



**NON-ALCOHOLIC  
FATTY LIVER DISEASE  
(NAFLD)**

**&**

**NON-ALCOHOLIC  
STEATOHEPATITIS  
(NASH)**

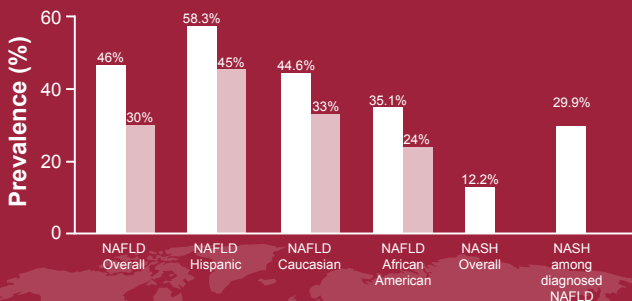
**ADDRESSING A  
GROWING SILENT  
EPIDEMIC**

# PREVALENCE OF NAFLD/NASH

## USA Prevalence in Middle Age Patients

■ San Antonio, Texas (Williams *et al.*, Gastroenterology 2011; 140:124-31)

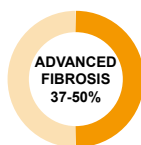
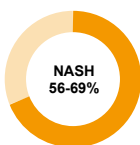
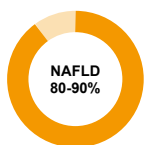
■ Dallas Heart Study Prevalence Numbers (Browning *et al.*, Hepatology 2004;40:1387-95)



## Worldwide prevalence of NAFLD: 20-30%

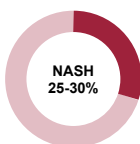
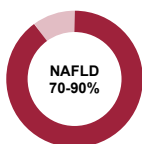
- 13-44% in Middle Eastern countries
- Approx. 20% in Asian countries
- Approx. 30% in European countries
- NASH worldwide prevalence unknown (estimate from U.S. study: 6-8%)

## NAFLD/NASH PREVALENCE AMONG PATIENTS WITH DIABETES



## NAFLD/NASH PREVALENCE AMONG OBESE PATIENTS

Prevalence among bariatric surgery patients



# NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

---

ISOLATED  
STEATOSIS

NON-NASH  
NAFLD

NASH WITH  
MILD FIBROSIS

NASH WITH  
ADVANCED FIBROSIS

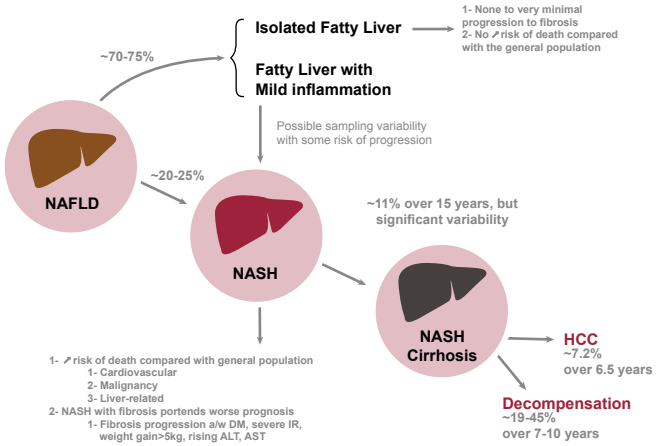
CIRRHOSIS

HEPATOCELLULAR  
CARCINOMA



NAFLD is an umbrella term that encompasses the spectrum of fatty liver disease, from isolated steatosis to cirrhosis and liver cancer with underlying CVD risk.

