

ACLF and combinatorial therapies

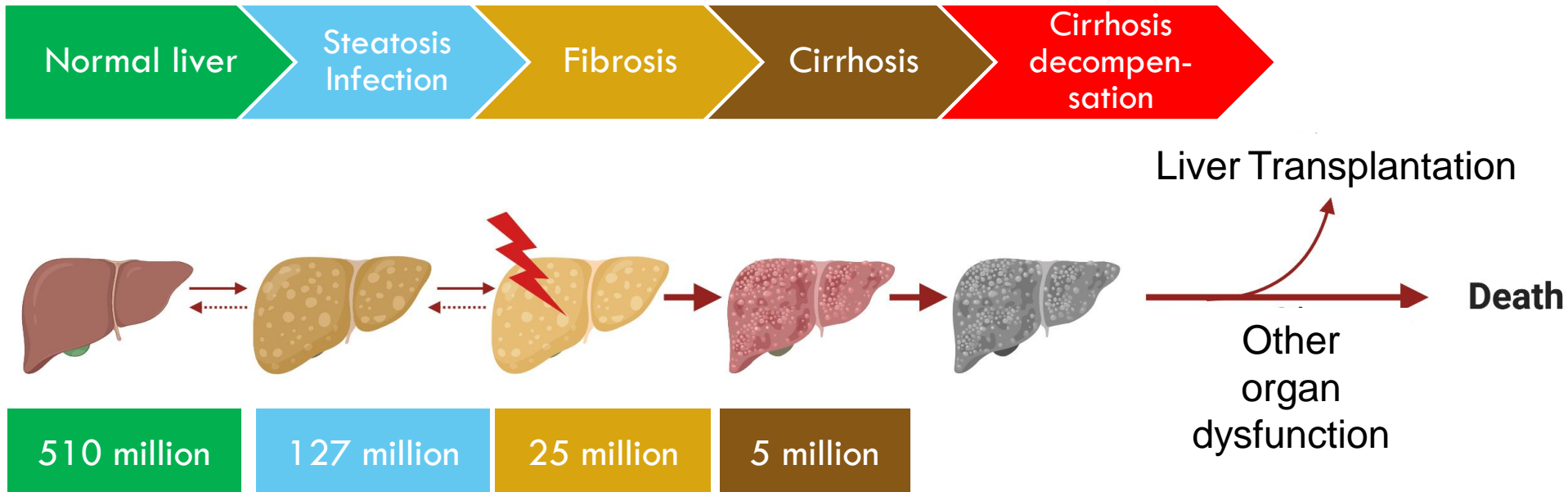
The **DECISION** project

**DECOMPENSATED CIRRHOSIS:
IDENTIFICATION OF NEW COMBINATORIAL THERAPIES
BASED ON SYSTEMS APPROACHES**

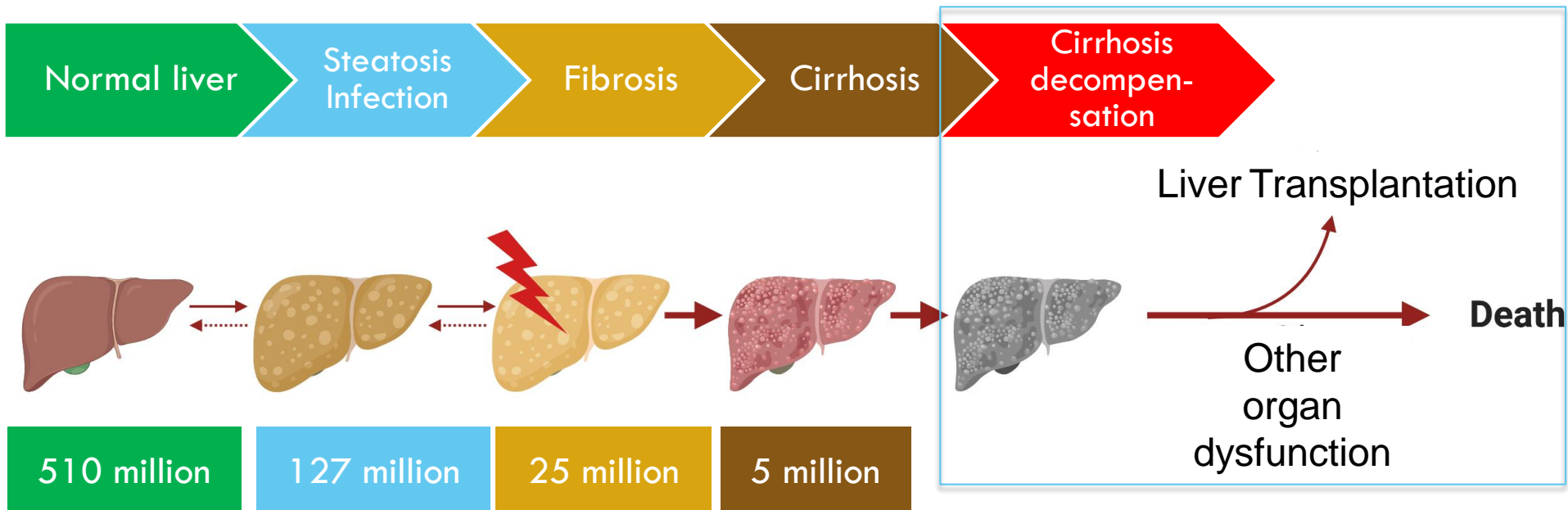
Pierre-Emmanuel RAUTOU

Inserm UMR-1149, Research center on Inflammation, Paris
Service d'hépatologie, Hôpital Beaujon, Clichy, France

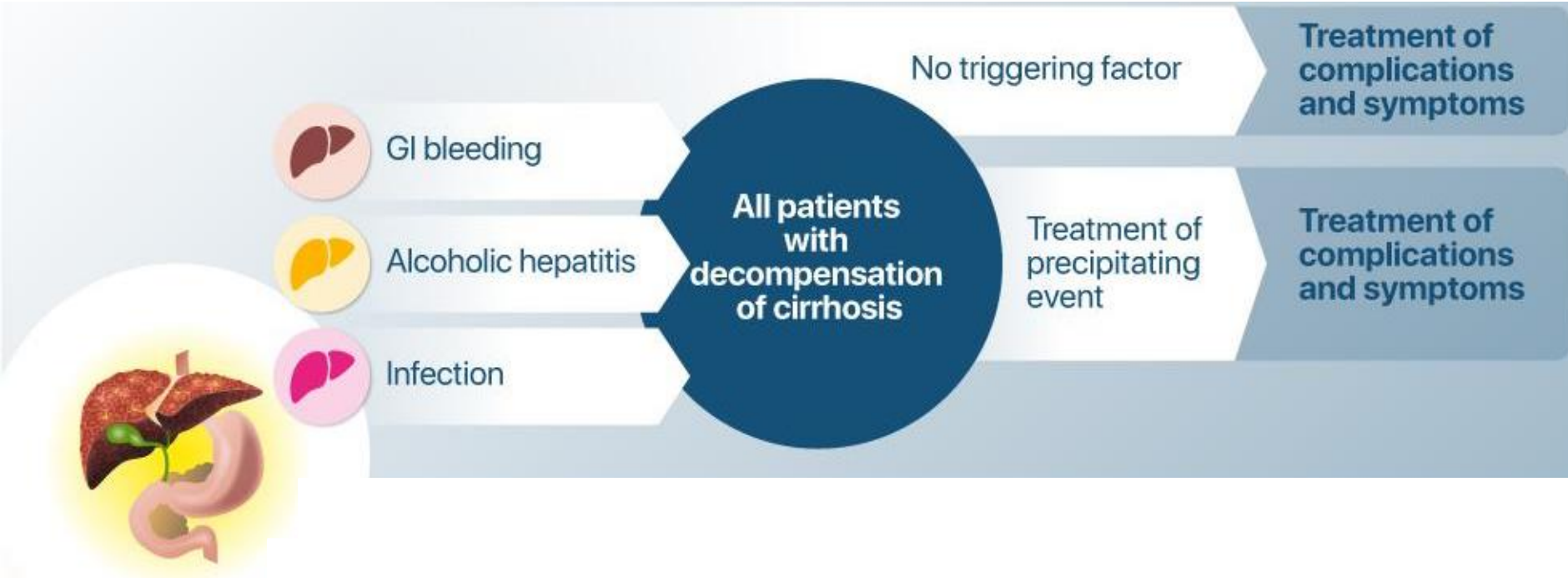
Chronic liver diseases: a public health issue



