Clinical insights for biologists
MICROB-PREDICT 2nd Master Class

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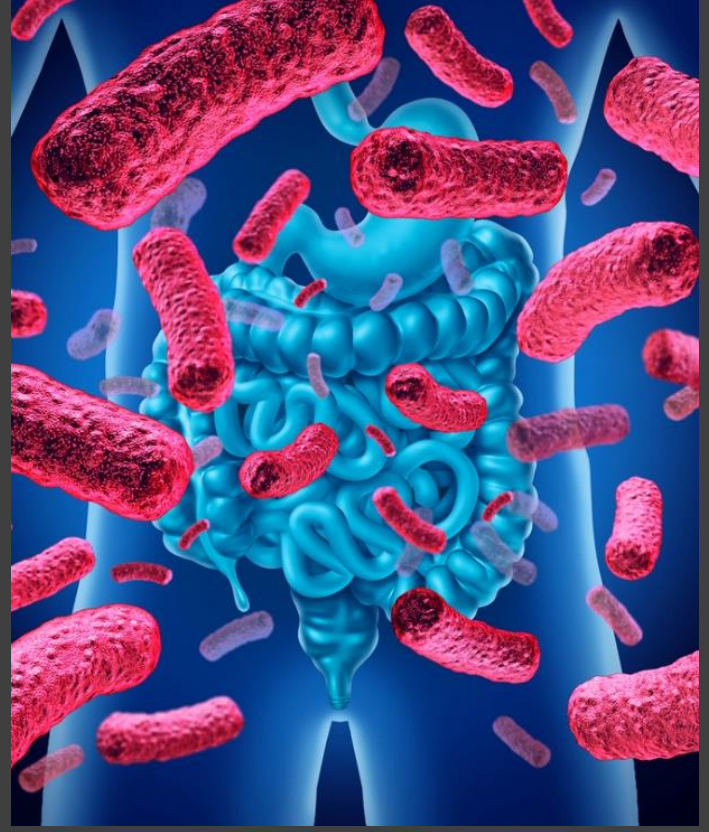
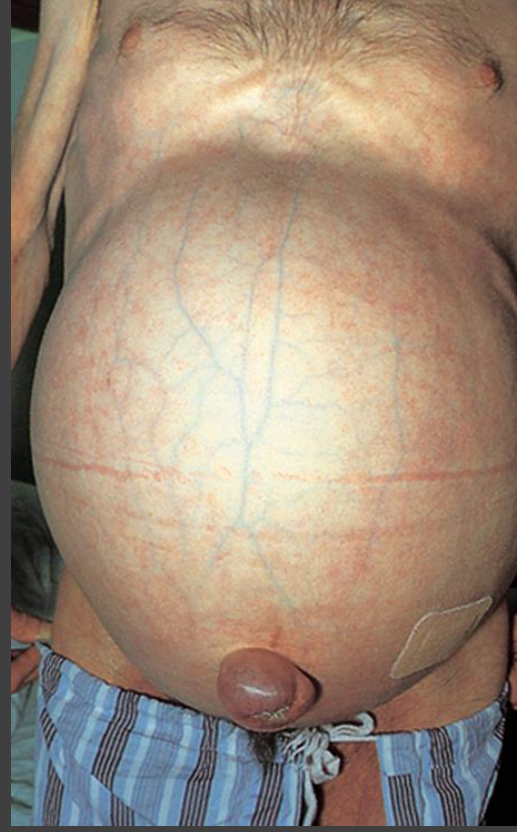
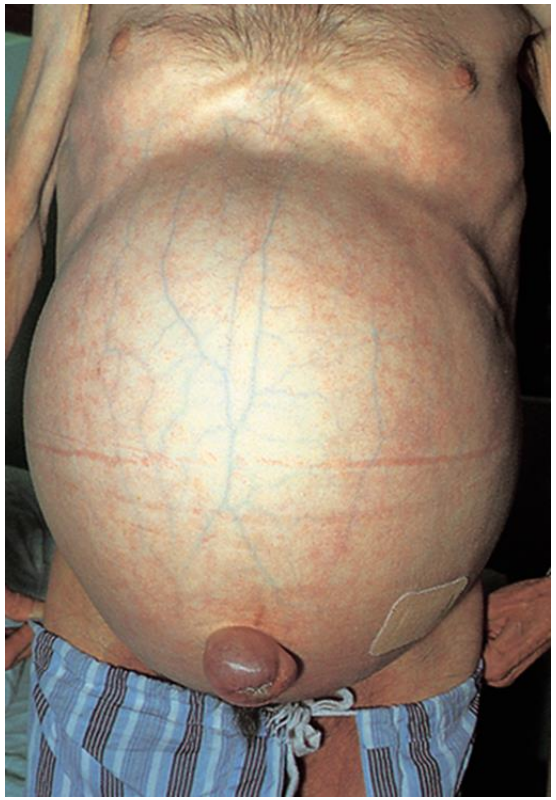
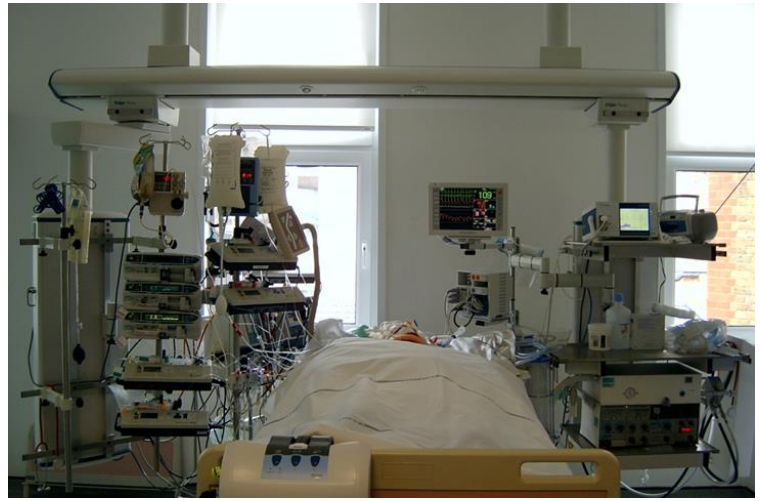
Talk Objectives

1. What is chronic liver disease?
2. Complications of chronic liver disease.
3. Pathophysiology of cirrhosis and ACLF
4. CANONIC AND PREDICT studies
5. Why are clinicians interested in the gut microbiome in cirrhosis?
6. Manipulating the gut microbiome in cirrhosis
7. Albumin
8. Rifaximin
9. MICROB-PREDICT Study from a clinician's standpoint



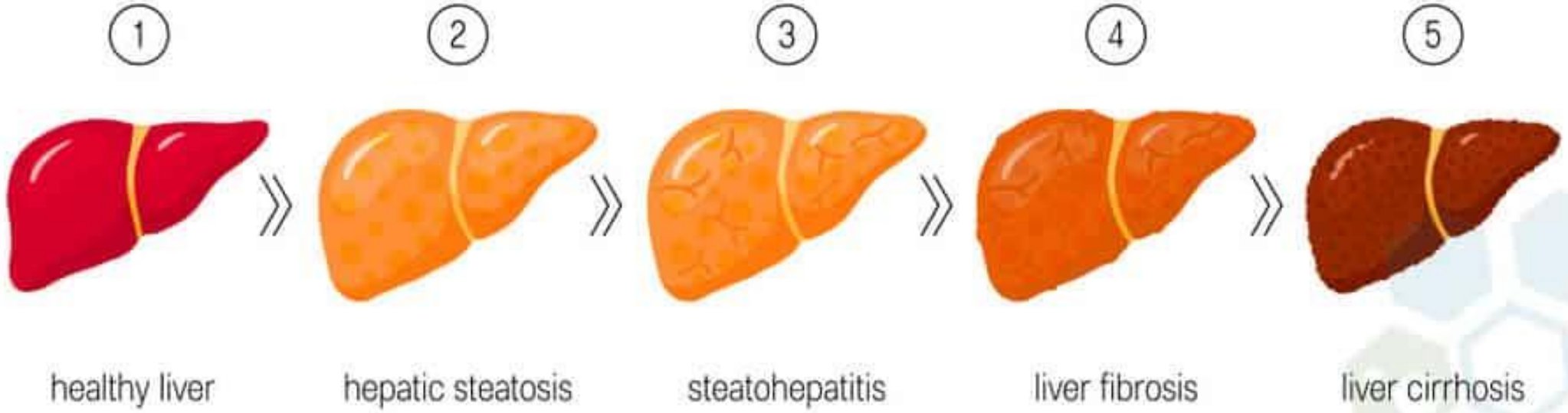






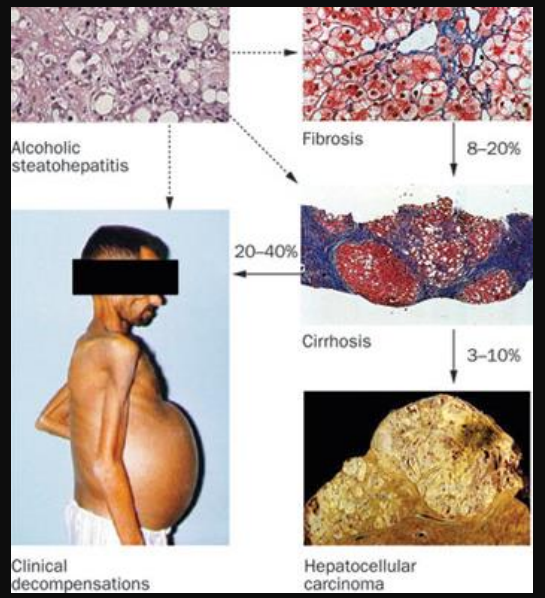
Chronic Liver Failure

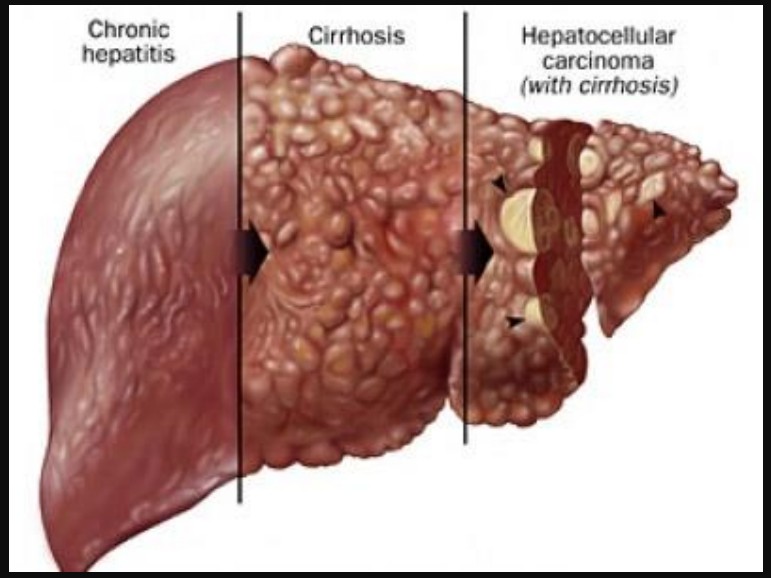
STAGES OF LIVER DAMAGE



Spectrum of Liver Disease

- Acute fulminant liver failure (rare)
  - 1 – 6 cases per million per year
- Chronic Liver Disease
  - 4% population
- Top 3 causes of cirrhosis in Europe
  1. Alcohol
  2. Fat
  3. Hepatitis C

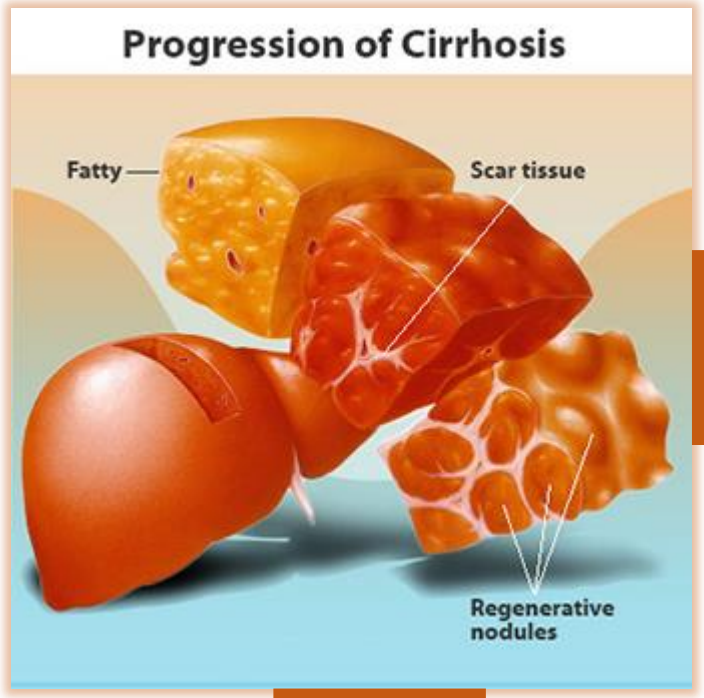




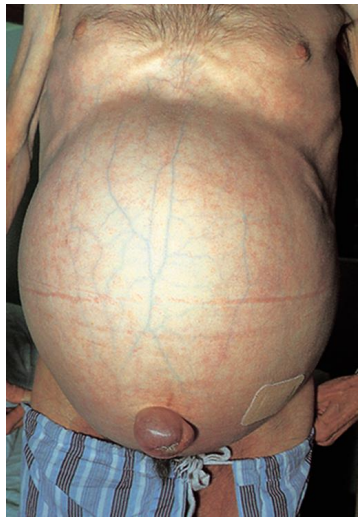
Classic Complications of Cirrhosis

5.5 million people in the US living with cirrhosis[1]

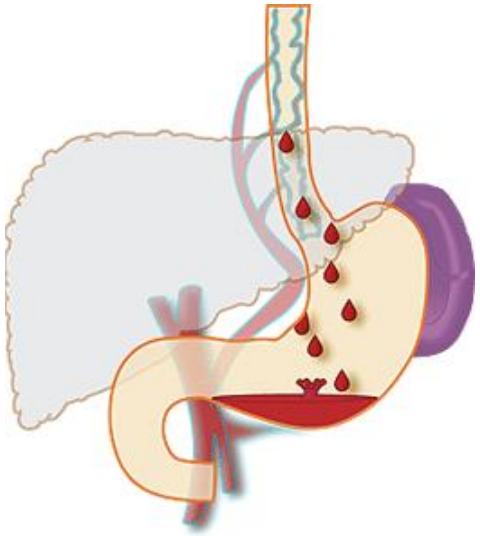
500,000 people in the EU living with advanced cirrhosis



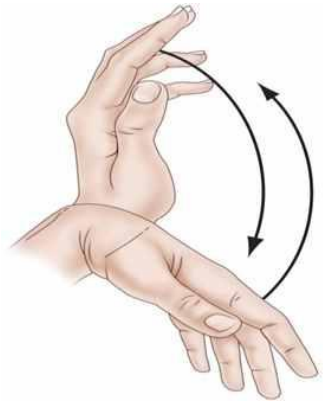
Ascites



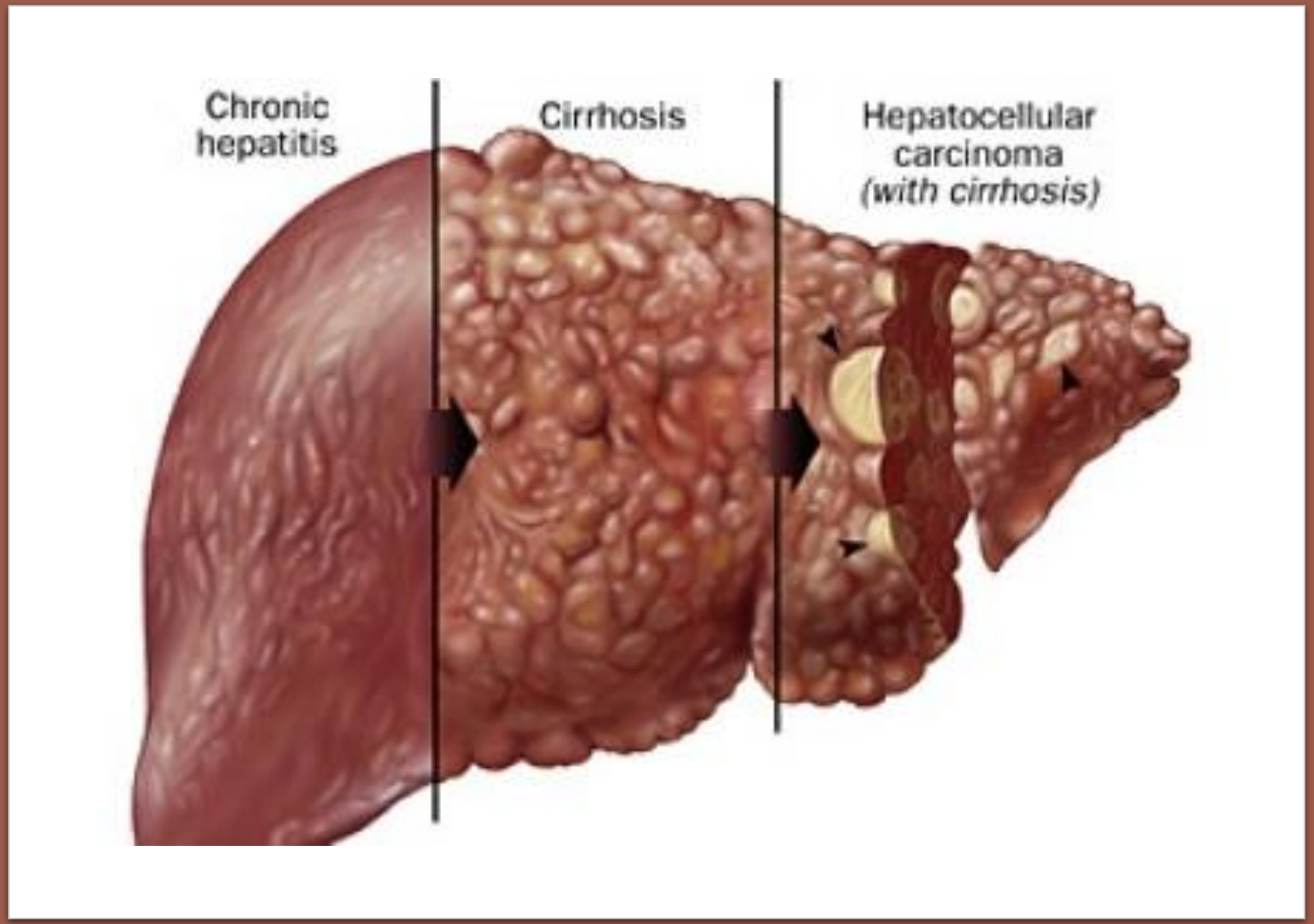
Variceal Bleeding



Hepatic Encephalopathy

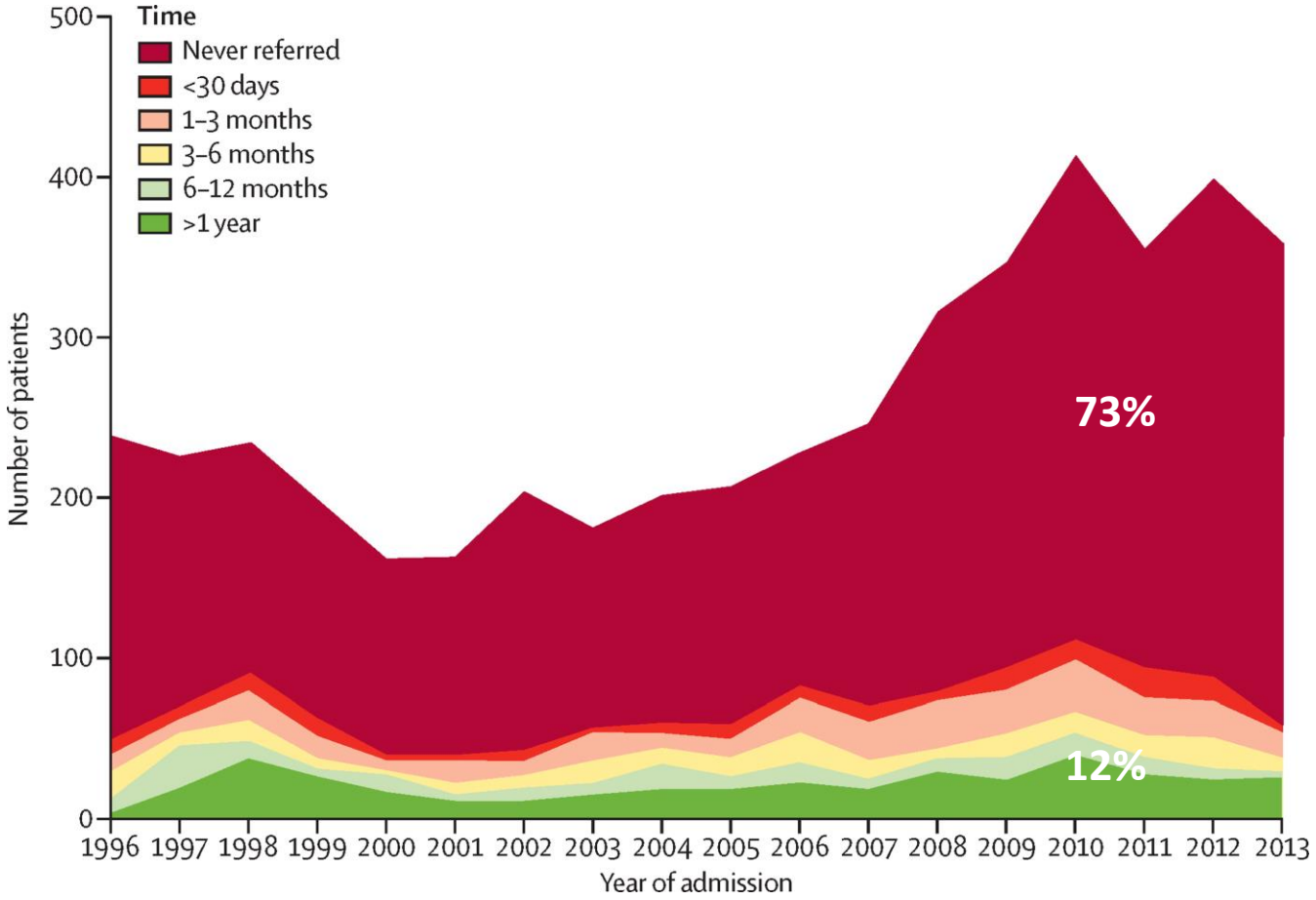


[1]Khungar V, Poordad F. *Clin Liver Dis* 2012;16:73-89.



