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Education

Non Alcoholic Fatty Liver Disease (NAFLD)

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- Dr. Cohen has disclosed that he serves on an advisory board for Pfizer.
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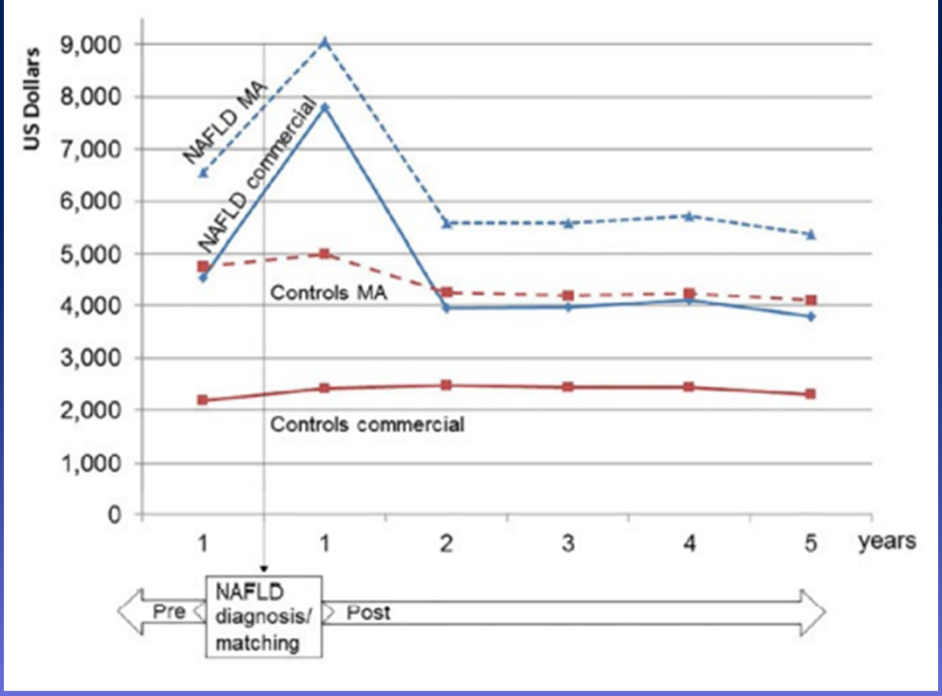
NAFLD: A Silent Epidemic

- Most prevalent liver disease in human history- 2 billion globally, 30% US population
- Established risk factor for the leading causes of death- Cancer, CVD and DMII
- Associated with increased health care costs

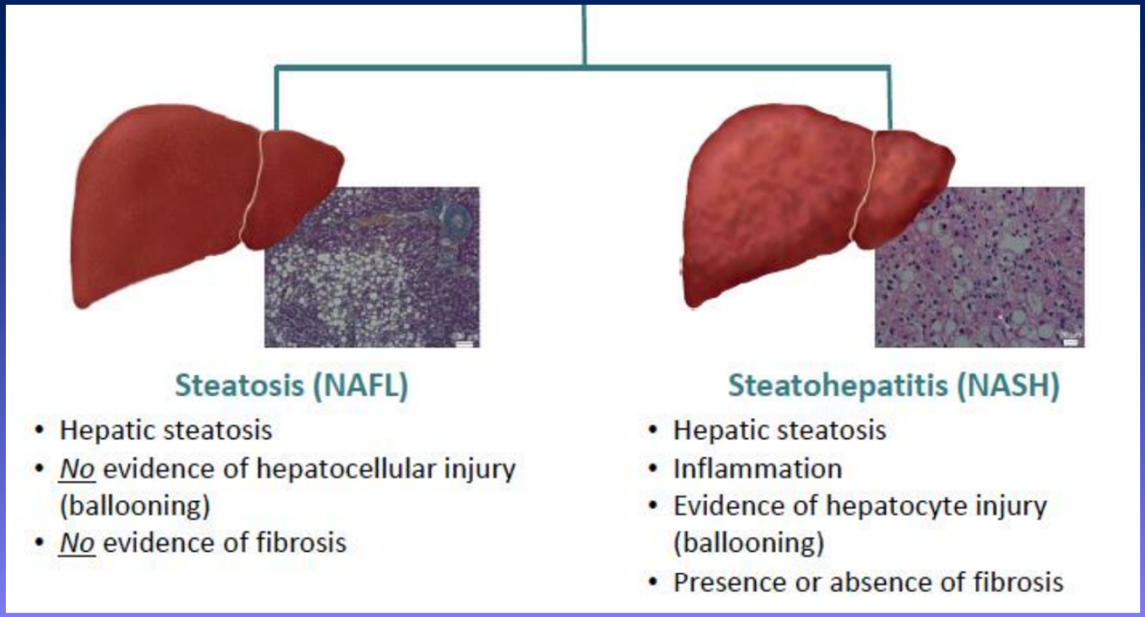


Annual total health care costs of NAFLD patients compared with matched controls in reference to the date of index (first) NAFLD diagnosis – Allen et al, Hepatology 2018; 68:2230-2238

Defining Nonalcoholic Fatty Liver Disease

- Requires evidence of hepatic steatosis- imaging or histology
- Absence of secondary etiologies of hepatic fat accumulation- such as significant alcohol consumption, long-term use of steatogenic medications, hepatitis C virus infection, monogenic hereditary disorders, severe malnutrition, and Wilsons

NAFLD = MAFLD (Metabolic associated fatty liver disease)



Chalasani N, et al. Hepatology 2018;67:328-357
Sanyal AJ, et al. Hepatology 2011;54:344-353

Alcohol is an important confounding factor

	AASLD (2018)	EASL (2016)	Asia-Pacific (2017)
Definition of significant alcohol consumption	• Men: 21 standard drinks/week or 294 g/week • Women: 14 standard drinks/week or 196 g/week	• Men: 30 g/day • Women: 20 g/day	• Men: 2 standard drinks/day or 140 g/week • Women: 1 standard drink/day or 70 g/week

- Arbitrary thresholds based on levels above which risk of cirrhosis is higher
- Moderate alcohol consumption associated with decreased improvement in steatosis or resolution of NASH*

*Ajmer V et al, Clinical Gastroenterol Hep 2018; 16:1511-1520

Chalasani N, et al. Hepatology 2018;67:328-357

European Association for the Study of the Liver. *J Hepatol* 2016;**64**:1388-1402

Wong VW, et al. *J Gastroenterol Hepatol* 2018;**33**:70-85

Pathogenesis of NAFLD

- Excessive importation of FFA from adipose tissue
- Diminished hepatic export of FFA

