

# The Liver Forum

## Compensated NASH Cirrhosis: Risk Stratification

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**THE trouble WITH FAT**

To get an inside look at how fat affects the body's organs, we asked two women—one morbidly obese, the other a healthy weight—to spend five hours under a state-of-the-art open scanner to get a high-resolution magnetic resonance imaging scan (MRI). Open scanners—as opposed to the more common enclosed MRI tubes—are in demand as patients get larger.

**MAGNETIC RESONANCE ANGIOGRAPHY OF A STROKE**  
**STROKE**  
The risk of having a stroke is two to four times higher in people with type 2 diabetes, 90 percent of whom are overweight. Stroke occurs either when a blood vessel ruptures or a blood clot blocks an artery in the brain, causing damage to nerve cells.

**OPHTHALMOLOGIC IMAGING: DAMAGED BLOOD VESSELS IN EYE**  
**TYPE 2 DIABETES**  
People with excess body fat—especially in the abdominal area—often become resistant to insulin, a substance that helps the body store glucose. When glucose levels soar, diabetes results. One side effect is damage to blood vessels in the retina, which can lead to blindness.

**MICROGRAPHIC FAT GLOBULES IN LIVER TISSUE**  
**LIVER DISEASE**  
Many obese people develop deposits of fat inside the liver, a condition that can progress to cirrhosis in about 10 percent of cases, and occasionally to liver failure.

**X-RAY: COLON CONSTRICTED FROM CANCER**  
**COLON CANCER**  
Obese people are at greater risk of colon cancer. Abdominal fat appears to increase risk more than fat elsewhere, which may explain why men (who tend to store fat in their abdomens) have a higher risk.

**X-RAY: ARTHRITIC KNEE JOINT**  
**OSTEOARTHRITIS**  
Being overweight places additional stress on the spine, hip, and knee joints, causing a loss of cartilage. As the cartilage deteriorates, joint space narrows and bones grind together.

**MICROGRAPHIC PLAQUE BUILDUP IN ARTERY**  
**HEART DISEASE**  
Obese people tend to have elevated cholesterol, which can lead to plaque buildup in the arteries. They are twice as likely to have hypertension.