1 in 6 patients with cirrhosis develop hepatocellular carcinoma

Time between referral to a liver clinic and the first admission with cirrhosis or liver failure

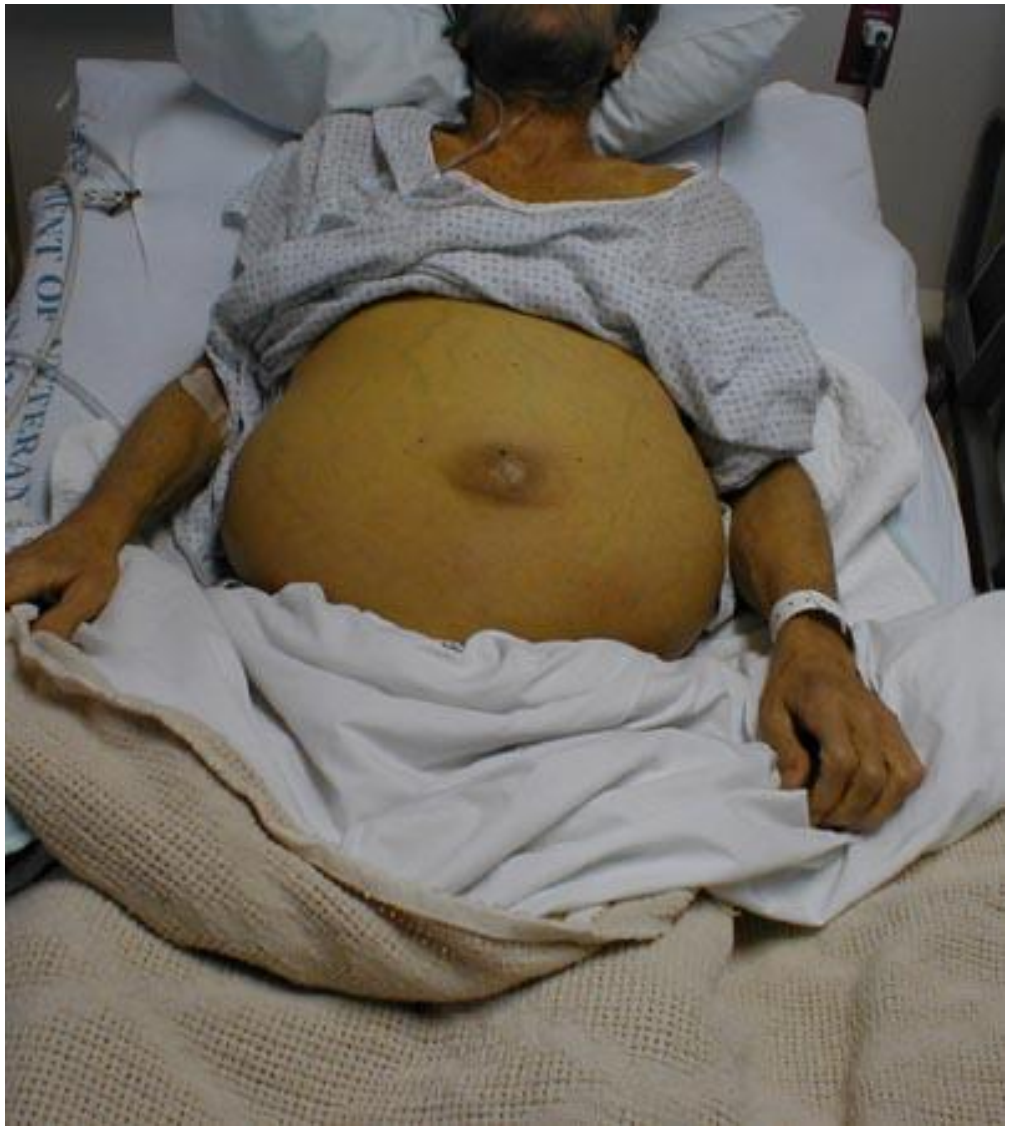


Original analysis of 4313 first admissions between 1996 and 2012 with cirrhosis or liver failure by International Classification of diseases-10 code to University Hospitals Southampton, UK. Data are from Emma Greatorex (University Hospital Southampton Trust, Southampton, UK, personal communication).
Analysed by Nick Sheron.

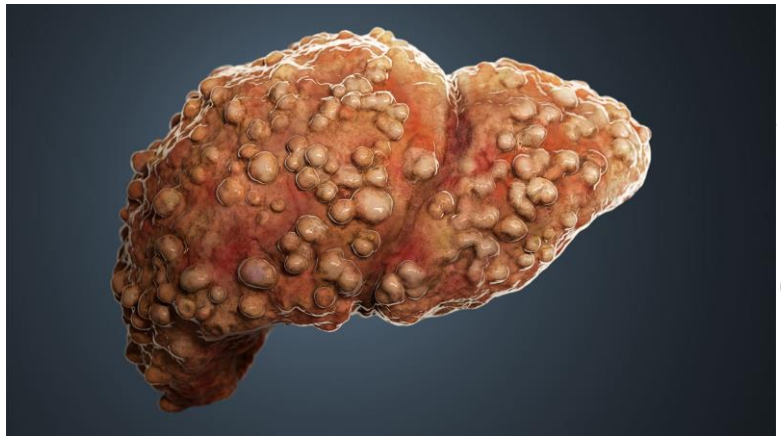
The Lancet 2014 384, 1953-1997DOI: (10.1016/S0140-6736(14)61838-9)

Consequences of Liver Decompensation and Chronic liver failure

- Jaundice
- Portal hypertension and bleeding
- Ascites
- Encephalopathy
- Renal Dysfunction
- Hyponatremia
- Anorexia
- Muscle Wasting
- Immune dysfunction and inflammation
- Infection
- Hepatocellular Cancer



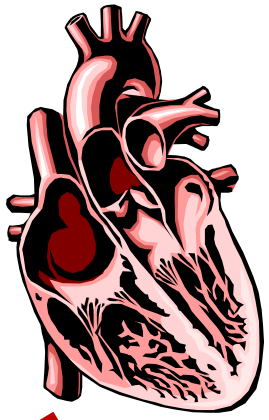
Pathogenesis of Ascites and Hepatorenal Syndrome



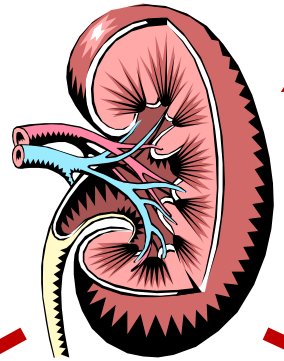
Cirrhosis & Portal HT
(Release of Nitric Oxide)

Splanchnic Vasodilatation

(Pooling of Blood)



Reduced arterial blood volume



Local Vasodilators (PGE2)

Renin-angiotensin activation

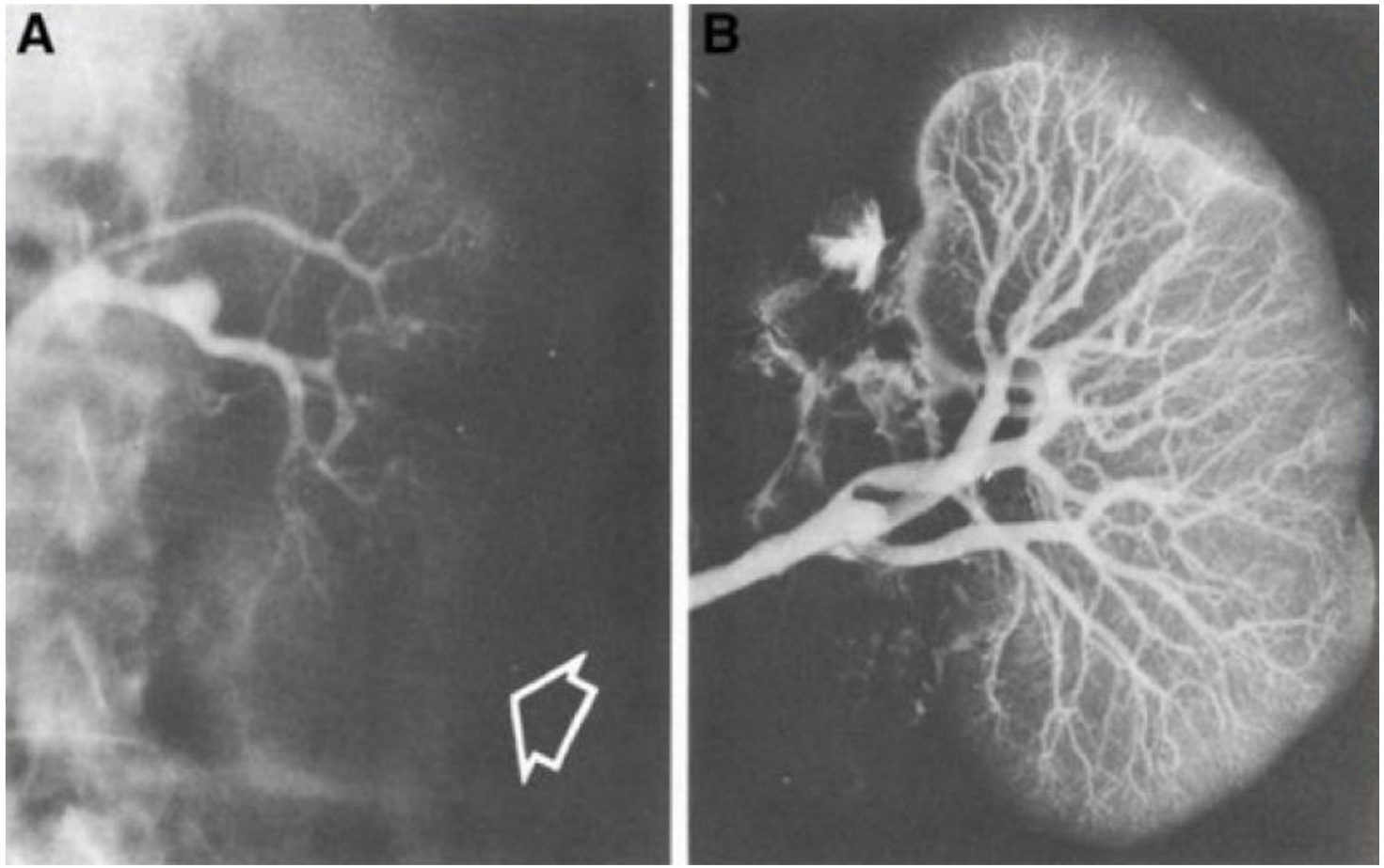
Sympathetic Nervous System

Reduced renal blood flow & Glomerular Filtration Rate

Hepatorenal Syndrome

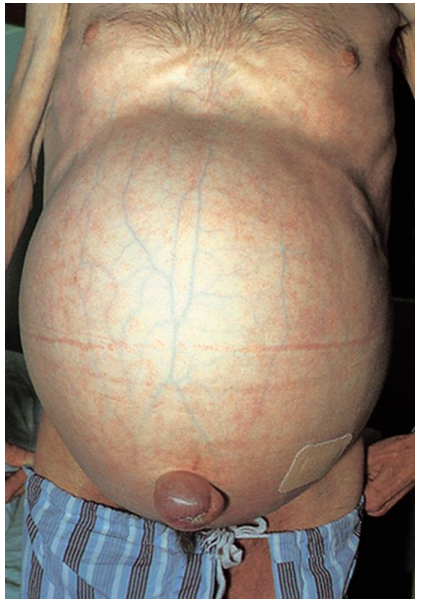
Hepatorenal Syndrome

Intense renal vasoconstriction secondary to activation of a number of vasoconstrictor mechanisms and an imbalance between intra-renal vasodilators and vasoconstrictors.



A – Angiogram in a patient with cirrhosis and HRS demonstrating intense vasoconstriction and poor arterial filling.
B – Post-mortem angiogram in same kidney demonstrating intact renal vasculature

Epstein O et al. 1970



Ascites formation

Portal Hypertension

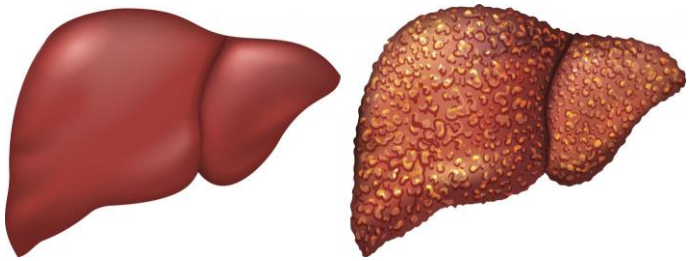
Splanchnic arteriolar vasodilatation

Arterial underfilling activating in salt and water retaining mechanisms

Increase in capillary pressure and permeability

Salt and water retention

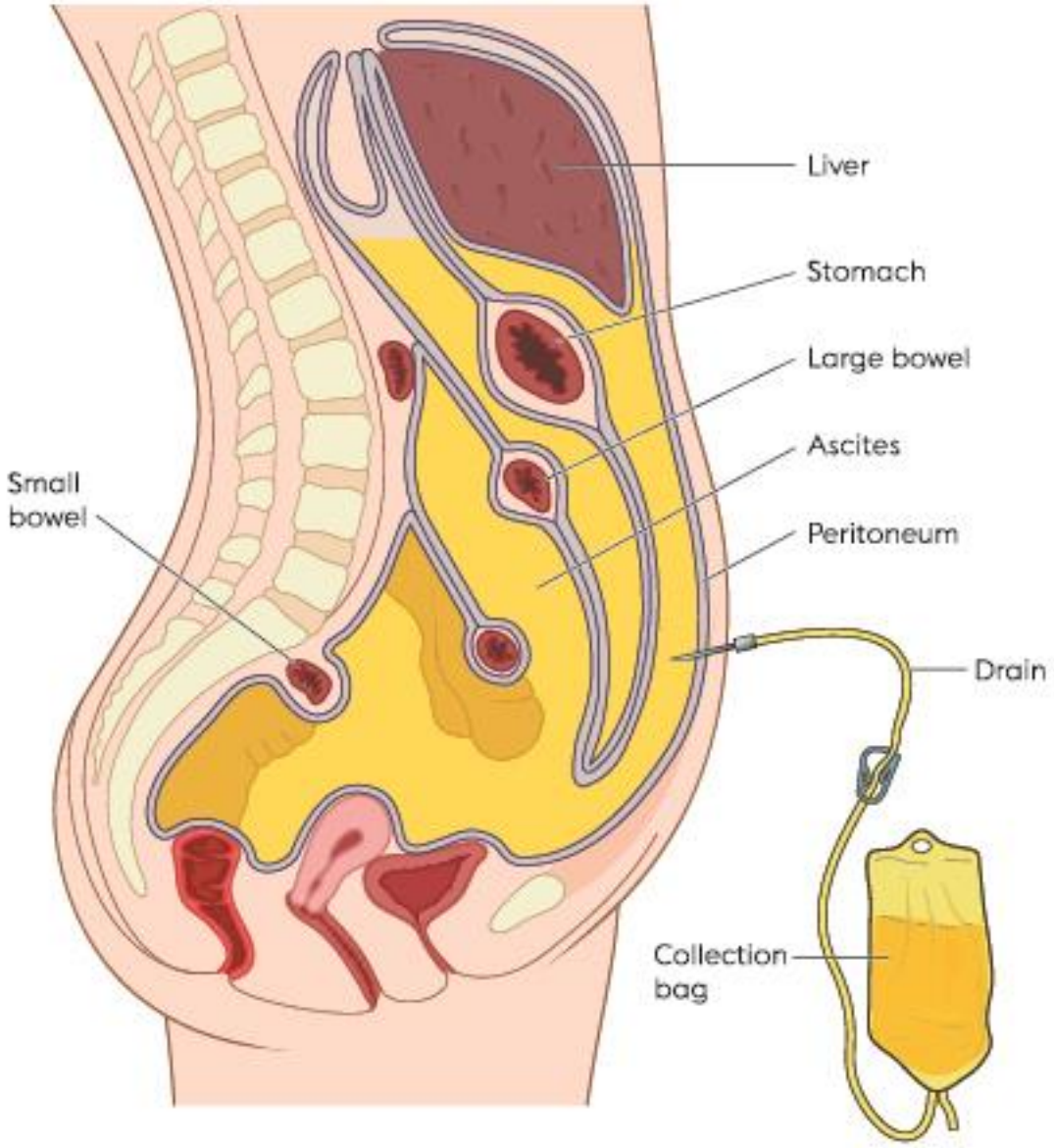
Lymph formation>lymph return



Intrahepatic vascular resistance

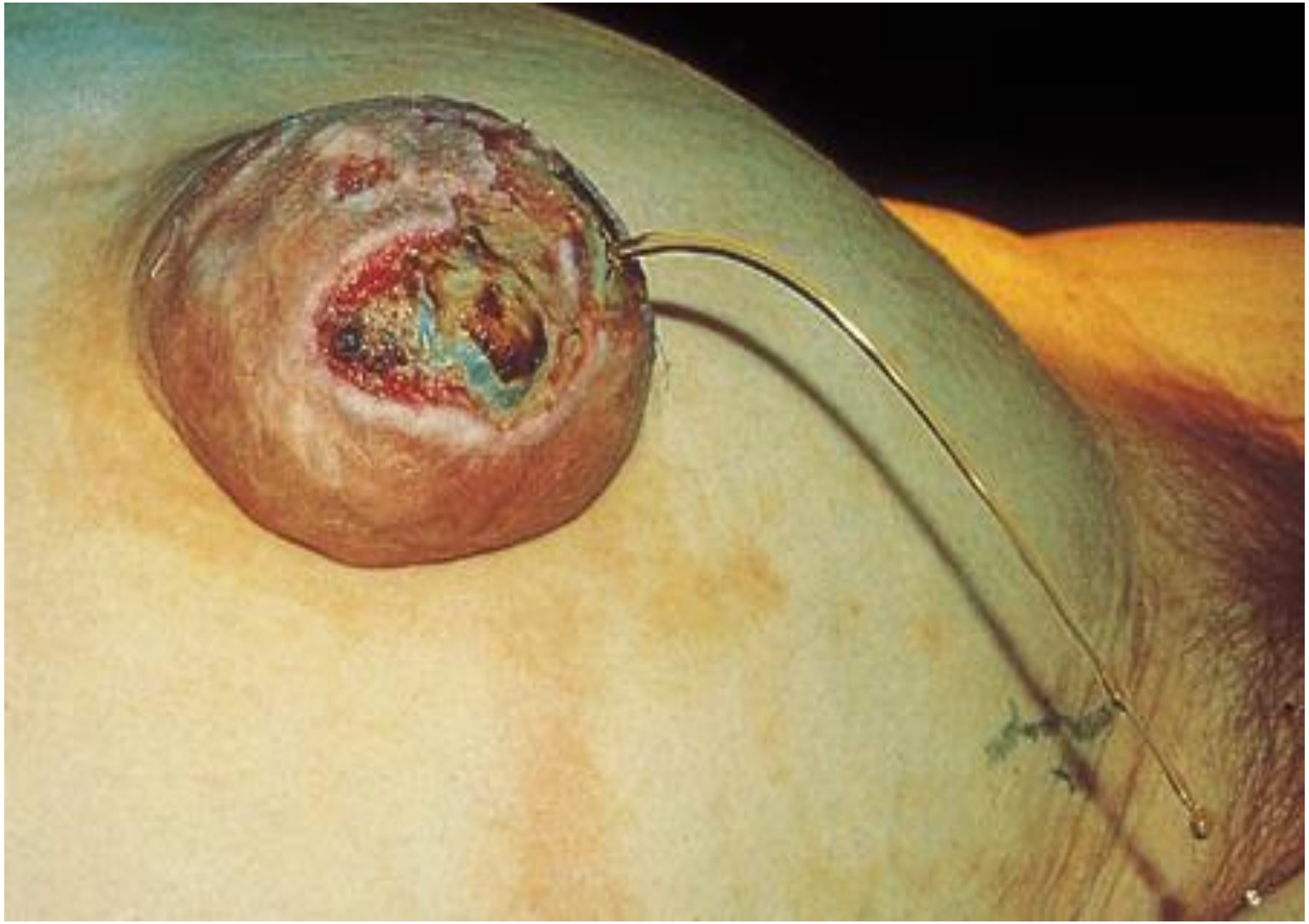
(Release of vasodilator substances)

