The Skinny on NAFLD: Moving beyond diagnosis and toward actionable interventions for your patients

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Disclosures

No conflicts of interest to disclose
Learning Objectives
At the completion of today’s talk, physicians will:

1. Appropriately screen and diagnose patients with NAFLD
2. Use evidence-based treatments for NAFLD
3. Monitor patients with NAFLD appropriately
4. Understand when specialty referral and/or co-management is indicated in patients with NAFLD
Disease Spectrum of NAFLD

NAFLD
Nonalcoholic Fatty Liver Disease

NAFL
Nonalcoholic Fatty Liver
25-30% of US population (82.4 million)

NASH
Nonalcoholic Steatohepatitis
2-6% of US population (6.6 million)

Chalasani N et al. The Diagnosis and Management of NAFLD: Practice Guidance From the AASLD. Hepatology 2018
Natural History of NAFLD

Steatosis

NASH ± F1–F2 fibrosis

Advanced F3 fibrosis

Cirrhosis

Death/ LTx

HCC

12–40%

14%

5–10%

0–50%

25–50%

25%

7%

8%

13%

EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J Hep 2016
NALFD is a **GLOBAL** epidemic

Younossi ZM et al. Epidemiology of NAFLD and NASH: Implications for Liver Transplantation. Transplantation 2019
Younossi ZM et al. The global epidemiology of NAFLD & NASH in pts with T2DM: A systematic review & meta-analysis. J Hep 2019
NALFD is a **GLOBAL** epidemic

In patients with T2DM, GLOBAL prevalence:
- NAFLD = 55.5%
- NASH = 37%
- Advanced fibrosis/cirrhosis = 17%

Younossi ZM et al. Epidemiology of NAFLD and NASH: Implications for Liver Transplantation. Transplantation 2019
Younossi ZM et al. The global epidemiology of NAFLD & NASH in pts with T2DM: A systematic review & meta-analysis. J Hep 2019
Economics of NA$$H

Cumulative $ 5-years with NAFLD:
↑ 80% with commercial
↑ 42% with Medicare

Alina AM et al. Healthcare Cost and Utilization in NAFLD: Real-World Data from a Large US Claims Database. Hepatology 2018
NAFLD increases mortality

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Deaths (2007-16)</th>
<th>Annual % Change*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td>155,894</td>
<td>0.96 [0.18-1.74]</td>
</tr>
<tr>
<td>CVD</td>
<td>38,444</td>
<td>1.59 [0.85-2.34]</td>
</tr>
<tr>
<td>Non-liver cancer</td>
<td>19,466</td>
<td>2.14 [0.25-4.06]</td>
</tr>
<tr>
<td>HCC</td>
<td>10,867</td>
<td>3.82 [3.20-0.44]</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8,113</td>
<td>2.23 [0.01-4.49]</td>
</tr>
<tr>
<td>Lung disease</td>
<td>5,683</td>
<td>2.13 [1.08-3.20]</td>
</tr>
</tbody>
</table>

* = Average annual percent increase [95% Confidence Intervals]
NASH in the year 2030...

63% increase in NASH!
137% increase in HCC!!
168% increase in decompensated cirrhosis!!!
178% increase in liver-related deaths!!!!
Case #1

A 32-year old man presents to your clinic to establish care. He has a history of anxiety and obesity. He lives alone, works as a programmer, and does not use tobacco, alcohol, or other illicit drugs. He recently went to a local health fair and had a normal CBC, CMP, lipids, and HgA1c 5.7. His BMI is 36.2 with an otherwise normal physical exam.

Would you screen this patient for NAFLD?

A. No
B. Yes
C. Maybe but need to do more laboratory tests first
Who should you screen for NAFLD?
# Who should you screen for NAFLD?

|---------------------------------------------------------------|--------------------------------------------------------|---------------------------------------------------------------|
| No screening recommended due to lack of evidence to support screening even in high-risk groups but maintain “vigilance” | Recommend screening in patients with:  
• Obesity  
• T2DM  
• Metabolic Syndrome  
• Abnormal LFT | Consider screening in patients with obesity or T2DM |

Ando Y et al. Nonalcoholic Fatty Liver Disease and Recent Guideline Updates. Clinical Liver Disease 2021
Approach to Screening

• Recommend US to screen for NAFLD in high-risk patients every 3-5 years:
  • Insulin resistance
  • Metabolic syndrome
  • Obesity

• Include alcohol use screening*

• Consider exclusion of secondary causes of CLD

*NIAAA high-risk alcohol use:
Men <65 = >14 drinks/week, >4 drinks/day
All others = >7 drinks/week, >3 drinks/day
Case #1 (Cont).