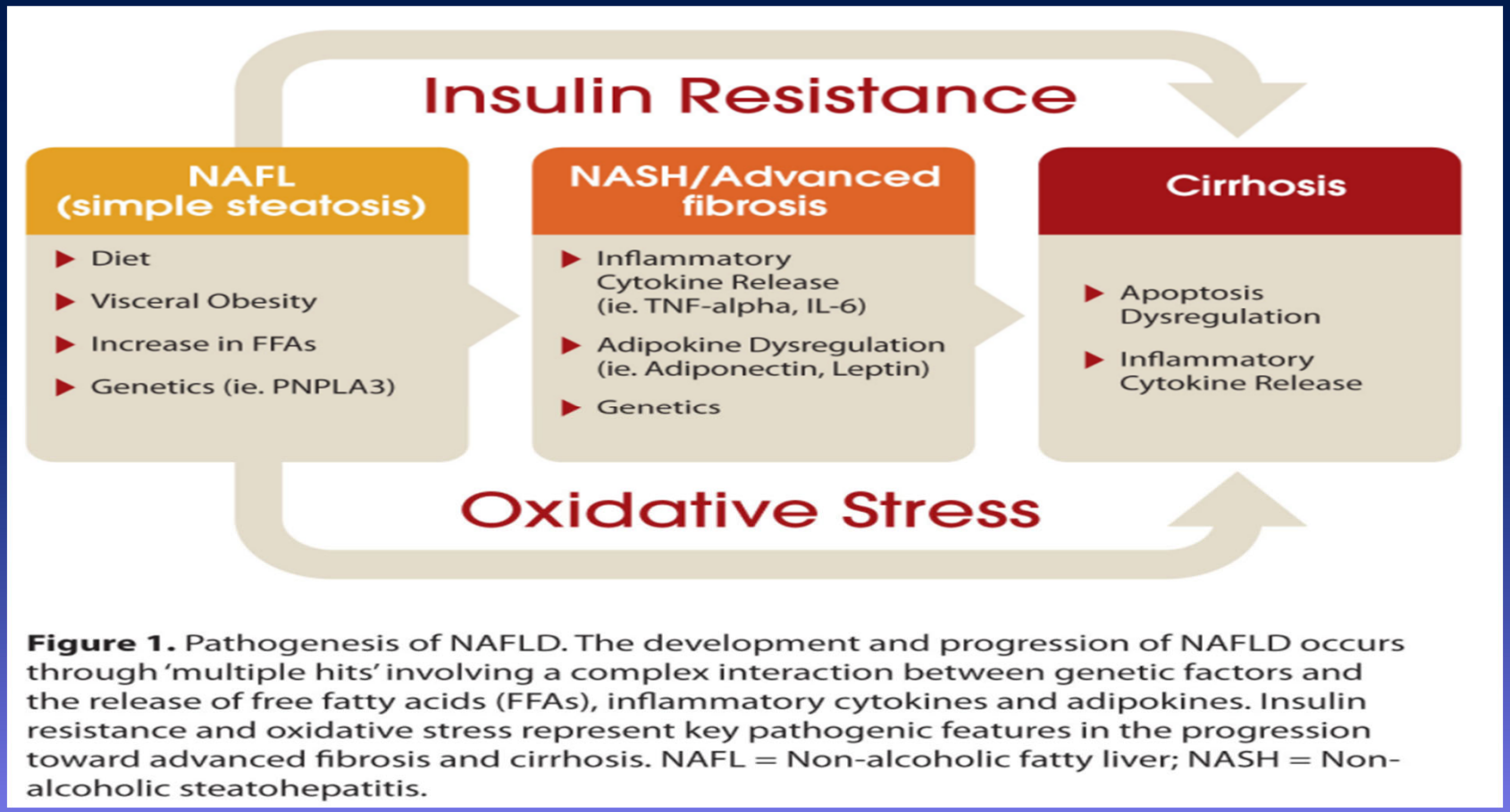
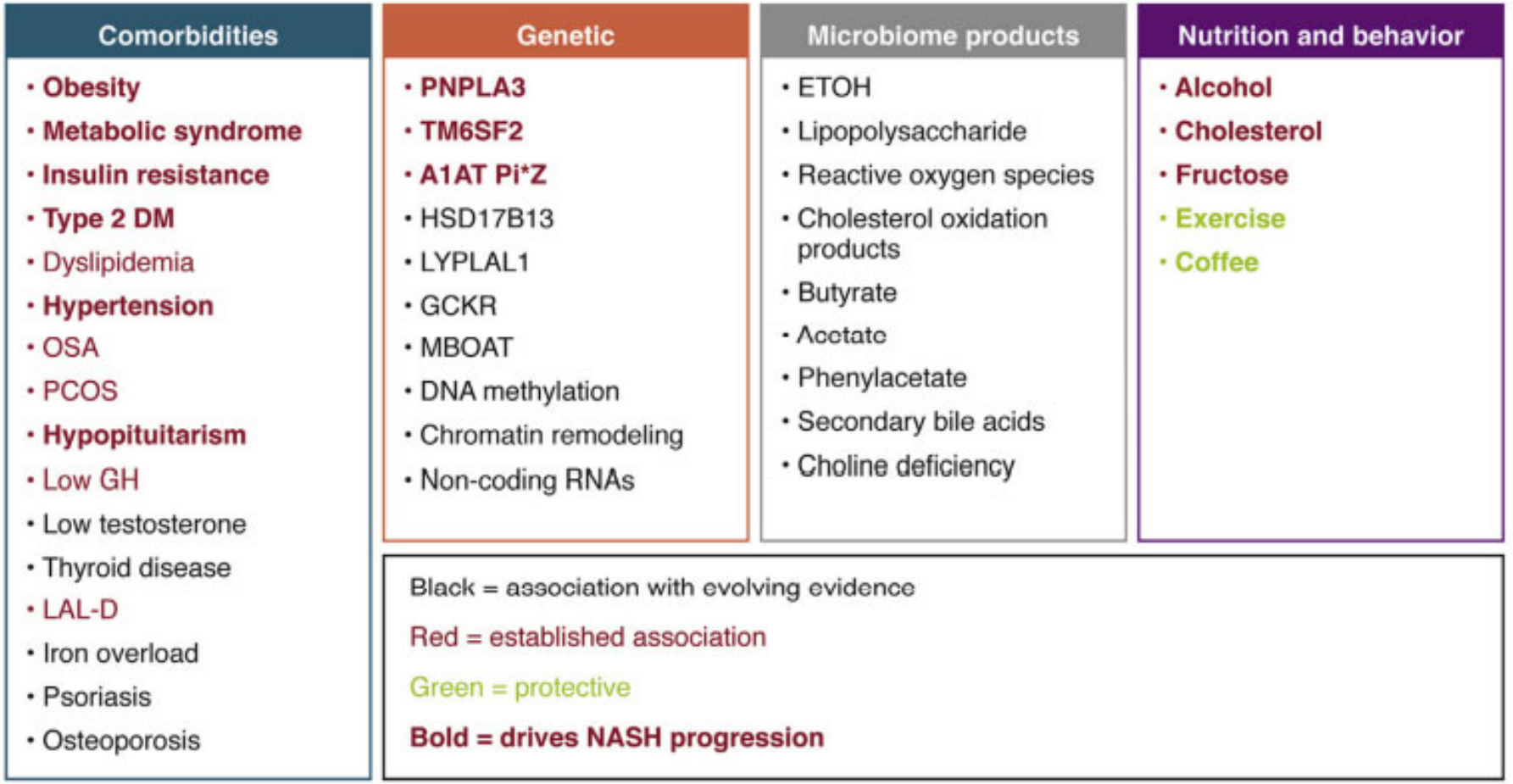


Figure 1. Pathogenesis of NAFLD. The development and progression of NAFLD occurs through 'multiple hits' involving a complex interaction between genetic factors and the release of free fatty acids (FFAs), inflammatory cytokines and adipokines. Insulin resistance and oxidative stress represent key pathogenic features in the progression toward advanced fibrosis and cirrhosis. NAFL = Non-alcoholic fatty liver; NASH = Non-alcoholic steatohepatitis.

