

NASH



Cirrhosis Strata for Risk Stratification and Enrollment in NASH Cirrhosis Trials

HOUSTON
Methodist
LEADING MEDICINE

Mazen Nouredin, MD, MHSc

Lynda K. and David M. Underwood Center for Digestive Disorders
Sherrie & Alan Conover Center for Liver Disease & Transplantation

Houston Methodist Hospital

Director Houston Research Institute

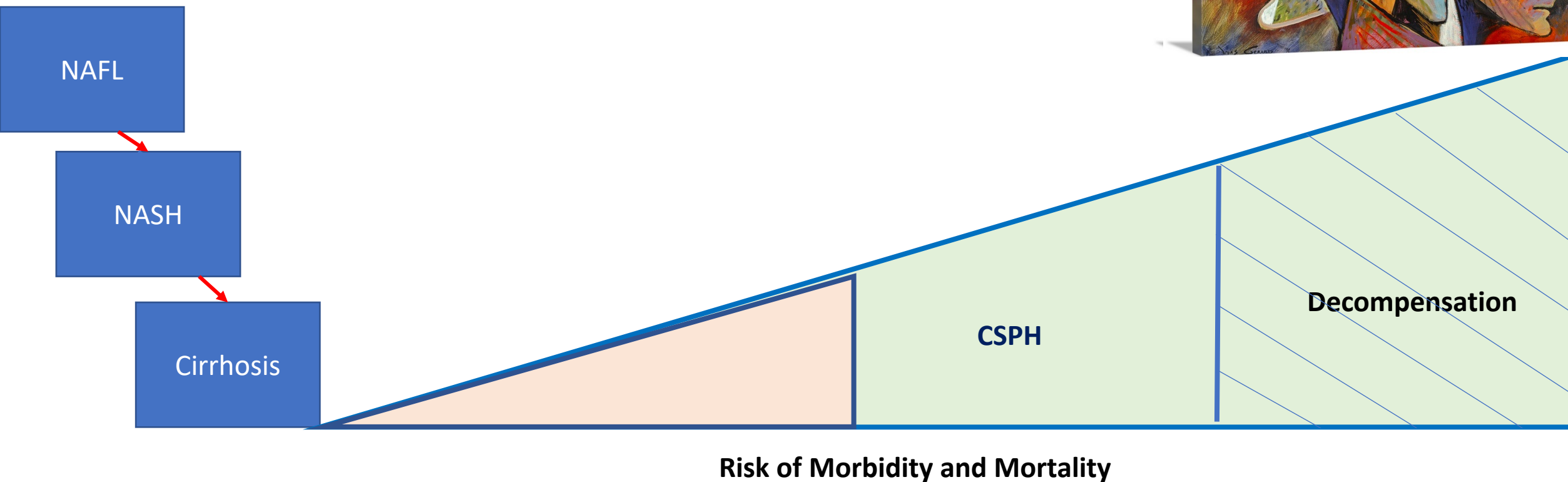
Houston, Texas



Disclosures

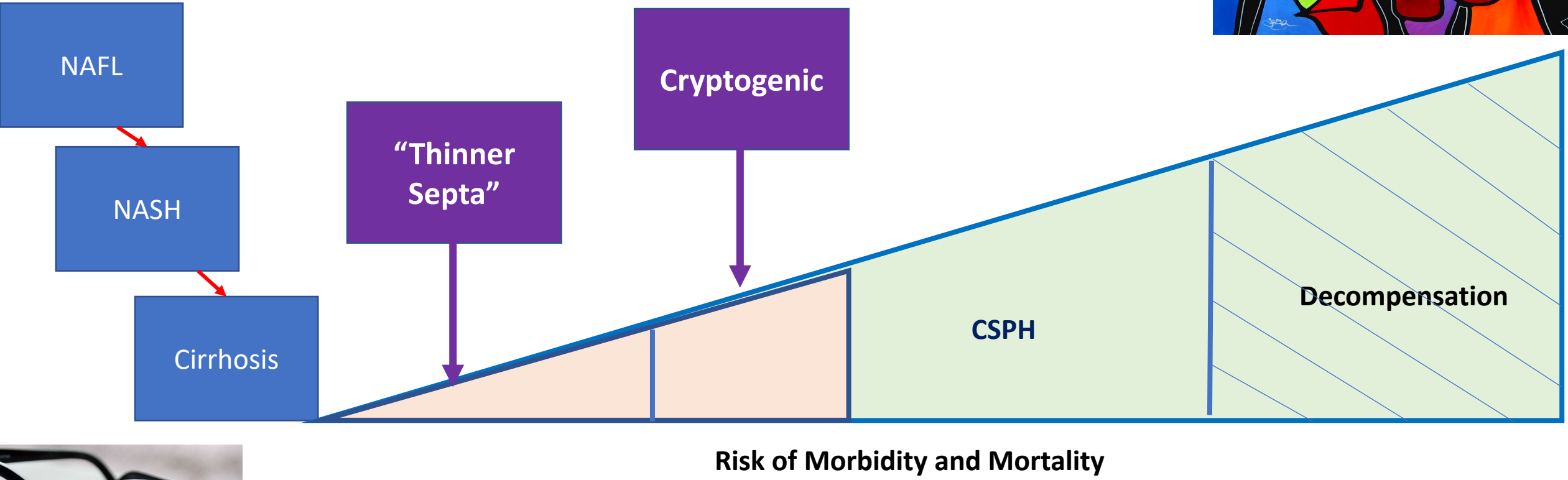
- Principal Investigator for a Drug Study: Allergan, Akero, BMS, Gilead, Galmed, Galectin, Genfit, Conatus, Enanta, Madrigal, Novartis, Novo Nordisk, Shire, TERNS, Viking and Zydus
- Advisory Board: 89BIO, Gilead, Intercept, Pfizer, Novo Nordisk, EchoSens, Fractyl, Terns, OWL, Prespecturm, Siemens and Roche diagnostic and Abbott
- Stockholder: Anaetos, Rivus Pharma, CIMA, Chrownwell and Viking
- Editorial Board : Gastroenterology , Clinical Gastroenterology and Hepatology
- Associate Editor: Clinical Gastroenterology and Hepatology
- Federal funding: NCI, NIH/NIDDK (Co-I)

