NASH Core Curriculum:
Risk Factors and Prognostic Indicators

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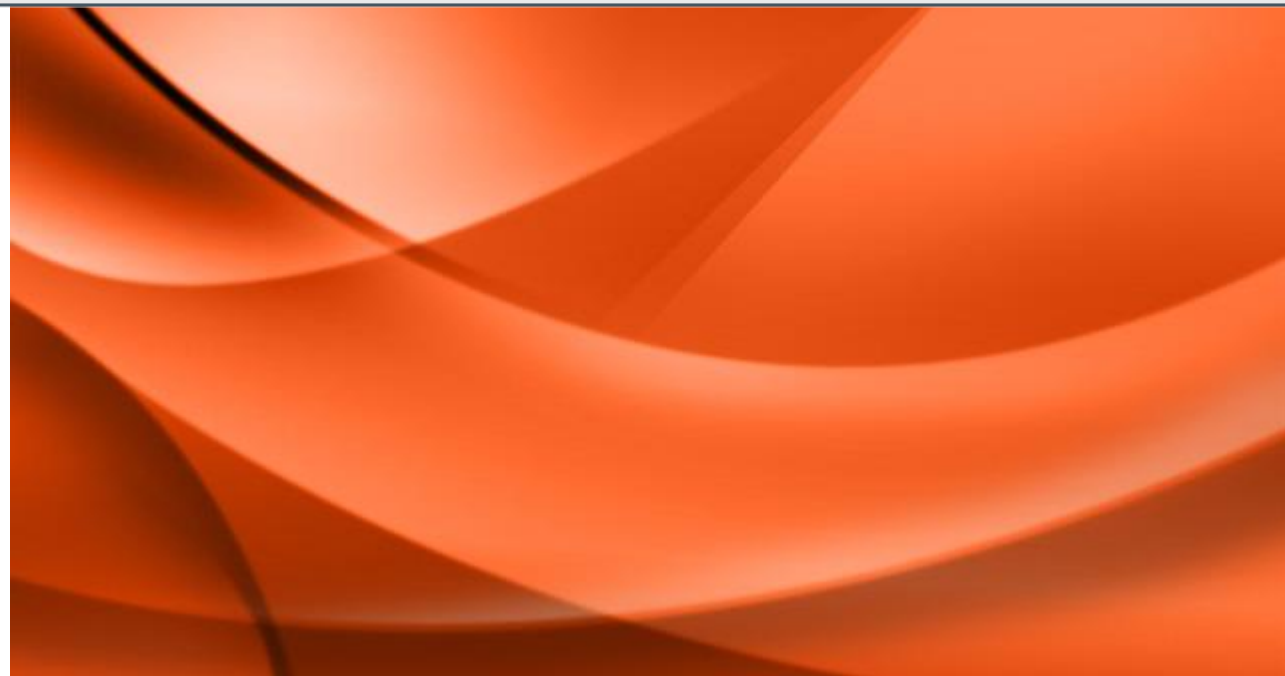

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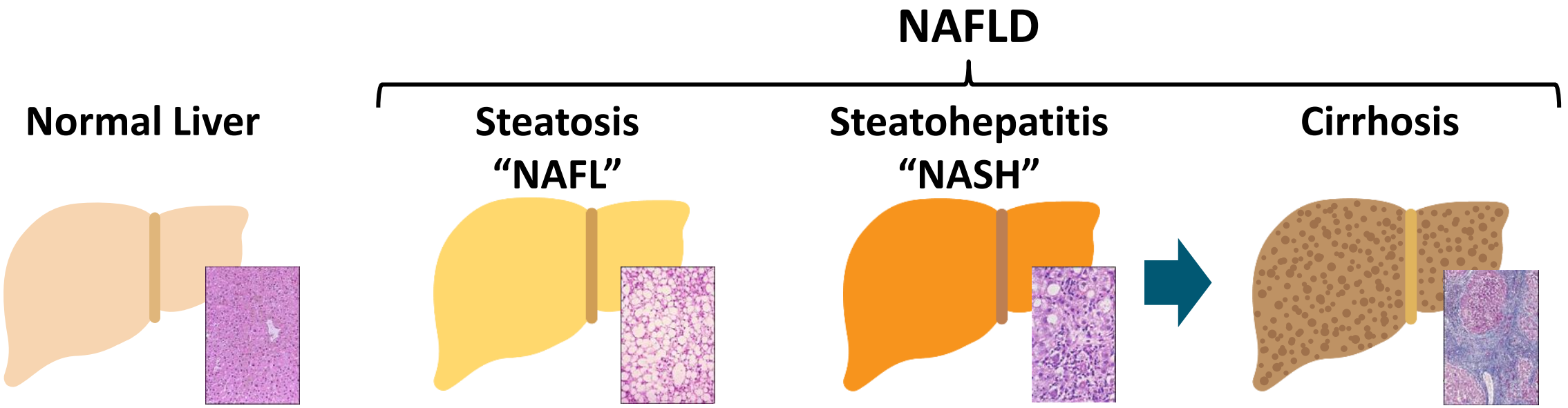
Agenda

