2023 NCSCG 8TH ANNUAL LIVER SYMPOSIUM

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NAFLD VS. MAFLD Are You BAFFLED?

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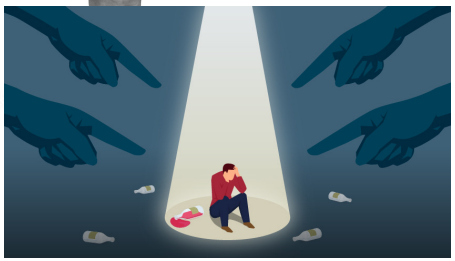
Why Is the Name Important?

- **N** = “non” can be see as “non”- important or “non” - well understood = **“non” - term**
- **A** = stigmatizing, especially in populations where alcohol consumption is forbidden
- **F** = stigmatizing, can be seen as “fat shaming”
- **L** = we seem to be OK with this
- **D** = is steatosis without inflammation or fibrosis a disease?

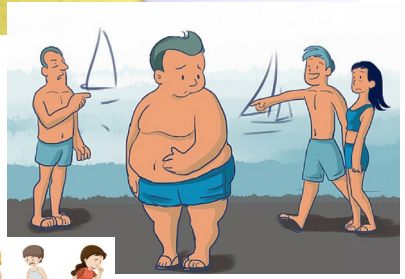


What Are the Downsides of Changing the Name?

- Implications for existing body of literature
- Implicating for research and funding
- Patients may be confused
- Difficulties in finding a fitting new name

Let's Give It a Try: MAFLD

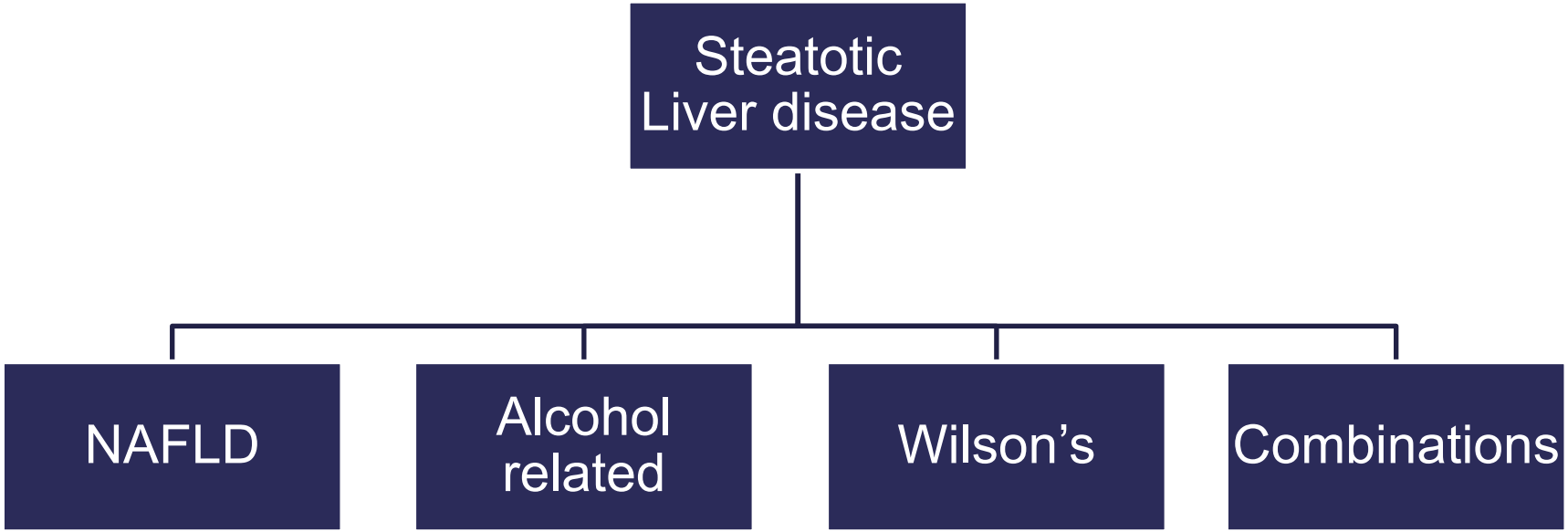
- **M** = what is metabolic liver disease?
  - A hepatic manifestation of metabolic syndrome?
  - Or is it an inborn error of metabolism in the pediatric world?
- **A** = associated
- **F** = "fat shaming"
- **L** = still OK here
- **D** = is steatosis without inflammation or fibrosis a disease? Perhaps more people are sick?