You decide to screen this patient for NAFLD with a liver ultrasound, which shows steatosis but is otherwise normal. In addition, you repeat liver tests, which are normal, and test him for HBV and HCV, both of which are negative. The patient sees his ultrasound report and sends you the following message through the patient portal:

“My ultrasound test shows fat in my liver. When I Googled ‘steatosis’ it said that this means chronic liver disease. Do I need any other tests or should I see a liver specialist?”

What would you recommend to this patient?

A. Biomarker testing to stage fibrosis
B. Transient elastography testing to stage fibrosis
C. Liver biopsy to evaluate for NASH and stage fibrosis
D. Refer him to Hepatology and let them figure it out
Fibrosis is the most important prognostic factor in NAFLD

Your tools:

Biomarker scores (NAFLD Fibrosis Score, FIB-4)
Transient Elastography

Chalasani N et al. The Diagnosis and Management of NAFLD: Practice Guidance From the AASLD. Hepatology 2018
EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J Hep 2016
Stage Risk: Low (≤F2) vs High (≥F3)

- FIB-4 (AUROC 0.80)
  - Age, ALT, AST, Plt
    - <1.30 Low Risk
    - >2.67* High Risk
    - Sensitivity 78%
    - Specificity 98%

- NAFLD Fibrosis Score (NFS) (AUROC 0.82)
  - FIB-4 + Albumin, IFG/Diabetes, and BMI
    - < -1.455 Low Risk
    - >0.672 High Risk
    - Sensitivity 90%
    - Specificity 97%

Shah AG. USE OF THE FIB4 INDEX FOR NON-INVASIVE EVALUATION OF FIBROSIS IN NAFLD. Clin Gastro Hep 2009
Angulo P et al. The NAFLD fibrosis score: a noninvasive system that identifies liver fibrosis in patients with NAFLD. Hepatology 2007
Transient Elastography

Vibration Controlled Transient Elastography

Images courtesy of Jerry Mabary
Comparison of Biomarker vs TE

*Individual Patient data Meta-Analysis of 37 Studies including 5735 Patients*

<table>
<thead>
<tr>
<th>Assay</th>
<th>Advanced fibrosis (≥F3)</th>
<th>Cirrhosis (F4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAFLD Fibrosis Score</td>
<td>0.73</td>
<td>0.78</td>
</tr>
<tr>
<td>FIB-4</td>
<td>0.76</td>
<td>0.80</td>
</tr>
<tr>
<td>Transient elastography</td>
<td>0.85</td>
<td>0.90</td>
</tr>
</tbody>
</table>

You perform a FIB-4 that is 0.88 (low likelihood of advanced fibrosis), but the patient is anxious and so transient elastography is performed. This shows elasticity of 14.5 kPa (cirrhosis). The patient sees his Fibroscan report and sends you the following message through the patient portal:

“I have cirrhosis...?!?!??! Am I going to die? Is this really just NASH?”

What would you recommend to this patient?

A. Reassurance and serial lab monitoring
B. MR Elastography
C. Liver biopsy
D. Refer him to Hepatology and let them figure it out
When to pursue liver biopsy

• In patients at increased risk of steatohepatitis or advanced fibrosis based on:
  • Biomarkers (NFS, FIB-4)
  • VCTE
  • Secondary liver disease

• NASH can **ONLY** be diagnosed with biopsy!

Histologic features of NASH:
- Steatosis
- Ballooning hepatocytes
- Portal inflammation

Chalasani N et al. The Diagnosis and Management of NAFLD: Practice Guidance From the AASLD. Hepatology 2018
When to pursue liver biopsy

- In patients at increased risk of steatohepatitis or advanced fibrosis based on:
  - Biomarkers (NFS, FIB-4)
  - VCTE
  - Secondary liver disease

**CLINICAL PEARL:** Biopsy should only be pursued if results will DETERMINE your patient management

- NASH can **ONLY** be diagnosed with biopsy!