- How Prevalent Are NASH and NASH with Advanced Hepatic Fibrosis?
- How Quickly Does NASH Progress?
- Who Is at Risk for Progression to Advanced Fibrosis?
- Who Should Be Evaluated?

How Prevalent Are NASH and NASH with Advanced Hepatic Fibrosis?

Worldwide Prevalence of NAFLD and NASH



Worldwide prevalence:	25%[1]	3% to 5%[1]	1% to 2% at risk*

*Based on analysis of NHANES data estimating 1.74% prevalence of NASH with advanced fibrosis[2]

1. Younossi. J Hepatol. 2019;70:351. 2. Kabbany. Am J Hepatol. 2017;112:581.

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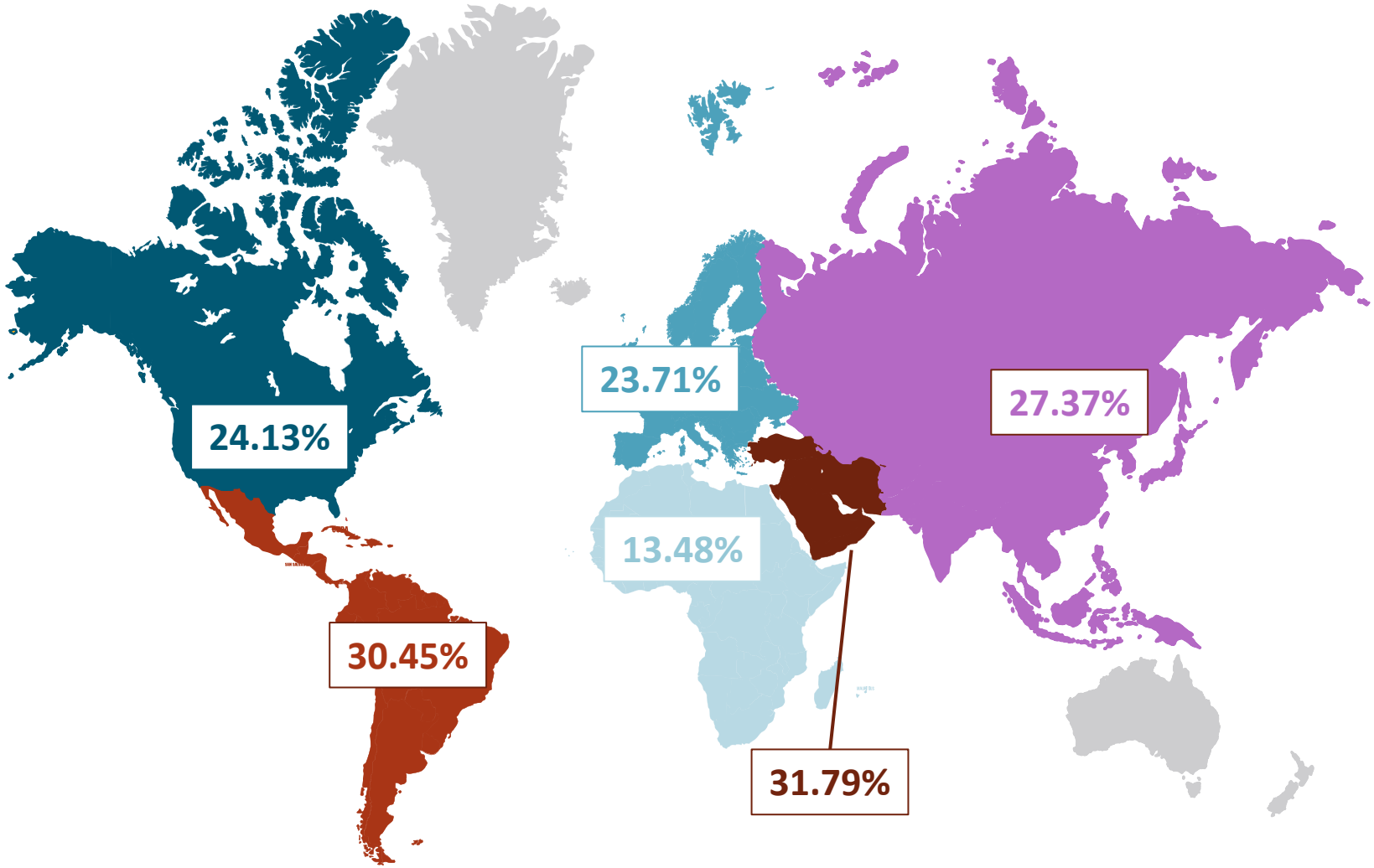
Prevalence of NAFLD