Hasham and Talal; Healio May 2016

Modifiers of NAFLD

- Factors influencing the course of NAFLD can be broadly divided into comorbid illness, genetic factors, microbial products, and nutritional/behavioral factors



Cotter and Rinella; Gastroenterology 2020;158: 1851-1864

Recommendations for screening for NAFLD

	AASLD (2018)	EASL (2016)	Asia-Pacific (2017)
Screening for NAFLD	Systematic screening of the general population not recommended		
	• No screening recommended due to lack of evidence of cost-effectiveness to support screening even in high-risk groups • "Vigilance" in high-risk groups	• Recommend screening in patients with obesity, T2DM, MetS (A2) • Recommend screening in patients with persistently abnormal liver enzymes (A1)	• Consider screening in patients with obesity or T2DM (B2)

- Lean NAFLD is prevalent in Asia, where almost a quarter of patients with NAFLD are not obese
- All guidelines agree that noninvasive tools should be used to stratify patients as low or high risk for advanced fibrosis

Chalasani N, et al. Hepatology 2018;67:328-357
European Association for the Study of the Liver. *J Hepatol* 2016;**64**:1388-1402
Wong VW, et al. *J Gastroenterol Hepatol* 2018;**33**:70-85

Common Clinical Scenarios

- Incidental Steatosis
- Persistently elevated liver enzymes

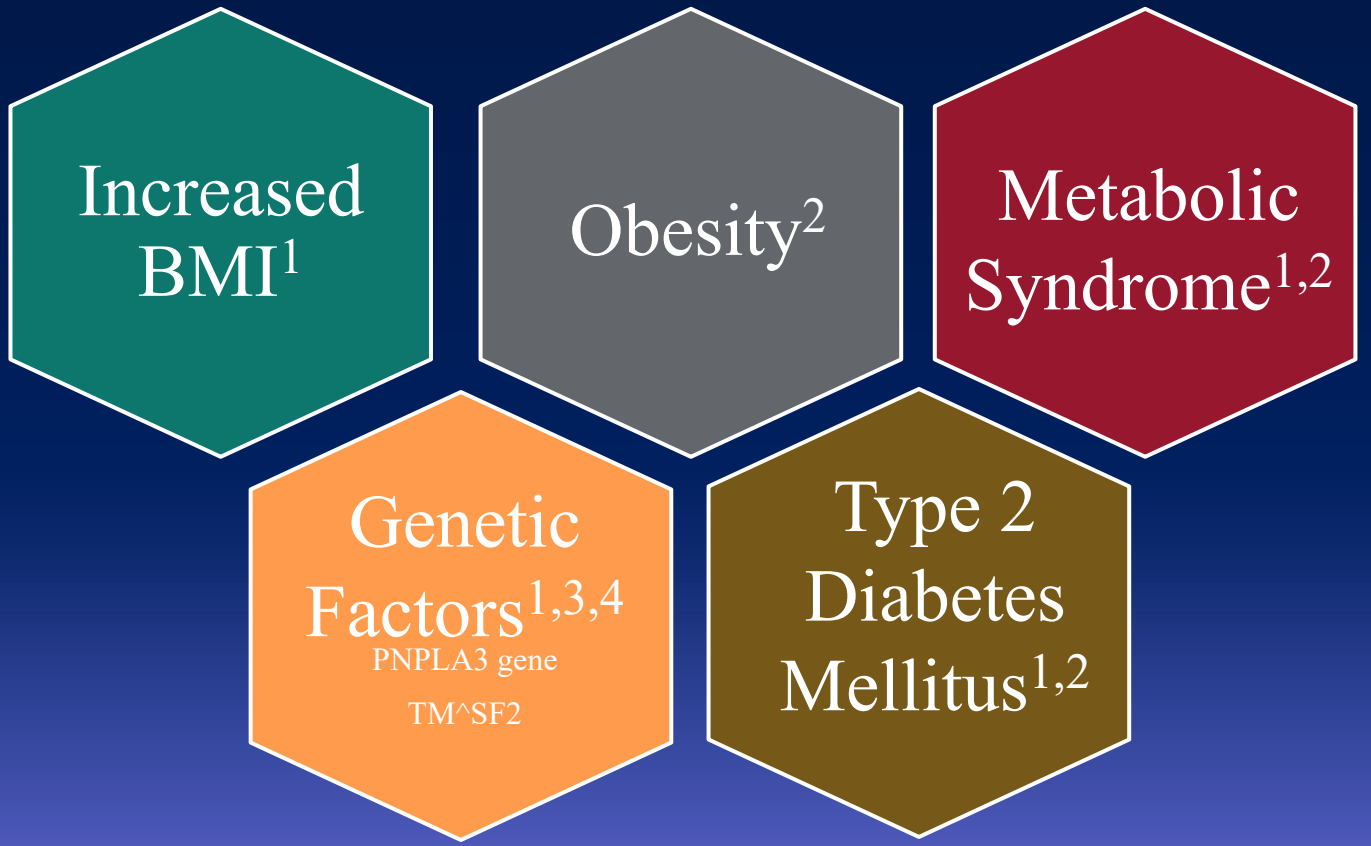
PCPs can consider fatty liver in at-risk patients with three questions:

1. Does the patient have risk factors for NAFLD?
2. If the answer is “yes”, does the patient have evidence of NAFLD?
3. If the answer is “yes”, does the patient have evidence of significant fibrosis by non-invasive tests?

Dinani A, et al. An algorithm for the management of non-alcoholic fatty liver disease in primary care. *Gastroenterol Hepatol Open Access*. 2021;12(4):114–122

NAFLD Risk Factors

- SEARCH FOR RISK FACTORS – Patients at higher risk of disease progression



- Increased waist circumference
- Insulin Resistance
- Hypertension
- Hypertriglyceridemia
- Low HDL cholesterol

BMI = body mass index; HDL = high-density lipoprotein; NASH = nonalcoholic steatohepatitis; *PNPLA3* = patatin-like phospholipase domain–containing protein 3; *TM6SF2* = transmembrane 6 superfamily member 2.

1. Marengo A, et al. *Clin Liver Dis.* 2016;20(2):313–324; 2. Chalasani N, et al. *Hepatology*. 2018;67(1):328–357; 3. Diehl AM, et al. *N Engl J Med.* 2017;377:2063–2072; 4. Anstee QM, et al. *Semin Liver Dis.* 2015;35:270–290.

When NAFLD is suspected

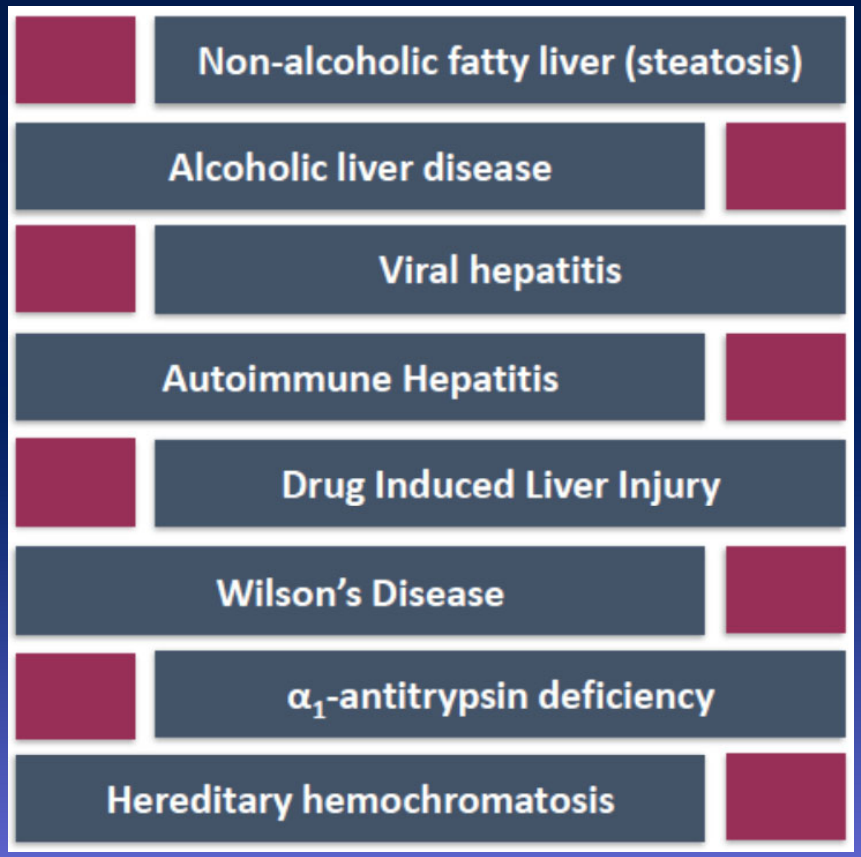
Recommendation 1: Identify patients at risk for NAFLD based on the presence of ≥1 of the following:

- Obesity, defined as body mass index (BMI) ≥30kg/m^2
  - Asian patients: ≥25kg/m^2
- Increased waist circumference (≥35 inches for women, ≥40 inches for men)
  - Asian patients: >32 inches for women, >35 inches in men
- Hyperglycemia
  - T2DM or glycosylated hemoglobin ≥5.7% or fasting glucose ≥100mg/dL
- Fatty liver on imaging

Dinani A, et al. An algorithm for the management of non-alcoholic fatty liver disease in primary care. *Gastroenterol Hepatol Open Access*. 2021;12(4):114–122

Consider other diseases that cause liver steatosis

Recommendation 2: All patients identified as at-risk for NAFLD should be investigated for other causes of chronic liver diseases and metabolic comorbidities



Dinani A, et al. Gastroenterol Hepatol Open Access. 2021;12(4):114–122
Chalasani N, et al. Hepatology 2018;67:328-357

- Typical lab panel
  - Hemogram
  - CMP
  - HBV, HCV
  - TSH
  - Celiac screen
  - Iron panel
  - Ferritin
  - Hemoglobin A1c
  - Lipid panel

  - A1AT quantification
  - Ceruloplasmin
  - ANA, ASMA, AMA,SPEP

Confusing lab findings to be aware of in NAFLD

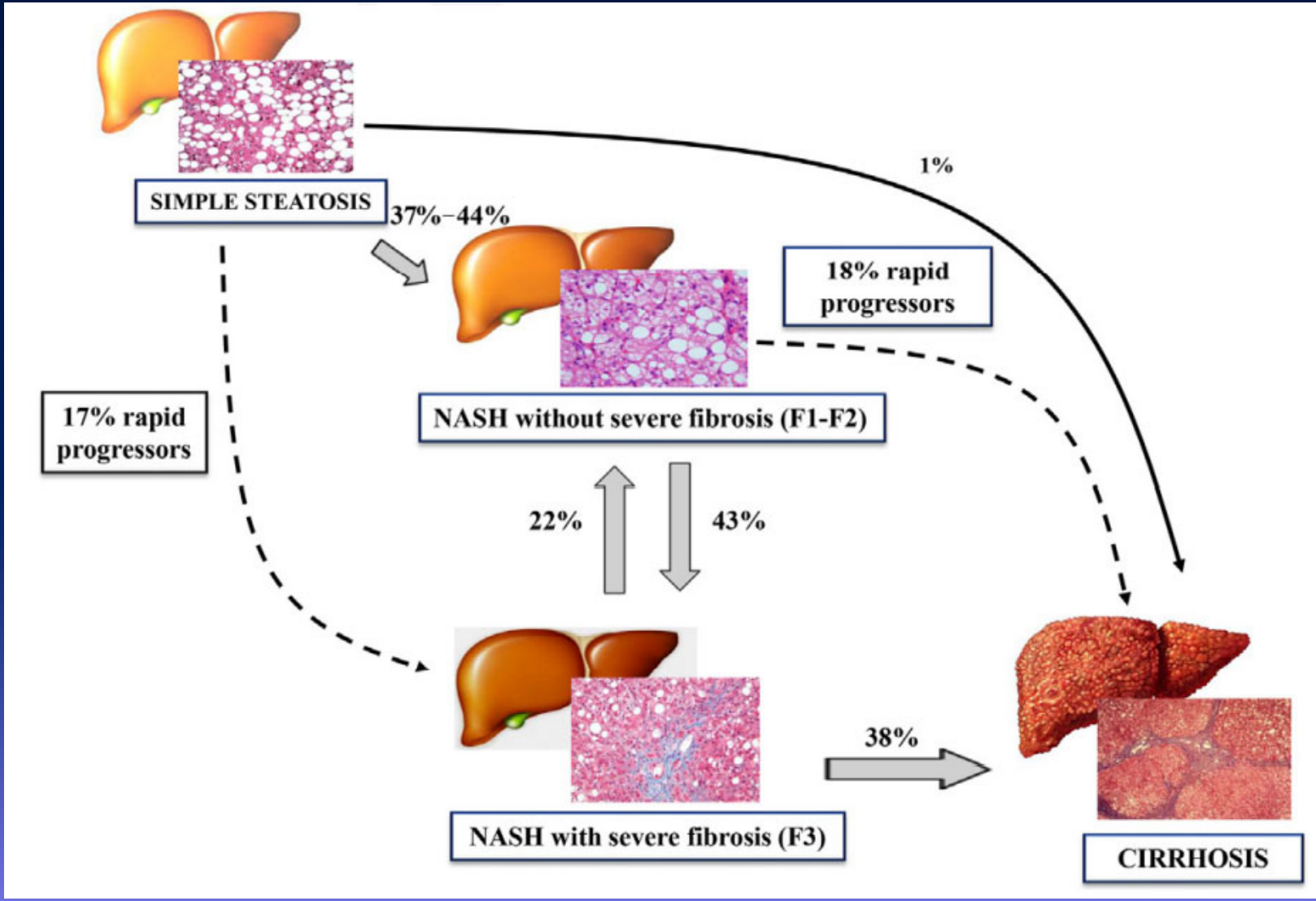
- *Serum ferritin*
  - Often mildly elevated, does not reflect iron overload
  - If ferritin and transferrin saturation are elevated
    - Exclude genetic hemochromatosis
    - Consider liver biopsy to assess hepatic iron quantitation

- *ALT can be normal in up to 50% of persons with NAFLD.*
  - elevated ALT and AST levels do not always correlate with the severity of liver damage.
  - An upper limit of normal for ALT of 35 U/L for men and 25 U/L for women is recommended to guide management decisions

- *Serum autoantibodies*
  - Frequently detected, often in low titers - epiphenomenon
  - Presence of antibodies does not impact natural history of NAFLD
  - Exclude autoimmune hepatitis if significant elevation of liver enzymes (>5x ULN) or elevated globulins

Valenti L, et al. Gastroenterology 2010;138:905-912
Vuppalanchi R, et al. Hepatol Int 2012;6:379-385
Sanyal D, et al. Indian J Endocrinol Metab. 2015;19(5):597–601.

Fibrosis: Predictor of Disease Progression and of Negative Outcomes



Marengo A, et al. Progression and Natural History of Nonalcoholic Fatty Liver Disease in Adults. Clin Liver Dis. 2016 May;20(2):313-24

Diagnosis of NASH

- Liver Biopsy is the gold standard by which NASH diagnosis is established
- Limitations:
  - Risks involved
  - Painful
  - Costs
  - Sampling errors
  - Histologic interpretation