Ascites

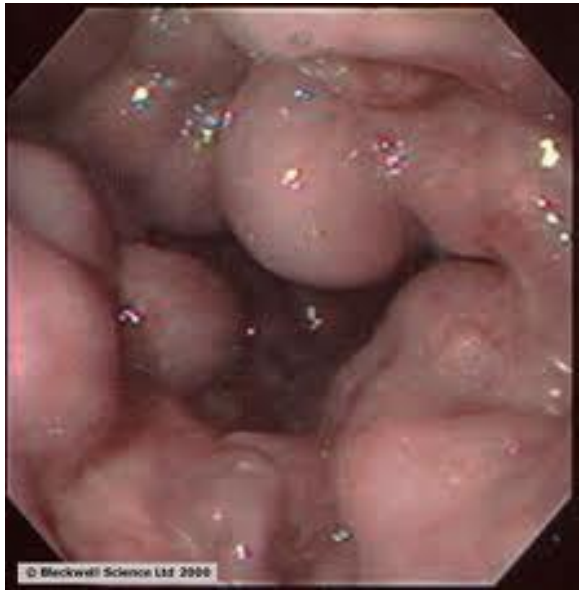

Liver
Stomach
Large bowel
Ascites
Peritoneum
Small bowel
Drain
Collection bag

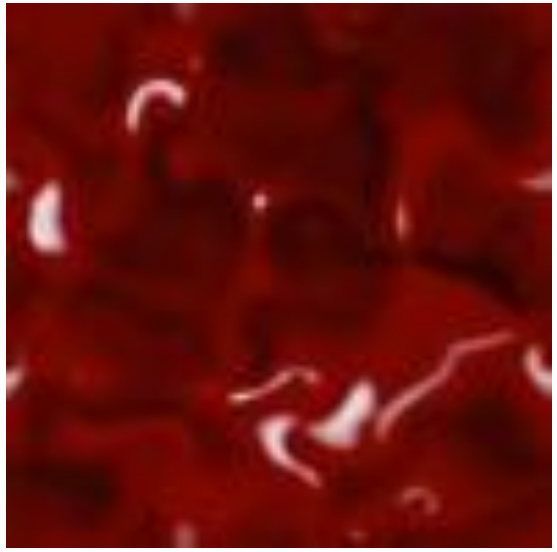

GRIFOLS
Albumin (Human) U.S.P.
Albutein® 5%
5%
GRIFOLS
GRIFOLS
GRIFOLS
Albumin (Human) U.S.P.
Albutein® 5%
5%

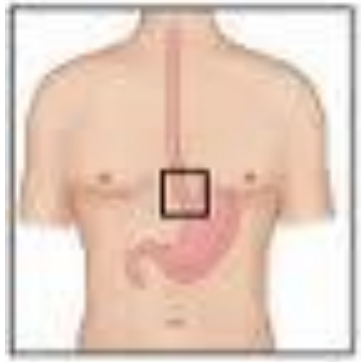
Ruptured umbilical hernia



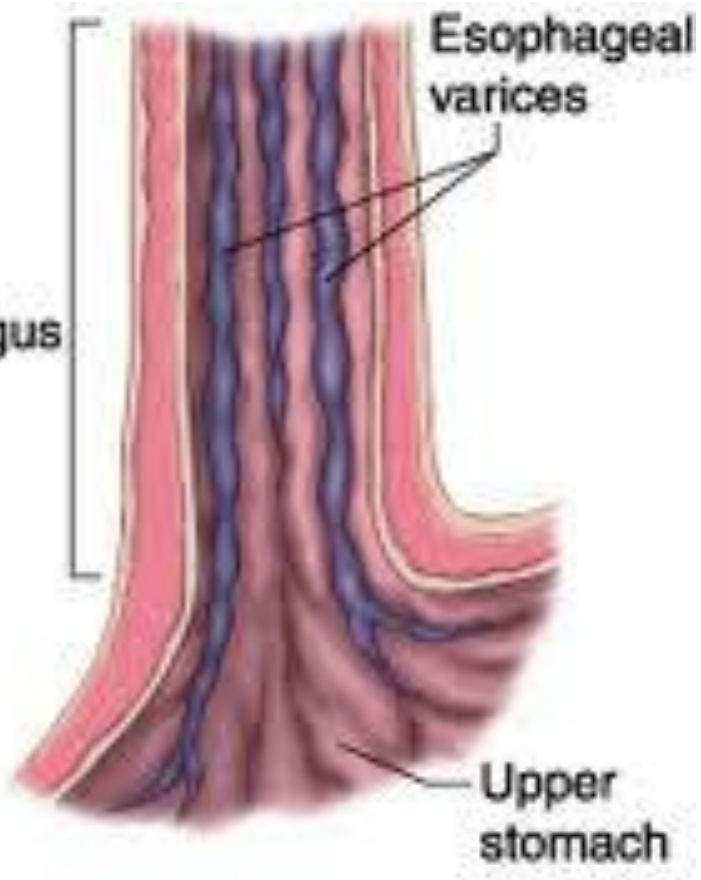
Varices



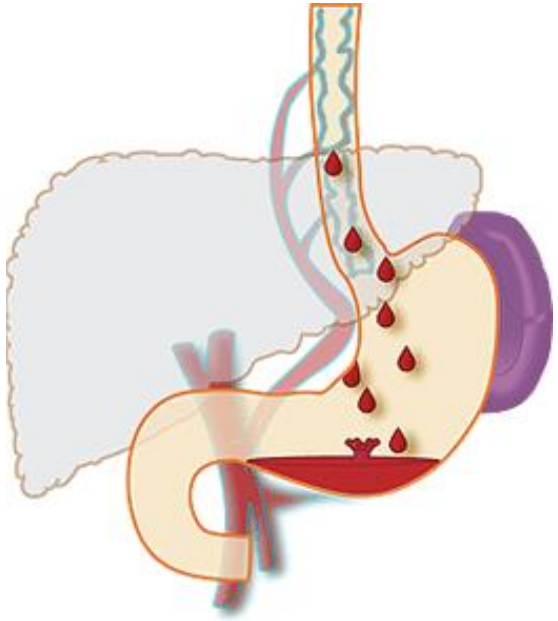




Lower esophagus



Portal Pressure >12mmHg

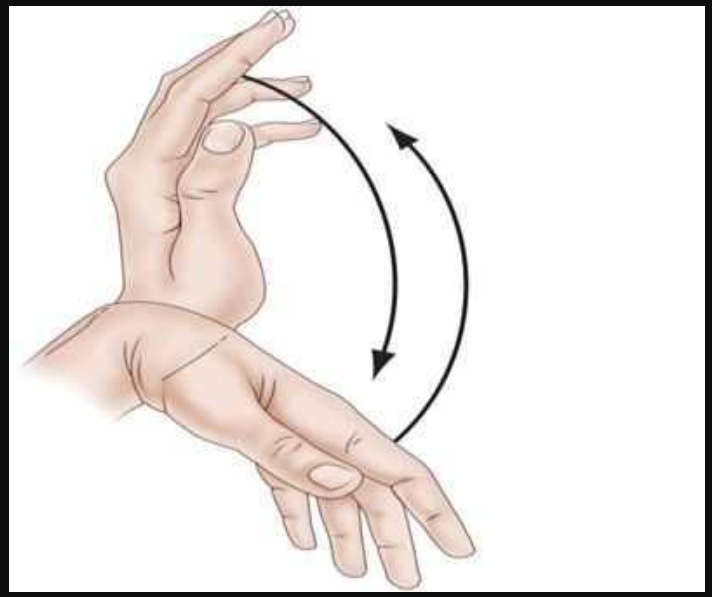


15% Bleed Annually

Hepatic Encephalopathy

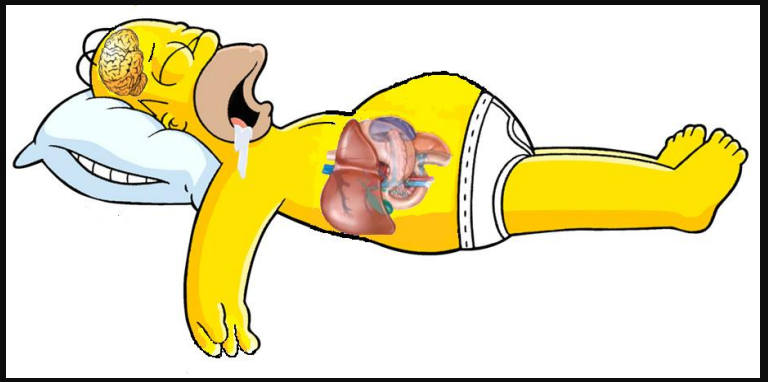
- 60-80% of patients with cirrhosis have evidence of neurocognitive dysfunction on neuropsychological function testing

- ❑ Short term memory loss
- ❑ Slow reaction times
- ❑ Impairs ability to drive and do fine motor tasks

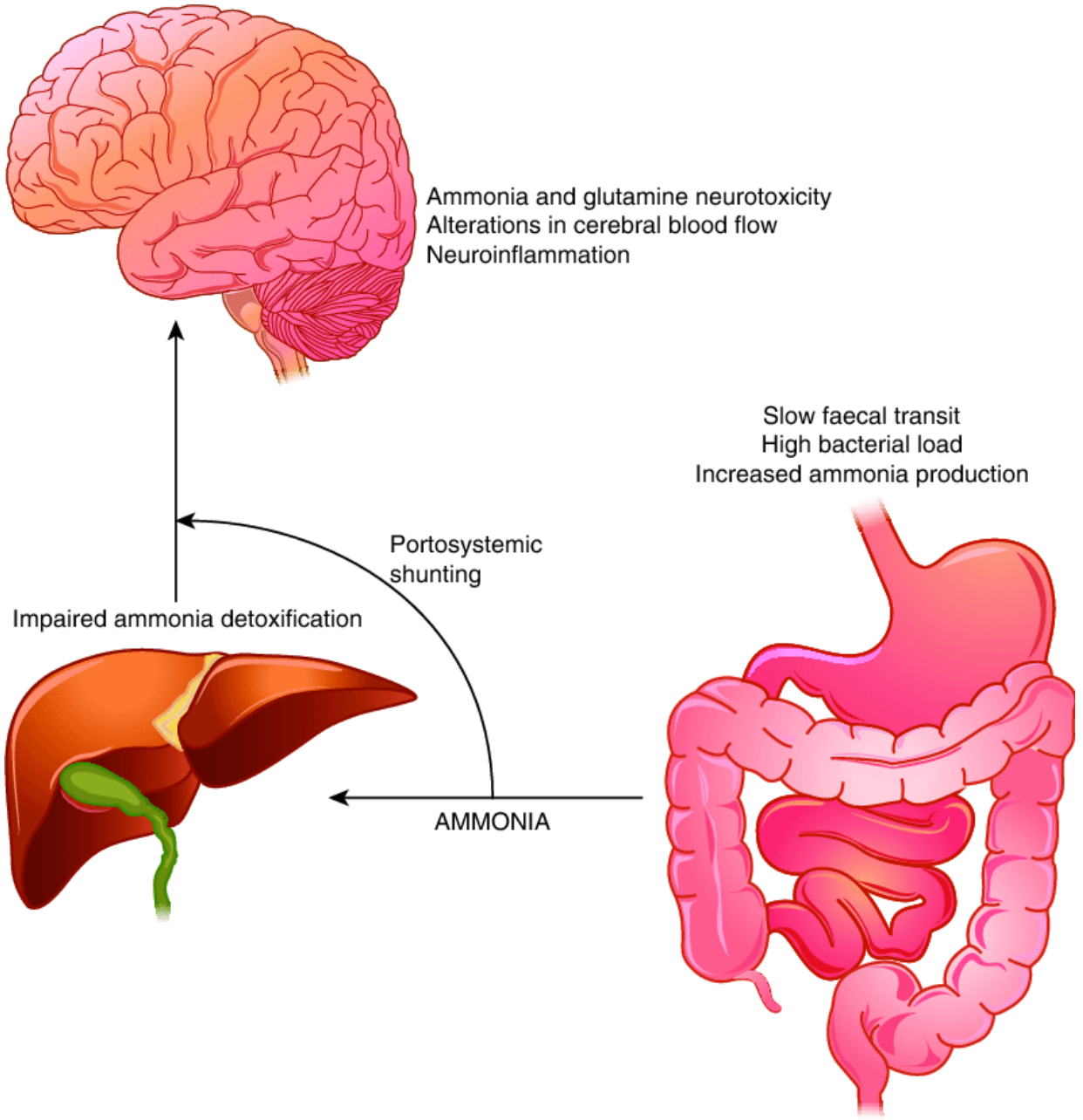


- Spectrum of hepatic encephalopathy

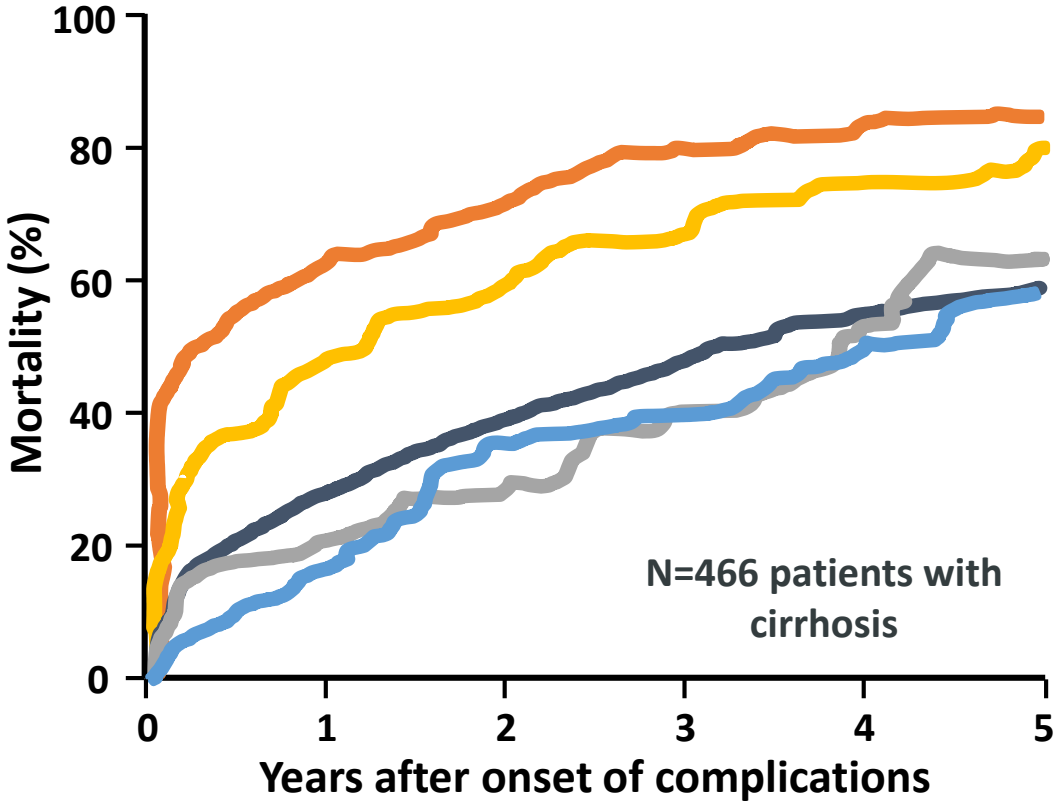
- ❑ Confusion
- ❑ Aggression
- ❑ Asterixis (liver flap)
- ❑ Disorientation
- ❑ Drowsiness
- ❑ Coma



Hepatic Encephalopathy



Mortality rates over 5 years for cirrhotic patients



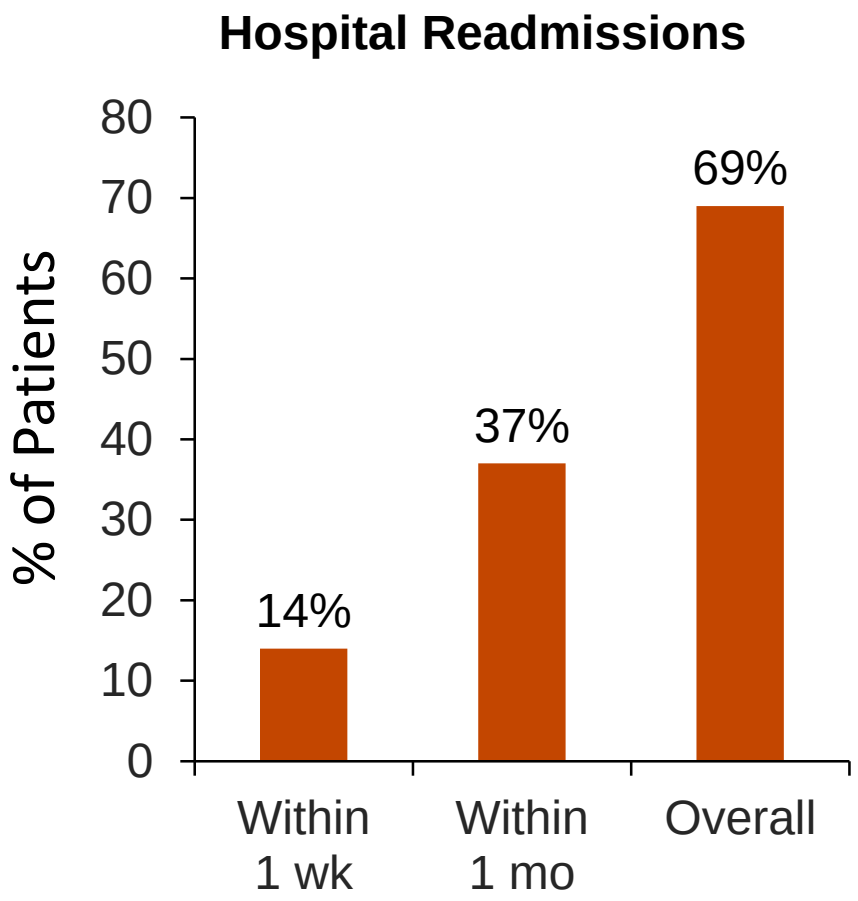
Complication of cirrhosis:

- Hepatic encephalopathy
- Ascites + variceal bleeding
- Ascites alone
- Variceal bleeding alone
- No complications

- **One-year mortality was 17% among patients with no initial complications and 64% following HE**

Jepsen P, *et al*. *Hepatology* 2010 51:1675–82.

Hospital re-admissions among patients with decompensated cirrhosis are common



- Retrospective study of 402 patients from an academic transplant centre
- Follow-up time censored at death, elective admissions such as transplant or post-procedure observation, or the date of last clinic note; median follow-up was 203 days
- Population included cirrhotic patients hospitalized for ascites, spontaneous bacterial peritonitis, renal failure, hepatic encephalopathy, or variceal hemorrhage
- Median time to first readmission was 67 days
- Median number of readmissions was 2 (range 0-40); overall rate was 3 hospitalizations/person-years

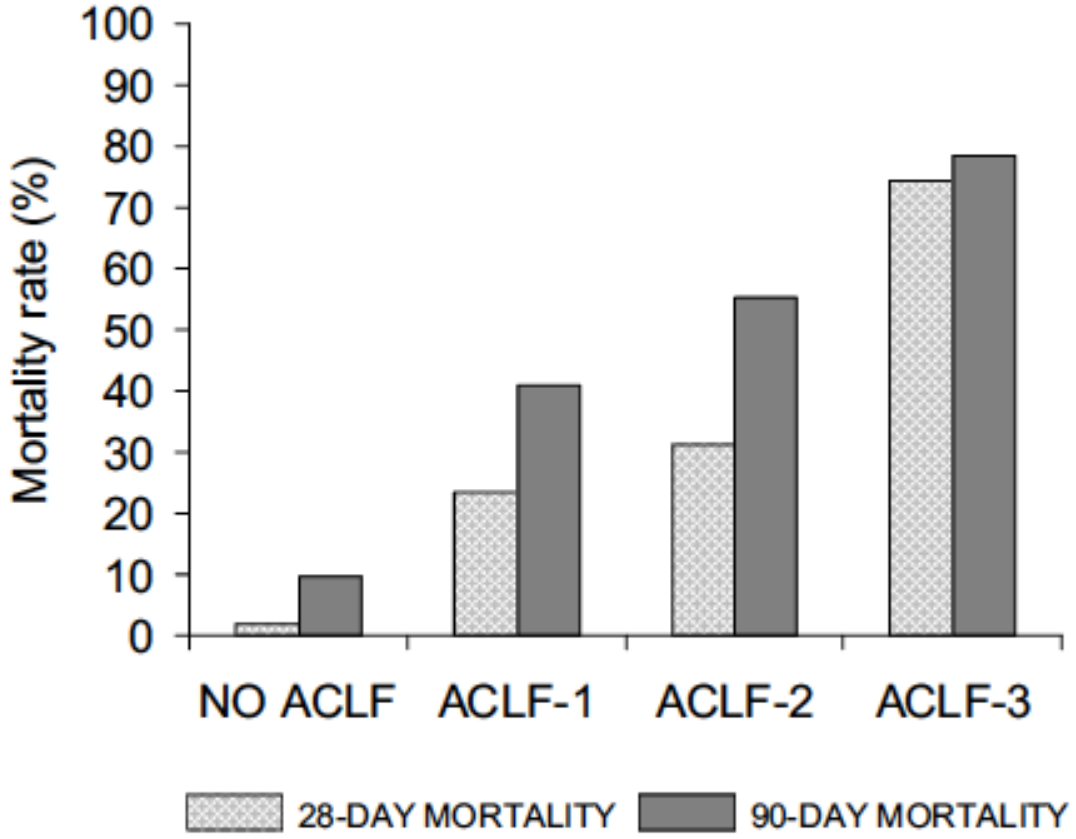
Volk ML et al. *Am J Gastroenterol* 2012;107:247-252.