Younossi. Hepatology. 2016;64:73

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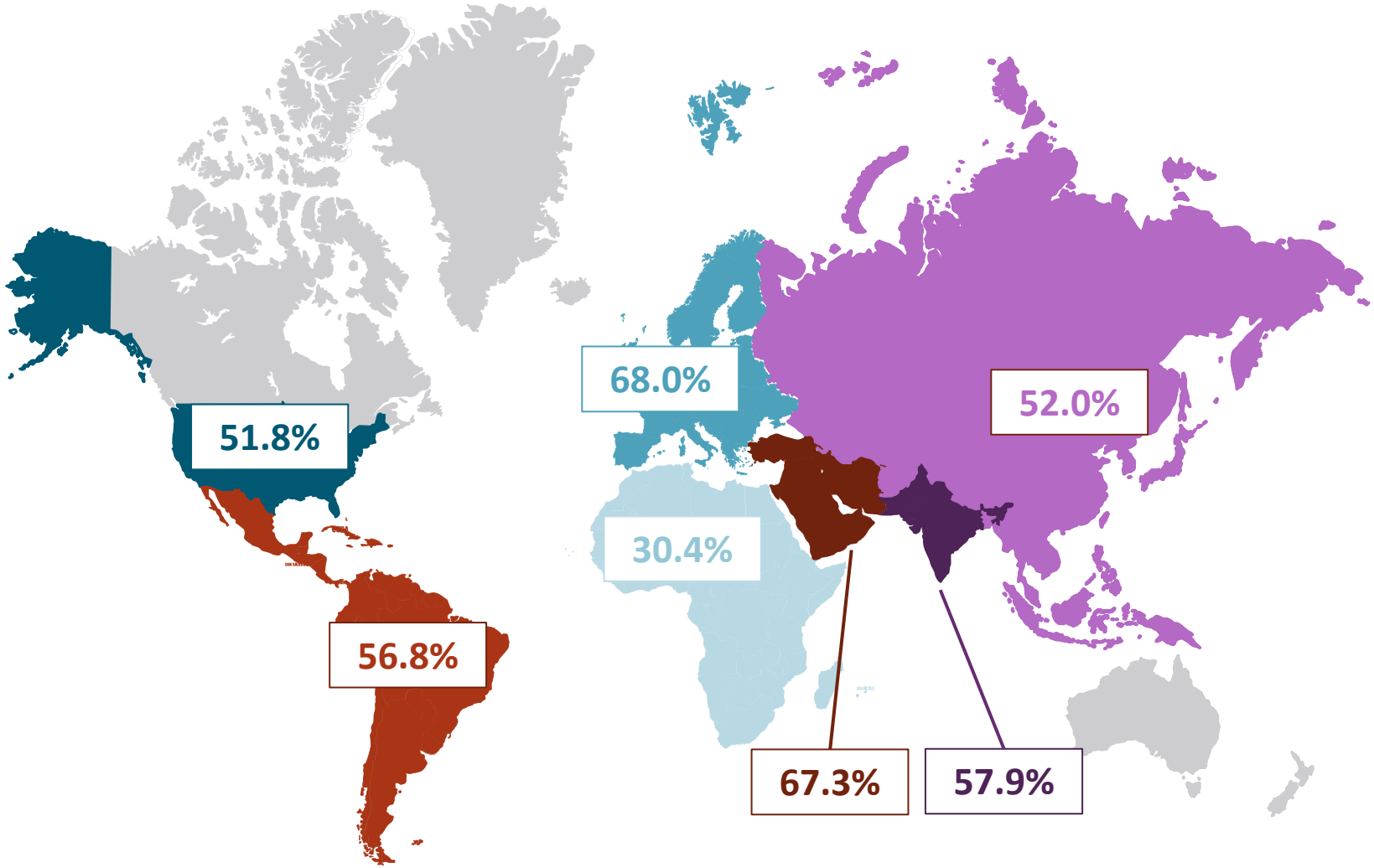
Prevalence of NAFLD in T2D