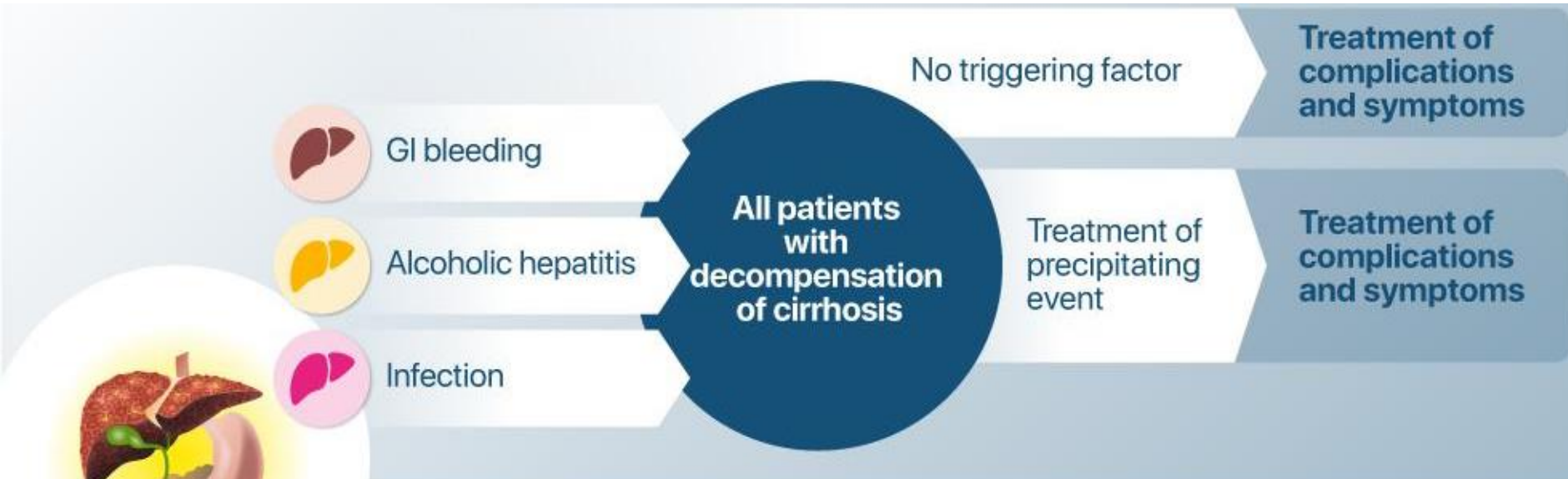
Chronic liver diseases: a public health issue



Current management of patients with acute decompensation of cirrhosis



Current management of patients with acute decompensation of cirrhosis



ACLF: 30% at 3 months
Mortality: 14% at 3 months



Need for:

- Better prediction
- Improved therapy

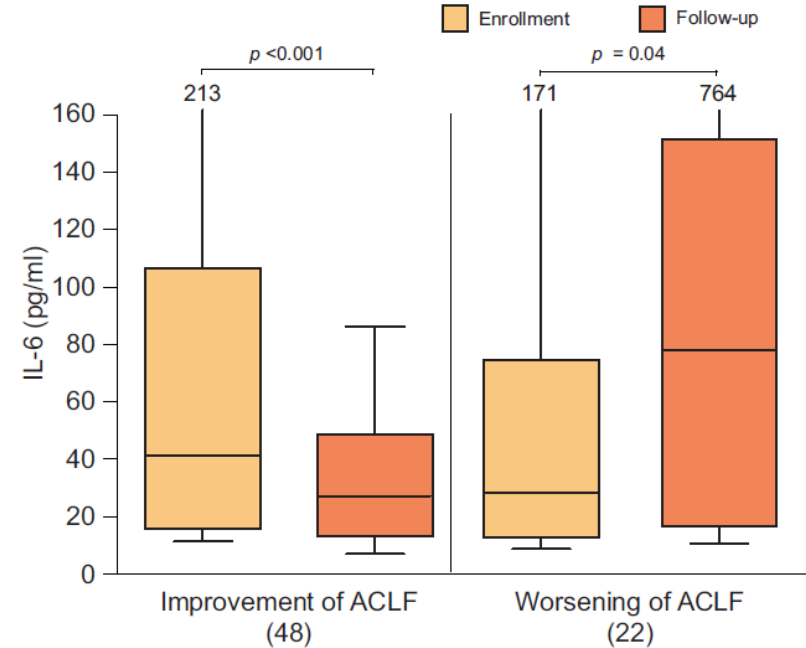
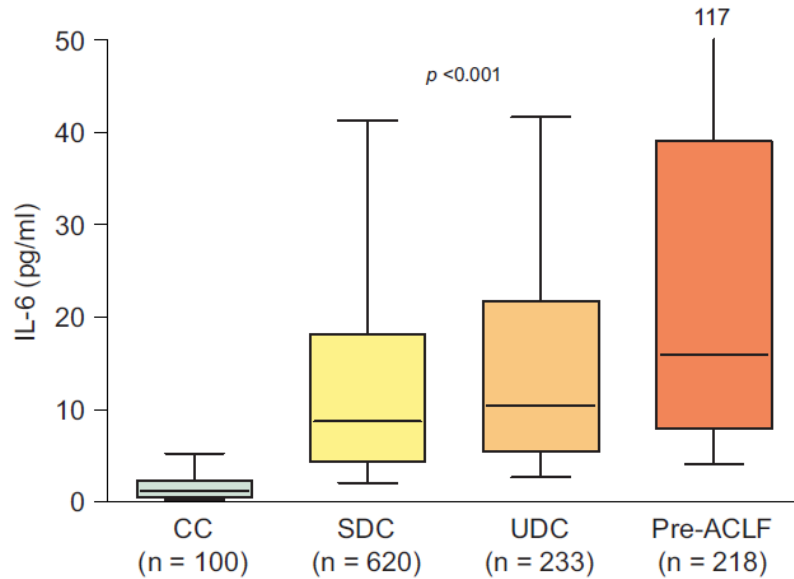
DECISION: New pathophysiological concepts



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Systemic inflammation in acute decompensation