Age: 40  
Weight: 250 lbs  
Height: 5' 9"  
Body Mass Index: 40.3

Age: 36  
Weight: 120 lbs  
Height: 5' 9"  
Body Mass Index: 20.0

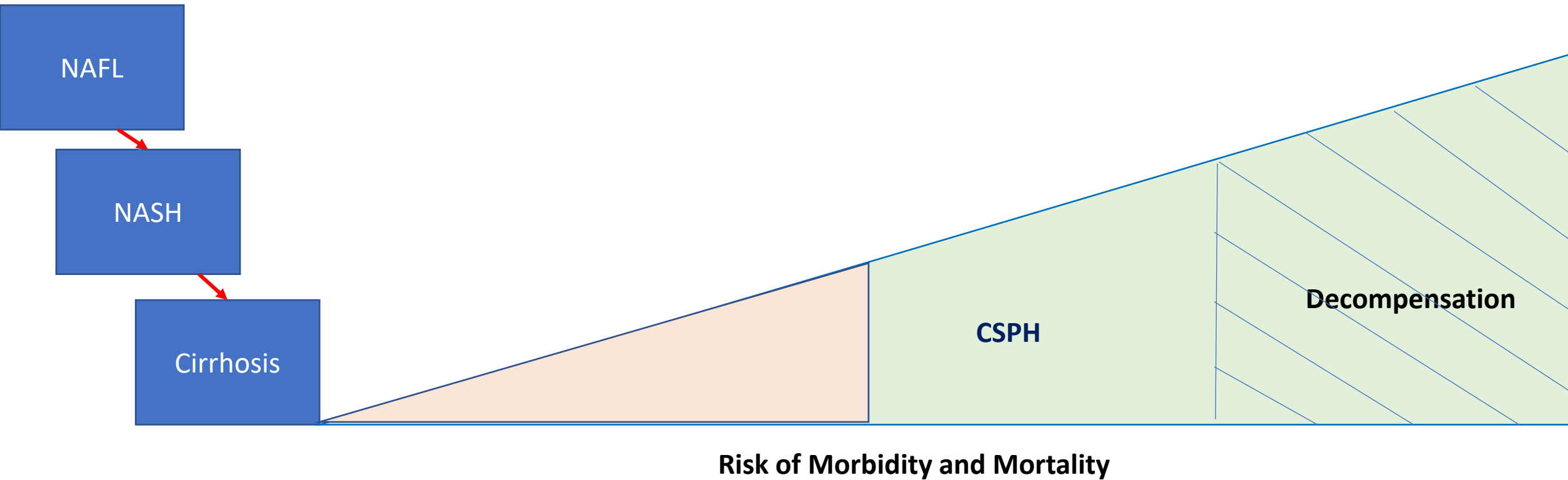
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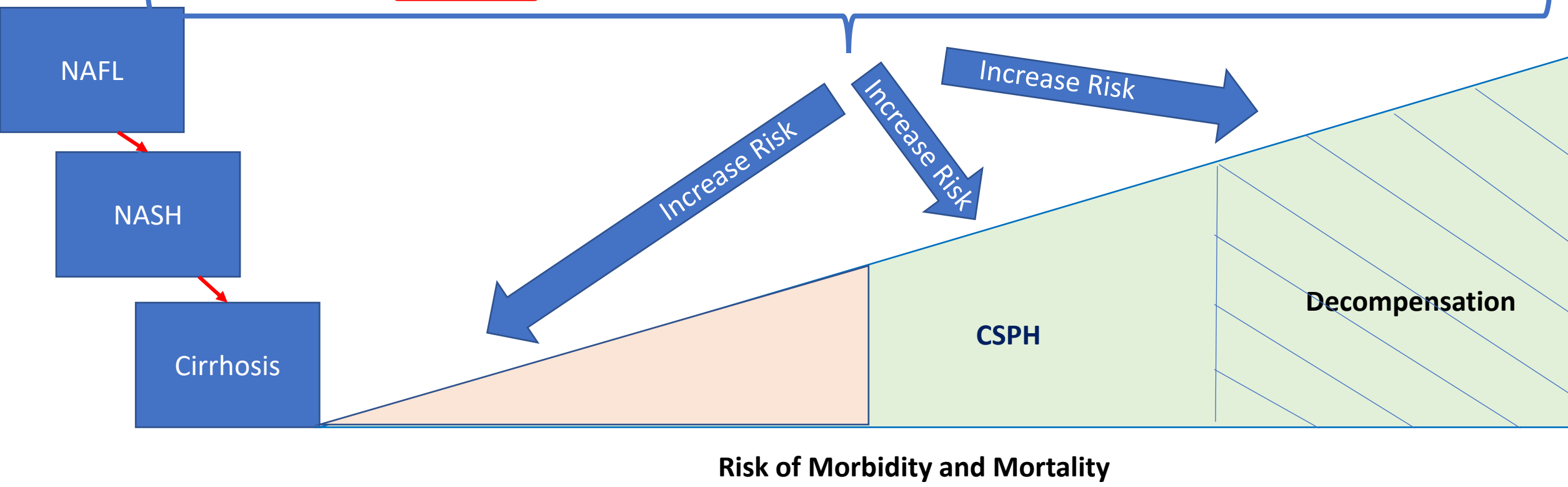
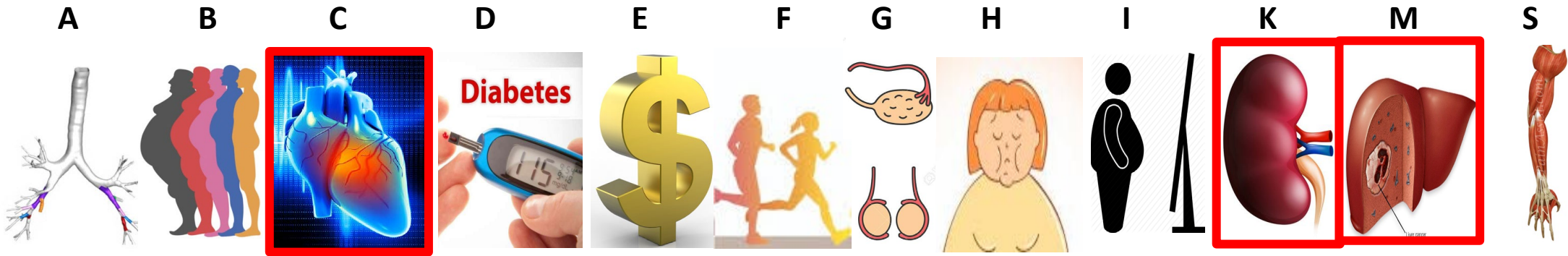
The NASH Cirrhosis Working Group has been split into two groups: Compensated and Decompensated. The groups has completed definitions of NASH as the etiology of cirrhosis. The groups now is focusing on risk stratification.