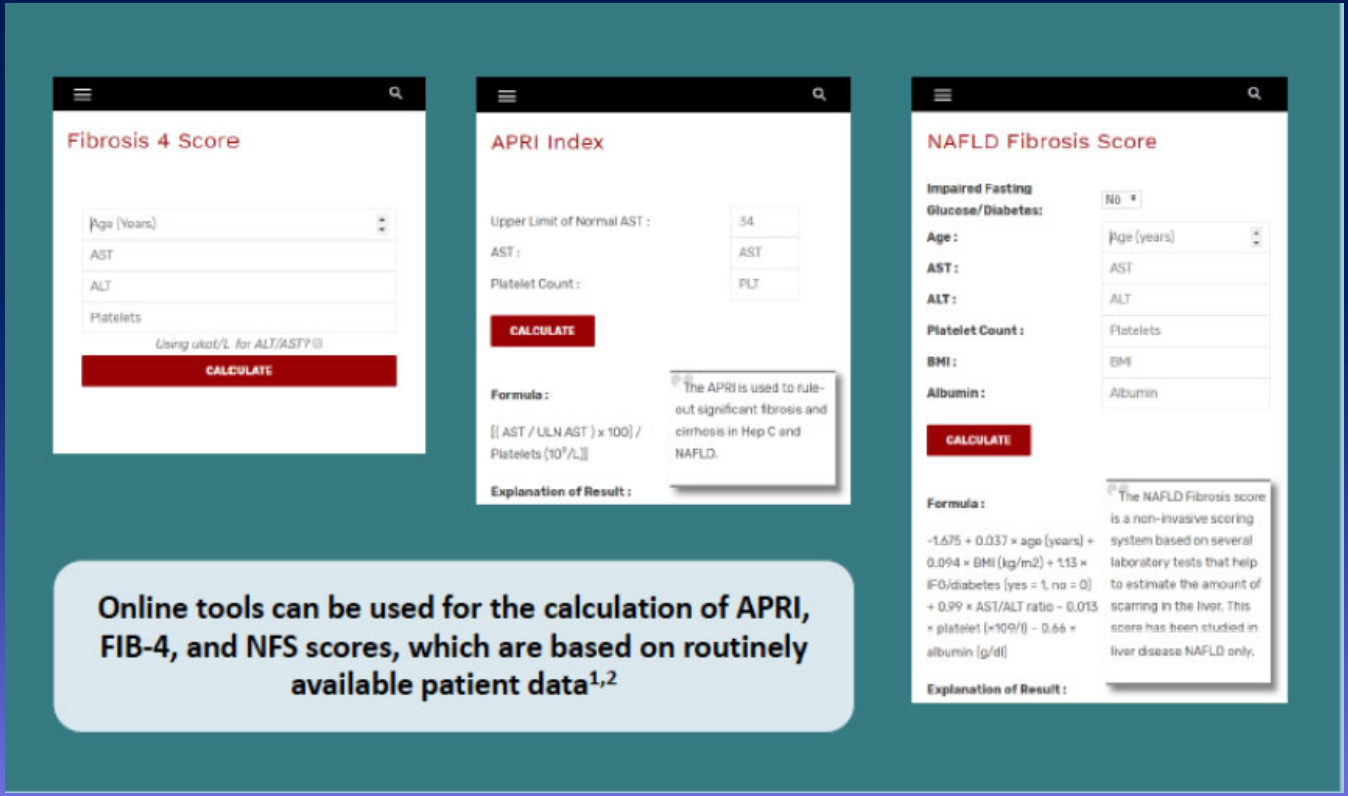
Diagnosis of NASH- Noninvasive Scores

Diagnostic Panel	N	AUROC	Cutoff Values	Se (%)	Sp (%)	PPV (%)	NPV (%)	Study Reference
BARD score	827	0.81 *0.78	2	91 72	66 64	43	96	Harrison et al.
NAFLD Fibrosis Score	733	0.88 *0.85	<-1.455 >0.676 <-1.455 >0.676	80 47 90 64	74 98 60 97	52 82	88 80	Angulo et al.
FIB4 index	541	0.80	<1.30 >2.67	74 33	71 98	43 80	90 83	Shah et al.
Fibrotest	267	0.88	0.3 0.7	95 25	71 97	31 56	99 91	Ratziu et al.
ELF panel	192	0.90	0.3576	80	90	71	94	Guha et al.

BARD score: Body mass index (BMI), AST/ALT ratio diabetes; **NAFLD Fibrosis score:** Age, hyperglycemia, BMI, platelet count, albumin, AST/ALT ratio; **FIB4 index:** age, ALT, AST, platelet count; **Fibrotest:** alpha-2 macroglobulin, haptoglobin, GGT, total bilirubin, apolipoprotein A1; **ELF panel** (Enhanced Liver Fibrosis Panel): age, hyaluronic acid, TIMP 1 (tissue inhibitor of metalloproteinase 1), PIIINP (amino-terminal propeptide of type III collagen).

Easy calculators of Fibrosis in Adults with NAFLD

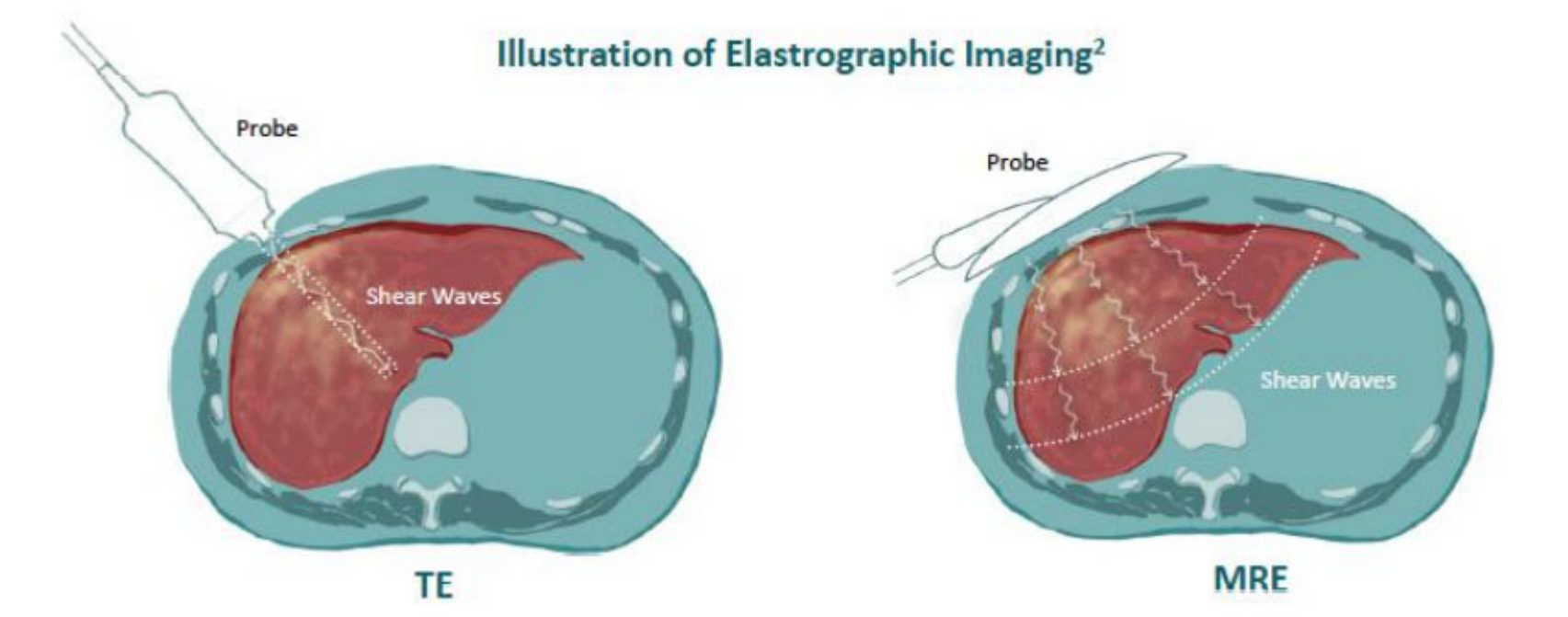
- Serologic markers – Simple:
- • FIB-4 – Fibrosis-4 Index
- • NFS – NAFLD Fibrosis Score
- • APRI index- Aspartate Aminotransferase to Platelet Ratio



1 Chalasani N, et al. Hepatology 2018;67:328-357
2 http://gihep.com/calculators/hepatology

Diagnosis of NASH- Imaging/ Elastography

- Liver stiffness steadily increases with increase in fibrosis[1]
- Non-invasive techniques can be used to measure liver stiffness (kPa) that correlates with fibrosis[2]
- Two clinically useful imaging tools for detecting advanced fibrosis are[3]
  1. Transient Elastography (TE)
  2. Magnetic Resonance Elastography (MRE)



1. Venkatesh SK, et al. *J Magn Reson Imaging*. 2013;37(3):544-555. 2. Mikolasevic I et al. *World J Gastroenterol* 2016;22(32):7236–7251; 3. Chalasani N, et al. *Hepatol*. 2018;67:328-357.

Transient Elastography

- Important to recognize its limitations

  May overestimate fibrosis when:

  - Non-fasting state
  - Flare of transaminases with hepatitis
  - Extrahepatic biliary obstruction
  - Liver congestion

Hugo Perazzo, et al, "Factors That Could Impact on Liver Fibrosis Staging by Transient Elastography", International Journal of Hepatology, 2015, 5 pages.