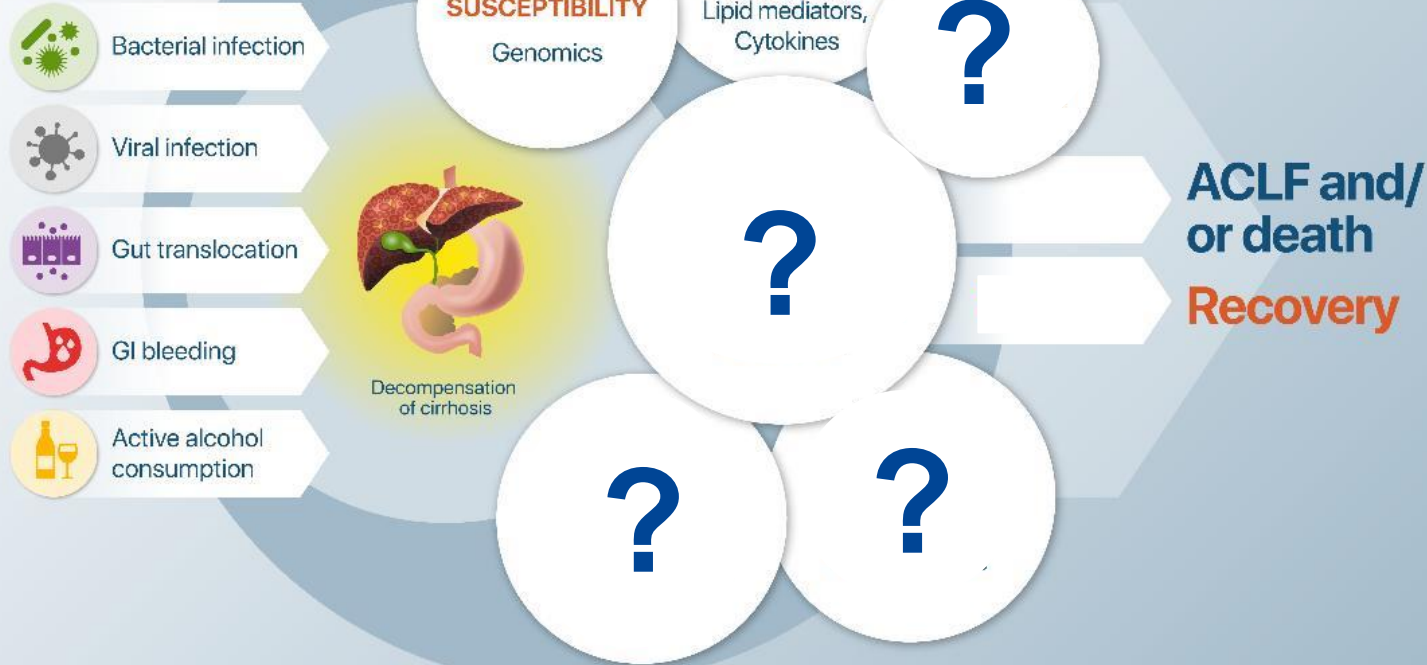


Trebicka, J Hepatol 2020

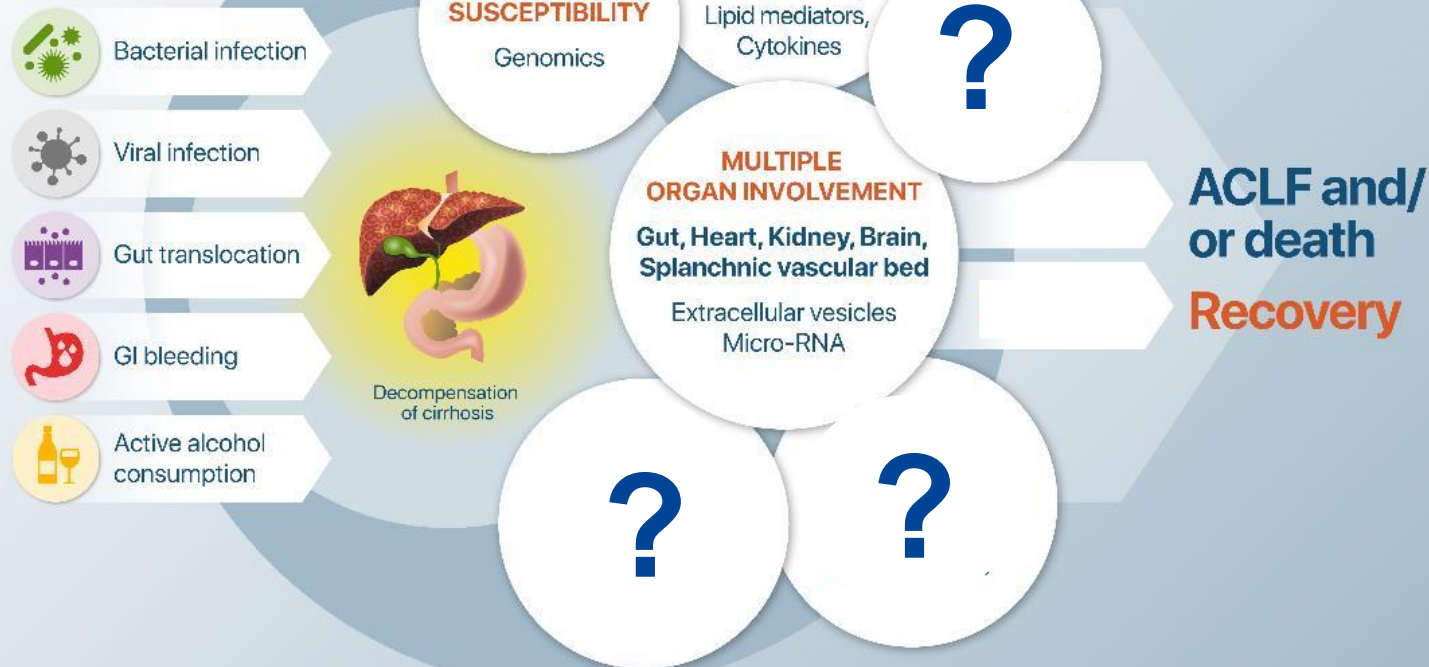
Jalan, J Hepatol 2021

DECISION: New pathophysiological concepts

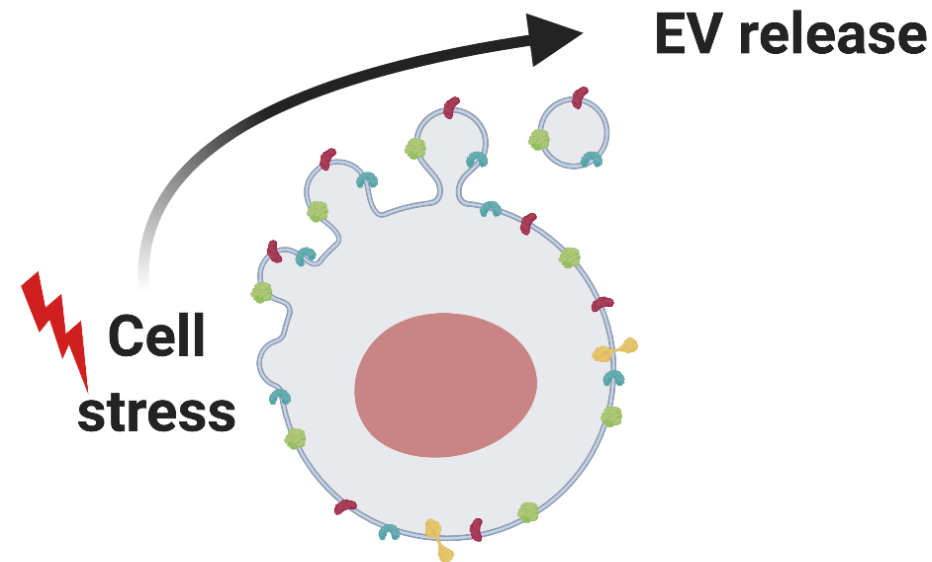
J. Claria



DECISION: New pathophysiological concepts



Extracellular vesicles (EV) in acute decompensation