Acute on Chronic Liver Failure

Three major features characterize this syndrome:

1. It occurs in the context of intense systemic inflammation
2. Frequently develops in close temporal relationship with proinflammatory precipitating events (e.g., infections or alcoholic hepatitis)
3. Is associated with single- or multiple-organ failure.

CANONIC STUDY



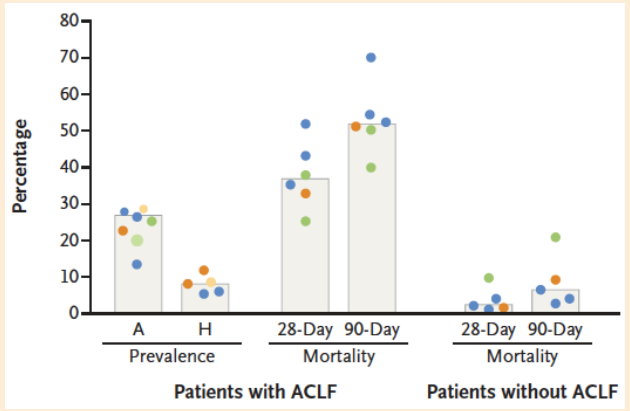
Supplementary Figure 2. Mortality rate at 28 days and 90 days according to the grade of ACLF.

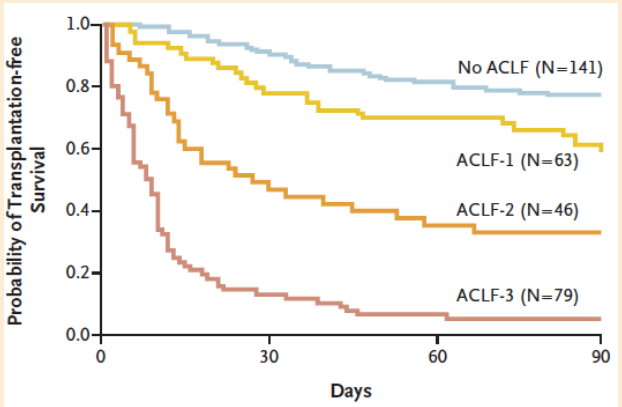
Moreau et al. Gastroenterology 2013

ACLF

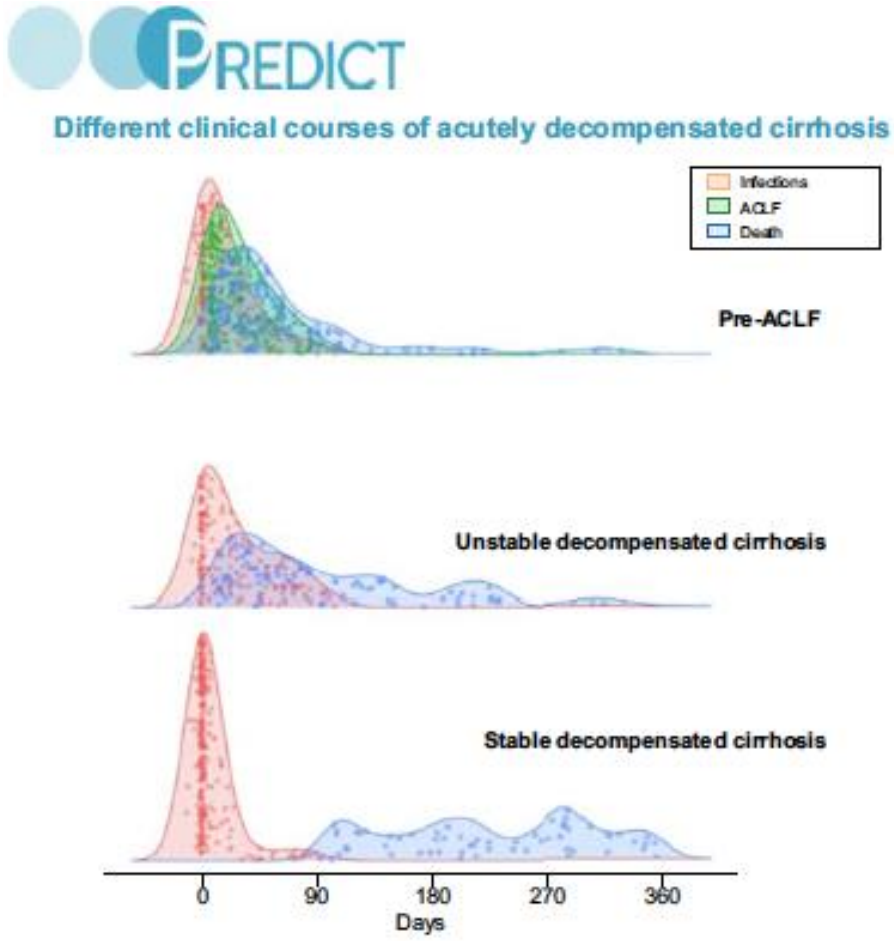
Organ System	1 Point	2 Points	3 Points
Liver	Bilirubin <6 mg/dl	Bilirubin 6.0–11.9 mg/dl	Bilirubin ≥12 mg/dl
Kidney	Creatinine <1.5 mg/dl Creatinine 1.5–1.9 mg/dl	Creatinine 2.0–3.4 mg/dl	Creatinine ≥3.5 mg/dl or RRT
Brain (West Haven criteria)	Grade 0	Grade 1–2	Grade 3–4
Coagulation	INR <2.0	INR 2.0–2.4	INR ≥2.5
Circulation	MAP ≥70 mm Hg	MAP <70 mm Hg	Vasopressor requirement
Respiration	Pao_2/Fio_2 >300 Spo_2/Fio_2 >357	Pao_2/Fio_2 201–300 Spo_2/Fio_2 215–357	Pao_2/Fio_2 ≤200 Spo_2/Fio_2 ≤214

EASL CLIF Score





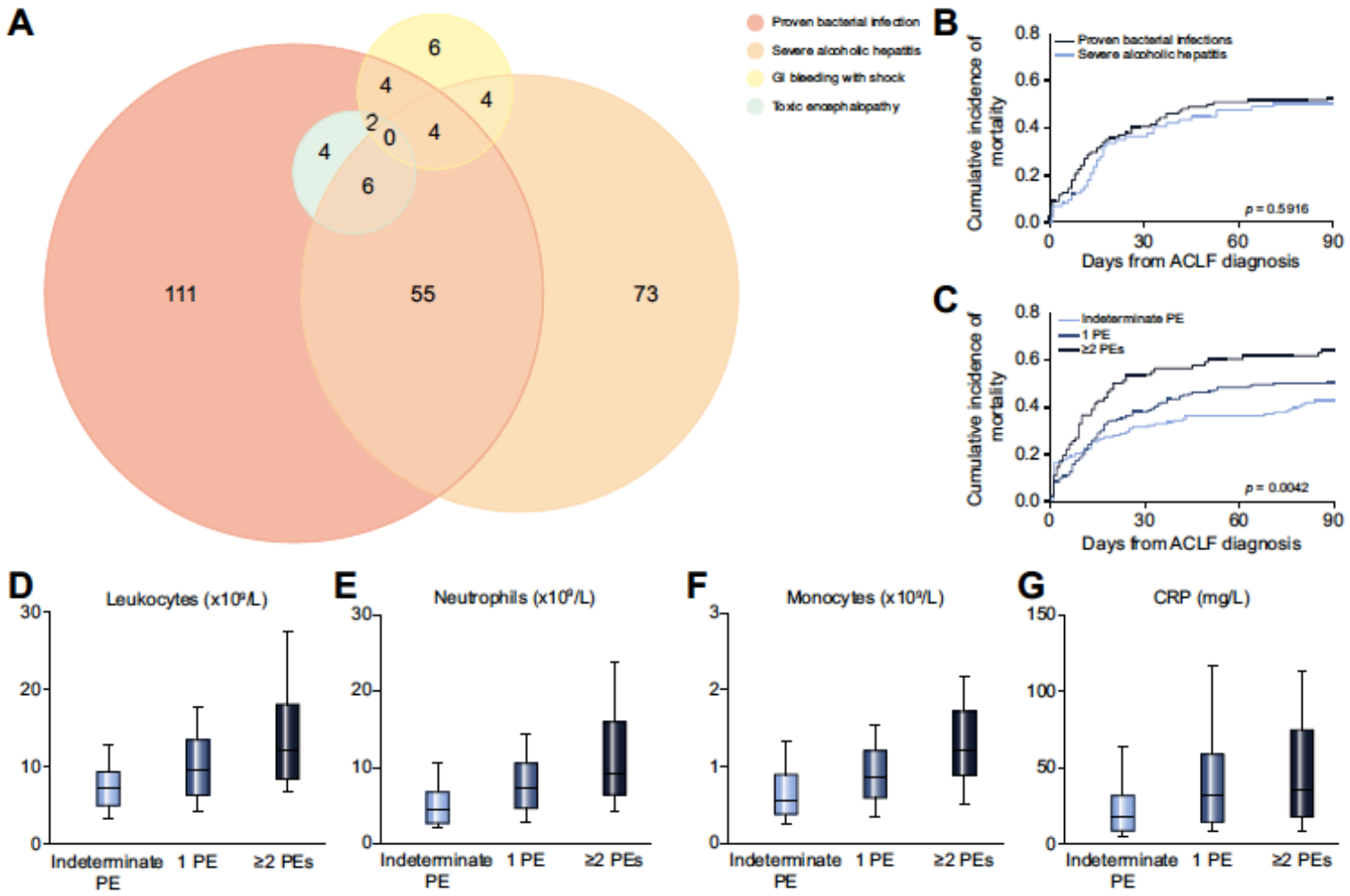
The PREDICT study uncovers three clinical courses of acutely decompensated cirrhosis that have distinct pathophysiology



- Patients with acutely decompensated cirrhosis without ACLF develop 3 different clinical courses.
- Patients with pre-ACLF develop ACLF within 90 days and have high systemic inflammation and mortality.
- Patients with unstable decompensated cirrhosis suffer from complications of severe portal hypertension.
- Patients with stable decompensated cirrhosis have less frequent complications and lower 1-year mortality risk.

Trebicka J et al. Journal of Hepatology 2020

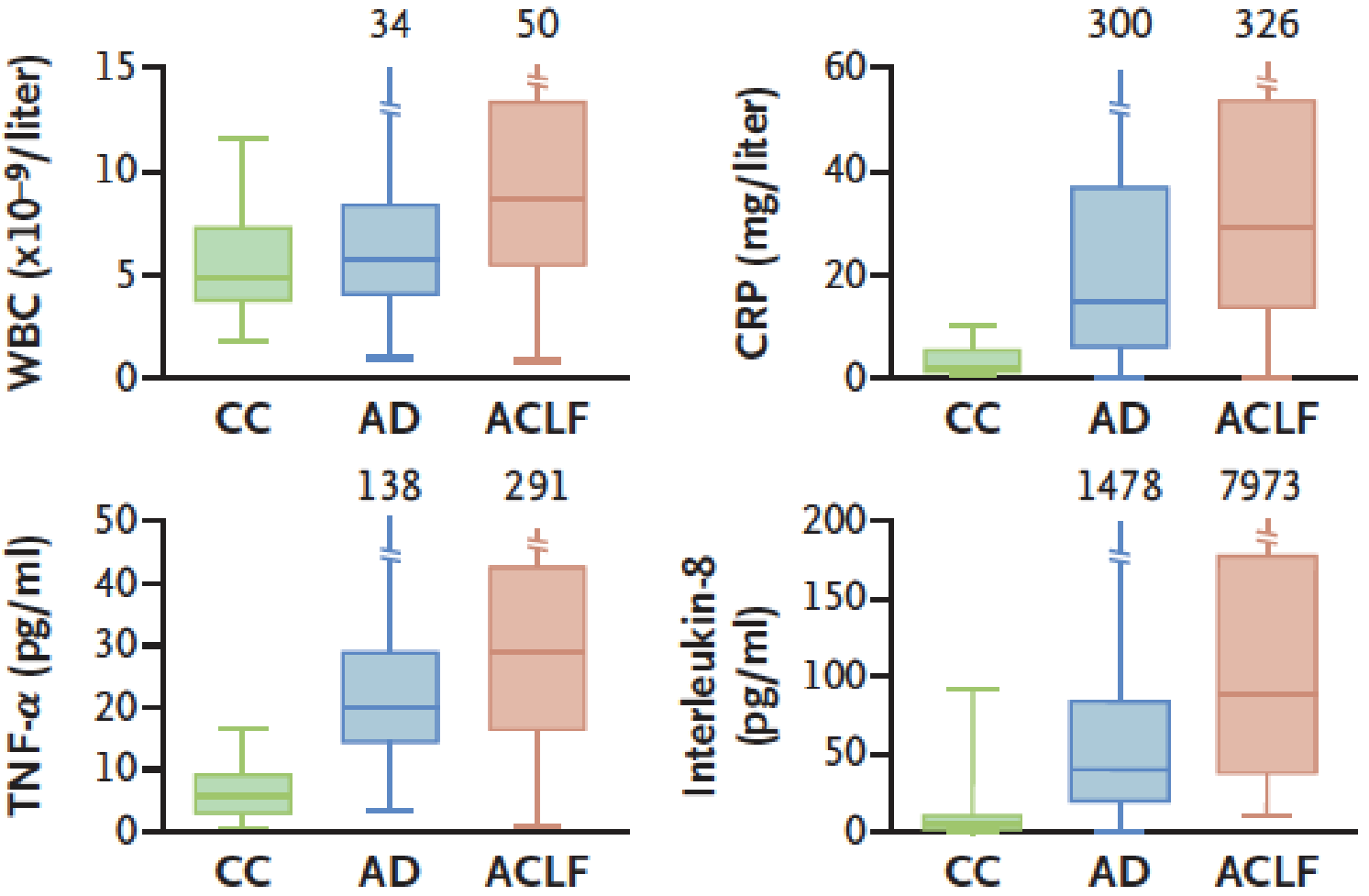
Infection as a precipitant of acute decompensation /ACLF



PREDICT identifies precipitating events associated with the clinical course of acutely decompensated cirrhosis

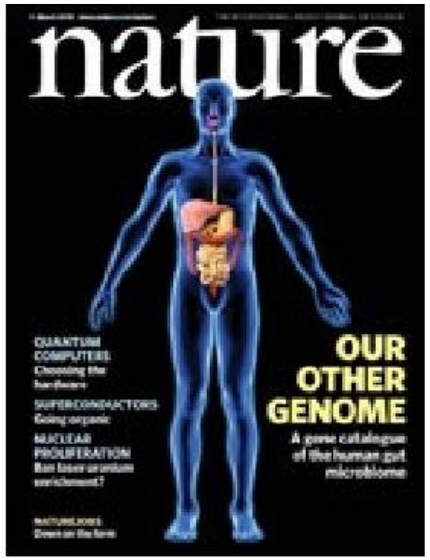
Trebicka J et al. Journal of Hepatology 2021

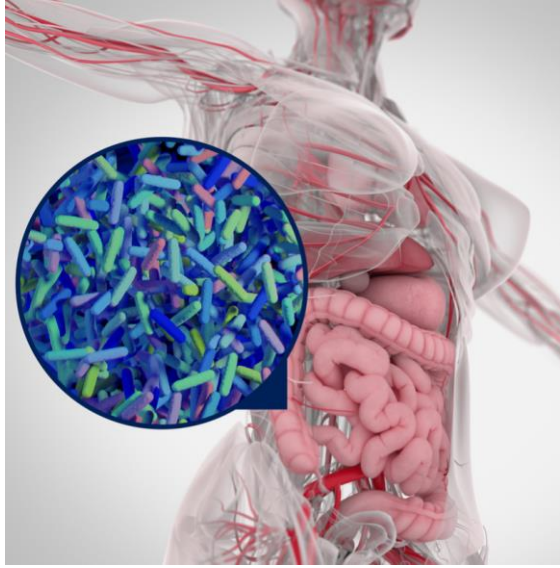
Role of inflammation and infection as a driver of ACLF



Casulleras M et al. Cells 2020

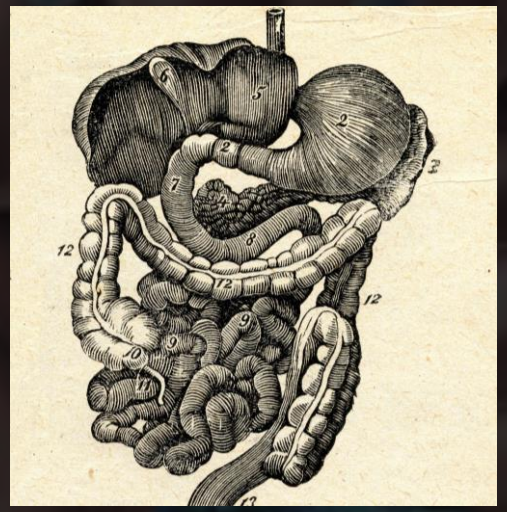
The rise of the gut microbiome

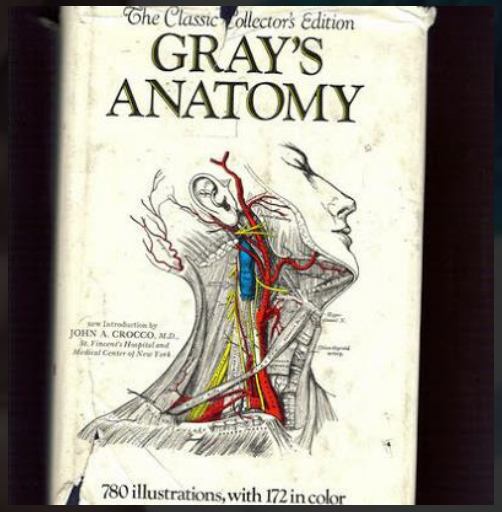




Your **gut microbiome** is a vast community of trillions of bacteria and fungi that inhabit your gastrointestinal tract, and have a major influence on your metabolism, body weight, propensity to illness, immune system, appetite and mood.