Histologic features of NASH:
- Steatosis
- Ballooning hepatocytes
- Portal inflammation

Chalasani N et al. The Diagnosis and Management of NAFLD: Practice Guidance From the AASLD. Hepatology 2018
How I approach testing/biopsy...

• Additional serologic testing for other causes of chronic liver disease **ONLY** if atypical for NAFLD

• If suspect NAFLD and...:
  • **LOW** non-invasive fibrosis stage (≤F2), no biopsy and monitor non-invasive fibrosis q2 years
  • **HIGH** non-invasive fibrosis stage (F3-F4), biopsy to confirm unless overt evidence of cirrhosis
  • **INDETERMINATE** non-invasive fibrosis stage, shared decision making with patient but typically no biopsy
Does the ALT help me at all...

ALT in 238 patients with biopsy proven NAFLD

<table>
<thead>
<tr>
<th>ALT value</th>
<th>&lt;35</th>
<th>36–52</th>
<th>53–70</th>
<th>&gt;70</th>
</tr>
</thead>
<tbody>
<tr>
<td>NASH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>88.9</td>
<td>88.9–72.2</td>
<td>72.2–50</td>
<td>50</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>28.6</td>
<td>28.6–50.6</td>
<td>50.6–60.7</td>
<td>60.7</td>
</tr>
<tr>
<td>Advanced fibrosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>68.9</td>
<td>68.9–48.9</td>
<td>48.8–40</td>
<td>40</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>22.6</td>
<td>22.6–43.5</td>
<td>43.5–57.6</td>
<td>57.6</td>
</tr>
</tbody>
</table>

**ALT (or AST) did NOT predict NASH or advanced fibrosis in multivariate analysis**

Verma S er al. Predictive value of ALT levels for NASH and advanced fibrosis in NAFLD. Liver Int 2013
Assessment for CVD

• NAFLD is a predictor of CVD beyond Metab Synd
  • HR 1.87 [1.2-2.6] for incident CVD

• Screening for CVD **mandatory** in NAFLD
  • How to screen remains unclear...

• Statin use is **NOT** prohibitive in NAFLD or NASH
  • “…not at higher risk for serious liver injury from statins. Thus, statins can be used to treat dyslipidemia…”
  • Pravastatin in decompensated cirrhotics (**NOT** CYP3A4)

Tager G et al. NAFLD Is Independently Associated With an Increased Incidence of Cardiovascular Events in Type 2 Diabetic Patients. Diabetes Care 2007
Longitudinal fibrosis progression

- Rate of 1 stage progression:
  - NAFL = 14.3 years
  - NASH = 7.1 years
  - Twice as fast if hypertension

- Regression is possible

- How to monitor:
  - Biomarkers (q2 years)
  - VCTE (q2-5 years)
  - Biopsy (q5+ years)
Longitudinal fibrosis progression

- Rate of 1 stage progression:
  - NAFL = 14.3 years
  - NASH = 7.1 years
  - *Twice* as fast if hypertension

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- How to monitor:
  - Biomarkers (q2 years)
  - VCTE (q2-5 years)
  - Biopsy (q5+ years)

**CLINICAL PEARL:** *If biopsy without VCTE, obtain VCTE AFTER biopsy to ensure this is consistent and useful longitudinally.*

Singh S et al. Fibrosis Progression in NAFLD vs NASH: A Systematic Review and Metaanalysis of Paired-Biopsy Studies. CGH 2015
Risk of HCC – When to Screen

• HCC in absence of cirrhosis occurs
  • In VA cohort, NAFLD increased risk of non-cirrhotic HCC by 5.4-fold compared to HCV-related HCC

• HCC in NASH cirrhosis may have unique risks
  • Incident HCC in LT candidates rising fastest in NASH
  • Gene polymorphisms (e.g., PNPLA3)

• Data supports HCC screening ONLY in cirrhosis
  • Ultrasound +/- AFP every 6 months
Portal HTN in non-cirrhotic NAFLD

354 patients
Non-invasive markers

292 patients
Direct HVPG

Signs of portal hypertension may be present WITHOUT cirrhosis but clinical sequelae rare

Moga L et al. Patients with NAFLD do not have severe portal hypertension in the absence of cirrhosis. J Hep 2021
Mendes FD G et al. Prevalence and Indicators of Portal Hypertension in Patients with NAFLD. CGH 2012
Case #2

A 52-year old woman presents to clinic for follow-up of diabetes for which she is on metformin. She also has an established diagnosis of biopsy proven NASH without advanced fibrosis (stage 2). She has read about NASH and is worried that this will worsen and wants you to prescribe medication to treat her NASH. Which of the following medications has been shown to reduce inflammation in NASH?