Younossi. J Hepatology. 2019;71:793

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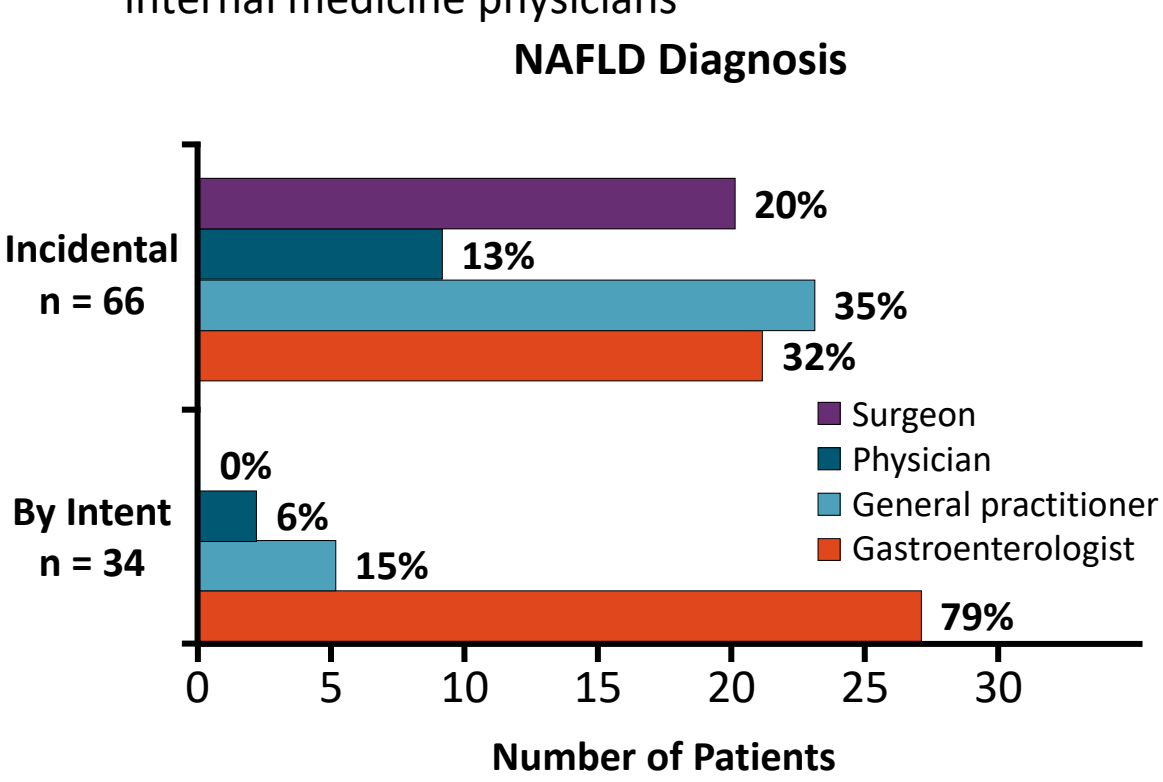
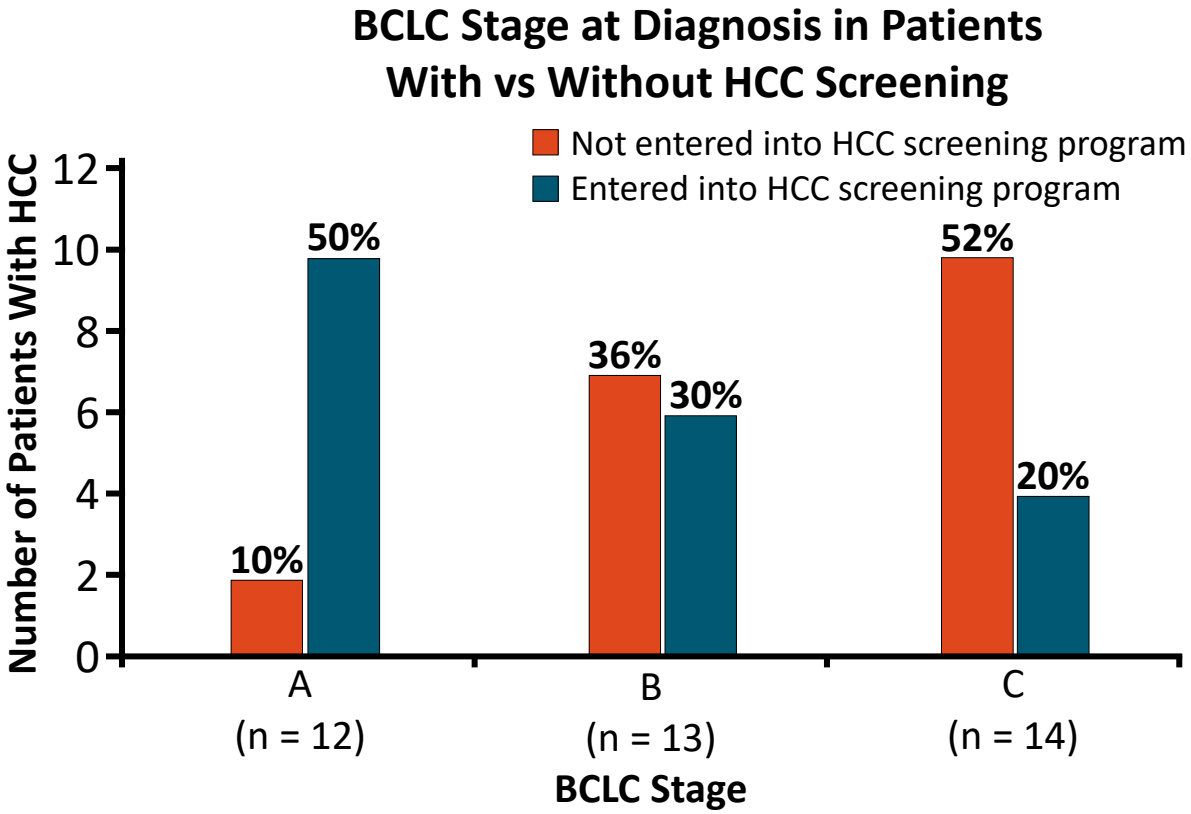
Despite Prevalence, NAFLD Is Rarely Examined, Referred