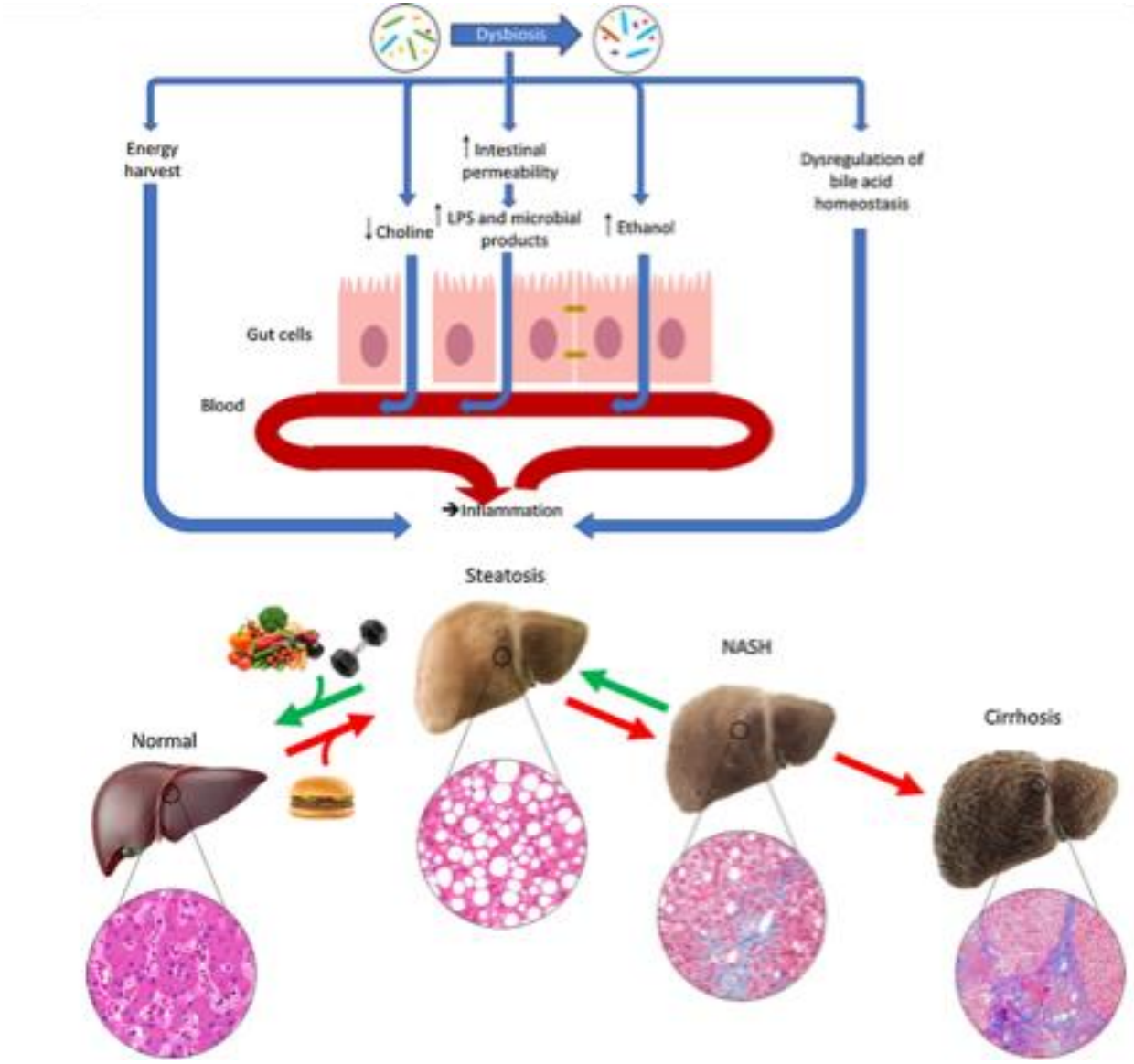
The gut and liver are intimately linked





As the liver receives the majority of its blood supply directly from the microbiota laden gut, via the portal vein, inherently the gut microbiome and the liver are intimately linked.

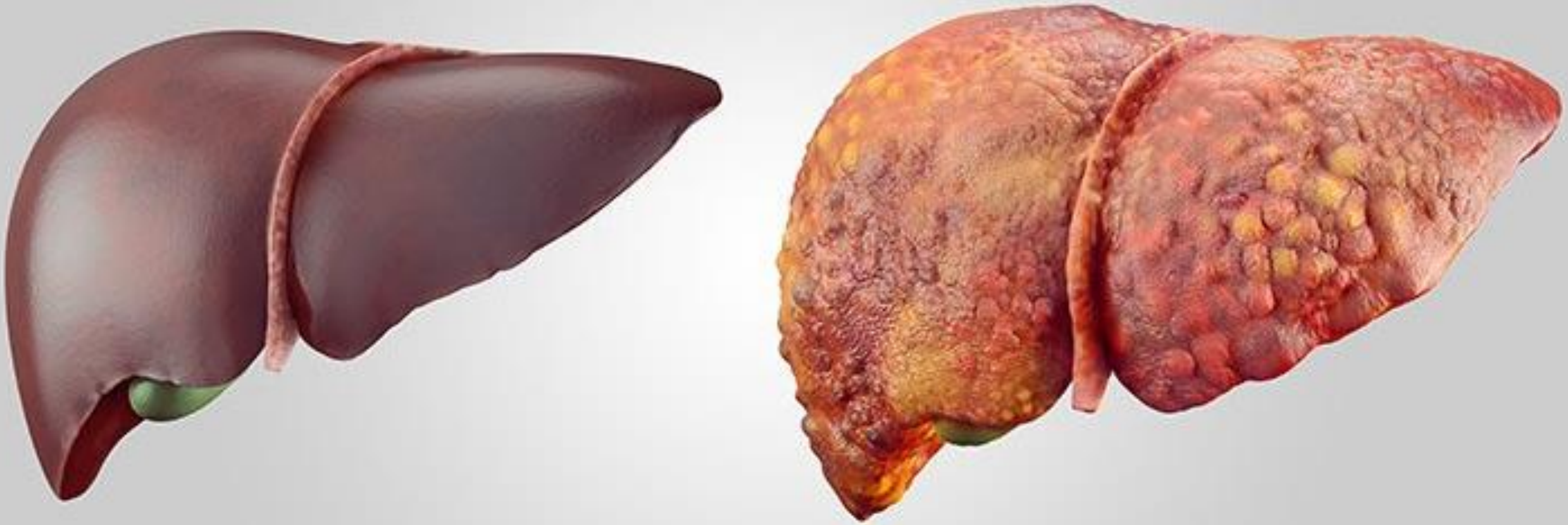
Mechanisms linking the microbiome to the development of hepatic steatosis



Intestinal microbiota can contribute to the development of hepatic steatosis through a variety of mechanisms:

1. Appetite regulation
2. Energy extraction from diet.
3. Endotoxin release from the cell wall of Gram-negative bacteria increases peripheral insulin resistance leading to an increased influx of free fatty acids from the adipose tissue to the liver.
4. Ethanol production can be used as a substrate for lipogenesis in the liver but can also affect the gut barrier
5. SCFA synthesis and bile acid homeostasis are perturbed.

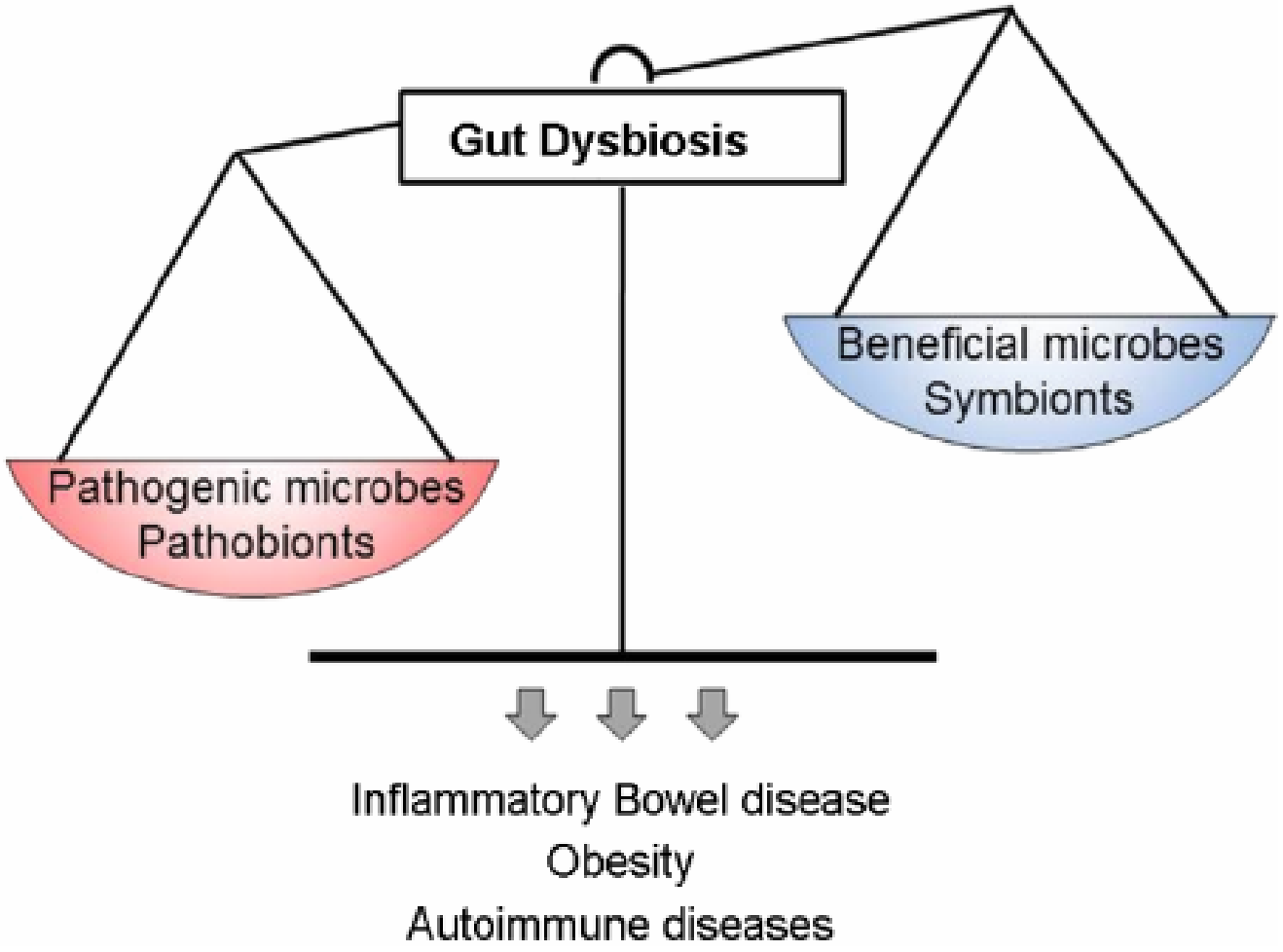
Safari Z and Gerard P. CMLS 2019); 76:1541–1558



Gut microbiome in cirrhosis

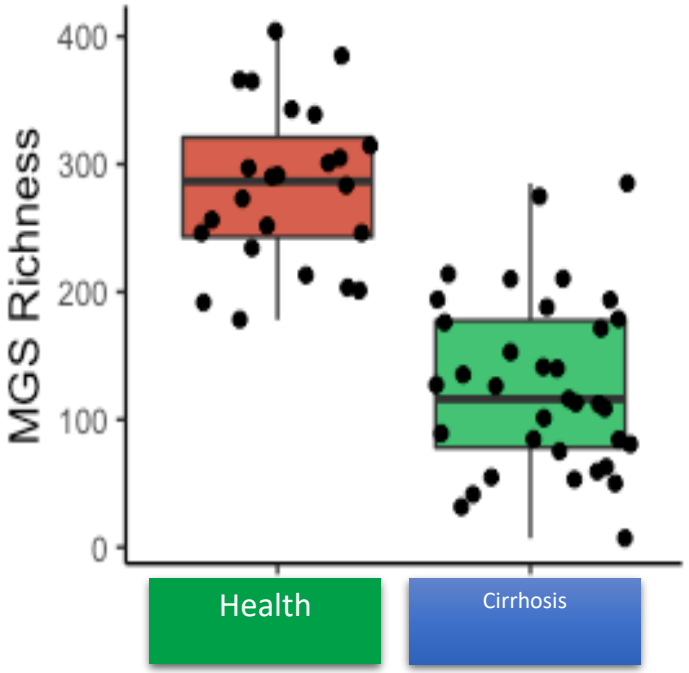
‘Gut dysbiosis’

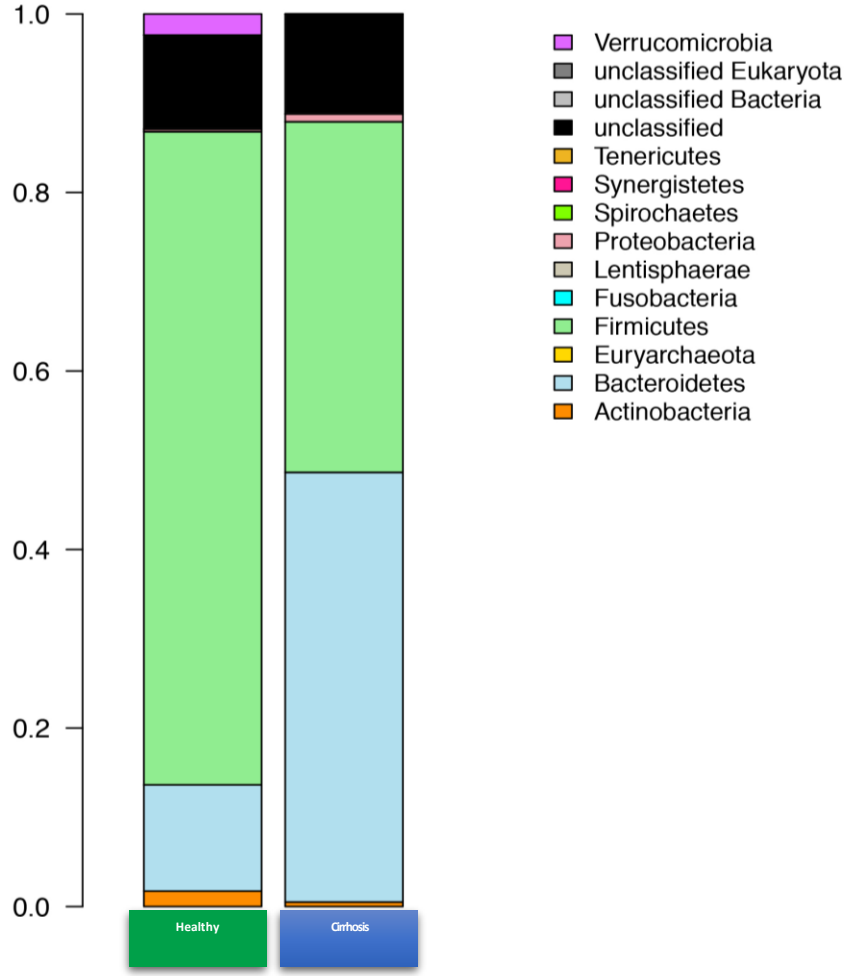
- Lose beneficial microbes in your gut
- Opportunistic bacteria take over (potentially harmful bacteria which are kept in check by beneficial microbes)
- You have less diversity in your gut



Imbalance of bacteria in your gut

Stool microbial diversity is reduced in cirrhosis



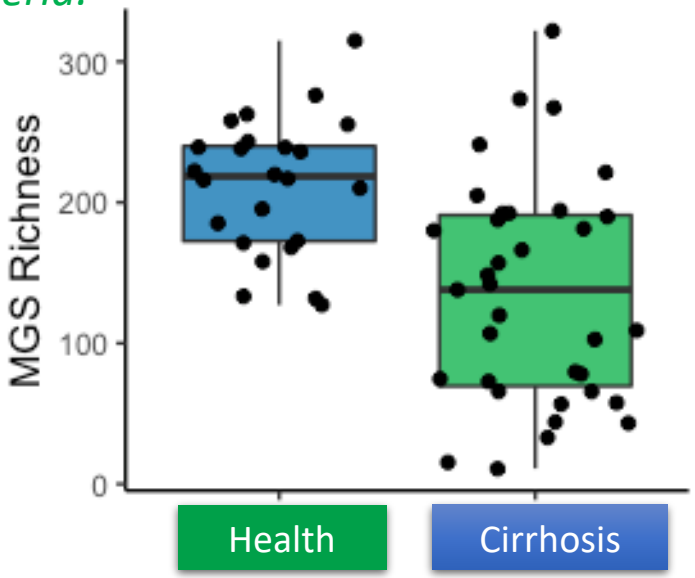


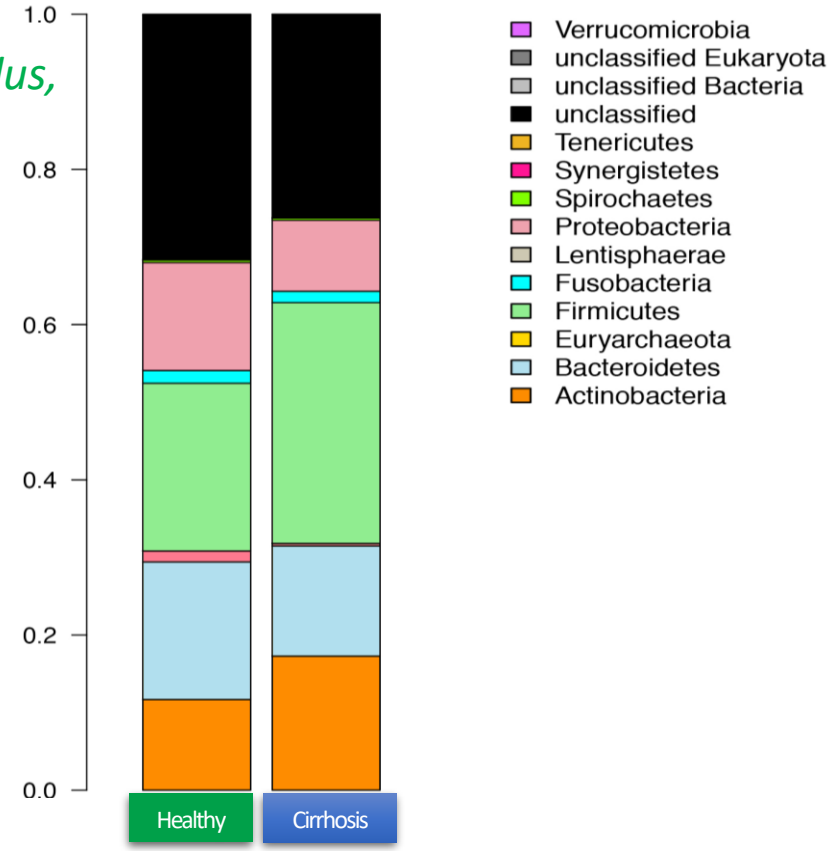
- Higher abundance of bacteroidetes
- Reduction in actinobacteria and firmicutes in cirrhosis

Patel VC et al. Results of a placebo-controlled double blind randomised trial to investigate the efficacy of rifaximin-α versus placebo in improving systemic inflammation in patients with cirrhosis and chronic hepatic encephalopathy (RIFSYS Trial). Journal of Hepatology 2018; 68: S105-364. LBA 005.

Saliva microbial diversity is reduced in cirrhosis

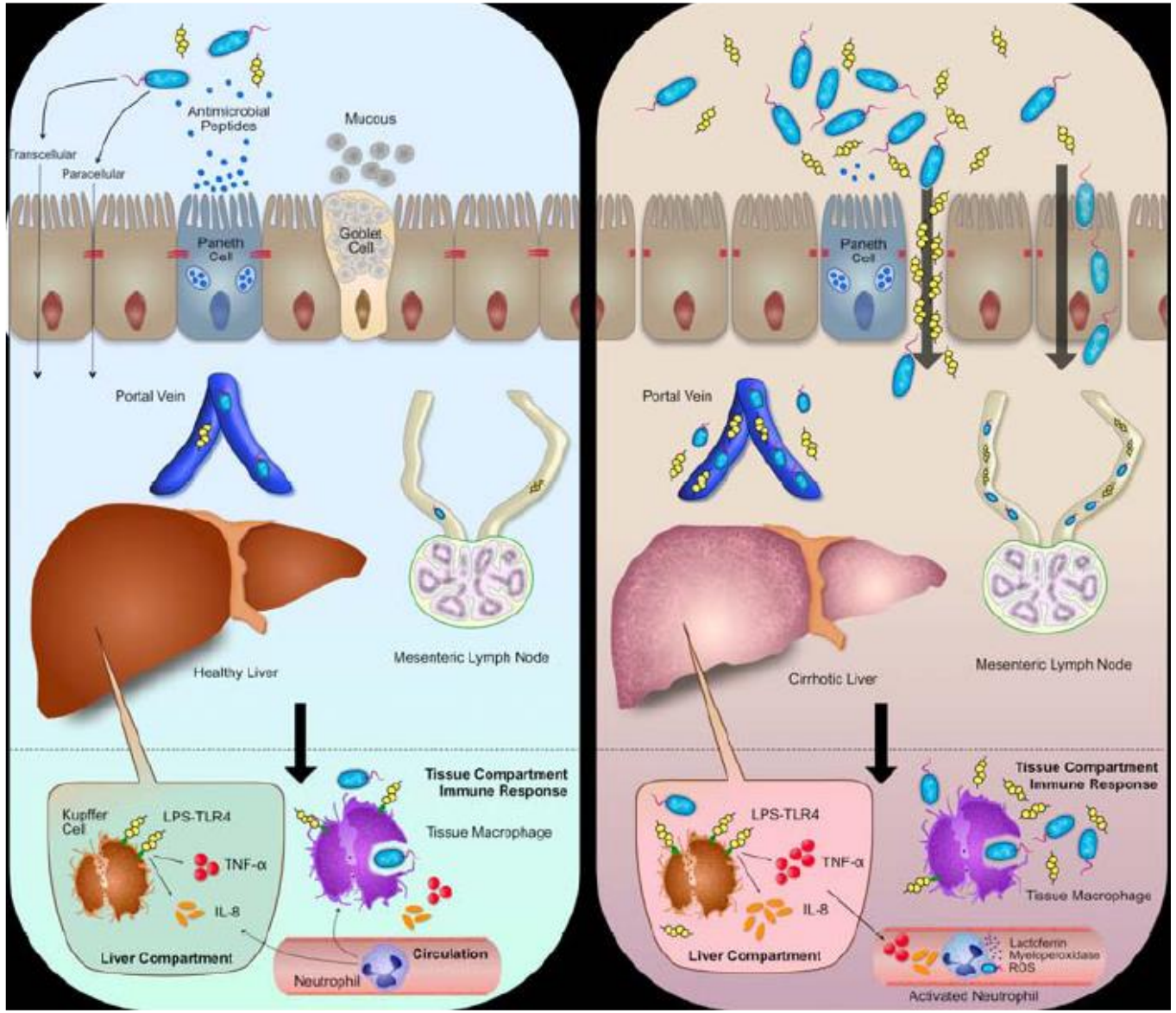
A reduction in genera associated with oral health: *Porphyromonas, Prevotella, Capnocytophaga, Haemophilus, and Neisseria.*





