

# **ALCOHOLIC LIVER DISEASE – NEW DEVELOPMENTS**

**MASSIMO PINZANI, MD, PhD, FRCP**  
Sheila Sherlock Chair of Hepatology  
UCL Institute for Liver and Digestive Health  
Royal Free Hospital, London, UK

# Alcoholic Liver Disease

Chronic alcohol misuse



Normal liver



Steatosis



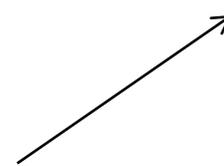
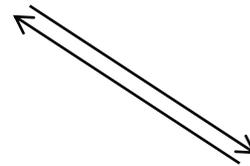
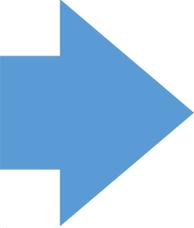
Steatohepatitis



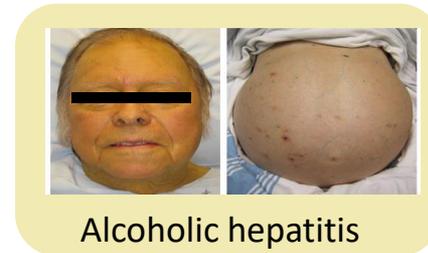
Cirrhosis



Decompensated cirrhosis

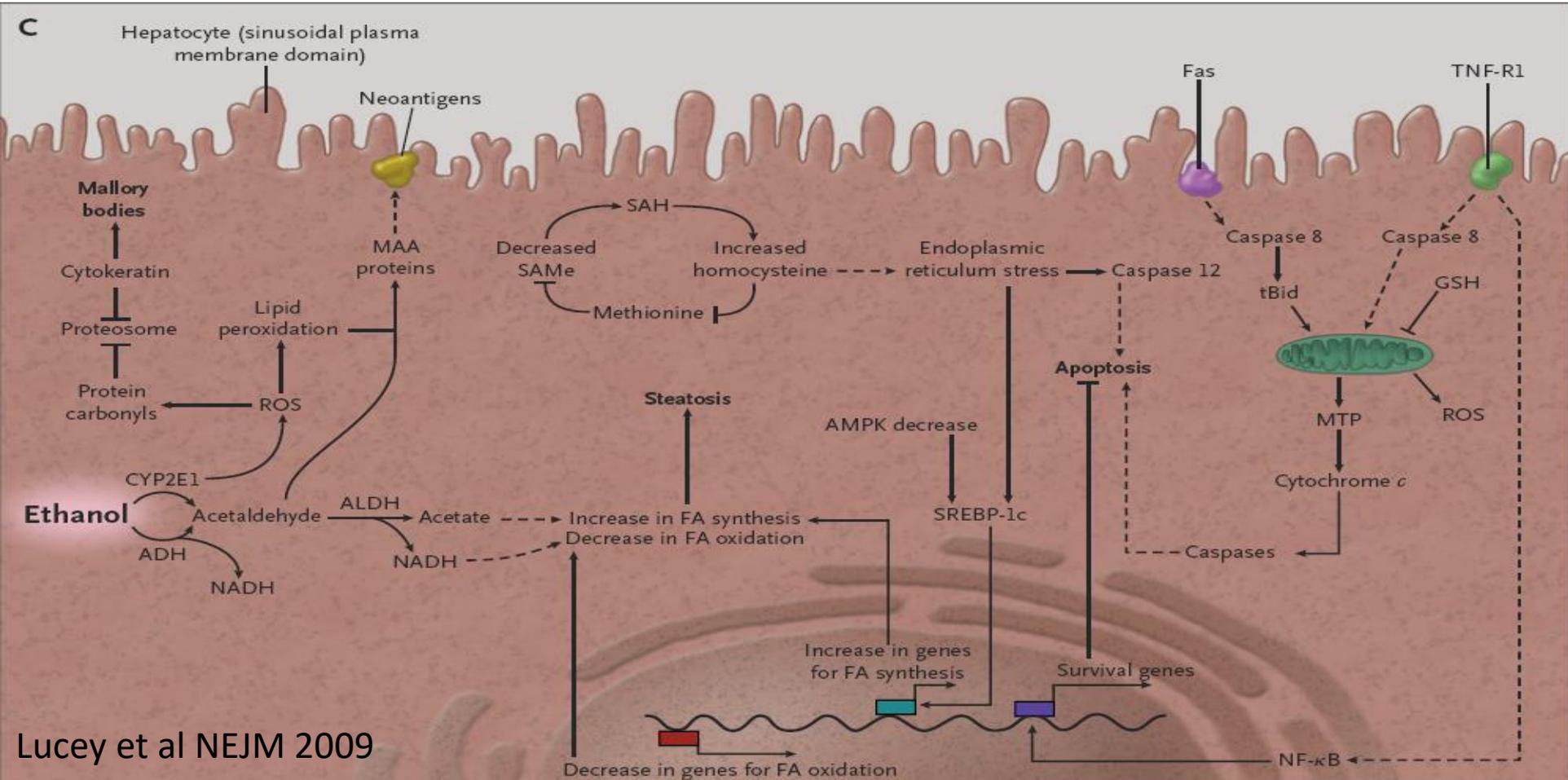


**BEST OF EASL**  
Addis Ababa



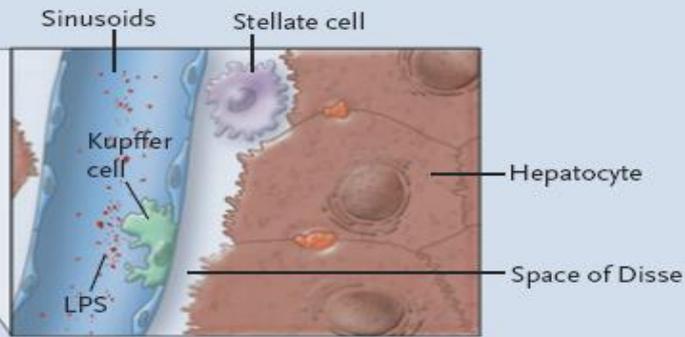
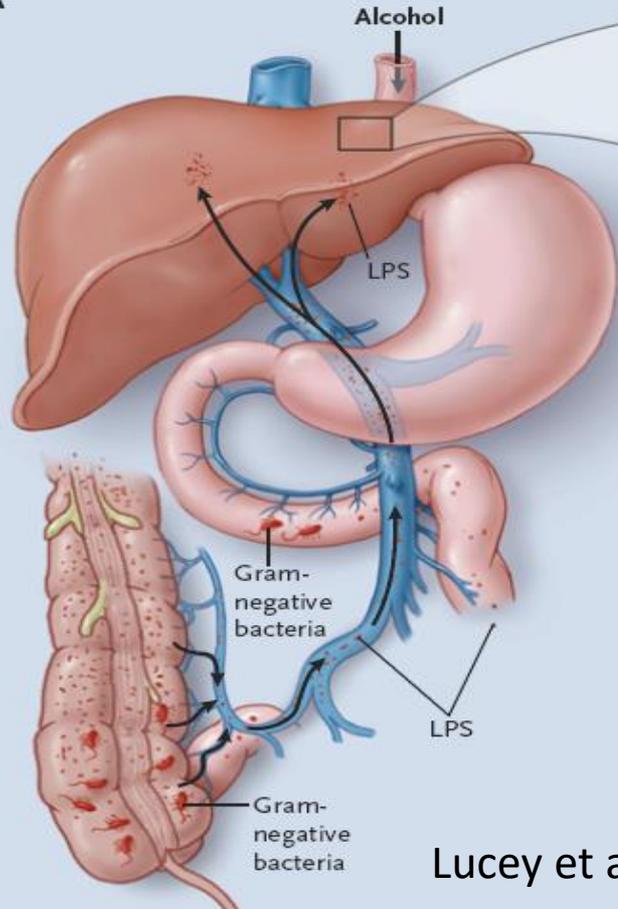
Alcoholic hepatitis