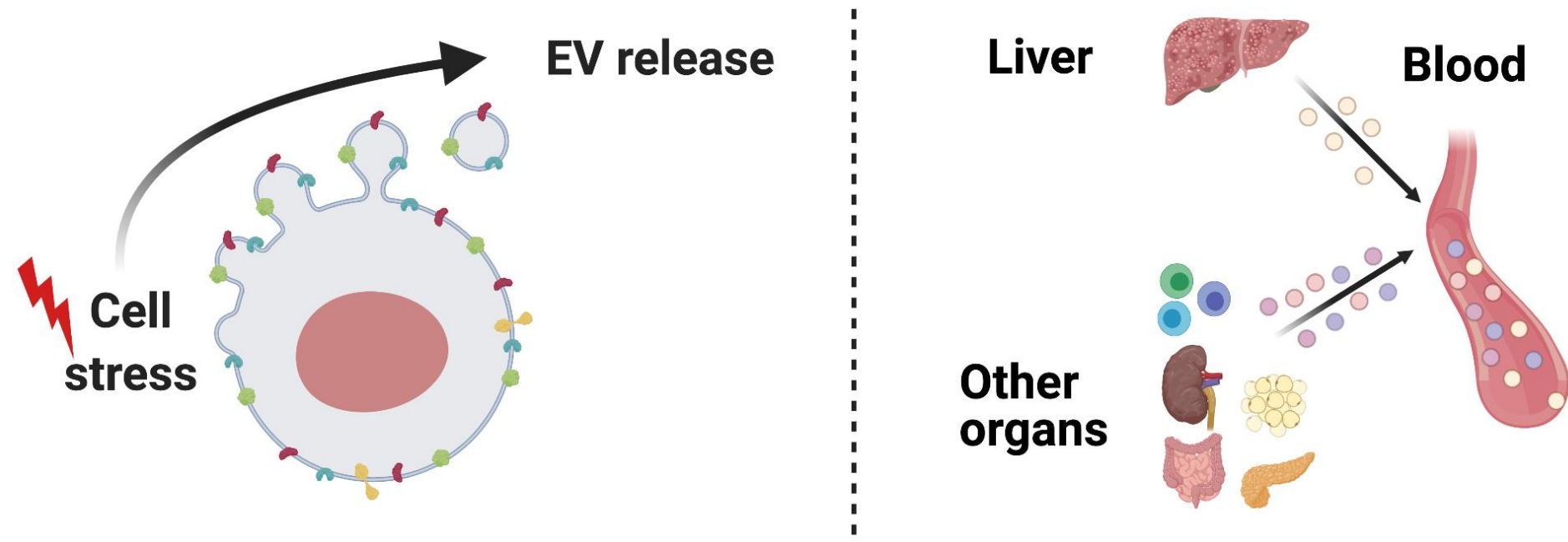
Signatures including EV subpopulations could be useful biomarkers

Thietart & Rautou, J Hepatol 2020



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 847949.

Extracellular vesicles (EV) in acute decompensation



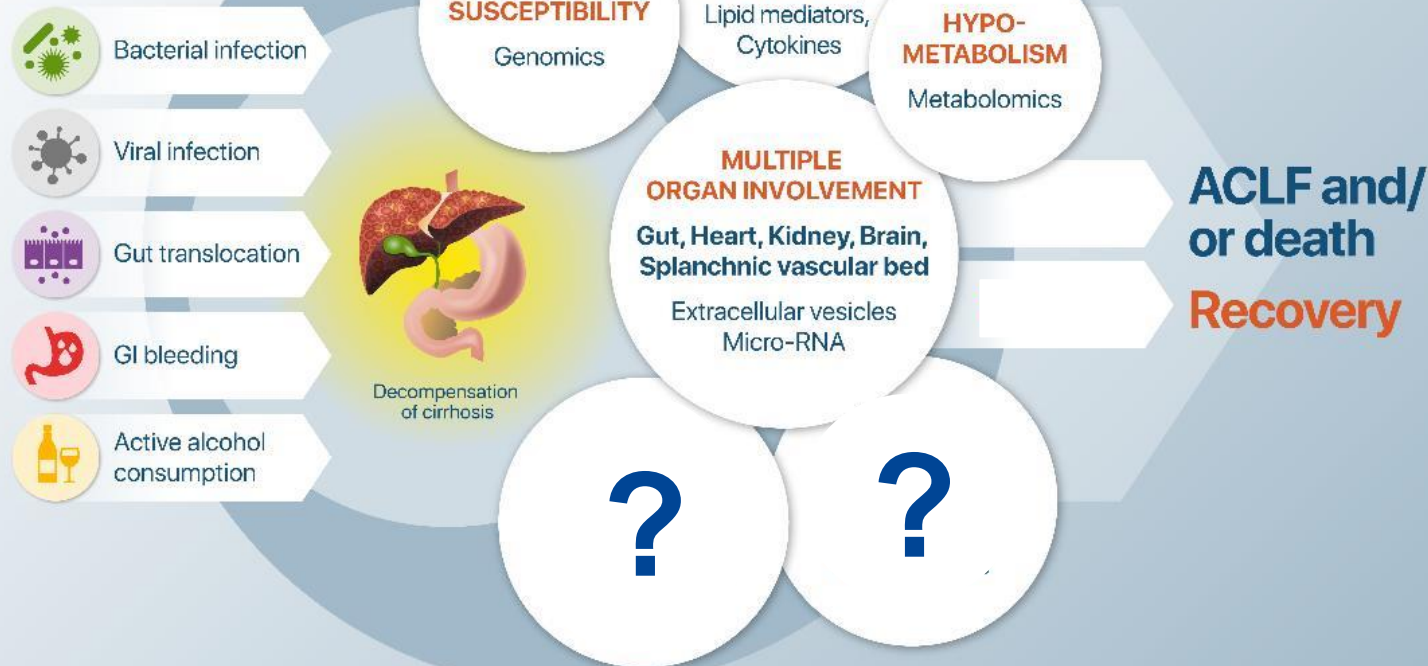
Signatures including EV subpopulations could be useful biomarkers