Let's Give It Another Try:

- Metabolic Liver Steatosis = **MLS**
- Steatosis Obesity Associated Liver disease = **SOLD**
- Insulin Related Steatosis = **IRS**
- Insulin Resistance Associated Liver Steatosis = **IRALS**

The Disease Formerly Known as …



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Is the Name Change a Distraction From the Real Issues?

- Who is at risk?
- How should we identify patients at highest risk?
- How do we incorporate screening into our practice?
- What are the treatment targets?
- Pharmacotherapies: are we there yet?

AASLD 2022 Guidance Updates: Hot Off the Press

- Pediatrics separated into an independent guidance document
- Screening for advanced fibrosis in high-risk populations
- Risk stratification algorithm
- Non-invasive diagnosis of at-risk NASH, advanced fibrosis and cirrhosis
- Off-label use of available medications
- Optimal care model

AASLD NAFLD Assessment Pearls

- AST and ALT levels are **frequently normal** in patients with advanced liver disease and should not be used to exclude presence of NASH with significant fibrosis
- “Normal” ALT levels reported by most labs are TOO HIGH
  - **ALT > 30 U/L is abnormal**
- Due to low sensitivity across the NAFLD spectrum **US should not be used** to identify hepatic steatosis
  - Increased echogenicity can be **FAT, INFLAMMATION or FIBROSIS**

Upcoming updates to AASLD NAFLD guidelines, presented at the Liver Meeting, November, 2022.

Screening for Advanced Fibrosis in High-Risk Populations

Screening recommended	Prevalence of advanced fibrosis
T2DM	6-19%
Medically complicated obesity*	4-33%
NAFLD in context of moderate alcohol use	17%
1st degree relative of patient with cirrhosis due to NAFLD	18%

- High burden and cost of disease
- Delayed diagnosis
- Higher prevalence of advanced fibrosis
- Off-label use of medications with overall mortality benefit and probable benefit on NAFLD (phase 2 trials)

**Complex chronic disease in which a person has a BMI ≥ 40 or ≥ 35 and is experiencing obesity-related health conditions*

Upcoming updates to AASLD NAFLD guidelines, presented at the Liver Meeting, November, 2022.

Key Updates: We Now Have Clearly Defined Populations for Screening

- General population based screening for NAFLD is not advised
- **High-risk patients should be screened**
  - T2DM, medically complicated obesity, family history of cirrhosis, concomitant alcohol use

Upcoming updates to AASLD NAFLD guidelines, presented at the Liver Meeting, November, 2022.

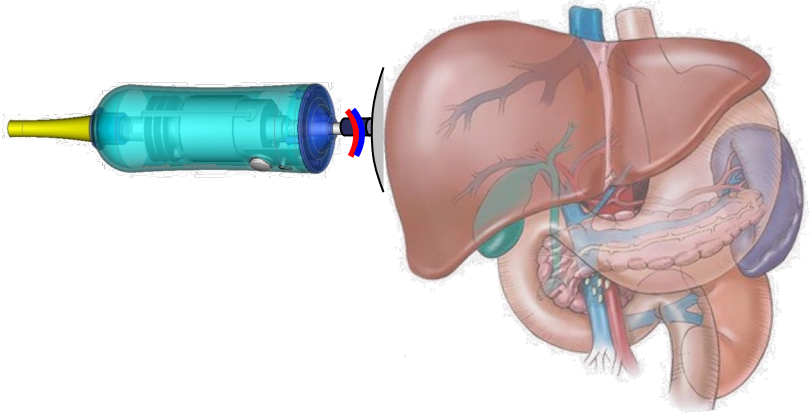
NIT: Blood Based = Simple = Fibrosis 4 (FIB-4)

- Based on age, platelet count, alanine aminotransferase (ALT) level and aspartate aminotransferase (AST) level
- Simple score that uses readily available patient data