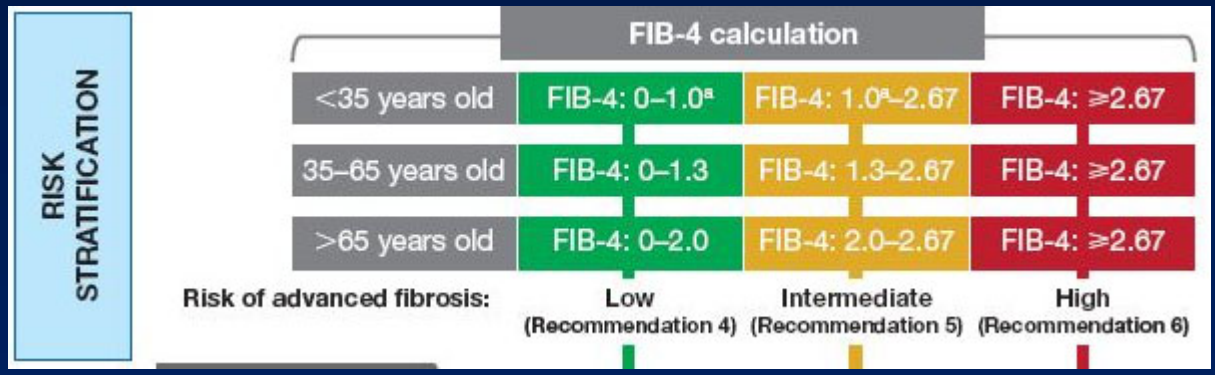
Recommendations for screening for NASH Fibrosis

	AASLD (2018)	EASL (2016)	Asia-Pacific (2017)
Fibrosis assessment	• NFS, FIB-4, and elastography • No algorithm provided for preferred sequence of testing	• NFS and FIB-4 to risk-stratify low versus medium/high risk for significant fibrosis • Hepatology referral for medium/high-risk patients for further testing with elastography and identifying those who need liver biopsy	• No specific recommendation regarding preferred tests or algorithm
	Liver biopsy remains the gold standard for differentiating NAFL from NASH and staging liver fibrosis. Proceed with liver biopsy if: (1) suspicion for NAFLD advanced fibrosis (2), or concern for coexisting or competing etiology of chronic liver disease (B2).		

Chalasani N, et al. Hepatology 2018;67:328-357
European Association for the Study of the Liver. *J Hepatol* 2016;**64**:1388-1402
Wong VW, et al. *J Gastroenterol Hepatol* 2018;**33**:70-85

Risk stratification and fibrosis assessment

- **Recommendation 3:** For each at-risk patient identified, calculate fibrosis-4 index (such as FIB-4) score to determine whether the patient has minimal (FIB-4: <1.3, F0-1), indeterminate (FIB-4: 1.3–2.67), or likely advanced fibrosis (FIB-4: >2.67, ≥F3)



- **Recommendation 4:** Patients with FIB-4 <1.3 have minimal fibrosis. These patients can be managed by their PCP
- **Recommendation 5:** Patients with FIB-4 1.3–2.67 have an indeterminate fibrosis score and should have a second non-invasive test such as Fibro Sure or ELF (serology-based tests) or liver stiffness (imaging based elastography)
- **Recommendation 6:** Patients with FIB-4 >2.67 have a 97% likelihood of advanced fibrosis and should be referred to a hepatologist

Dinani A, et al. Gastroenterol Hepatol Open Access. 2021;12(4):114–122

Recommendations for management of NAFLD

	AASLD (2018)	EASL (2016)	Asia-Pacific (2017)
Lifestyle intervention	Target weight loss of 7% to 10% TBW (B1). Achieve with 500-1000 daily caloric deficit and moderate-intensity exercise, preferably in a structured weight loss program (C2).		
	• No specific recommendations related to specific macronutrient diets or exercise regimens	• Mediterranean diet, avoidance of processed foods and added fructose (B1)	• No specific recommendations related to specific macronutrient diets or exercise regimens
Pharmacological intervention	There are currently no approved drugs to treat NAFLD or NASH. However, multiple drugs are in phase 3 development. In patients with cardiovascular indications, statins can be safely used in patients with NASH and compensated cirrhosis (B1)		
	• Vitamin E 800 IU daily can be considered in nondiabetic patients with biopsy-proved NASH *without* cirrhosis • Pioglitazone 30 mg daily can be considered in patients with and without T2DM with biopsy-proved NASH	• Pharmacotherapy should be reserved for patients with NASH fibrosis (stage F2 or higher) or NASH with high risk for disease progression (T2DM, MetS, elevated ALT) (B1) • No firm recommendations can be made for the use of pioglitazone or vitamin E (B2)	• Pioglitazone recommended only in patients with prediabetic or diabetic NASH for short-term use (B2) • No firm recommendation can be made regarding the use of vitamin E due to insufficient evidence (A2)

Chalasani N, et al. Hepatology 2018;67:328-357
European Association for the Study of the Liver. *J Hepatol* 2016;**64**:1388-1402
Wong VW, et al. *J Gastroenterol Hepatol* 2018;**33**:70-85

TREATMENTS

Weight loss

- Lifestyle
- Bariatric Surgery

Insulin sensitizers

- Metformin
- Thiazolidinediones (pioglitazone)

- Glucagon-like Peptide-1

Analogues

- Vitamin E
- Statins
- Coffee
- Vitamin D

Weight loss is the cornerstone of NASH management

Increased likelihood of NASH resolution and fibrosis improvements was associated with higher degrees of weight loss[1]

Weight loss, %	5%	7%	10%	P-value
Resolution of steatohepatitis,[a] %	10%	26%	64%	90%	<0.01
Fibrosis regression,[b] %	16%	18%	16%	45%	<0.01
Steatosis improvement,[c] %	35%	65%	76%	100%	<0.001
Patients achieving weight loss, %	70%	12%	9%	10%	
N =293	n=205	n=34	n=25	n=29	

In this study, only 1 in 5 patients may achieve weight loss sufficient (≥7%) to significantly improve liver histology[1]

The presence of diabetes, BMI ≥35, female sex, and many ballooned cells at baseline reduced the probability of NAS improvement or resolution of steatohepatitis[1]

Weight loss through lifestyle interventions can be difficult to sustain[2,3]

[a]Resolution of steatohepatitis was defined as absence of the histologic features of definite steatohepatitis, which required lack of hepatocellular ballooning with no fibrosis impairment. [b]Regression was defined as a decrease of at least 1 point in the fibrosis score. [c]Improvement in steatosis, ballooning, lobular formation, and portal inflammation scores were defined as a reduction of at least 1 point as compared with baseline values with no fibrosis impairment.

1 Vilar-Gomez E, et al. Gastroenterology 2015; 2:367-378
2 Managing Overweight and Obesity in Adults. *NIH 2013 accessed December 19th 2021*
3 Anderson JW,et al. *Am J Clin Nutr 2001; 74*:579-584

Interventions - Exercise

- The majority of NAFLD patients are engaged in minimal physical activity.
- Exercise improves hepatic steatosis
- Optimal exercise regimen
  - Maintain physical activity >150 min/week
  - Exercise > 5x week
- Best outcomes if exercise is combined with weight loss

Kistler KD, et al. Physical activity recommendations, exercise intensity, and histological severity of nonalcoholic fatty liver disease. Am J Gastroenterol 2011;106:460-468.

Interventions – Dietary modifications

- Mediterranean diet
- Caloric control
- Ingestion of food without labels
- 60 ml of extra virgin olive oil
- Nuts
- Avoidance of high fat foods: animal fat and red meat
- Coffee > 2 cups/day

Ryan M.C. et al. *J. Hepatol.* 2013;59:138–143
Vilar-Gomez E, et al. Gastroenterology 2015; 2:367-378
Chalasani N, et al. Hepatology 2018;67:328-357
Kennedy OJ, et al. Alimentary Pharm Therap 2016; 5:562-574.