Thietart & Rautou, J Hepatol 2020

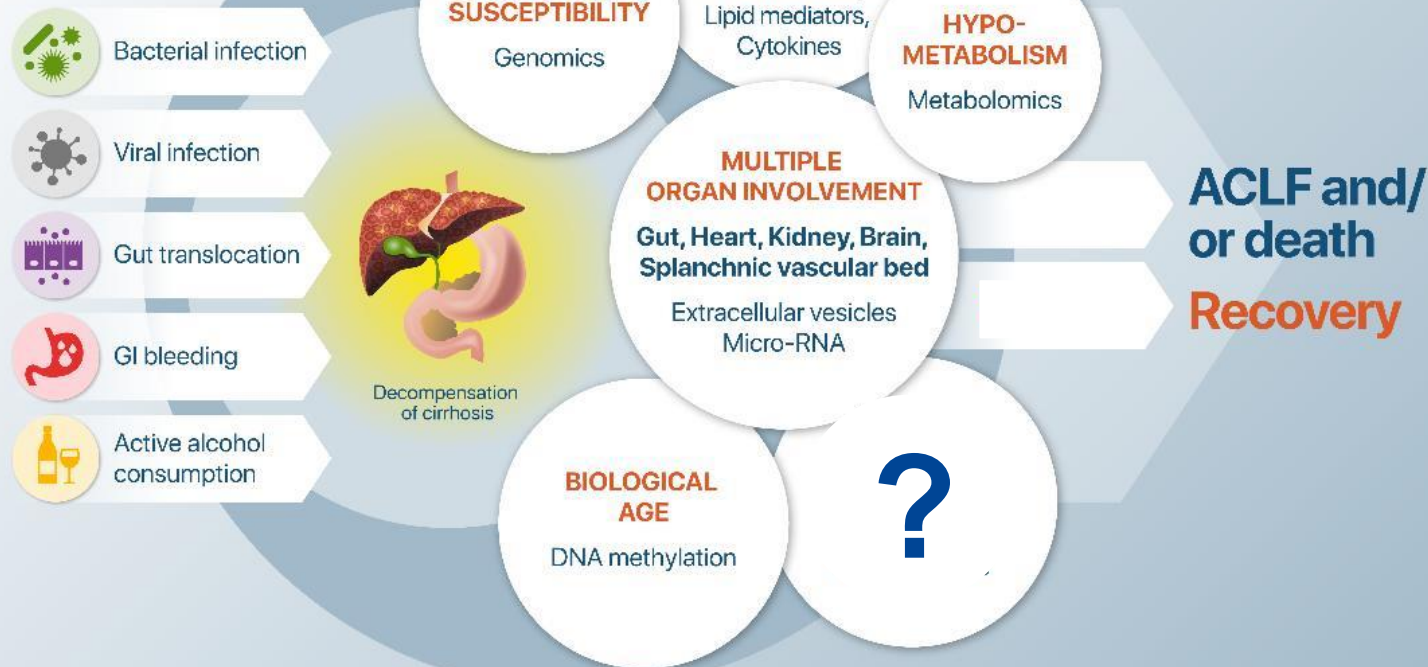


DECISION: New pathophysiological concepts

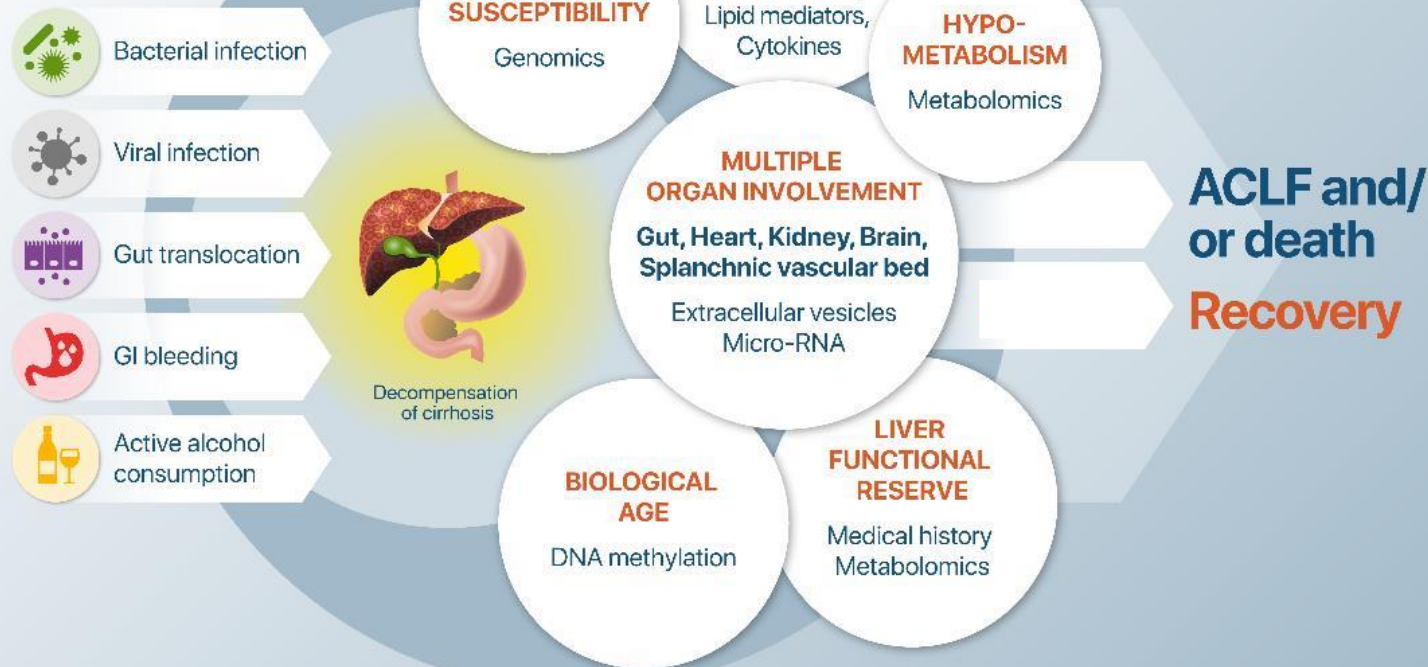
C. Junot, 3PM



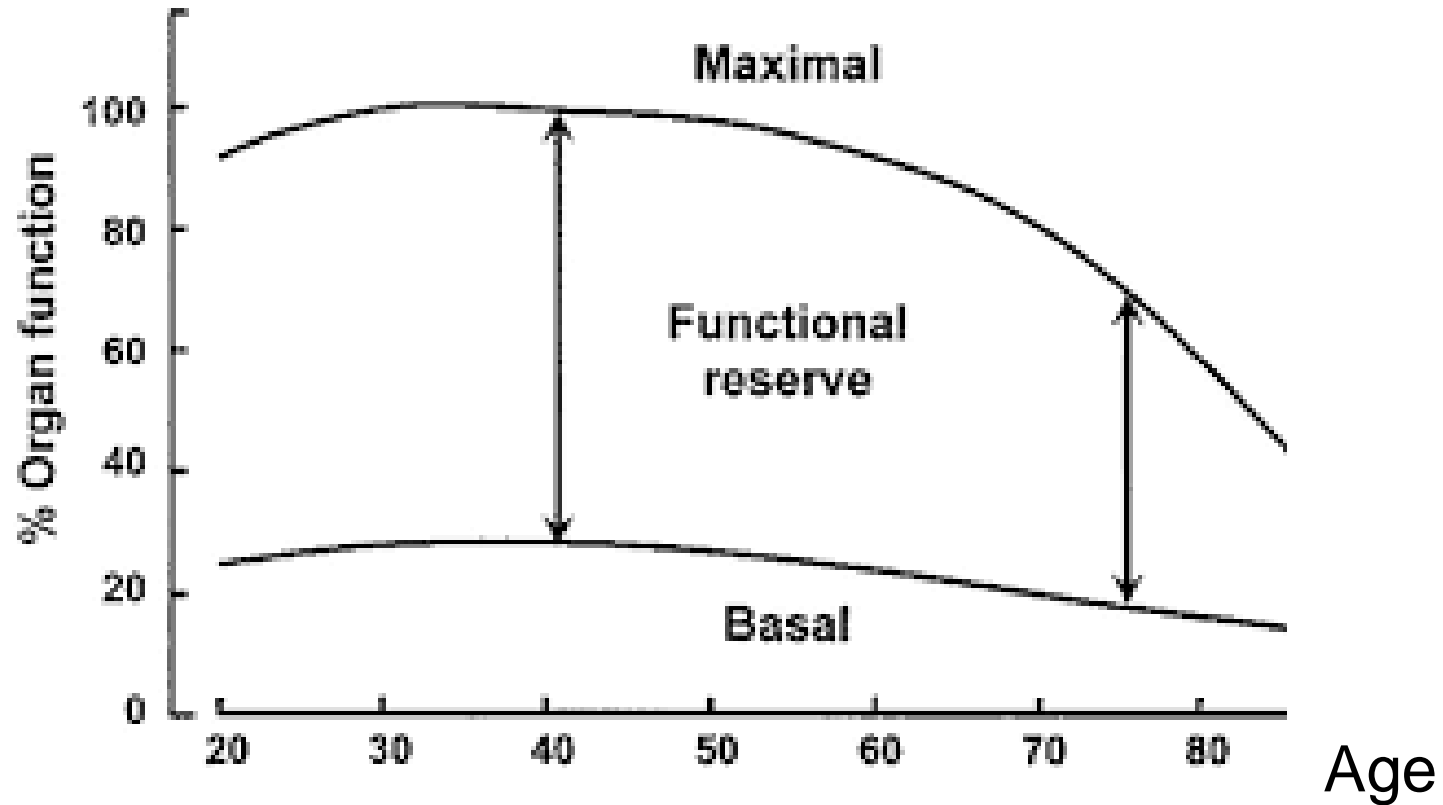
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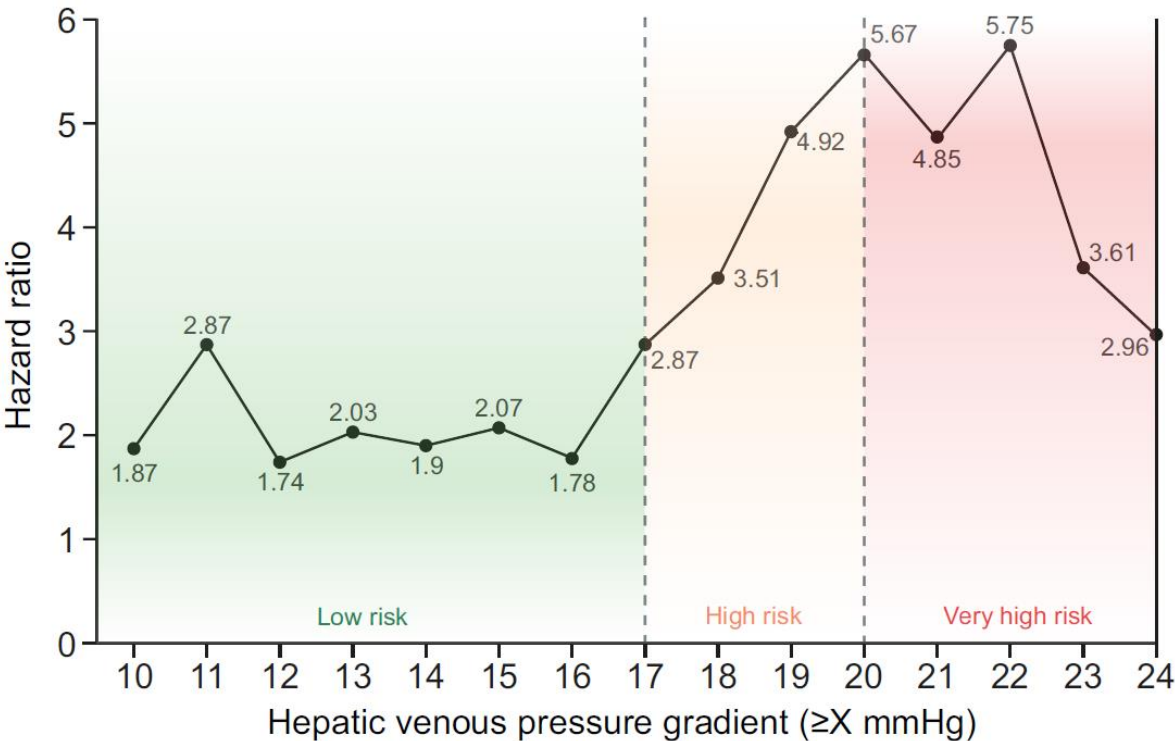