# NATURAL HISTORY OF NAFLD

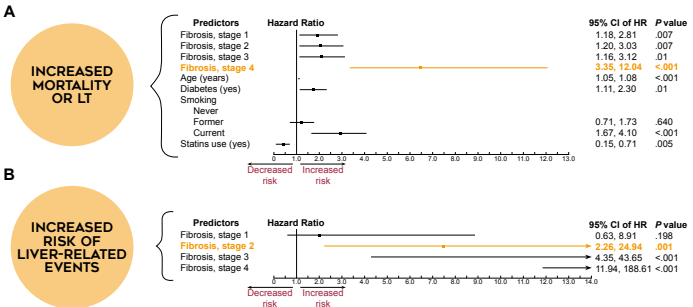


Modified from Torres DM et al. Features, diagnosis, and treatment of NAFLD. Clin Gastro Hepatol 2012;10:837-858

- Progression of isolated steatosis to cirrhosis is very rare
- Fatty liver with inflammation but not NASH may progress but at a slower rate than NASH
- NASH with fibrosis is at greater risk for disease progression
- Patients with NASH and metabolic syndrome are also an enriched population for disease progression
- NAFLD/NASH is now the second leading cause for liver transplantation in the U.S.

## HIERARCHY OF HISTOLOGIC FEATURES

Associated with disease progression and mortality



## C MAJOR PROGNOSIS FACTORS



## NAFLD & MORTALITY: TOP 3 CAUSES

1

CARDIOVASCULAR DISEASE (CVD)

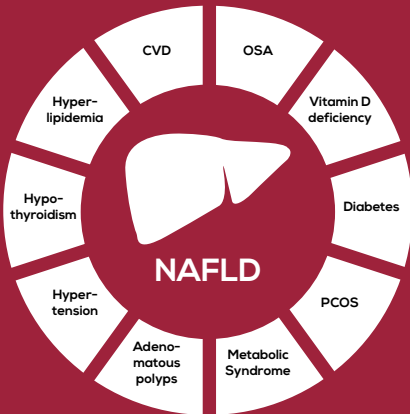
2

ALL CAUSE MALIGNANCY

3

LIVER-RELATED DEATH

## CONDITIONS ASSOCIATED WITH NAFLD



Modified from Torres DM et al. Features, diagnosis, and treatment of NAFLD. Clin Gastro Hepatol 2012; 32:30-38

## DIAGNOSIS

- AASLD practice guidelines require liver biopsy to diagnose NASH
- Liver enzymes can be normal in up to 60% of patients with NASH
- No non-invasive test with sufficient sensitivity or specificity to rule in or rule out NASH

## RED FLAGS INCREASING PROBABILITY FOR NASH

*When deciding who to biopsy*

- Age
- Gender
- Hispanic
- Hypertension
- Obesity
- ALT and AST level
- AST/ALT ratio
- Insulin level
- PNPLA3

**No lab test or imaging study will be able to predict with 100% accuracy**

**All variables have been shown to predict NASH**

## TREATMENT

---

- Diet, lifestyle modification and exercise remain the top priority. Ultimate goal is to achieve 10% weight loss as this has been shown to improve all histopathologic parameters of NASH.
- No approved therapies for the treatment of NASH.

Diet and exercise are not always satisfactory options, and there is a lack of treatment. To address this unmet need, enrollment in one of the clinical trials underway can be considered.

## NASH: KEY CONSIDERATIONS

---

- NASH is the liver manifestation of metabolic diseases. NASH patients are often obese, have type 2 diabetes, and cardiovascular disease.
- NASH is the underlying cause of cirrhosis and its complications: treating NASH is the appropriate approach to prevent progression to cirrhosis.
- Liver biopsy is required to diagnose NASH.
- How to reverse NASH: stop the disease activity i.e. necroinflammation (ballooning + inflammation) that is the driver leading to liver fibrosis and progressive liver fibrosis.
- NASH therapies should be efficacious against both the underlying liver disease and comorbid conditions associated with NAFLD such as insulin resistance, diabetes, and hyperlipidemia.
- Because NASH is a chronic and silent disease, therapies should be safe and well tolerated.



- 🔍 [www.the-nash-education-program.com](http://www.the-nash-education-program.com)
- ✉ [the-nash-education-program@genfit.com](mailto:the-nash-education-program@genfit.com)
- 🐦 NASH\_Education
- 📺 The NASH Education Program