The different Faces of NASH Cirrhosis



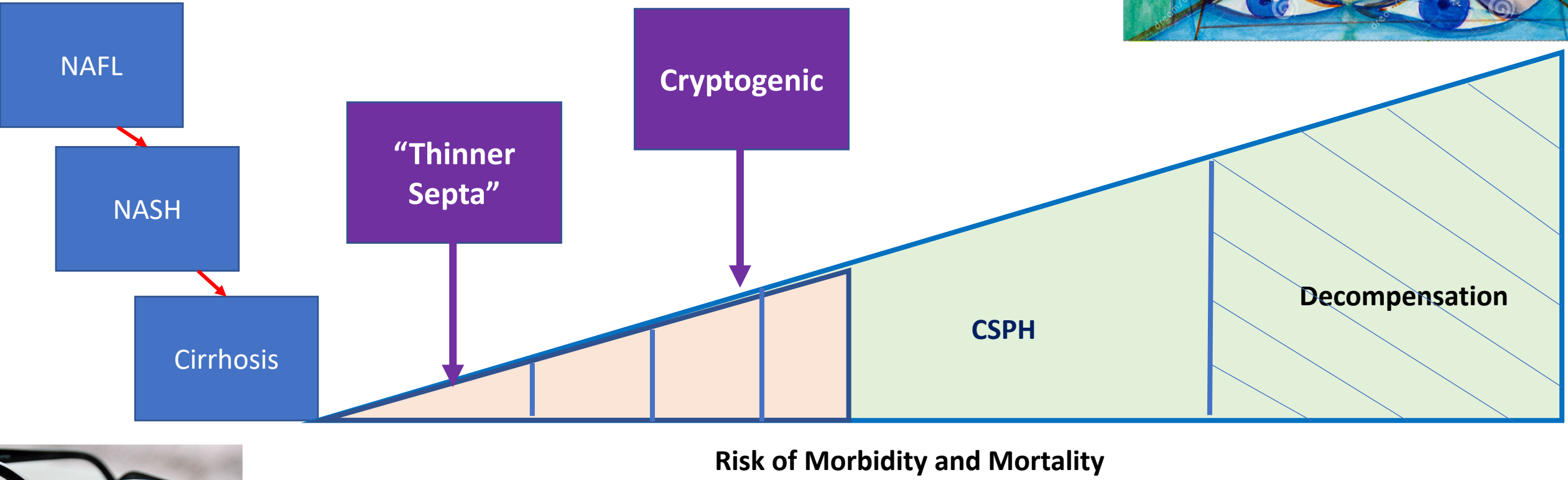
The different Faces of NASH Cirrhosis