# Mechanism of Alcohol Damage 1

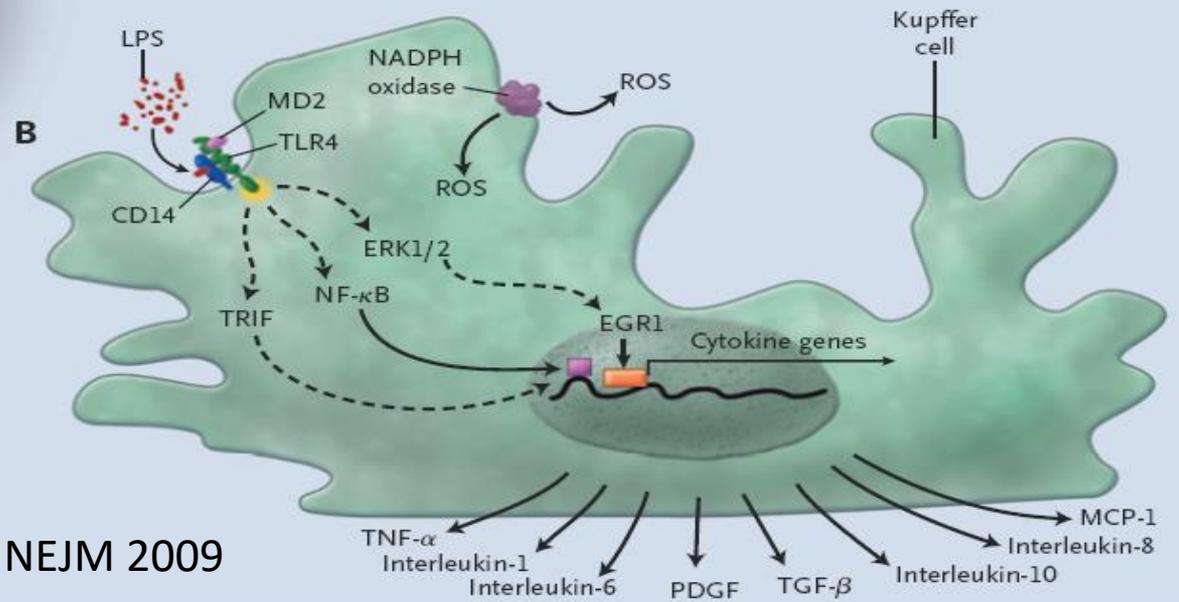


# Mechanism of Alcohol Damage 2

**A**



**B**



Lucey et al NEJM 2009

# ALD Presentation

- Abnormal LFTs
- Cirrhosis
- Alcoholic Hepatitis



**BEST OF EASL**  
Addis Ababa

# Diagnosis of Alcoholic Hepatitis

- AST raised
- AST:ALT > 2
- Bilirubin > 80  $\mu\text{mol}$
- INR > 1.3
- Neutrophilia
- Recent (< 6 weeks) alcohol abuse
- Exclude other causes of liver disease