- Increase in abundance of actinobacteria and firmicutes
- Reduction in bacteroides, proteobacteria and fusobacterium

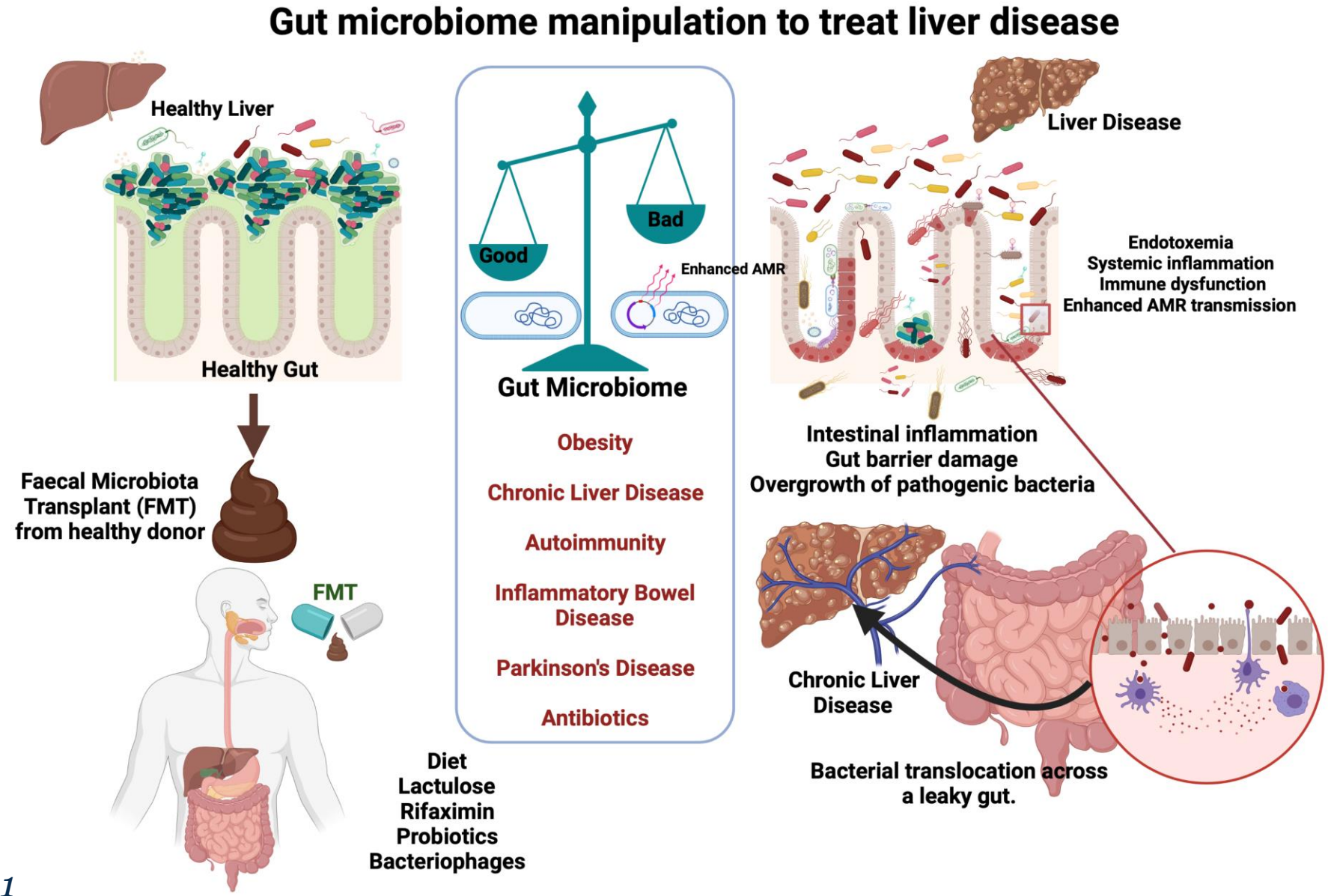
Patel VC et al. Results of a placebo-controlled double blind randomised trial to investigate the efficacy of rifaximin-α versus placebo in improving systemic inflammation in patients with cirrhosis and chronic hepatic encephalopathy (RIFSYS Trial). Journal of Hepatology 2018; 68: S105-364. LBA 005.



Movement of bacteria from the gut lumen to the liver in health and in cirrhosis generates inflammation

Woodhouse C et al. APT 2018;47(2):192-202.

Gut microbiome manipulation to treat cirrhosis

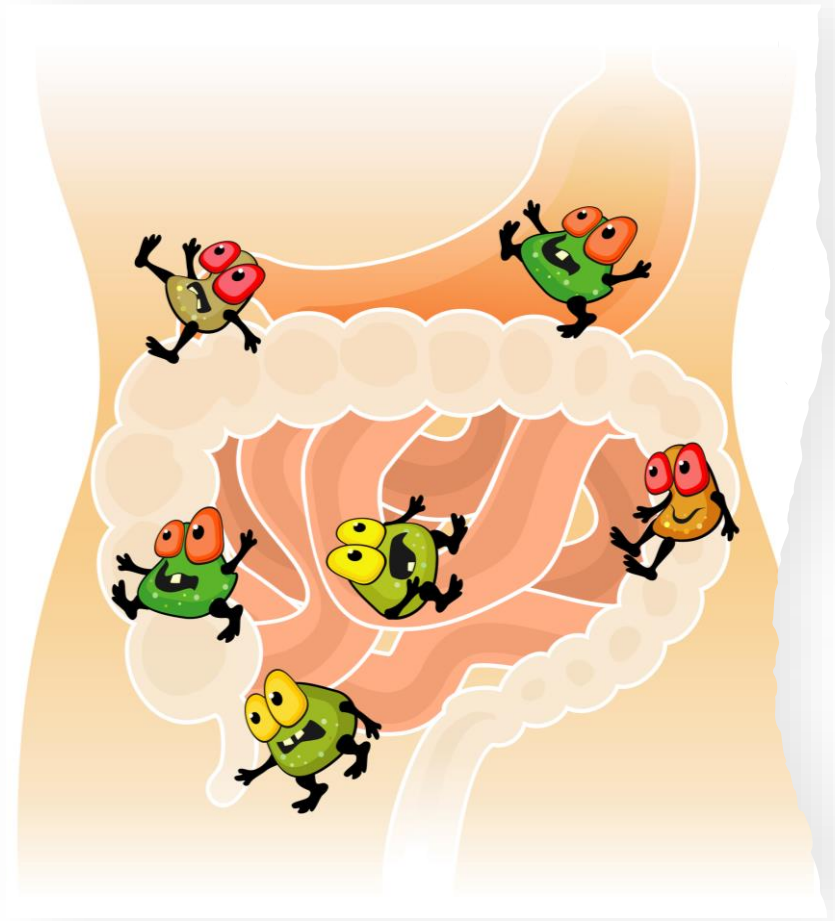


Shawcross 2021

Existing and novel therapies that manipulate the gut microbiome in cirrhosis

Existing Therapies

- ❑ Diet
- ❑ Lactulose (prebiotic)
- ❑ Antibiotics (Rifaximin)
- ❑ Probiotics

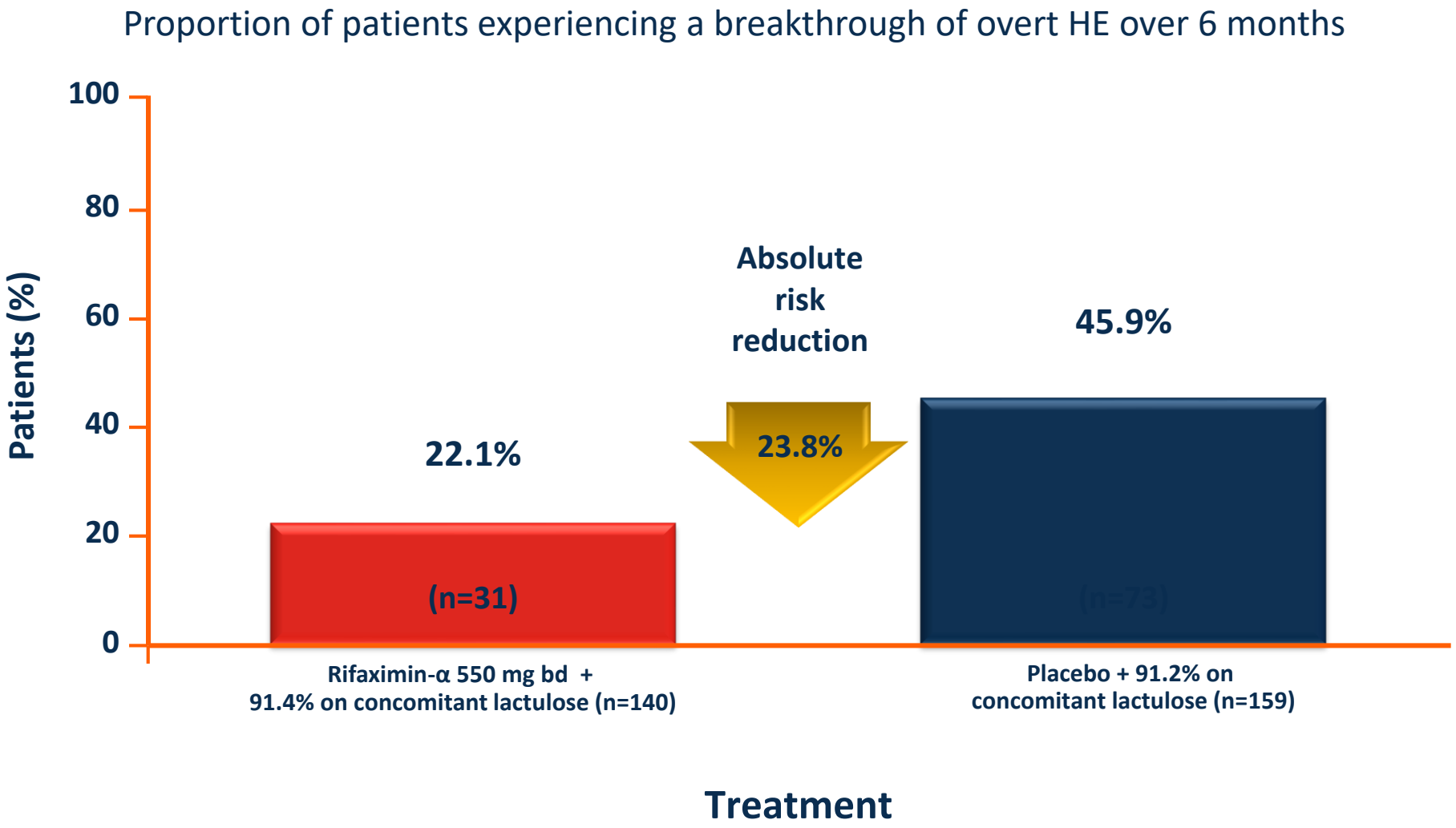


Novel therapies

- ❑ FMT
- ❑ Bacteriophages
- ❑ Carbalive™ beads
- ❑ Albumin?

Rifaximin

Secondary prevention of Hepatic Encephalopathy with rifaximin



Bass N, et al. New Engl J Med 2010;362:1071–81

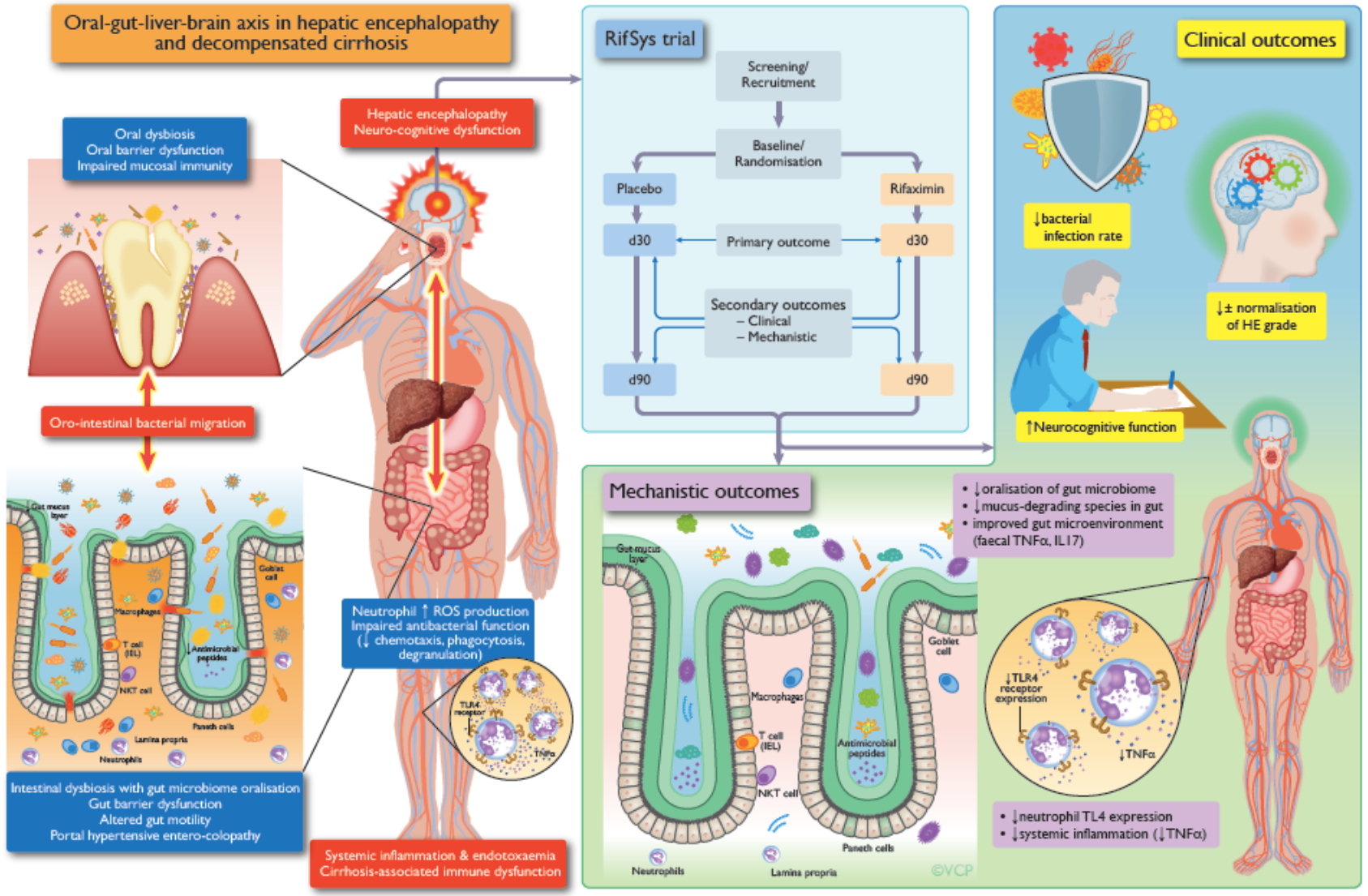
Rifaximin: Numbers Needed to Treat

Primary endpoint:
Four patients would need to be treated with Rifaximin-α 550 mg bd for 6 months to prevent one breakthrough of overt HE episode

Secondary endpoint:
Nine patients would need to be treated with Rifaximin-α 550 mg bd for 6 months to prevent one hospitalisation involving hepatic encephalopathy

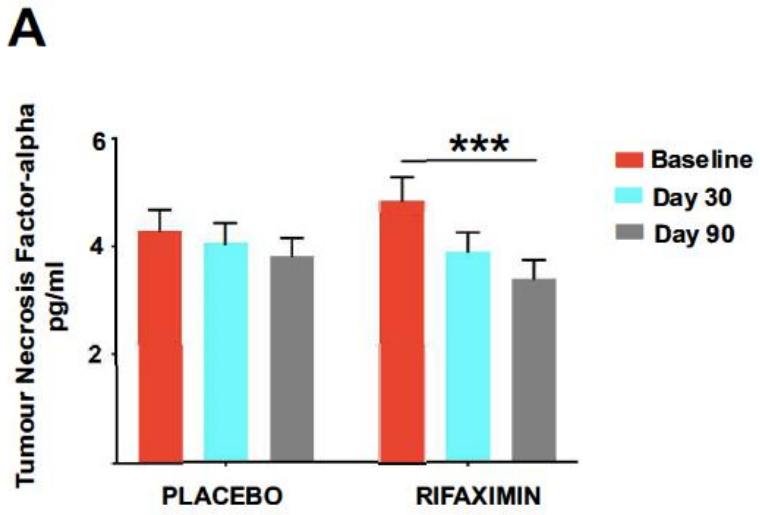
Bass N, et al. New Engl J Med 2010;362:1071–81

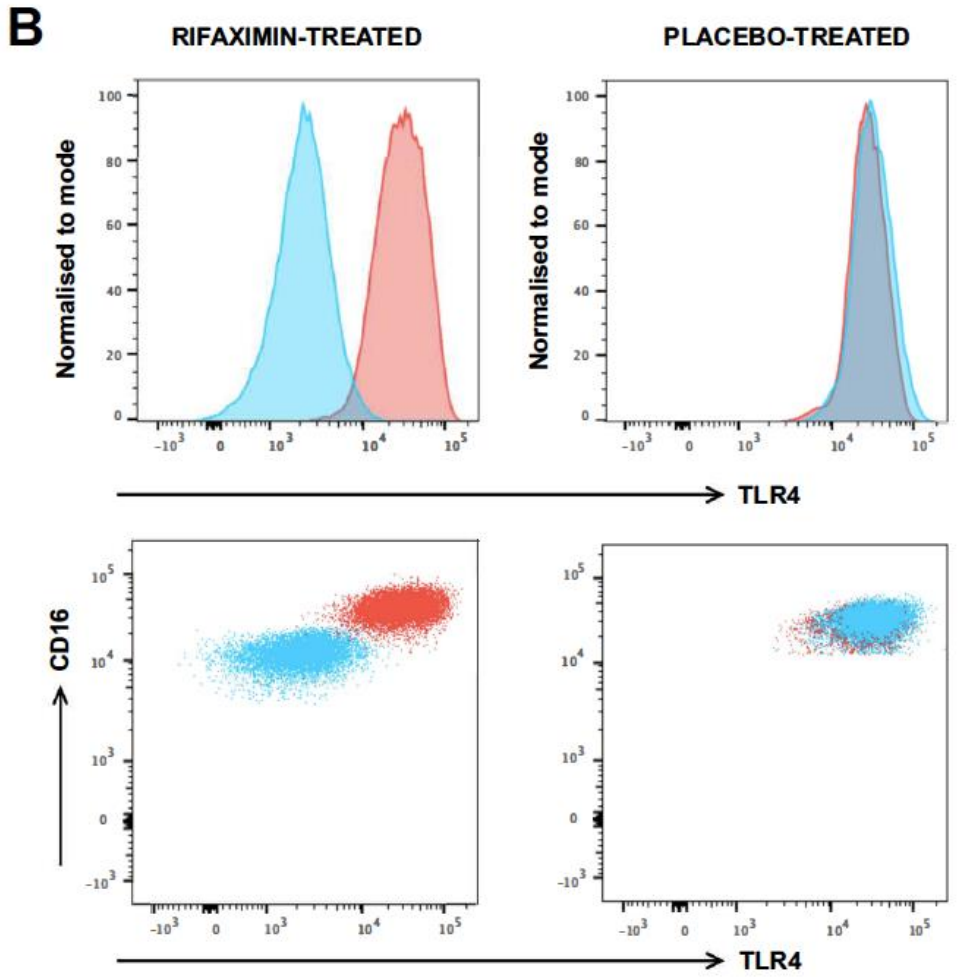
RIFSYS Trial



Patel VC, Lee S et al. Journal of Hepatology 2021 (in press)

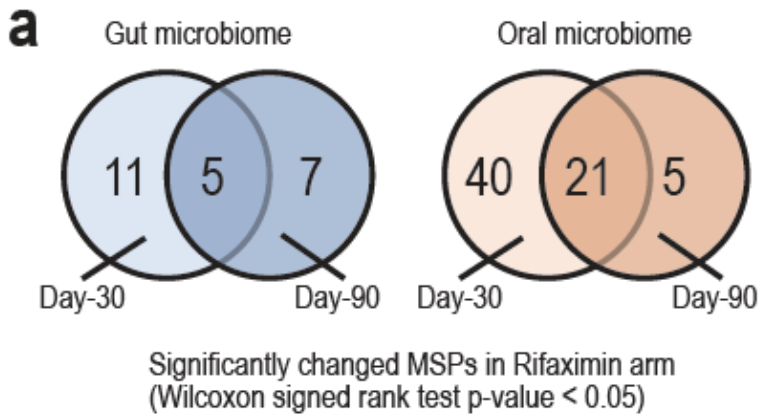
Rifaximin reduces gut-derived systemic inflammation