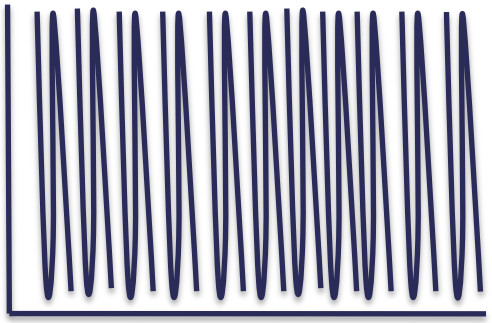
$$\text{FIB-4} = \frac{\text{Age (Years)} \times \text{AST Level } (U/L)}{\text{Platelet Count } (10^9/L) \times \sqrt{\text{ALT } (U/L)}} =$$

Calculator available at: https://www.mdcalc.com.

NIT: Imaging Based = Vibration Controlled Transient Elastography (VCTE)

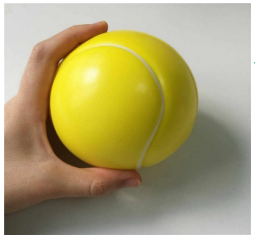


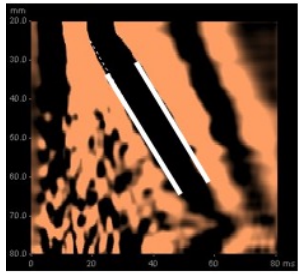
Probe mechanically induces shear wave …



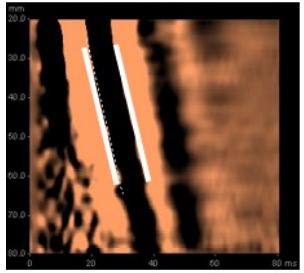
Shear Wave

VCTE: Surrogate Marker of Fibrosis





5.5 kPa



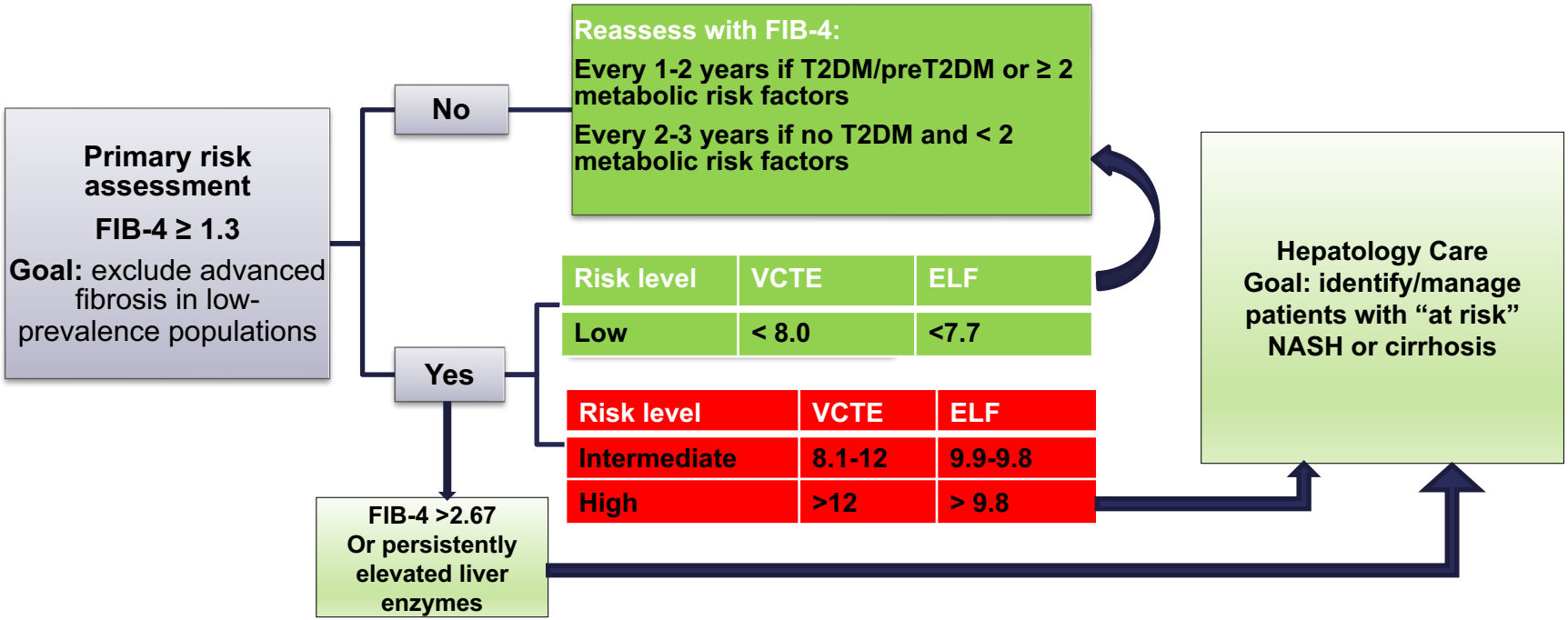
36.3 kPa

NIT: Blood Based = Complex = Enhanced Liver Fibrosis (ELF)

- Combines three biomarkers of fibrosis: hyaluronic acid, tissue inhibitor of metalloproteinase 1 and amino-terminal peptide of procollagen III

Alkhouri N et al. *Gastroenterol Hepatol* (NY). 2012;8(10): 661–668; 2. Siemens Healthineers. ELF instructions for use. Available at: https://doclib.healthcare.siemens.com.