DECISION: New pathophysiological concepts



Functional reserve



Functional reserve in cirrhosis?

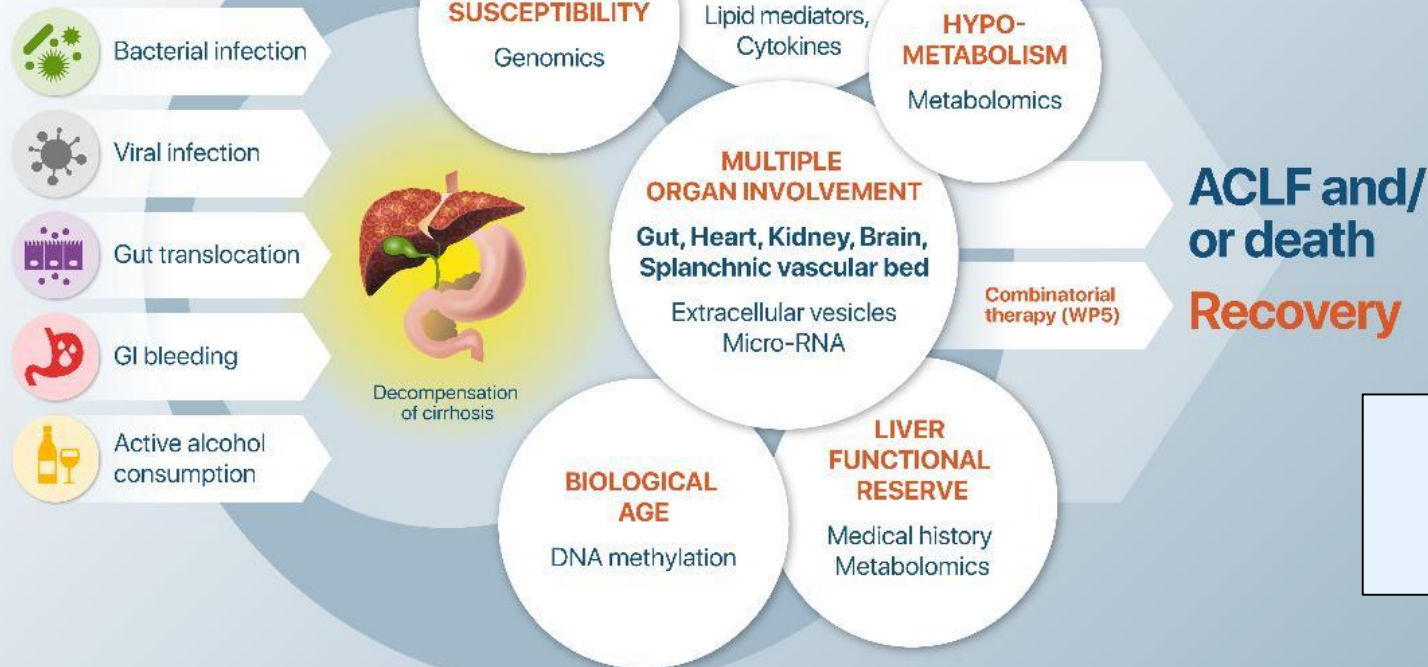


HVPG before
extrahepatic surgery

Events	22	22	20	20	19	18	16	16	15	14	14	11	6	4	3
Patients	116	104	98	92	88	75	65	56	46	36	32	20	10	8	7