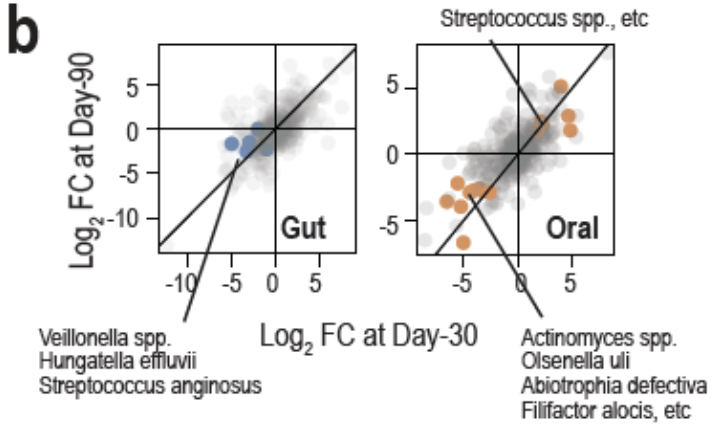


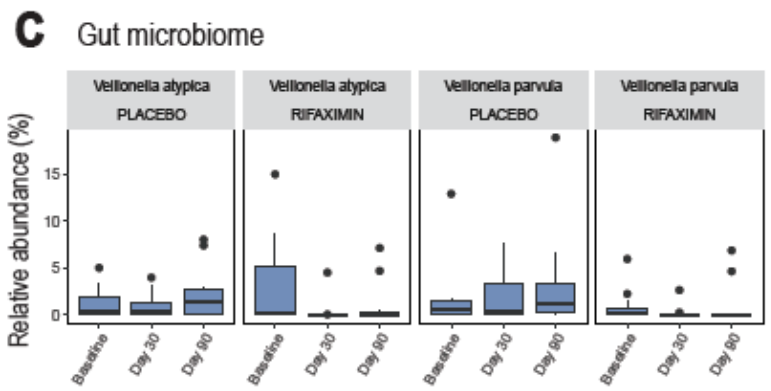


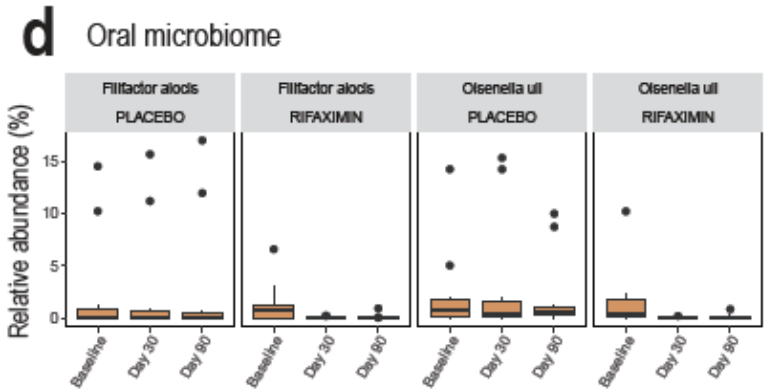
Patel VC, Lee S et al. Journal of Hepatology 2021 (in press)

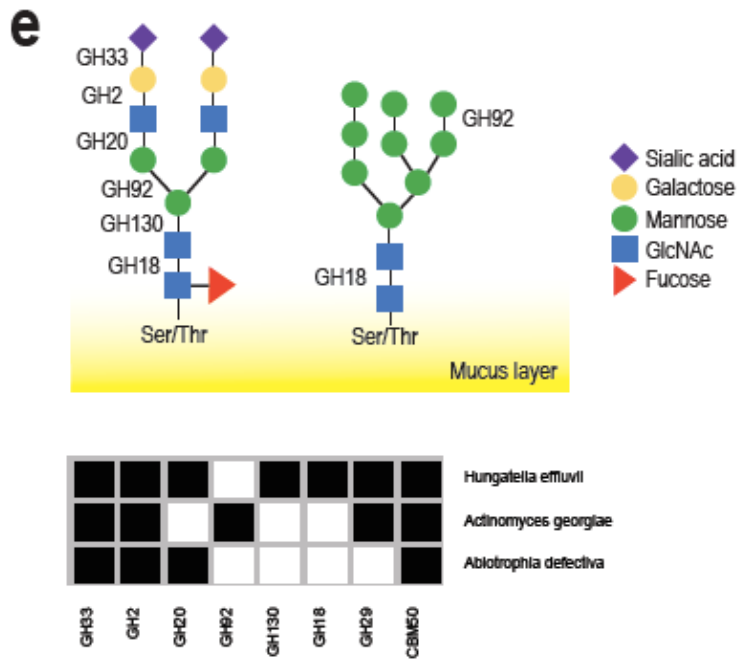
Rifaximin suppresses the growth of oral originating species in the gut microbiome and bacteria with mucin-degrading capacities





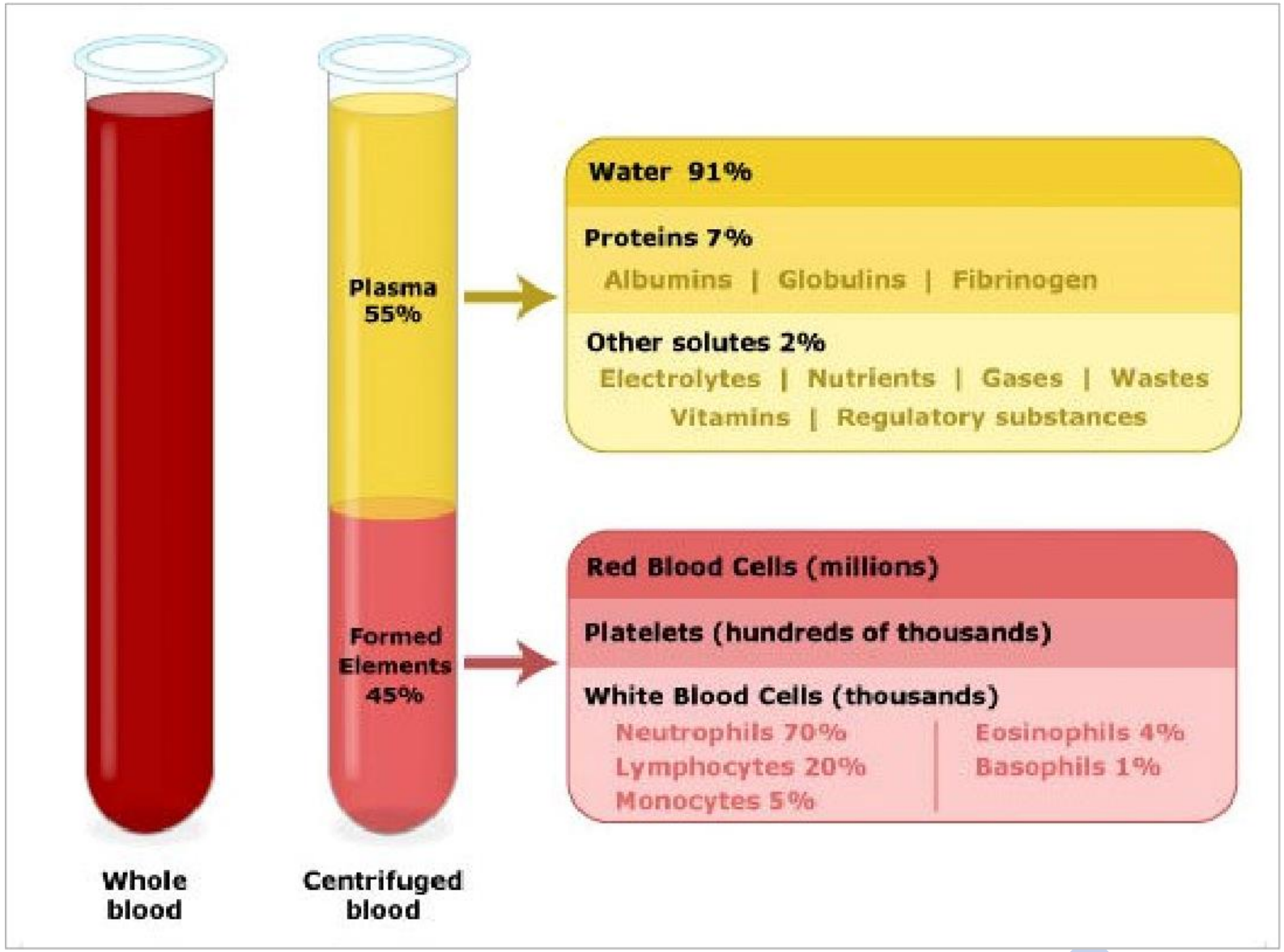






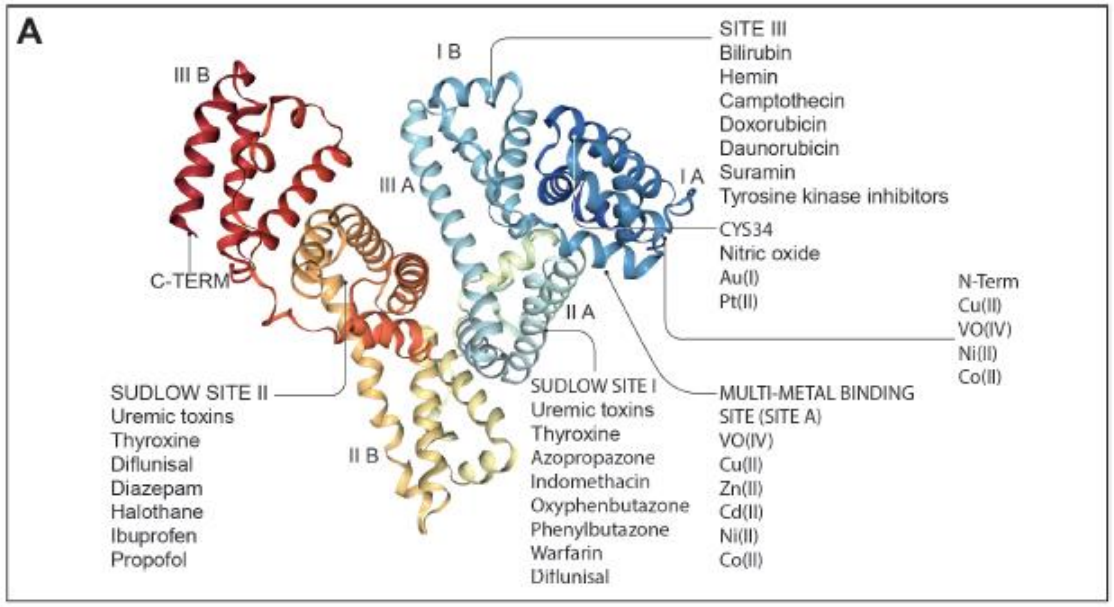
Patel VC, Lee S et al. Journal of Hepatology 2021 (in press)

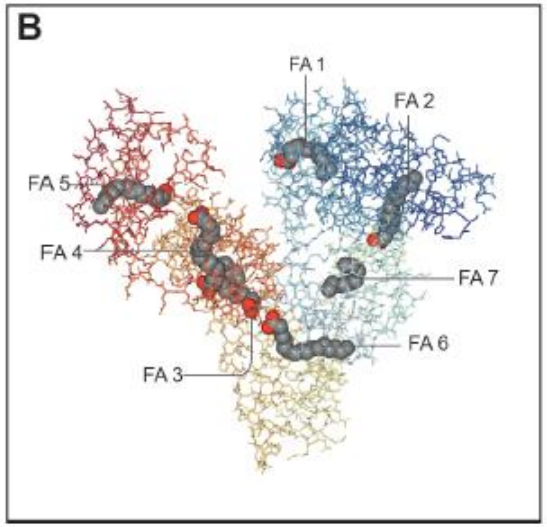
Human Albumin Solution

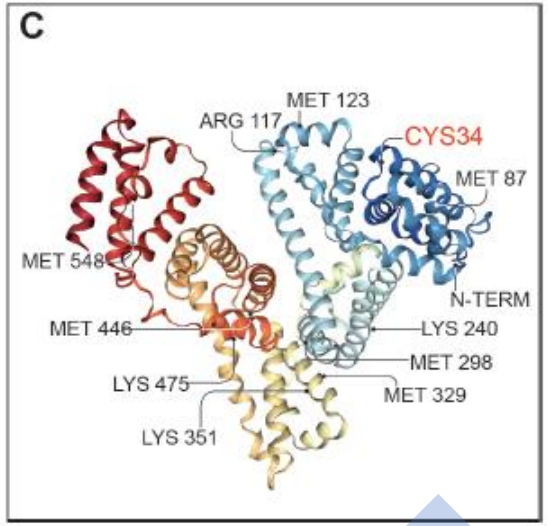

Plasma
55%
Formed
Elements
45%
Whole
blood
Centrifuged
blood
Water 91%
Proteins 7%
Albumins | Globulins | Fibrinogen
Other solutes 2%
Electrolytes | Nutrients | Gases | Wastes
Vitamins | Regulatory substances
Red Blood Cells (millions)
Platelets (hundreds of thousands)
White Blood Cells (thousands)
Neutrophils 70%
Lymphocytes 20%
Monocytes 5%
Eosinophils 4%
Basophils 1%

Endogenous and exogenous binding sites in the albumin molecule

Many of the physiological functions of human serum albumin rely on its ability to reversibly bind to an extremely wide range of ligands to increase their solubility in plasma, to transport to specific tissues or organs or to dispose of them when they are toxic.







Albumin is the most important regulator of extracellular oxidative stress and presents many binding sites for reactive oxygen species.

The most important site is the Cys-34 residue, which can be reversibly or irreversibly oxidized.

Albumin and Cirrhosis

- The systemic proinflammatory and pro-oxidant state of patients with decompensated cirrhosis drives structural and functional changes in the albumin molecule
- This interferes with its antioxidant, scavenging, immune- modulating and endothelium protective functions.
- International guidelines recommend the use of human albumin solution after large-volume paracentesis in patients with spontaneous bacterial peritonitis and hepatorenal syndrome.
- The optimal dosage and administration schedule and identification of patients who would benefit most from long-term albumin administration remains to be defined.

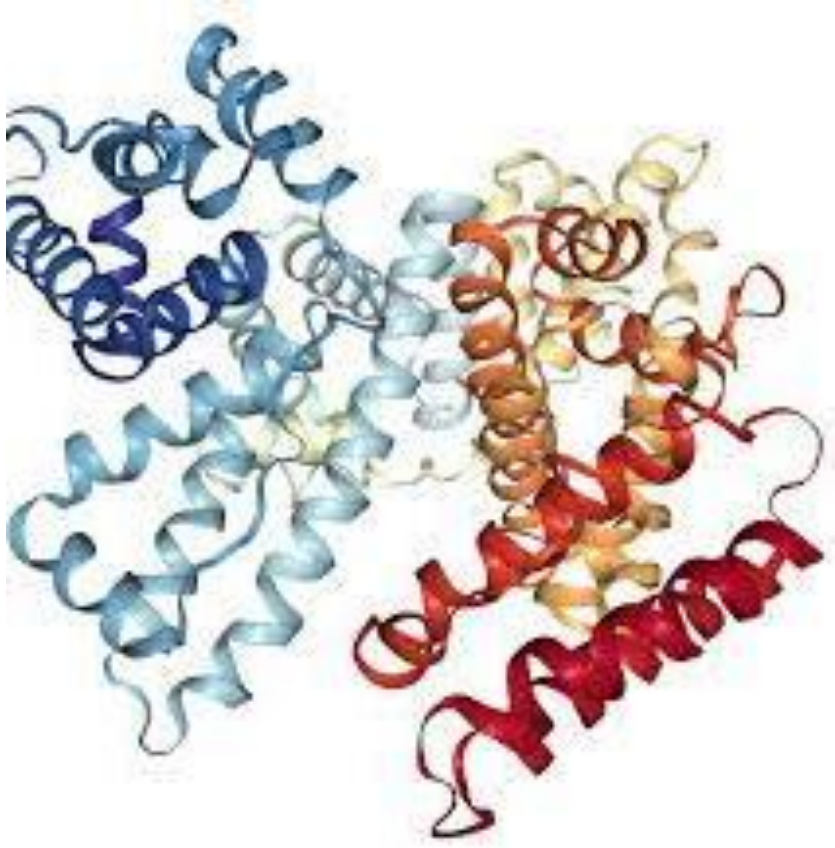


Table 1 Plasma concentrations of cytokines, C reactive protein and irreversible oxidised albumin in healthy subject and patients with cirrhosis with and without ACLF (data gathered from Clària *et al*[22])

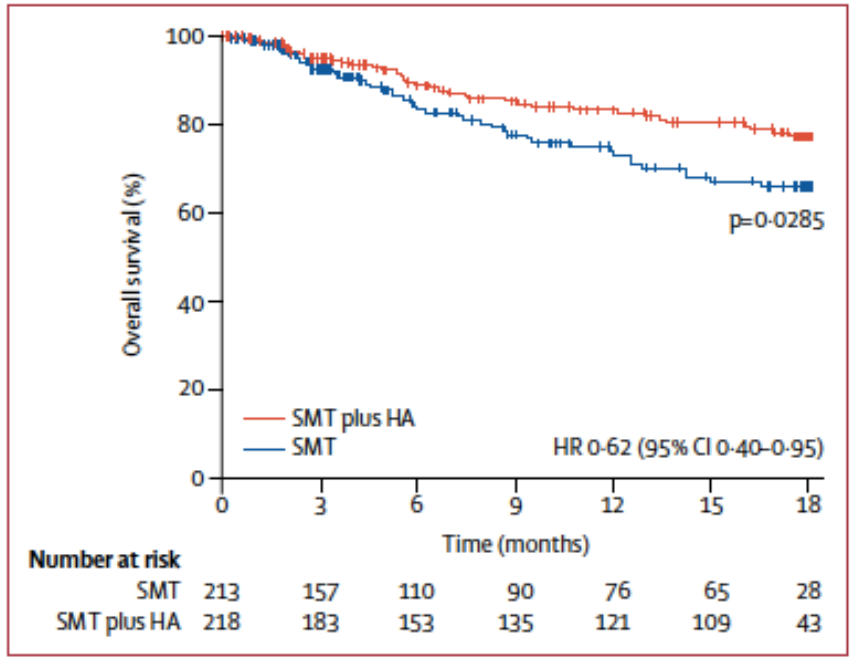
	Healthy controls	Patients without ACLF	Patients with ACLF	
	n=40	n=285	n=237	P value*
Proinflammatory cytokines				
TNF-α (pg/mL)	9 (7–12)	20 (14–27)	29 (17–41)	<0.001
IL-6 (pg/mL)	0.3 (0.3–0.3)	21 (11–41)	39 (17–115)	<0.001
IL-8 (pg/mL)	1.6 (0.6–3.3)	37 (20–76)	84 (41–169)	<0.001
GM-CSF (pg/mL)	2.1 (1.8–11)	23 (11–50)	32 (14–83)	<0.001
Anti-inflammatory cytokines				
IL-10 (pg/mL)	1.1 (0.4–1.1)	3.4 (1.1–9.2)	8.1 (2.1–29.9)	<0.001
IL-1ra (pg/mL)	7 (3–9)	10 (5–22)	23 (9–63)	<0.001
C reactive protein and irreversible albumin oxidised albumin				
CRP	<3	18 (6–35)	27 (12–20)	
HNA2 (% of total albumin)	1.3 (0.3–1.9)	4.5 (2.5–8.8)	9.8 (5.6–14.8)	<0.001

Data are expressed as median (IQR).
*P value between ACLF and no ACLF.
HNA2, irreversibly oxidised human nonmercaptalbumin.ACLF, acute-on-chronic liver failure; CRP, C reactive protein; GM-CSF, granulocyte macrophage colony-stimulating factor; IL, interleukin; TNF-α, tumour necrosis factor alpha.

Casulleras M et al. Cells 2020

Albumin Trials

- In a randomized trial (ANSWER Trial) involving outpatients with ascites, weekly albumin infusions reduced the incidences of infection and kidney dysfunction and were associated with a lower probability of death than standard care.
- In contrast, there was no effect in a smaller trial in which albumin was administered less frequently than weekly.
- In patients hospitalized with decompensated cirrhosis, albumin infusions to increase the albumin level to a target of 30 g per litre or more was not more beneficial than the current standard care in the UK (ATTIRE Trial).