A. Vitamin E
B. Pioglitazone
C. Empagliflozin
D. Pentoxyfylline
E. All of the above
F. None of the above
FDA-approved medications for indication NAFLD/NASH: 0!
Why no liver-directed therapy...?

• Clinical trial end points/surrogates remain a challenge
  • Phase 3 end points:
    • Resolution of NASH with no worsening of fibrosis
    • Improvement in fibrosis by 1 stage

• NAFLD is a systemic metabolic disease

• Liver-specific therapeutic targets vary
  • Metabolic
  • Anti-inflammatory
  • Anti-fibrotic
PIVENS Trial – What started it all

• Key study design points:
  • 247 patients with biopsy proven NASH \textit{without} diabetes randomized to one of following for 96 weeks:
    • Placebo
    • Vitamin E 800mg PO daily
    • Pioglitazone 30mg PO daily
  • Required 2 biopsies (0 and 96 weeks)
  • Primary outcome was composite histologic improvement in NASH with no increase in fibrosis
  • Given two arm comparison, p-value $<0.025$

Sanyal AJ et al. Pioglitazone, Vitamin E, or Placebo for Nonalcoholic Steatohepatitis. NEJM 2010
PIVENS Trial – What started it all

Histologic Improvement:
- Placebo 19%
- Pio 34% (p=0.04)
- VitE 43% (p=0.001)

No change in fibrosis stage in any cohort

AASLD supports Vitamin E in non-cirrhotic, non-diabetic NASH with aggressive histology
Consider Pioglitazone in similar cohort with T2DM

Sanyal AJ et al. Pioglitazone, Vitamin E, or Placebo for Nonalcoholic Steatohepatitis. NEJM 2010
Belfort R et al. A placebo-controlled trial of pioglitazone in subjects with nonalcoholic steatohepatitis. NEJM 2006
GLP-1 Agonists

- Liraglutide
  - Increase NASH resolution ± T2DM (39% vs 9%, p=0.04)
    - LEAN (placebo-controlled RCT 1.8mg/d, N=52)
  - Reduces intrahepatic fat (IHF) ± metformin

- Semaglutide
  - Double-blind, placebo-controlled RCT
    - Increase NASH resolution ± T2DM (40% vs 19%, p=0.001)
    - No improvement in fibrosis stage (43% vs 33%, p=0.46)

- DPP4 inhibitors may have similar effect (sitagliptin)

Yan J et al. Liraglutide, Sitagliptin, and Insulin Glargine Added to Metformin: The Effect on Body Weight and Intrahepatic Lipid in Patients With T2DM and NAFLD. Hepatology 2019
Feng W. Randomized trial comparing the effects of gliclazide, liraglutide, and metformin on diabetes with NAFLD. J Diabetes 2017
Newsome et al. A Placebo-Controlled Trial of Subcutaneous Semaglutide in Nonalcoholic Steatohepatitis. NEJM 2021
Additional antidiabetic medications

• SGLT2 Inhibitors (+T2DM)
  • Improve non-invasive measures (e.g., ALT, BMI)
  • Single open label biopsy-proven NASH + T2DM
    • Empagliflozin 25mg/d x 24 weeks; 4/9 NASH resolution

• Metformin
  • No histologic improvement independent of lifestyle intervention
    • Meta-analysis of 4 RCT (N=115)
Lipid lowering therapy

• Statins
  • ↓ ALT without clear histologic improvement
  • Clinical benefit is in CVD risk reduction
  • Evolving evidence that statins of benefit in advanced liver disease/cirrhosis (NIH-funded U01 longitudinal study)

• Ezetimibe
  • No histologic or steatosis benefit

• Omega-3 PUFA
  • ↓ ALT without clear histologic/fibrosis improvement

Satiya J et al. Narrative review of current and emerging pharmacological therapies for NASH. Transl Gastroenterol Hepatol 2021
Loomba R et al. Ezetimibe for the treatment of nonalcoholic steatohepatitis: assessment by novel magnetic resonance imaging and magnetic resonance elastography in a randomized trial (MOZART trial). Hepatology 2015
Statins are underutilized in NAFLD