NAFLD Suspected:



Upcoming updates to AASLD NAFLD guidelines, presented at the Liver Meeting, November, 2022.

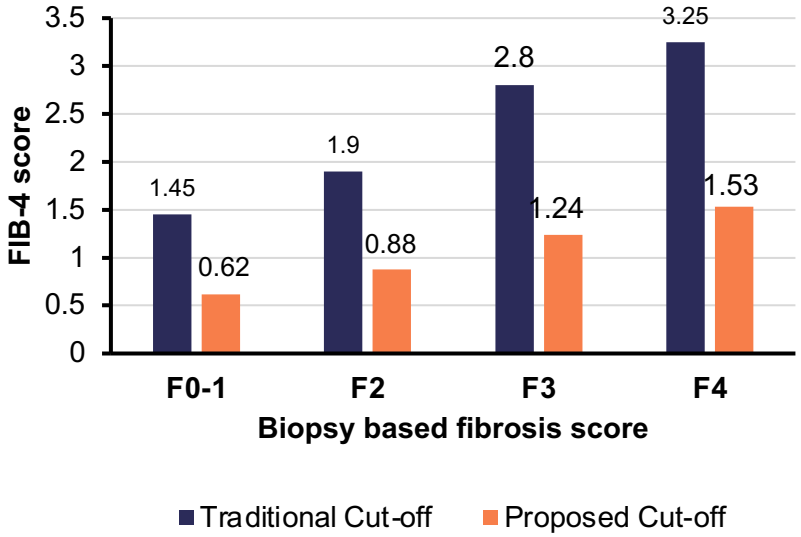
Key Updates: We Now Have an Algorithm for Screening in Primary Care Setting

- All patients with hepatic steatosis or clinically suspected NAFLD based on the presence of risk factors should undergo **primary risk assessment with FIB-4**
- Patients with T2DM, preT2DM, or ≥ 2 metabolic risk factors or steatosis on imaging should have FIB-4 repeated every **1-2 years**
  - When available, secondary assessment may be considered (VCTE or ELF)
- **If FIB-4 ≥ 1.3 secondary assessment (VCTE, ELF, MRE) should used** to exclude advanced fibrosis

Upcoming updates to AASLD NAFLD guidelines, presented at the Liver Meeting, November, 2022.

FIB-4: Are lower cut-offs needed for NAFLD?