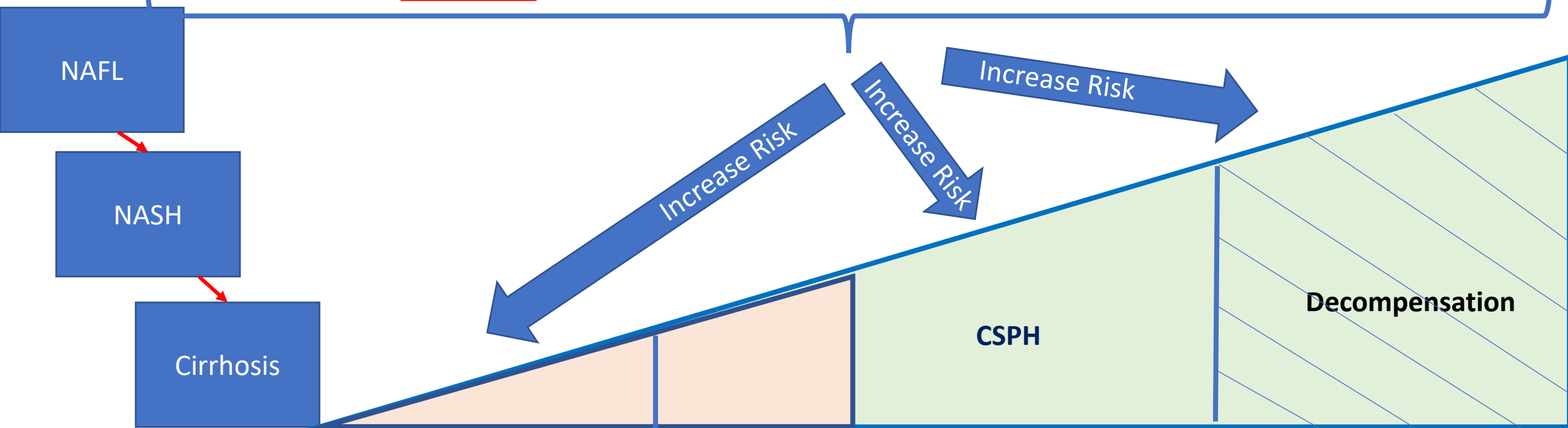
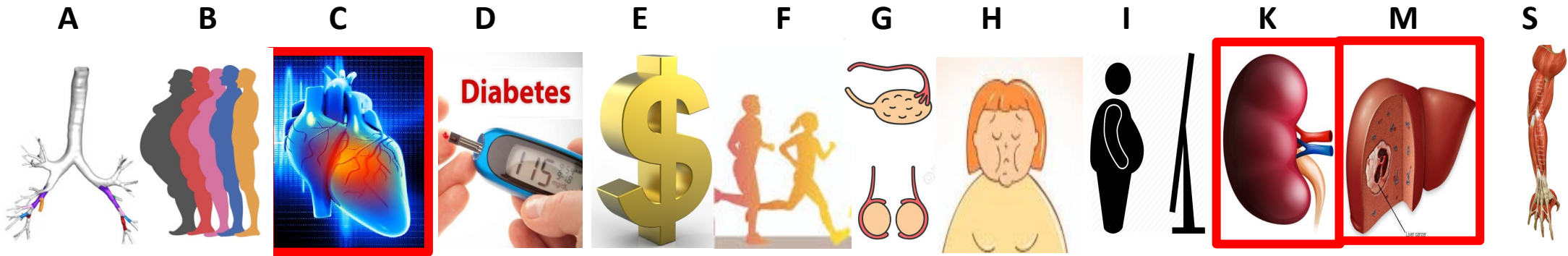
Different Lenses to be Used?