**Women have lowest rates of statin utilization!**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Total Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one indication</td>
<td>2214</td>
</tr>
<tr>
<td>More than one indication</td>
<td>692</td>
</tr>
<tr>
<td>Clinical ASCVD</td>
<td>641</td>
</tr>
<tr>
<td>LDL &gt;= 190 mg/dL</td>
<td>23</td>
</tr>
<tr>
<td>T2DM + age 40-75</td>
<td>1803</td>
</tr>
<tr>
<td>10-year ASCVD risk &gt;= 7.5%</td>
<td>536</td>
</tr>
</tbody>
</table>
Statins are underutilized in NAFLD

Women have lowest rates of statin utilization!

CLINICAL PEARL: Statins prevent CVD in NAFLD..., no contraindication even in decompensated cirrhosis*
(use pravastatin [10mg] or low dose atorvastatin [20mg])
Novel PPAR dual/pan-agonists

A. Cariello et al. Transcriptional Regulation of Metabolic Pathways via Lipid-Sensing Nuclear Receptors PPARs, FXR, and LXR in NASH. CGH 2021

Cariello M et al. Transcriptional Regulation of Metabolic Pathways via Lipid-Sensing Nuclear Receptors PPARs, FXR, and LXR in NASH. CGH 2021
Novel PPAR dual/pan-agonists

- Saroglitazar magnesium (PPAR-α/γ agonist)
  - Multicenter, placebo-controlled RCT in India with histologic regression, no worsening fibrosis after 52 weeks
  - Phase II trial ongoing in US; interim analysis at 16 weeks with improved ALT

- Elafibranor (PPAR-α/δ agonist)
  - Phase 3 RCT in 1070 patients failed to reach 1° end point

- Lanafibranor (PPAR-α/γ/δ)
  - Phase 2b, placebo-controlled RCT in 247 patients
    - Increase NASH resolution (49% vs 22%)
    - One stage fibrosis regression (35% vs 9%)

Sarin SK et al. A prospective, multi-center, double-blind, randomized trial of saroglitazar 4 mg compared to placebo in patients with NASH. Hep Int 2020
Pan-PPAR is Pan-NAFLD

“NASH-cycled” liver agents

- Obeticholic Acid (FXR agonist)
  - Phase 3 trial 931 patients show improvement in fibrosis (23% vs 12%) without increased NASH resolution (12% vs 8%)
  - FDA did **NOT** approve
  - Re-vamped Phase 3 trial ongoing

- Pentoxyfylline (↑ erythrocyte flexibility, ↑ tissue O2)
  - Two placebo-controlled RCT with histologic improvement and same/better fibrosis
  - Limited inclusion of patients with diabetes

Satiya J et al. Narrative review of current and emerging pharmacological therapies for NASH. Transl Gastroenterol Hepatol 2021
Obeticholic Acid (FXR agonist)

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Pentoxyfylline (↑ erythrocyte flexibility, ↑ tissue O2)

- Two placebo-controlled RCT with histologic improvement and same/better fibrosis.
- Limited inclusion of patients with diabetes.

Satiya J et al. Narrative review of current and emerging pharmacological therapies for NASH. Transl Gastroenterol Hepatol 2021


Case #3

A 62-year old man presents to clinic for follow-up of NASH. He also has diabetes, HL, and HTN. He has had serial transient elastography of good quality with progression to now stage 3 fibrosis (advanced fibrosis). A friend recently passed away and he wants to make some meaningful lifestyle modifications. Currently, his weight is 220 lb, he does not exercise, and he drinks 1-2 glasses of wine 3-4 days per week. Which of the following would have the greatest impact on NASH?

A. Dietary changes leading to 15 lb weight loss
B. Exercise 150 min/week without weight loss
C. Alcohol cessation
D. Medical optimization of his metabolic diseases
Managing obesity in NAFLD

• Weight loss is the most effective treatment for NASH
• Modest weight loss helps!
  • 3-5% TBW loss leads to improvement in steatosis
  • 7-10% TBW loss leads to improvement/resolution of NASH
• AASLD guidelines support lifestyle modifications:
  • Reduce daily caloric intake by 500-1000 kcal
  • Exercise (150-200 min/week of moderate exercise)
• Lifestyle modifications >>> pharmacotherapy

Chalasani N et al. The Diagnosis and Management of NAFLD: Practice Guidance From the AASLD. Hepatology 2018
Bariatric surgery is effective

Resolution of NASH according to weight loss

Evolution of Fibrosis after Bariatric Surgery

Alcohol in NASH is...???