**BEST OF EASL**  
Addis Ababa

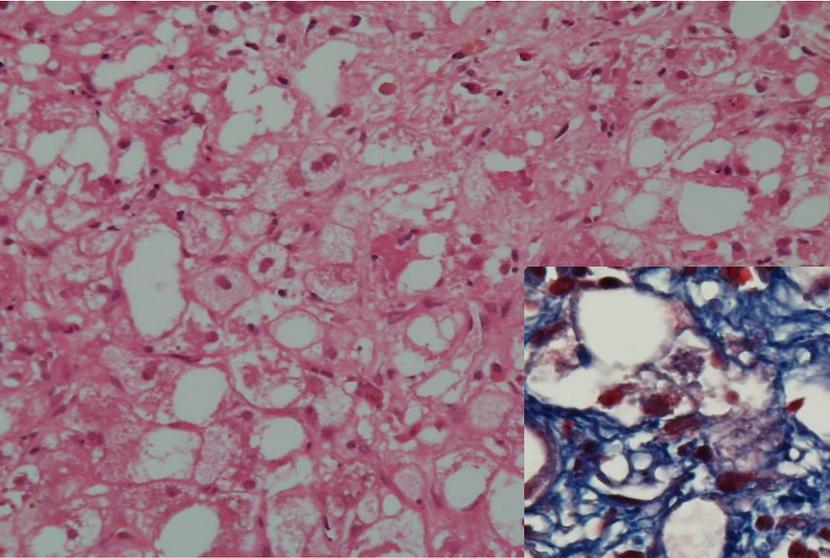
# Diagnosis of Alcoholic Hepatitis

- AST raised
- AST:ALT > 2
- Bilirubin > 80  $\mu\text{mol}$
- INR > 1.3
- Neutrophilia
- Recent (< 6 weeks) alcohol abuse
- Exclude other causes of liver disease
  
- Do you need a liver biopsy?

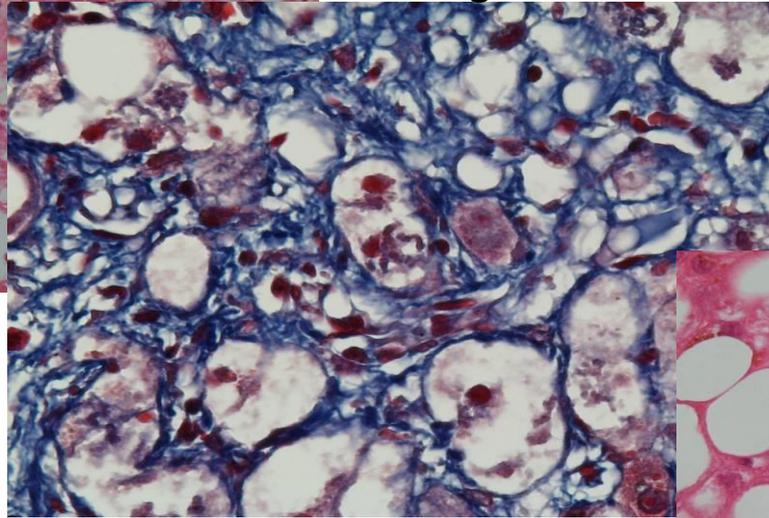


**BEST OF EASL**  
Addis Ababa

# Histological Appearance

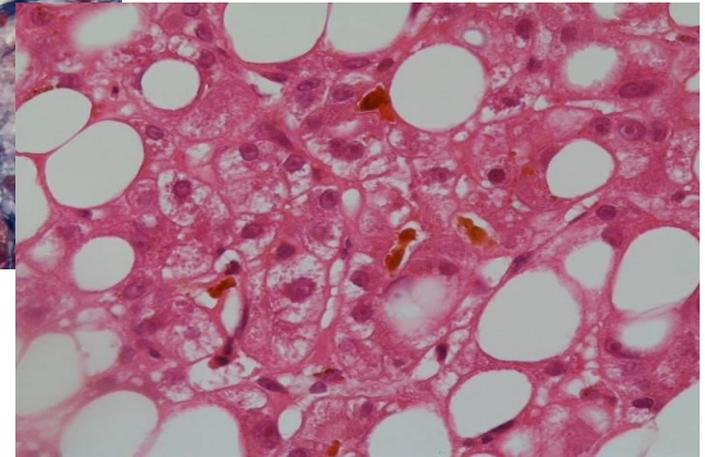


Steatosis  
Ballooning  
Mallory's Hyaline  
Mega mitochondria



Pericellular & perivenular  
fibrosis

Bile plugging



# Alcoholic Hepatitis Severity Scores

- Maddrey's discriminant function
  - $[4.6 \times (\text{patient's prothrombin time} - \text{control prothrombin time, in seconds})] + \text{serum bilirubin (mg/dl)}$
- MELD
  - $9.57 \times \log(\text{creatinine (mg/dl)}) + 3.78 \times \log(\text{bilirubin (mg/dl)}) + 11.20 \times \log(\text{INR}) + 6.43$