Reverter E, J Hepatol 2019

DECISION: New pathophysiological concepts



**Systems
medicine**

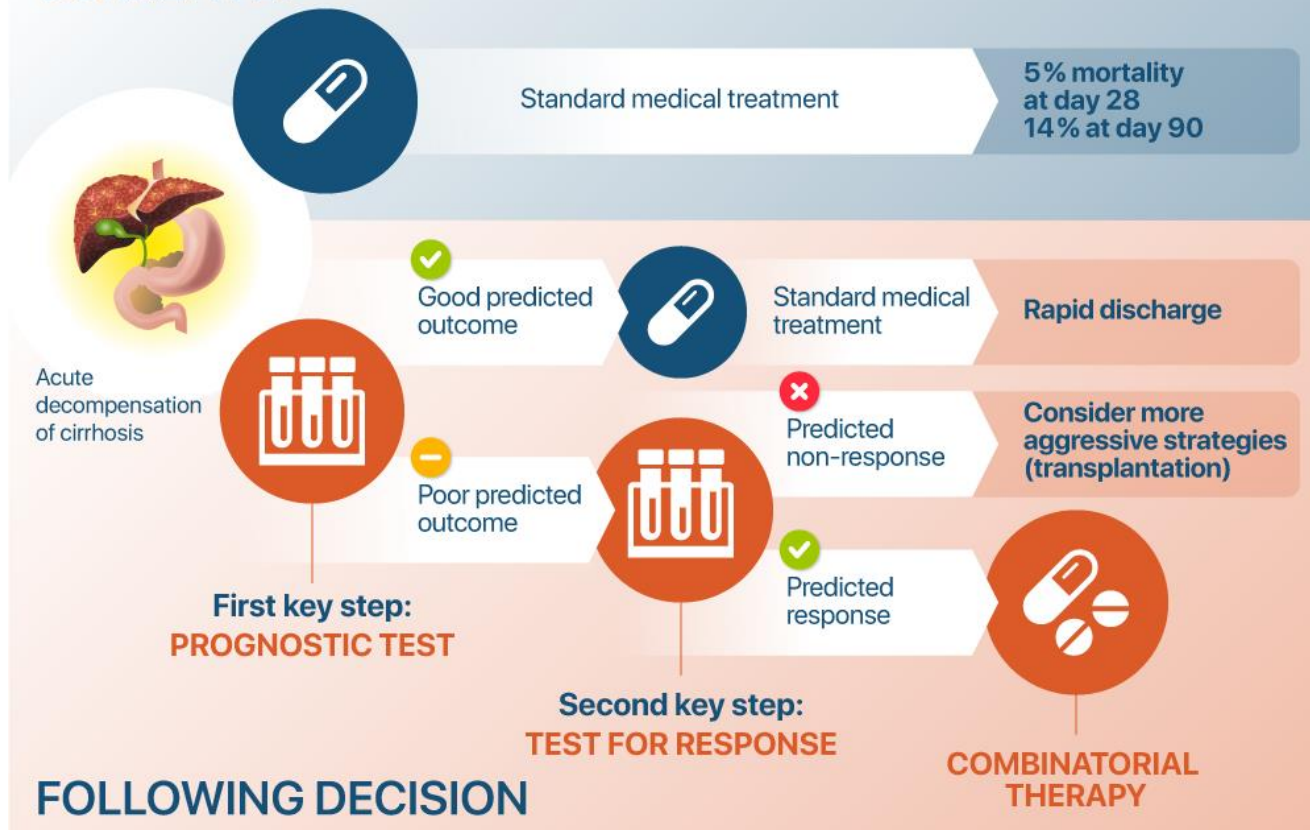
The DECISION project: basis

Cohort (Country)	CANONIC (EU)	PREDICT (EU)	ACLARA (South America)
Owner	EFCLIF	EFCLIF	EFCLIF
Samples	yes	yes	yes
Study Description	Decompensated cirrhosis 10 countries in Europe N=800 patients	Decompensated cirrhosis 10 countries in Europe N=700 patients	Decompensated cirrhosis 7 countries in South America N=700 patients

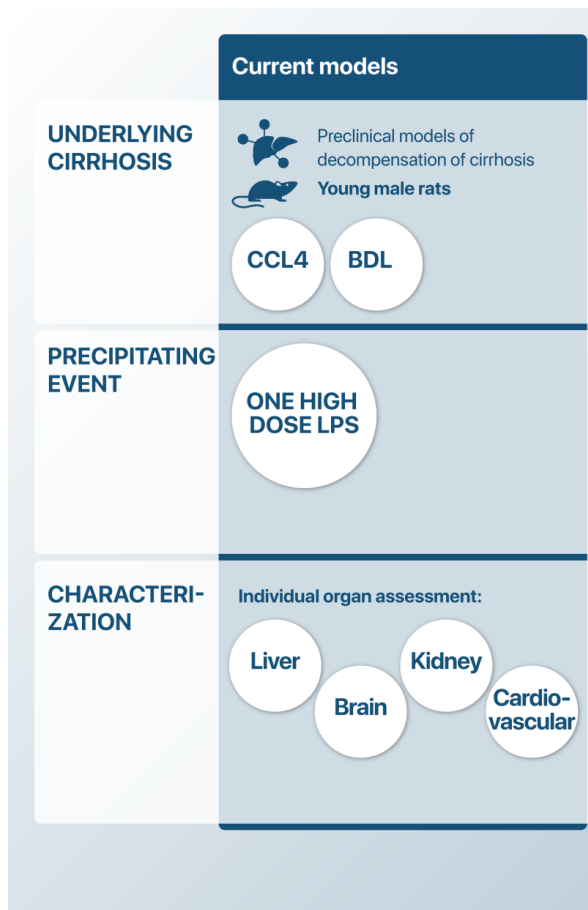
DECISION: new prognostic and response tests