Framing the work by separating risk stratification into hepatic and extra-hepatic- the goal is to ensure clinical trials are not lumping all patients with cirrhosis into one category.

Need to determine the subgroups that could impact the trial outcomes, and to what degree.

# NASH Cirrhosis Risk Stratification: Different Lenses to be Used?





# Frame of work/Outline:

- **Hepatic :**

- **HVPG (solid data)**

- Varices, Ascites, HE
  - MELD score
  - Plt count
  - Thick vs thin Septa and nodule size
  - Total collagen content, path AI and Histoindex
  - Functional tests: Frailty/Hep Quant
  - Breath test (Stravitz et al J Hep 2015)
  - NITs: VCTE, MRE, cT1, ELF,...

	Stratum A	Stratum B	Stratum C
<b>High Evidence Tier</b>			
<b>Portal pressure related measurements</b>			
HVPG (mm Hg) <sup>&amp;</sup>	~ 5	6-10	> 10 mm
Varices	Absent	Absent	Present*
Ascites	Absent	Absent	Seen on Imaging only or recompensated
Hepatic encephalopathy	Absent	Absent	Absent-Minimal and recompensated
Platelets count (10 <sup>9</sup> /L)**	> 150,000	<150,000	<150,000
Child-Pugh Score	CTP-5	CTP-5	CTP-6
<b>Fibrosis related measurements</b>			
?Ishak Fibrosis stage	5	5-6	6
<b>Function related measurements</b>			
MELD	<10	10-12	>12*
Albumin (gm/dl)	> 3.5	2.8-3.5	≤2.8
Bilirubin (mg/dl)	< 1.3 mg/dL	1.3-2 mg/dL	>2 mg/dL
INR	<1.2	>1.2	>1.2
eGFR <sup>^</sup>	>60	>60	30-60 <sup>^</sup>
<b>Activity related measurements</b>			
NAS score	≥4	≥4	≥4

# Good Evidence Tier

## Portal Pressure or/And Fibrosis (stiffens) related measurements

VCTE~	14-20	21-25	> 25
MRE	4.7-6.48 kPa	4.7-6.48 kPa	>6.48 kPa
Liver cT1	825 – 875	>875	>875
ELF	<9.8	9.8-11.29	≥11.3
FIB-4	<1.3	1.3-2.67	>2.67 >3.25

## Function related measurements

Liver Frailty Index	<3.2	3.2-4.3	≥4.4
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## Emerging Evidence Tier

### Portal pressure related measurements

<i>Histoindex (SGH or B Index)</i> <i>SNOF score (see below)</i>	SNOF <10.85	SNOF >10.85 <11.78	SNOF <11.78
<i>PathAI (ML -HVPG)</i>	~1.51	1.93-2.59	<2.60
Spleen cT1 (needs more studies)	<1282	1282-1376	>1376

### Fibrogenesis related measurements

<i>ProC3</i>	>16.5 ng/mL	>16.5 ng/mL	>16.5 ng/mL
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### Function related measurements

<i>HepQuant (DSI)</i>	<21	<21	≥21
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