Treatment and Monitoring

Recommendation 7: All patients identified with NAFLD should be counselled on lifestyle modification around weight loss and physical activity

- Weight loss is the best therapy for NAFLD
- Carbohydrate restriction is the most effective diet
  - Patients who lose 10% body weight typically resolve NAFLD
  - Weight loss usually results in improved AST and ALT and improved metabolic parameters
- Exercise reduces hepatic fat but should be recommended in combination with weight loss
- Alcohol use should be discouraged

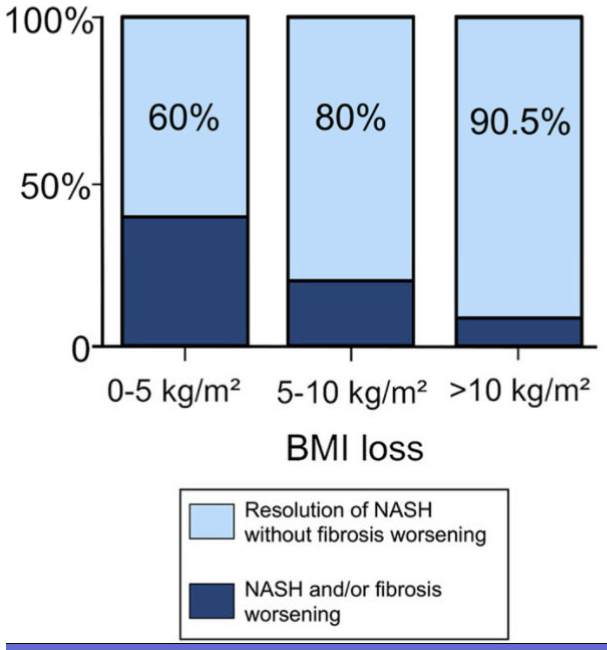
Dinani A, et al. Gastroenterol Hepatol Open Access. 2021;12(4):114–122

Interventions – Bariatric Surgery

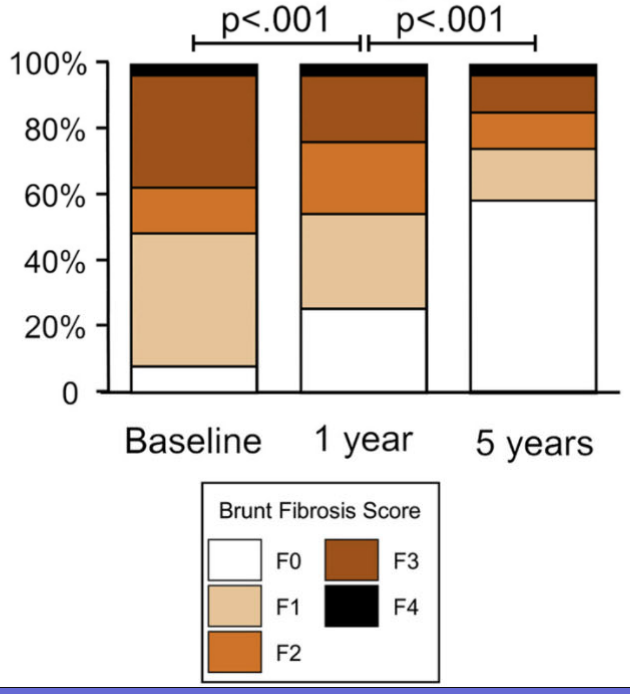
In a long-term follow-up of 180 patients with NASH who underwent bariatric surgery in France

- resolution of NASH in liver samples from 84% of patients 5 years later.
- reduction of fibrosis is progressive, beginning during the first year and continuing through 5 years

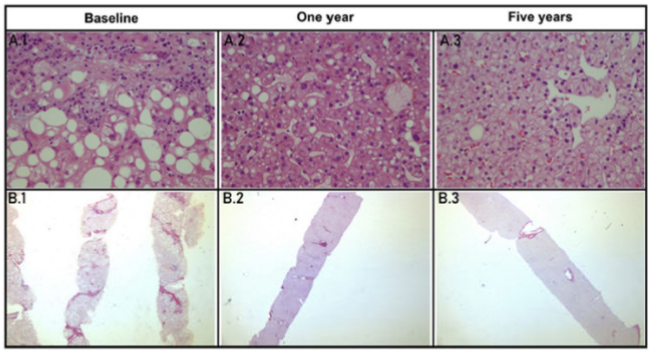
Resolution of NASH according to weight loss



Evolution of Fibrosis after Bariatric Surgery



Histological Evolution of NASH and Fibrosis after Bariatric Surgery



A: Upper panel H&E staining, (X400)

B: Lower panel Sirus Red staining, (X25)

Gastroenterology

Lassailly G, et al. Bariatric Surgery Provides Long-term Resolution of Nonalcoholic Steatohepatitis and Regression of Fibrosis. Gastroenterology. 2020 Oct;159(4):1290-1301.

AASLD Guidance – Bariatric Surgery

1. Bariatric surgery can be considered in otherwise eligible obese individuals with NAFLD or NASH
2. Bariatric surgery is not yet an established option to specifically treat NASH
3. Type, safety and efficacy of bariatric surgery in otherwise eligible patients with cirrhosis is not established

Chalasani N, et al. Hepatology 2018;67:328-357

Insulin Sensitizers-AASLD Guidance

1. Metformin may improve serum aminotransferases
2. Improves insulin resistance
3. No significant improvement in liver histology

Not recommended for treatment of NASH but should be considered as first-line pharmacologic therapy for those with NAFLD and T2DM

Marchesini G, et al. Lancet 2001;358:893-894

Nair S, et al. Aliment Pharmacol Ther 2004;20:23-28

Bugianesi E, et al. Am J Gastroenterol 2005;100:1082-1090

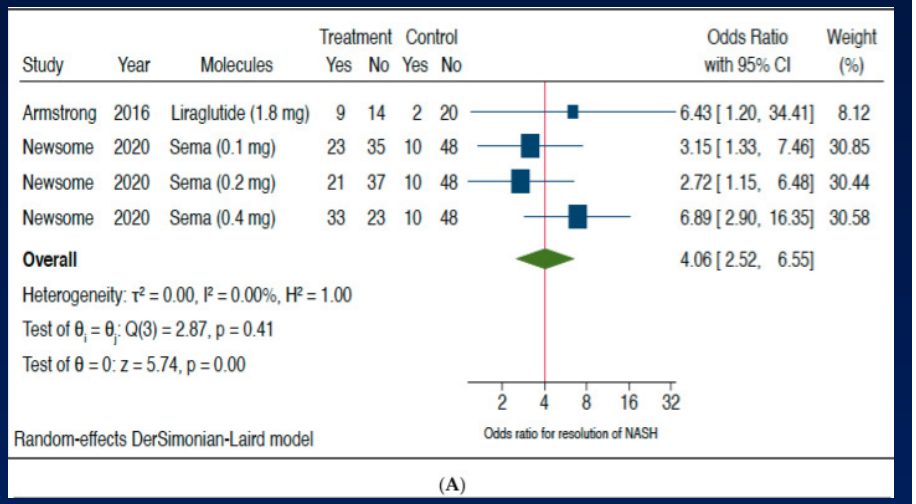
PPARγ agonist - AASLD Guidance

1. In biopsy proven NASH, Pioglitazone improves histology in patients with and without diabetes
2. Risks and benefits should be discussed with each patient
3. Should not be used to treat NAFLD without biopsy proven NASH