- Review of N = 100 Australian patients with cirrhosis from a prospectively collected NAFLD database
- NAFLD diagnosis more likely to be made **incidentally** by general practitioners, surgeons, internal medicine physicians



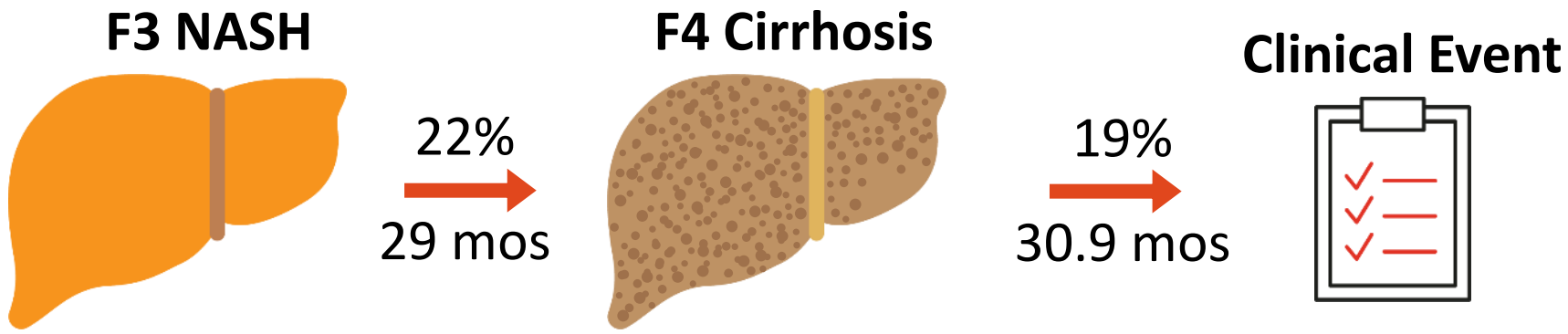
- Patients not put into an HCC screening more likely to have stage C cancer at time of HCC diagnosis



Bertot. Hepatol Commun. 2017;1:53.

How Quickly Does NASH Progress?

NASH Advanced Hepatic Fibrosis May Quickly Progress to Cirrhosis



- In n = 217 NASH patients with F3, after median 29 mos, **22% had cirrhosis**
- In n = 258 NASH patients with F4, after median 30.9 mos, **19% had a clinical event**
  - Death, ascites, hepatic encephalopathy, esophageal variceal bleed, new varices, ≥ 2-pt increase in Child-Pugh score and or MELD ≥ 15

Sanyal. Hepatology. 2019;70:1913.