Caraceni P et al. Lancet 2018

Table 2. End Points.*

Variable	Albumin Group (N=380)	Standard-Care Group (N=397)	Adjusted Odds Ratio (95% CI)†	P Value
Composite primary end point — no. (%)	113 (29.7)	120 (30.2)	0.98 (0.71–1.33)	0.87
Components of composite primary end point — no. (%)‡				
Incidence of new infection	79 (20.8)	71 (17.9)	1.22 (0.85–1.75)	
Incidence of kidney dysfunction	40 (10.5)	57 (14.4)	0.68 (0.44–1.11)	
Incidence of death	30 (7.9)	33 (8.3)	0.95 (0.56–1.59)	
Death at 28 days	53 (14.0)	62 (15.6)	0.86 (0.57–1.30)	
Death at 3 mo	92 (24.2)	93 (23.4)	1.05 (0.74–1.48)	
Death at 6 mo	132 (34.7)	119 (30.0)	1.27 (0.93–1.73)	
Total median albumin infused per patient (IQR) — g	200 (140–280)	20 (0–120)	143 (127–158)§	

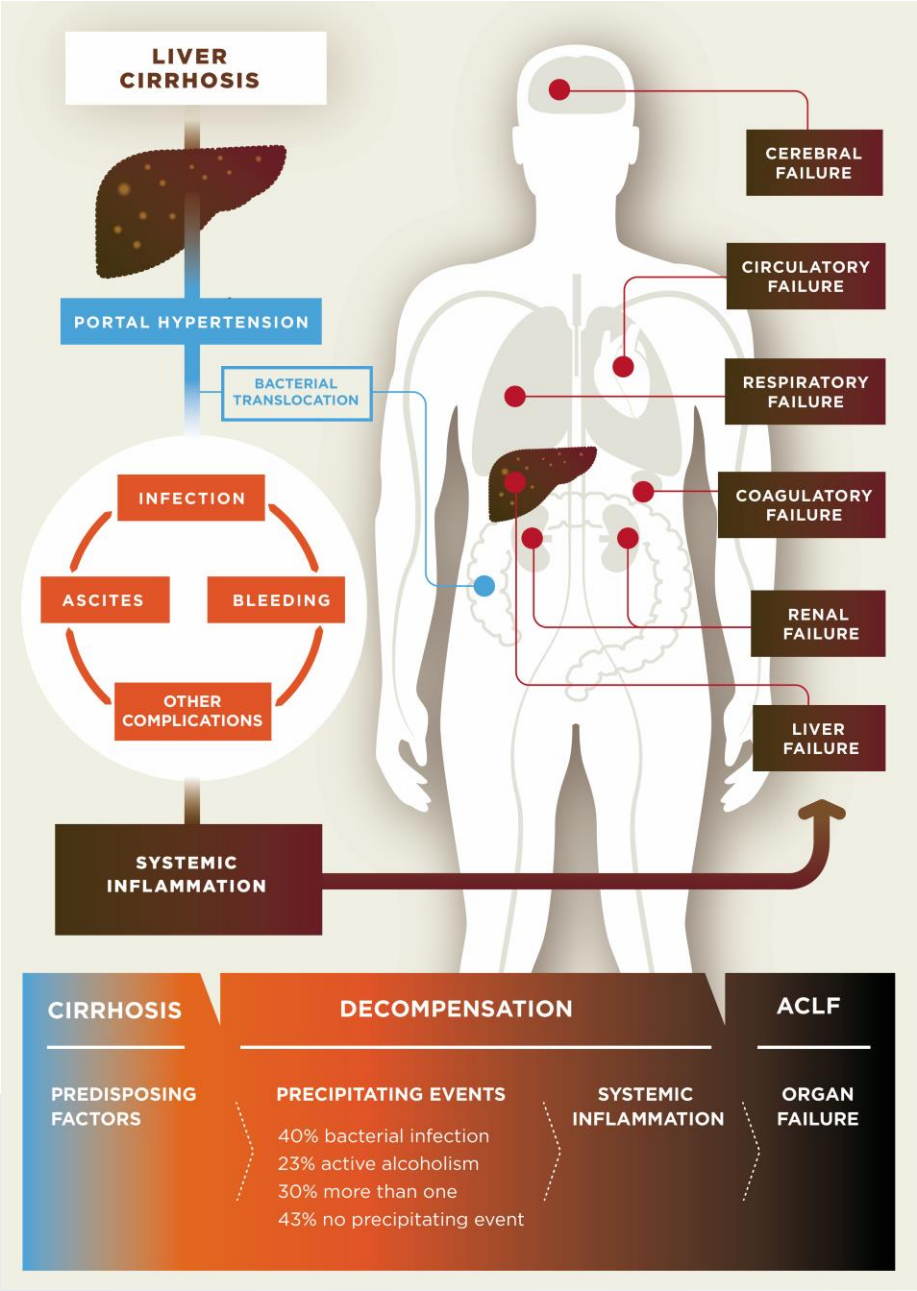
* Unless stated, the time of the end point is during the trial treatment period (15 days after randomization).
† Odds ratios are adjusted for stratification variables, with sites as random intercept terms.
‡ The end points are defined in the original trial protocol.[26]
§ This is the adjusted mean difference between the groups.

China L et al. NEJM 2021

MICROB-PREDICT - MICROBiome-based biomarkers to PREDICT decompensation of cirrhosis and treatment response

Better stratification of cirrhotic patients enabling microbiome-based intelligent treatment

Chief Investigator - Jonel Trebicka



This project hast received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 825694.

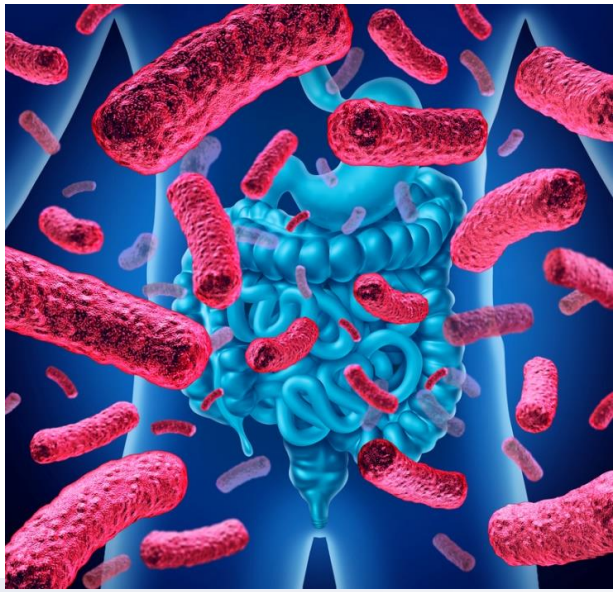
Objectives

MICROB-PREDICT will investigate the human microbiome to:

1) Identify predictors and mechanisms associated with the development of decompensation and progression to ACLF and death.

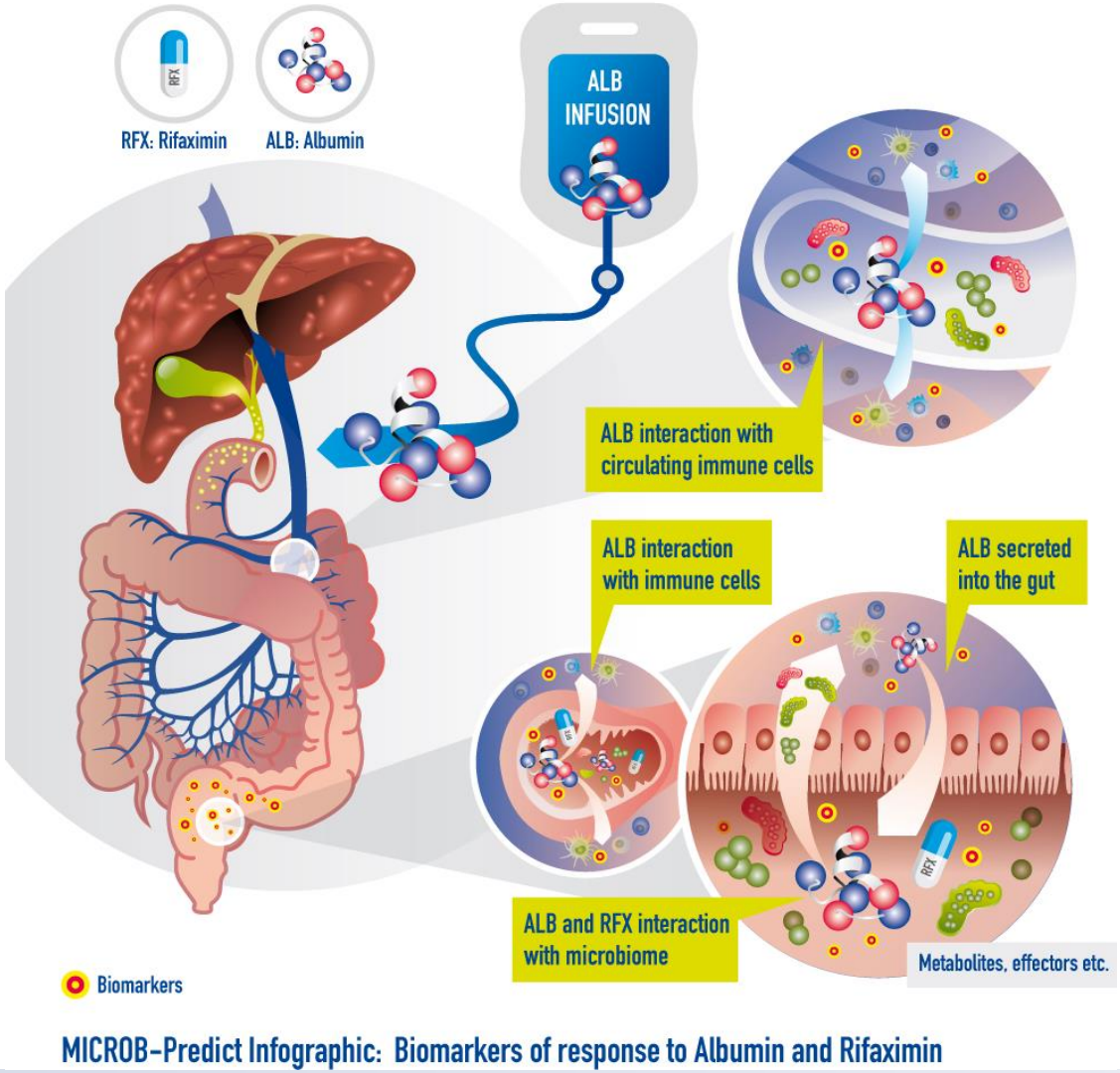
2) This will result in better stratification of cirrhotic patients enabling microbiome-based intelligent and personalized allocation to treatment, and ultimately prevent ACLF reducing mortality.

3) The identified microbiome-based markers will be validated in a clinical trial and translated into three new clinical tests useful for patients.



This project hast received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 825694.

Two interventions and their interaction with the gut microbiome



MICROB-Predict Infographic: Biomarkers of response to Albumin and Rifaximin

This project hast received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 825694.

Approach and cohorts

Data and samples:

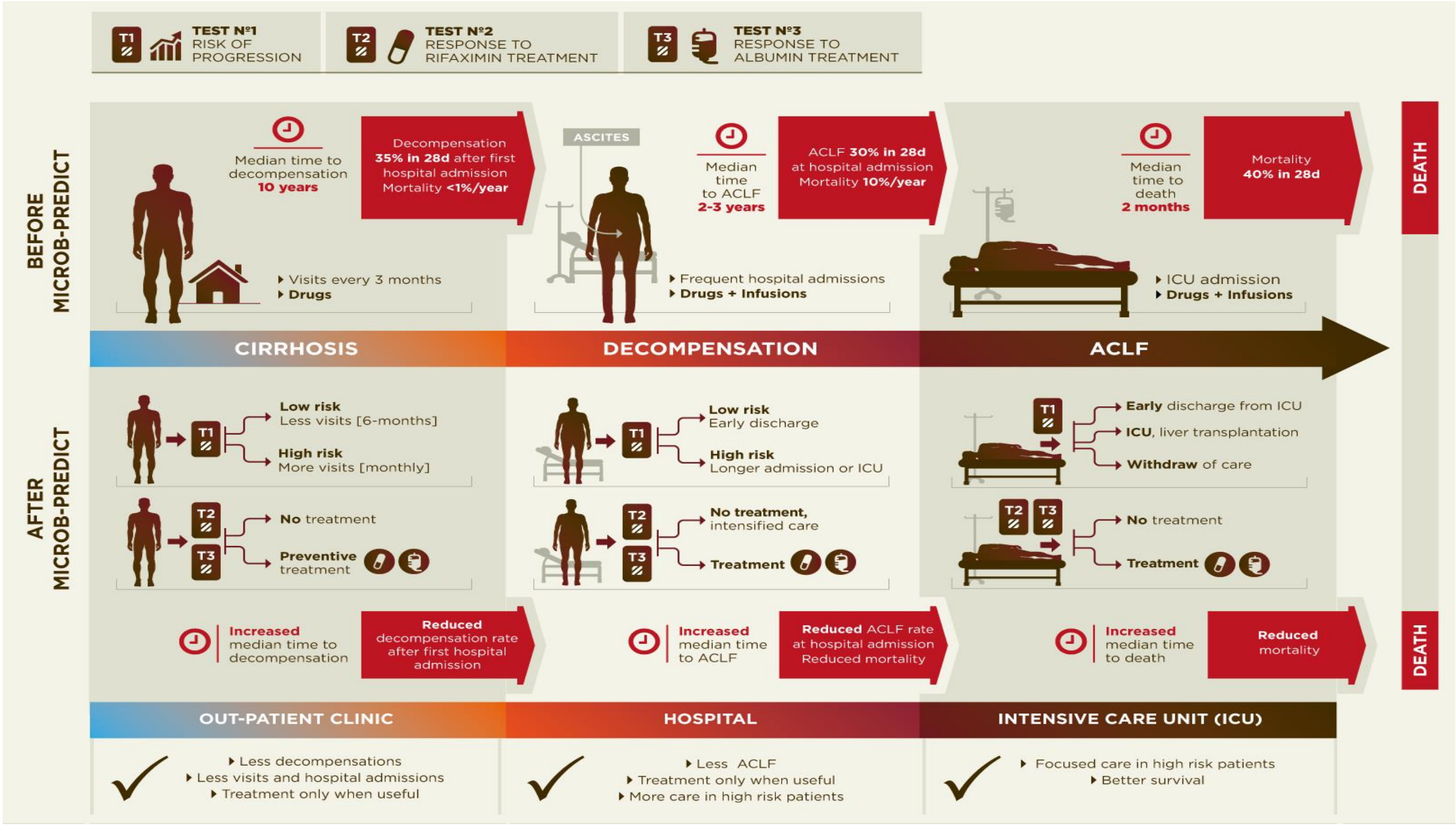
- 12 microbiome initiatives in the field of hepatology including >10,000 patients and controls
- Existing metadata and -omics data from >2500 patients and >7000 controls
- Multiomics analysis of 1050 patients

Cohort (Country), Reference, Owner	Sub-cohort	(D) Study Description and (R) Rationale in MICROB-PREDICT	Status	n	Vts.	Ctrls.	Data	Samples	Used in WP
PREDICT (EU) Owners: EFCLIF, UNIDEB	MUCOSA-PREDICT (including mucosa biopies)	**D:** Decompensated cirrhosis and ACLF, wide range of biological samples, **R:** discovery and validation of signatures	Existing data and samples.	100	2-3	-	- clinics, biochemics - drugs - G	stool blood BC saliva urine GI biopsy	WP2-5
	STOOL-PREDICT (only stool samples)		Existing data and samples.	100		100		stool	WP2-5
	VALIDATION-PREDICT (for validation WP5)		Existing data and samples.	400					WP5
GALAXY/ MICROB-LIVER (EU) Owners: OUH, UCPH	GALAXY (alcoholic liver fibrosis)	**D:** alcoholic fibrosis and cirrhosis, decompensated cirrhosis with TIPS, wide range of biological samples, longitudinal data with minimum 1 visit, sub-cohort with rifaximin RCT, follow-up up to 8 years **R:** discovery and validation of signatures	Existing data.	400	1	150	- Clinics, biochemics - MG, MT, 16S, F, V - Sal. 16S - METAB, BA, C, G	-	WP4
	TIPS-MICROB-LIVER (decompensated cirrhosis)		Existing data.	100	1			-	WP4
	CIRRHOSIS-GALAXY (decompensated cirrhosis)		Planned study in MICROB-PREDICT	100	1	-		stool	WP2, 4, 5
EMBL-cohort (EU) Owner: EMBL		**D:** individuals (no cirrhosis) from large well phenotyped and genotyped cohorts **R:** controls for in silico validation	Existing data.	-	-	6000	- Clinics, biochemics - drugs, diet - MG, MT	-	WP4
RIFSYS-RCT (EU) Owner: KCL		**D:** Decompensated cirrhosis receiving rifaximin in RCT R: in silico validation of signatures, controlling for different region and technique	Existing data.	38	2	18	- Clinics, biochemics - MG, Sal. MG - BA, C, G	-	WP4
FCRB-cohort (EU) Owner: FCRB		**D:** compensated, decompensated cirrhosis and ACLF, first MG study in ACLF **R:** in silico validation of signatures, controlling for different technique	Existing data.	200	1	40	- Clinics, biochemics - MG	-	WP4
DCH-NG cohort (EU) Owner: UCPH		**D:** Decompensated cirrhosis, their relatives, medication and medical trajectory, **R:** validation of signatures, controlling for family and environmental effects	Planned study in MICROB-PREDICT	100	1	100	- Clinics, biochemics - drugs	stool	WP5
META-HIT (EU) Owners: UCPH, EMBL, INRA		**D:** individuals (no cirrhosis) from large well phenotyped and genotyped cohorts **R:** controls for in silico validation	Published data (see Section 5.1)	-	-	780	- Clinics, biochemics - MG, G	-	WP4
VA-US-cohort (USA)		**D:** compensated and decompensated cirrhosis, longitudinal up to 7 visits, wide range of biological samples **R:** in silico validation of signatures, controlling for different region and techniques	Published data (see Section 5.1)	315	3	38	- Clinics, biochemics - 16S, F, Sal. 16S - METAB, C, G	-	WP4
CANONIC (EU),		**D:** Decompensated cirrhosis and ACLF, 10 countries in Europe, longitudinal data, first description of ACLF **R:** in silico validation of signatures	Published data (see Section 5.1)	800	2	40	- Clinics, biochemics - METAB, G, C	-	WP4
QIN-cohort (China)		**D:** compensated cirrhosis, first MG study in cirrhosis **R:** in silico validation of signatures, controlling for different region and techniques	Published data (see Section 5.1)	123	1	114	- Clinics, biochemics - MG	-	WP4
ALBUMIN-PILOT-RCT (EU)		**D:** decompensated cirrhosis receiving albumin in a RCT, longitudinal data with minimum 3 visits, **R:** discovery of albumin response signature	Ethics approval ongoing, study starts 2018 and ends 2019	50	3	-	- Clinics, biochemics - drugs	stool	WP2,4,5
LIVERHOPE-RCT (EU)		**D:** Decompensated cirrhosis receiving rifaximin and statins in RCT **R:** validation of signatures for Rifaximin response	Ethics approval ongoing, study starts on 2018 and ends 2020	200	1	-	- Clinics, biochemics - drugs	stool	WP5
Total				**3.026**		**7.380**			

Vts. – visits, Ctrls – controls, - Clinics, biochemics - Clinical and biochemical data, 16S – 16S sequencing, BA – bile acids, BC – buffy coat, C – cytokines, F – fungome, G- genomics, GI – gastrointestinal, METAB – metabolomics, MG – metagenomics, MT – metatranscriptomics, Sal. 16S – saliva 16S sequencing, Sal. MG – saliva metagenomics

This project hast received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 825694.

Our vision


T1 TEST Nº1 RISK OF PROGRESSION
T2 TEST Nº2 RESPONSE TO RIFAXIMIN TREATMENT
T3 TEST Nº3 RESPONSE TO ALBUMIN TREATMENT
BEFORE MICROB-PREDICT
Median time to decompensation 10 years
Decompensation 35% in 28d after first hospital admission Mortality <1%/year
ASCITES
Median time to ACLF 2-3 years
ACLF 30% in 28d at hospital admission Mortality 10%/year
Median time to death 2 months
Mortality 40% in 28d
DEATH
Visits every 3 months
Drugs
Frequent hospital admissions
Drugs + Infusions
ICU admission
Drugs + Infusions
CIRRHOSIS
DECOMPENSATION
ACLF
AFTER MICROB-PREDICT
Low risk
Less visits [6-months]
High risk
More visits [monthly]
Low risk
Early discharge
High risk
Longer admission or ICU
Early discharge from ICU
ICU, liver transplantation
Withdraw of care
No treatment
Preventive treatment
No treatment, intensified care
Treatment
No treatment
Treatment
Increased median time to decompensation
Reduced decompensation rate after first hospital admission
Increased median time to ACLF
Reduced ACLF rate at hospital admission Reduced mortality
Increased median time to death
Reduced mortality
DEATH
OUT-PATIENT CLINIC
HOSPITAL
INTENSIVE CARE UNIT (ICU)
Less decompensations
Less visits and hospital admissions
Treatment only when useful
Less ACLF
Treatment only when useful
More care in high risk patients
Focused care in high risk patients
Better survival

THANK YOU

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