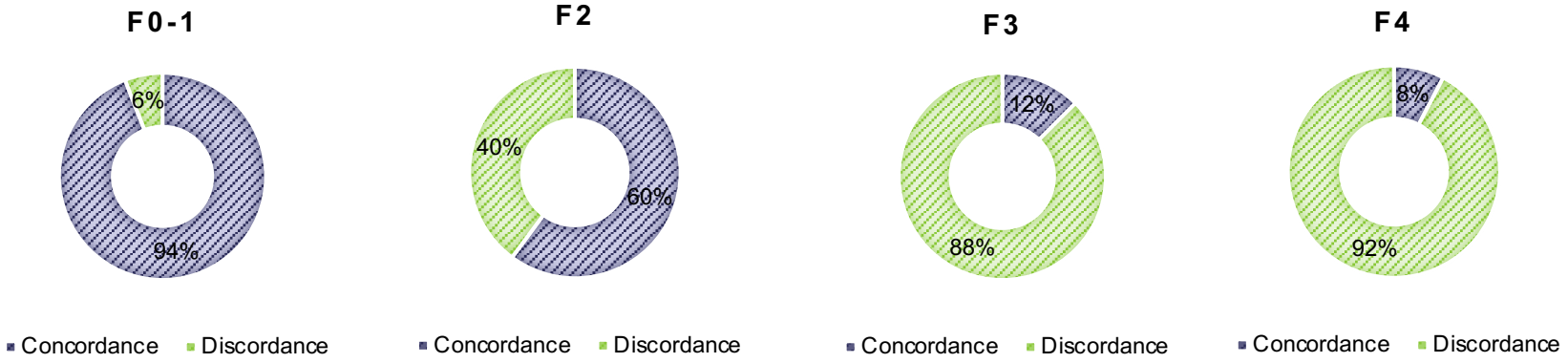
- FIB-4 score was developed for patients with HCV-HIV co-infection
- New AASLD guidelines lowered the cut-off from **< 1.45 to < 1.3**
  - Is it enough to capture the patients at highest risk?
- UCSF Fresno study
  - **632 patients** undergoing bariatric surgery
  - Pre-op VCTE, FIB-4 and intra-op liver biopsy
  - Mean age was 41 (18-75)
  - Mean **BMI is 45.73** (28.57-79.21)



In this study, most patients with advanced fibrosis would have been missed using traditional cut-off values

Green V, Roytman M. Liver Meeting November 2022.

Can We Rely on Vibration Controlled Transient Elastography in Patients With Severe Obesity?



VCTE	F0-1	F2	F3	F4
Overestimated fibrosis	36%	87.3%	87.5%	92.3%
Underestimated Fibrosis	4%	3.8%	0%	0%

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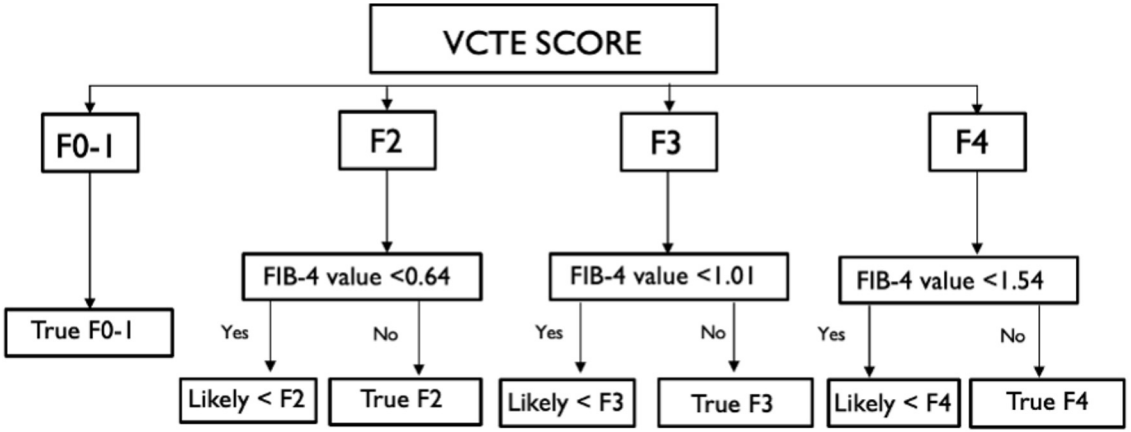
NAFDL-F to the Rescue! (or MAFLD-F)



From
60% concordance
with biopsy

To 88%

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What Have We Learned?

- There is **no consensus** on name change for NAFLD
- Soon to be published AASLD guidelines:
  - Define populations **at risk**
  - Recommend **screening** for advanced fibrosis in high risk populations
  - Provide a **risk stratification algorithm** through use of NIT
- We are in the very beginning of our journey of understanding NAFLD
  - **There is a lot to study and learn**

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