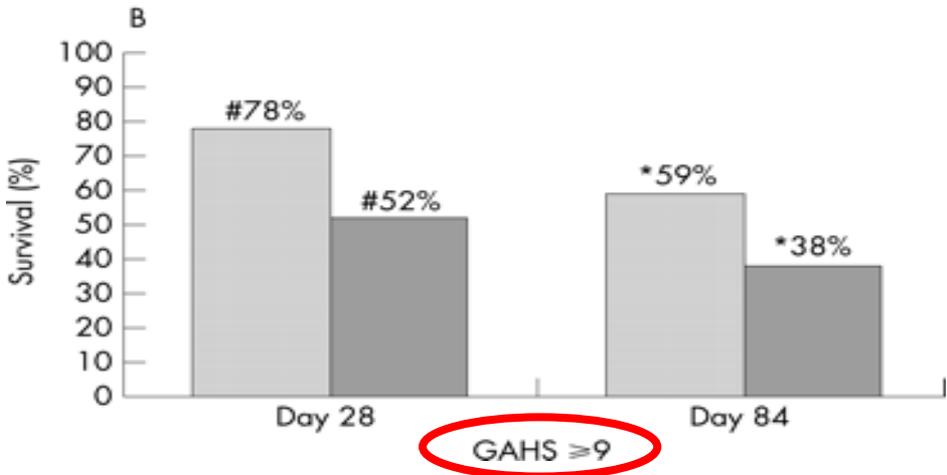
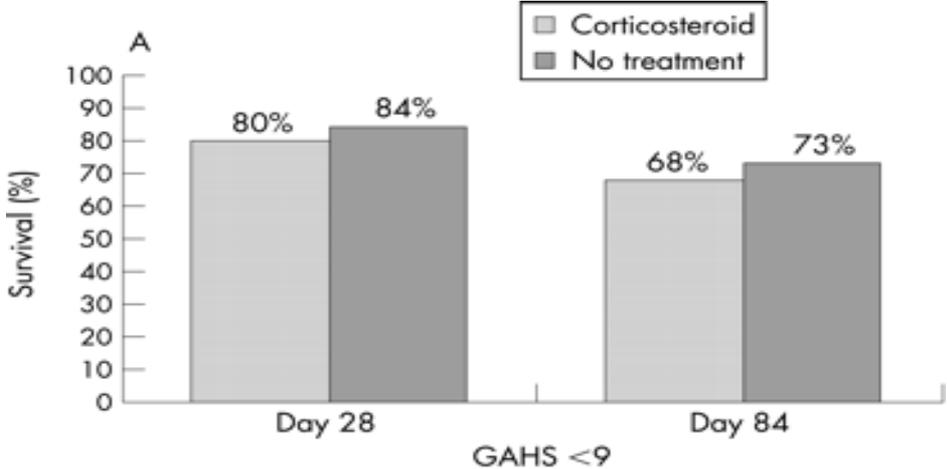
# Glasgow Alcoholic Hepatitis Score

Parameter	1	2	3
Age	<50	≥50	-
WBC (x 10 <sup>9</sup> )	<15	≥ 15	-
Urea (mmol)	<5	≥ 5	-
Prothrombin ratio	<1.5	1.5 – 2.0	>2.0
Bilirubin (umol)	<125	125 – 250	>250

# GAHS Predicts response to steroids



BEST OF EASL  
Addis Ababa



Forrest et al  
Gut 2007

# Lille Score

3.19

- 0.101 \* (age in years)