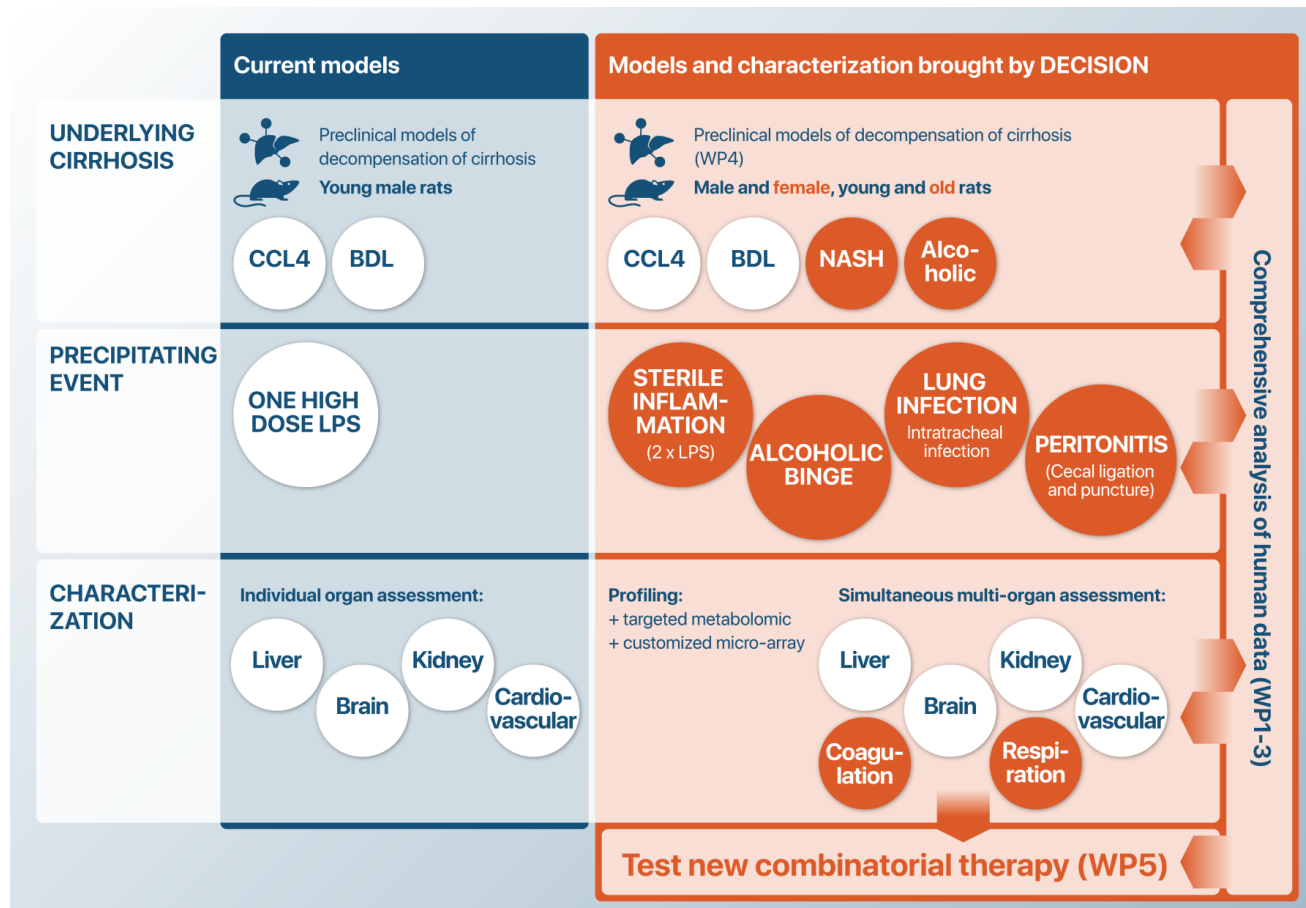
CURRENTLY



Animal models of acute decompensation / ACLF



DECISION: Refined and new animal models



The **DECISION** project: Aims

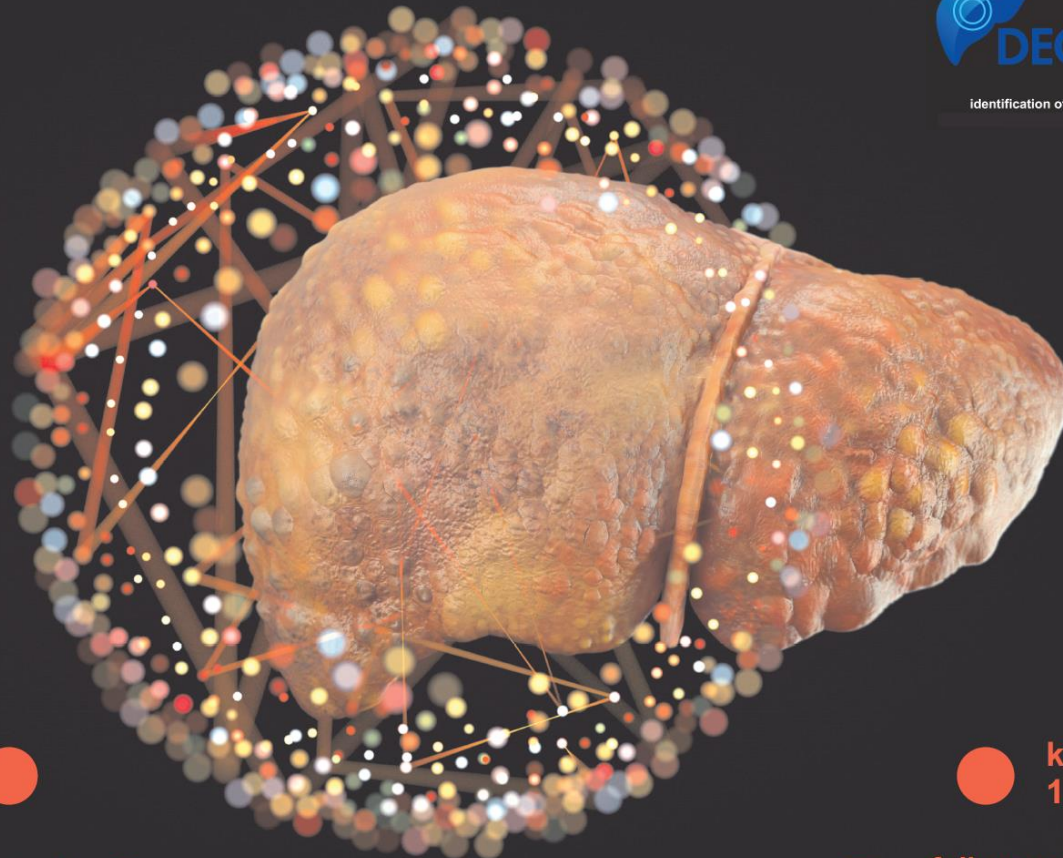
- **Understand** pathophysiology of acute decompensation
- Refine existing and develop new **animal models** of decompensation of cirrhosis leading to organs failure
- Identify **new combinatorial therapies**
- **Develop novel tests**

The DECISION project: Work packages

1. Extensive characterization using omic approaches (Prof. Joan Clària)
2. Data management (Dr. Cristina Sanchez)
3. Systems approaches (Dr. David Gomez-Cabrero)
4. Selection of combinatorial therapies in animal models (Prof. Jonel Trebicka)
5. Phase II prospective randomized controlled study (Prof. Paolo Caraceni)
6. Ethics, Health and Socio-Economics (Dr. Itziar de Lecuona)
7. Dissemination, communication, exploitation, guideline development, and training (Dr. Ameli Schwalber)
8. Project Management (Prof. Pierre-Emmanuel Rautou)

DECISION: Expected impact





project duration
5 ½ years

grant amount
6 million €

10 countries
21 institutions

kick-off
1st April 2020

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