• Modest drinkers (≤ 2 drinks/day) have lower odds of steatohepatitis than non-drinkers (OR 0.49 [0.33-0.72])

1

• Modest drinkers (≤ 2 drinks/day) less likely to have NASH resolution compared to non-drinkers (OR 0.32 [0.11-0.92])

2

• Modest drinkers (<70 g/week) with NASH, particularly wine in non-binge pattern, had lower fibrosis stage than non-drinkers

3

1. Dunn W et al. Modest alcohol consumption is associated with decreased prevalence of steatohepatitis in patients with NAFLD. J Hep 2012
2. Ajmera V et al. Among Patients With NAFLD, Modest Alcohol Use Is Associated With Less Improvement in Histologic Steatosis and Steatohepatitis. CGH 2018
3. Mitchell T et al. Type and Pattern of Alcohol Consumption is Associated With Liver Fibrosis in Patients With NAFLD. AJG 2018
Alcohol in NASH is...?

- Modest drinkers (≤ 2 drinks/day) have lower odds of steatohepatitis than non-drinkers (OR 0.49 [0.33–0.72])

**CLINICAL PEARL:** Phosphatidylethanol (PeTH) is a good tool to determine if moderate-heavy alcohol use in past 30 days if question of ASH +/- NASH (e.g., AST>ALT)

- Modest drinkers (<70 g/week) with NASH, particularly wine in non-binge pattern, had lower fibrosis stage than non-drinkers

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Comprehensive NAFLD care

**What**
- Develop guidance on screening and testing with non-invasive tests
- Establish patient-centred pathways tailored to the disease stage
- Outline actions to prevent disease progression
- Develop guidance on treatment strategies related to disease stage

**Who**
- Define the composition and structure of the multidisciplinary team responsible for managing patients with NAFLD

**Where**
- Articulate the roles of and interactions between primary, secondary and tertiary care providers
- Establish where co-location of services for the treatment of NAFLD and common comorbidities is feasible

**How**
- Establish systems for coordinating and integrating care across the health-care system

Lazarus JV et al. Defining comprehensive models of care for NAFLD. Nat Rev Gastro Hep 2021
Referral pathways are key

Enhance Liver Fibrosis test (biomarker)

Satiya J et al. Narrative review of current and emerging pharmacological therapies for NASH. Transl Gastroenterol Hepatol 2021
Referral pathways are key

Pre-pathway, 470 referrals to get 36 (7.7%) high risk (≥F3)

Satiya J et al. Narrative review of current and emerging pharmacological therapies for NASH. Transl Gastroenterol Hepatol 2021
Practical guidance

- **DO** screen high-risk patients (T2DM, obesity) for NAFLD with LFT and/or US
- **DON’T** biopsy patients to establish NASH if otherwise typical pattern unless will change management
- **DO** identify NAFLD patients at risk for advanced fibrosis with biomarkers (e.g., FIB-4) **AND** reassess
- **DON’T** refer patients with NAFL or no fibrosis NASH to specialty providers unless additional questions
- **DO** prescribe statin therapy when indicated and consider GLP-1 agonists in T2DM with NAFLD
- **DO** emphasize importance of modest weight loss and consider bariatric surgery if refractory
Practical guidance

• **DO** screen high-risk patients (T2DM, obesity) for NAFLD with LFT and/or US

• **DON’T** biopsy patients to establish NASH if otherwise typical pattern unless will change management

• **DO** identify NAFLD patients at risk for advanced fibrosis with biomarkers (e.g., FIB-4) AND reassess

• **DON’T** refer patients with NAFL or no fibrosis NASH to specialty providers unless additional questions

• **DO** prescribe statin therapy when indicated and consider GLP-1 agonists in T2DM with NAFLD

• **DO** emphasize importance of modest weight loss and consider bariatric surgery if refractory

**CLINICAL PEARL:** FDA approval of liver-directed NASH therapy will result in a shift from passive approach to NAFLD to a biopsy-dependent treatment algorithm
Thank You!

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