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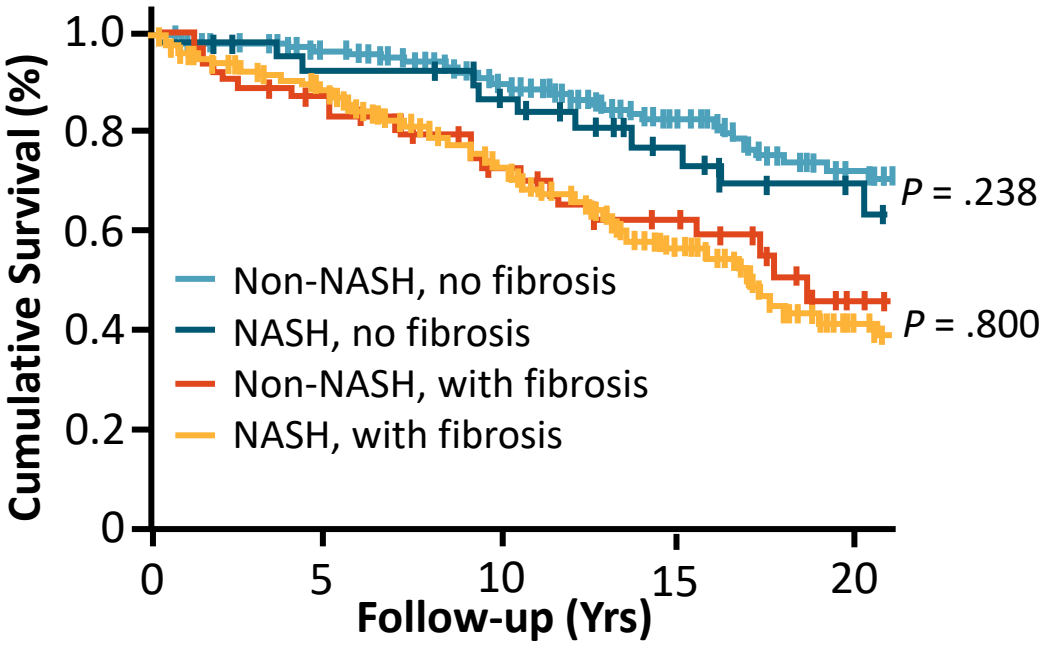
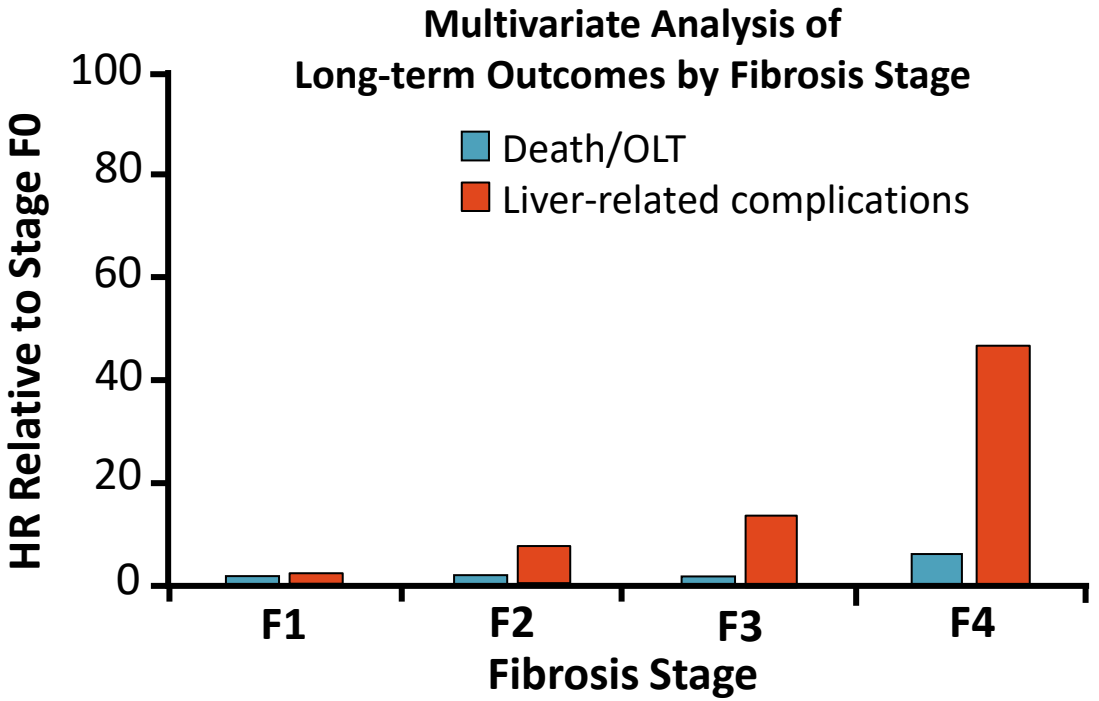
PRELHIN Study: Liver Fibrosis Associated With Long-term Outcomes in Patients With NAFLD

