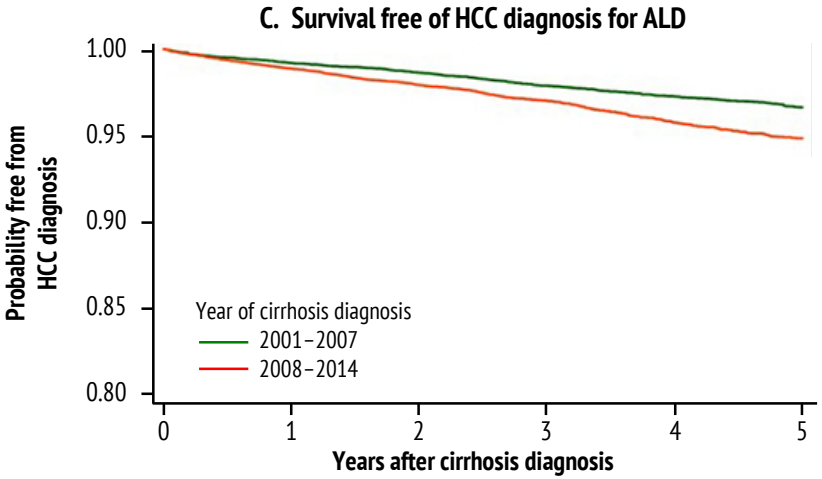
AFP, alpha-fetoprotein; ALD, alcoholic liver disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body-mass index; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; NAFLD, non-alcoholic fatty liver disease; py, patient years

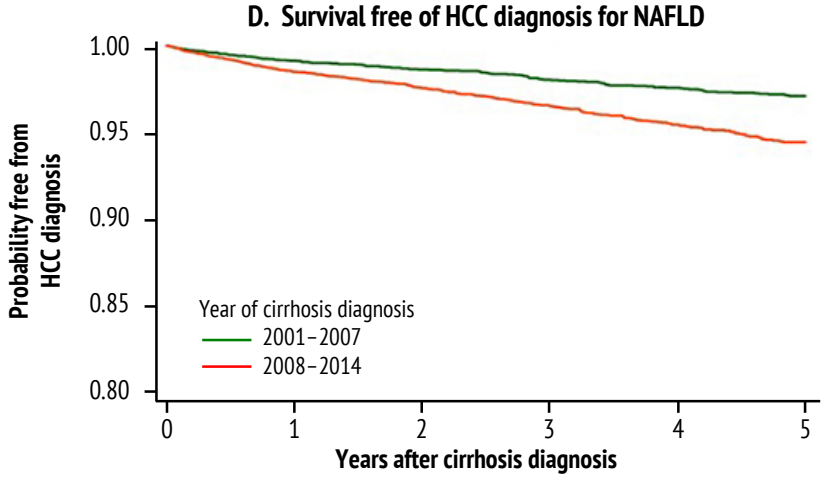
Ionnou G, et al. AASLD 2018. Abstract 274

RESULTS









ALD, alcoholic liver disease; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; NAFLD, non-alcoholic fatty liver disease

Ionnou G, et al. AASLD 2018. Abstract 274

CONCLUSIONS

- HCC risk is 3 times greater in cirrhotic patients with HCV than ALD or NAFLD
  - This strongly suggests that the hepatitis C virus itself may have a direct carcinogenic effect
- HCC risk continues to increase over time in analyses extending to 2017 in cirrhosis of all etiologies
  - There was a remarkable 1.6-fold increase in HCC incidence in the 7-year interval between the two cohorts
- Multiple readily available risk factors for HCC were identified that were influenced by cirrhosis etiology
  - These could be used to develop HCC risk estimation models

ALD, alcoholic liver disease; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; NAFLD, non-alcoholic fatty liver disease

Ionnou G, et al. AASLD 2018. Abstract 274

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