The different Faces of NASH Cirrhosis

Different Lenses to be Used?





Risk of Morbidity and Mortality

Cirrhosis is a spectrum of disease

Stage	Clinical classification	Dominant mechanisms	Symptoms	MELD	VCTE (kPa)	MRE (kPa)	HVPG (mmHg)	ELF
≤ F3	Non-cirrhotic	Fibrogenesis and angiogenesis	None		< 8	2.93-4		
F4	Compensated Childs A/B Minimal PHTN	Scar and x-linking Decreased NO/Increased Intrahepatic Vascular Resistance	None (No varices)		≥ 14	>3.65	≥5-10	>9.8
F4	Compensated Childs B CSPH	Dense, acellular scar and nodules	None (+varices)	<12	≥ 20	≥ 5	≥10	
F4	Decompensated Childs C	Insoluble scar	Ascites, VH, encephalopathy	>15	≥ 25 ≥ 20	≥ 6.5	>12	>11.3

Ideal point for intervention?

- Antifibrotics
- Disease modifying agents

Too late?

- Portal pressure lowering agents
- Antifibrotics ?

NASH Cirrhosis Working Group Planning Call: February 2022

Cirrhosis Strata and Guidance from Stakeholders for Risk Stratification and Enrollment in NASH Cirrhosis Trials

Table: Liver related measurements in NASH cirrhosis Trials

	Stratum A	Stratum B	Stratum C
High Evidence Tier			
Portal pressure related measurements			
HVPG (mm Hg) ^{&}	~ 5	6-10	> 10
Varices	Absent	Absent	Present e*
Ascites	Absent	Absent	Seen on Imaging only or recompensated
Hepatic encephalopathy	Absent	Absent	Absent-Minimal and recompensated
Platelets count (10 ⁹ /L)**	≥ 150,000	<150,000	<150,000
Child-Pugh Score	CTP-5	CTP-5	CTP-6
Histology Related Measures			
?Ishak Fibrosis stage	5	5-6	6
NAS score	≥3 or 4	≥3 or 4	None (cryptogenic)
Function related measurements			
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

Good Evidence Tier

Portal Pressure or/And Fibrosis (stiffens) related measurements

VCTE~	14-20	21-25	> 25
MRE	4.3-6.5 kPa	5-6.5 kPa	>6.5 kPa
Liver cT1	825 – 875	>875	>875
ELF	<9.8	9.8-11.29	≥11.3
FIB-4	1.3-2.67 [#]	>2.67-3.25 [#]	>3.25
Function related measurements			
Liver Frailty Index	<3.2	3.2-4.3	≥4.4

Portal pressure and Fibrosis related measurements

<i>Histoindex (SGH or B Index)</i>	<10.85	>10.85 <11.78	>11.78
<i>SNOF score (see below)</i>			
<i>PathAI (ML -HVPG DELTA)</i>	~1.51	1.93-2.59	<2.60
Spleen cT1 (needs more studies)	<1282	1282-1376	>1376
<i>ProC3</i>	16.5 ng/mL	?	?
Function related measurements			
<i>HepQuant (DSI)</i>	<19	19-22	≥22
<i>Methacetin breath test</i>	Collect more data	Collect more data	Collect more data
MRI measured adverse muscle composition	Collect more data	Collect more data	Collect more data

Thank you



 • @nouredinmd