- Retrospective analysis in patients with NAFLD (N = 619); median follow-up: 12.6 yrs (range: 0.3-35.1)





Only fibrosis stage was associated with overall mortality, OLT, and liver-related events. Presence of NASH, NAS (or any of its components) had no independent prognostic effect.

Angulo. Gastroenterology. 2015;149:389.

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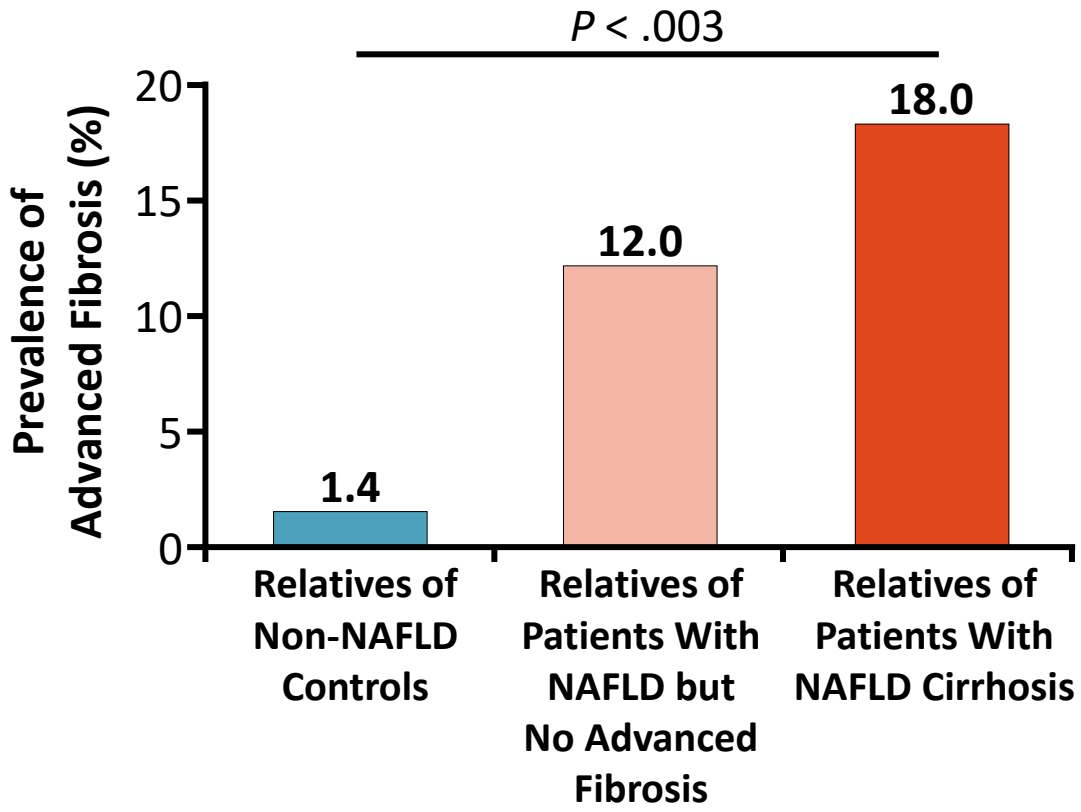
Who Is at Risk for Progression to Advanced Hepatic Fibrosis?

Who Is at Risk for NASH and Advanced Hepatic Fibrosis?

Risk Factors for NAFLD[1]
Type 2 diabetes
Obesity
Dyslipidemia
Metabolic syndrome
Polycystic ovary syndrome



- Risk of advanced fibrosis higher in first-degree relatives of patients with NAFLD cirrhosis[2]

1. Chalasani. Hepatology. 2018;67:328. 2. Caussy. J Clin Invest. 2017;127:2697.

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Case Finding and High-Risk Populations

Strong Clinical Predictors of NASH and Fibrosis

- Age > 50 yrs
- T2D
- First-degree relative with NAFLD cirrhosis

Other Risk Factors

- Sedentary lifestyle/Western diet (high fructose consumption)
- Overweight/obese
- Metabolic syndrome (3 or more features)
- Ethnicity (Hispanic/Asian)
- Dyslipidemia
- Polycystic ovary syndrome
- Endocrinopathies (panhypopituitarism)
- Obstructive sleep apnea

Angulo. NEJM. 2002;346:1221. Caussy. J Clin Invest. 2017;127:2697. Chalasani. Hepatology. 2018;67:328.