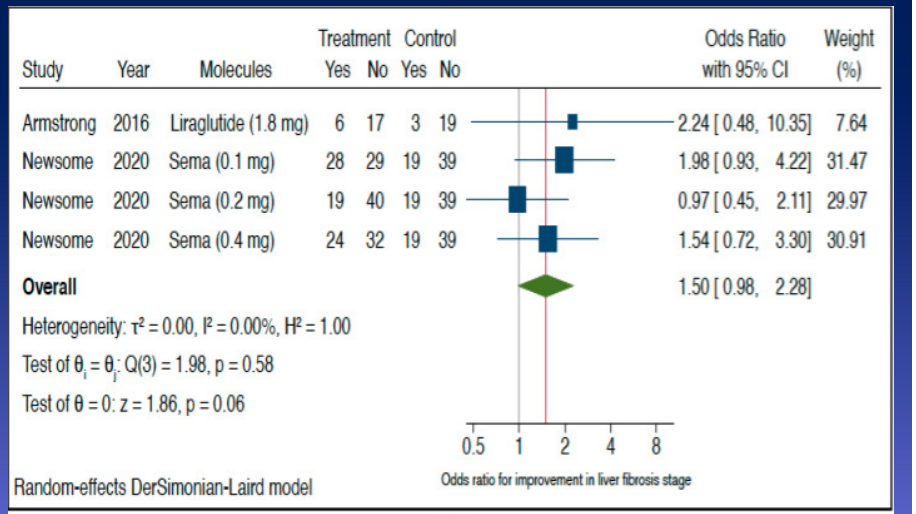
Chalasani N, et al. Hepatology 2018;67:328-357

Glucagon-like Peptide-1

- Forest plot and pooled estimates of the effect of GLP-1 RAs (*n* = 2 RCTs included using either liraglutide 1.8 mg/day or semaglutide at a dose of 0.1 mg, 0.2 mg or 0.4 mg/day subcutaneously) on
- A- histologic resolution of NASH with no worsening of liver fibrosis
- B- improvement in liver fibrosis stage without worsening of NASH as compared with placebo.



(A)



(B)

Mantovani A, et al. Glucagon-Like Peptide-1 Receptor Agonists for Treatment of Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis: An Updated Meta-Analysis of Randomized Controlled Trials. Metabolites. 2021 Jan 27;11(2):73.

Treatment and Monitoring

Recommendation 8: All patients identified with NAFLD should work with their PCP to manage medical comorbidities

- Treat components of metabolic syndrome with medication as indicated
  - Statins should be used if indicated – not contraindicated in patients with liver disease
  - Antihypertensive agents as indicated – beta-blockers should not be used as first-line treatment (may promote weight gain)
  - Preferred medications for diabetes include metformin, sodium-glucose co-transporter-2 inhibitors (SGLT2i), and glucagon-like peptide-1 (GLP-1) agonists
  - Pioglitazone may cause weight gain but may benefit patients with NAFLD
  - Insulin and sulphonylureas should be avoided
  - Consider bariatric surgery referral in those with clinical indication

Dinani A, et al. Gastroenterol Hepatol Open Access. 2021;12(4):114–122

Treatment and Monitoring

Recommendation 9: At each clinic visit, patient smoking status and detailed alcohol history should be obtained

- Smoking is a risk factor for the development of hepatic fibrosis and HCC
- Advice on keeping alcohol consumption to a minimum should be encouraged

Dinani A, et al. Gastroenterol Hepatol Open Access. 2021;12(4):114–122

Vitamin E- PIVENS trial

Vitamin E at 800 IU/day

Pioglitazone 30mg/day

Placebo

247 patients in total

NASH CAN RESOLVE

BUT FIBROSIS STAYS

THE SAME

Variable	Placebo	Vitamin E	Pioglitazone	P Value*	
				Vitamin E vs. Placebo	Pioglitazone vs. Placebo
Primary outcome†					
No. of subjects randomly assigned	83	84	80		
Subjects with improvement (%)	19	43	34	0.001	0.04
Changes from baseline in histologic features					
No. of subjects with biopsy specimens at baseline and 96 wk	72	80	70		
Steatosis					
Subjects with improvement (%)	31	54	69	0.005	<0.001
Mean change in score	−0.1	−0.7	−0.8	<0.001	<0.001
Lobular inflammation					
Subjects with improvement (%)	35	54	60	0.02	0.004
Mean change in score	−0.2	−0.6	−0.7	0.008	<0.001
Hepatocellular ballooning					
Subjects with improvement (%)	29	50	44	0.01	0.08
Mean change in score	−0.2	−0.5	−0.4	0.03	0.01
Total NAFLD activity score (mean change)	−0.5	−1.9	−1.9	<0.001	<0.001
Fibrosis‡					
Subjects with improvement (%)	31	41	44	0.24	0.12
Mean change in score	−0.1	−0.3	−0.4	0.19	0.10
Resolution of definite nonalcoholic steatohepatitis (% of subjects)	21	36	47	0.05	0.001

Sanyal AJ, Chalasani N, Kowdley KV, et al; NASH CRN. Pioglitazone,vitamin E, or placebo for nonalcoholic steatohepatitis. N Engl J Med 2010; 362: 1675–85.

Vitamin E - AASLD Guidance

1. Vitamin E 800 IU/day improves liver histology in nondiabetic with biopsy proven NASH
2. Risk and benefits should be discussed with each patient
3. Vitamin E is not recommended to treat NAFLD without biopsy proven NASH

Chalasani N, et al. Hepatology 2018;67:328-357

Interventions- Vitamin D

- Vitamin D deficiency (<20ng/ml) is present in 55% of patients with biopsy proven NAFLD
- Vitamin D may be protective against inflammation

Nelson JE, et al. Vitamin D Deficiency Is Associated With Increased Risk of Non- alcoholic Steatohepatitis in Adults With Non-alcoholic Fatty Liver Disease: Possible Role for MAPK and NF-κB? Am J Gastroenterol. 2016 Jun;111(6):852-63.

PROPOSED ALGORITHM

Identify patients at risk for NAFLD
1 or more of the following
Obesity
Increased waist circumference
Hyperglycemia
Fatty liver on ultrasound

If liver enzymes are elevated, assess for other causes of liver disease

Reassess risk every 2 years.

Determine risk of advanced fibrosis

Calculate FIB-4 or NAFLD Fibrosis Score

FIB-4		
≤ 1.3	1.3 to 2.67	>2.67
NFS		
≤ -1.45	-1.45 to 0.67	>0.67

Higher cut offs, <2 (FIB-4) and <0.12 (NFS) for patients > 65 years of age.

LOW RISK of advanced fibrosis ← < 7.8 kPa ← Transient Elastography → > 7.8 kPa → HIGH RISK of advanced fibrosis

Manage in Primary Care
- Weight loss and exercise, vaccinate
- Metabolic syndrome
- Diabetes/HTN/Hyperlipidemia
- Stop smoking
- Avoid alcohol
- Consider bariatric surgery

Manage with Hepatology Clinic
- For assessment of liver disease
- For management of advanced fibrosis
- HCC screening and management
- Portal HTN and varices
- Clinical trials

Conclusions

- NAFLD is an epidemic with a rising mortality and healthcare cost.
- Non invasive tests for fibrosis are a cost-effective method of stratifying patients in low- and high-risk groups.
- Weight loss is a crucial part of NASH management. No current FDA approved medications are available.
- PCPs are overburdened, so the addition of ancillary staff to assist with dietary and lifestyle changes are essential to the effective management of these patients.

Acknowledgements/Recommended reading

Non-Alcoholic Fatty Liver Disease An Update in Diagnosis, Management and Treatment Guidelines 2021 by Federico Rodríguez-Pérez, MD, AGAF, FAASLD San Juan, Puerto Rico

NAFLD/NASH – Optimizing Therapies for Maximal Benefit by Karen L. Krok, MD,ACG 2021

Dinani A, Sussman N, Noureddin M, et al. An algorithm for the management of non-alcoholic fatty liver disease in primary care. *Gastroenterol Hepatol Open Access*. 2021;12(4):114–122

Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, Harrison SA, Brunt EM, Sanyal AJ. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018 Jan;67(1):328-357