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Who Should Be Evaluated?

Case Finding and Screening

Need to identify individuals at risk of progression BEFORE bad outcomes occur

Guideline Recommendations: Who Is at Risk for NASH and Advanced Fibrosis?

AASLD[1]	EASL-EASD-EASO[2]	ADA[3]
In T2D, **suspect NAFLD and NASH** and determine patient's risk of advanced fibrosis	NASH and advanced fibrosis **screening recommended** in persons at high risk (age > 50 yrs, T2D, metabolic syndrome)	NASH and fibrosis **screening recommended** in persons with T2D or prediabetes and elevated ALT or fatty liver
Increasing number of metabolic diseases = **increasing risk of progressive liver disease**		

AASLD, EASL, and ADA guidelines call out **patients with T2D** as warranting workup

1. Chalasani. Hepatology. 2018;67:328. 2. EASL, EASD, EASO. J Hepatol. 2016;64:1388. 3. ADA. Diabetes Care. 2019;42:S34.

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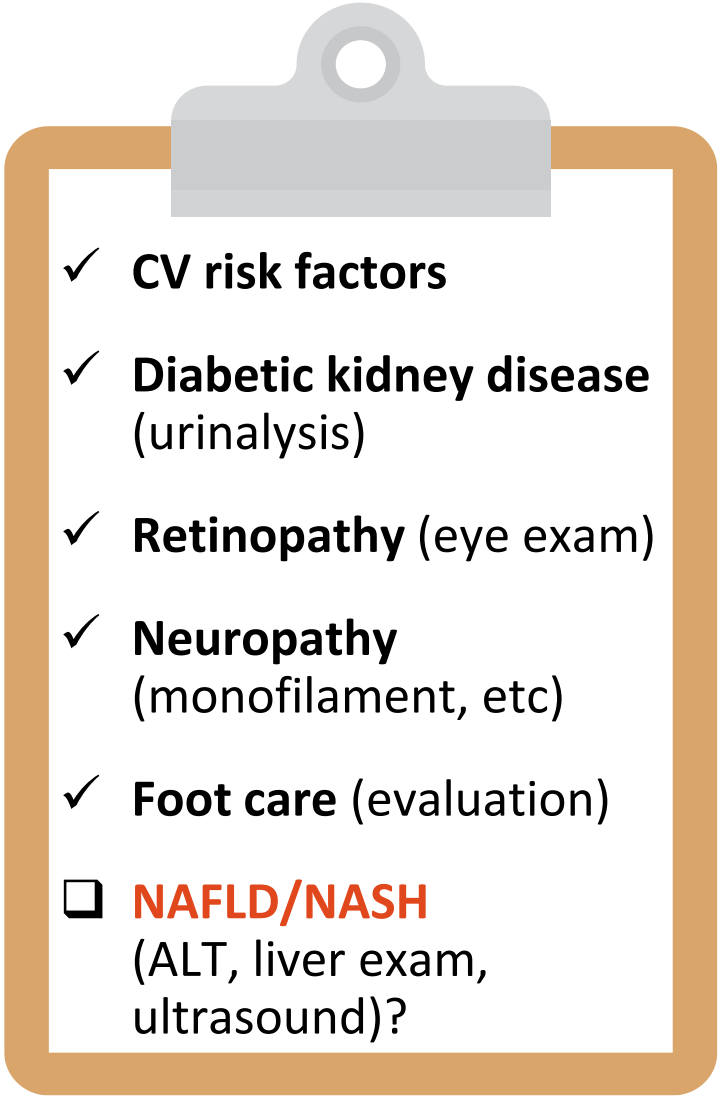
Should NASH be Part of Standard Screening for Everyone With T2D?



Summary

- NAFLD is **highly prevalent** with variable rates of progression to NASH and advanced hepatic fibrosis
- Crucial to identify those with **NASH advanced hepatic fibrosis** because it can quickly progress to cirrhosis and HCC, liver transplant, mortality
- Patients with **T2D** warrant evaluation
  - Other risk factors include obesity, metabolic syndrome, first-degree relative with NASH cirrhosis
- Non-invasive prognostic biomarkers may facilitate risk-stratification

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