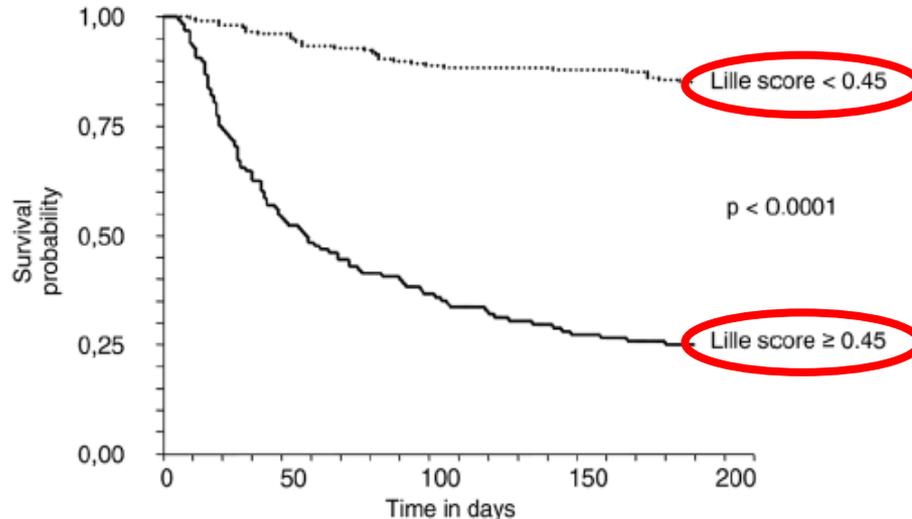
+ 0.147 \* (albumin day 0 in g/L)

+0.0165 \* (evolution in bilirubin level in uM)

-0.206 \* (renal insufficiency)

-0.0065 \* (bilirubin day 0 in uM)

-0.0096 \* (prothrombin time in seconds)



# Detection of Alcohol Use Disorders

- **CAGE**
  - Brief (4 question) screening tool
- **AUDIT**
  - 10 domain questionnaire to determine if alcohol dependence is present
- **SADQ**
  - The SADQ measures the severity of dependence:
    - · physical withdrawal symptoms
    - · affective withdrawal symptoms
    - · relief drinking
    - · frequency of alcohol consumption
    - · speed of onset of withdrawal symptoms

# Treatment of Alcohol Use Disorders

Recognition of AUD in  
GP / outpatient consultation

Admission for alcohol  
related disorder

Assess Dependence

Refer to alcohol services

Brief Intervention

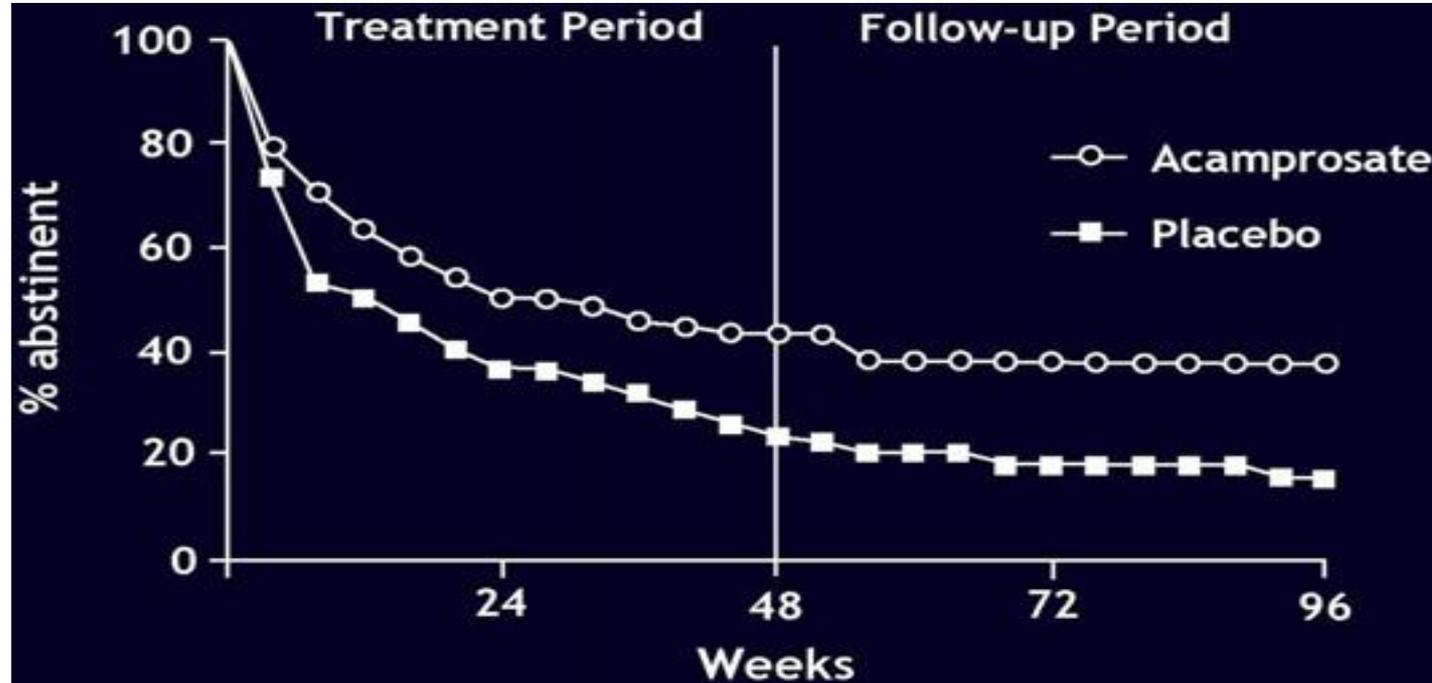
Psychosocial Interventions:

- Behavioural Self Control Therapy
- Motivational Enhancement Therapy
- Family therapy
- Social skills training

Pharmacological Intervention

- Acamprosate
- Disulfiram
- Naltrexone
- Baclofen

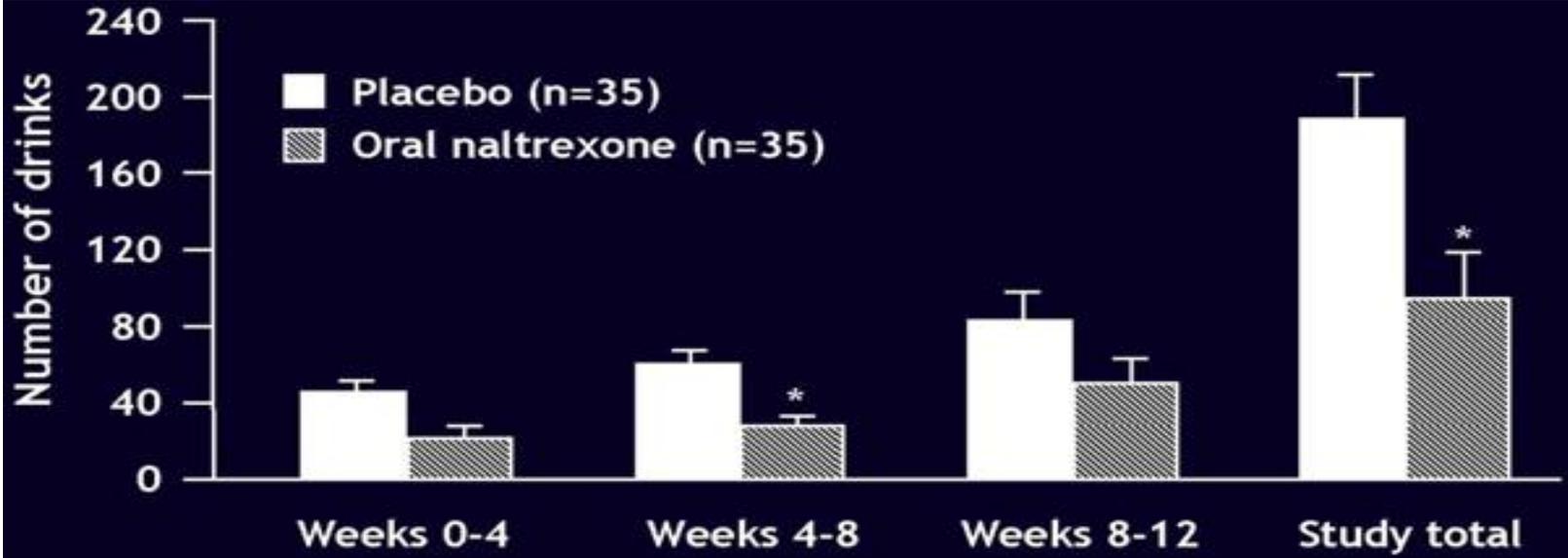
# Acamprosate in Alcohol Dependence



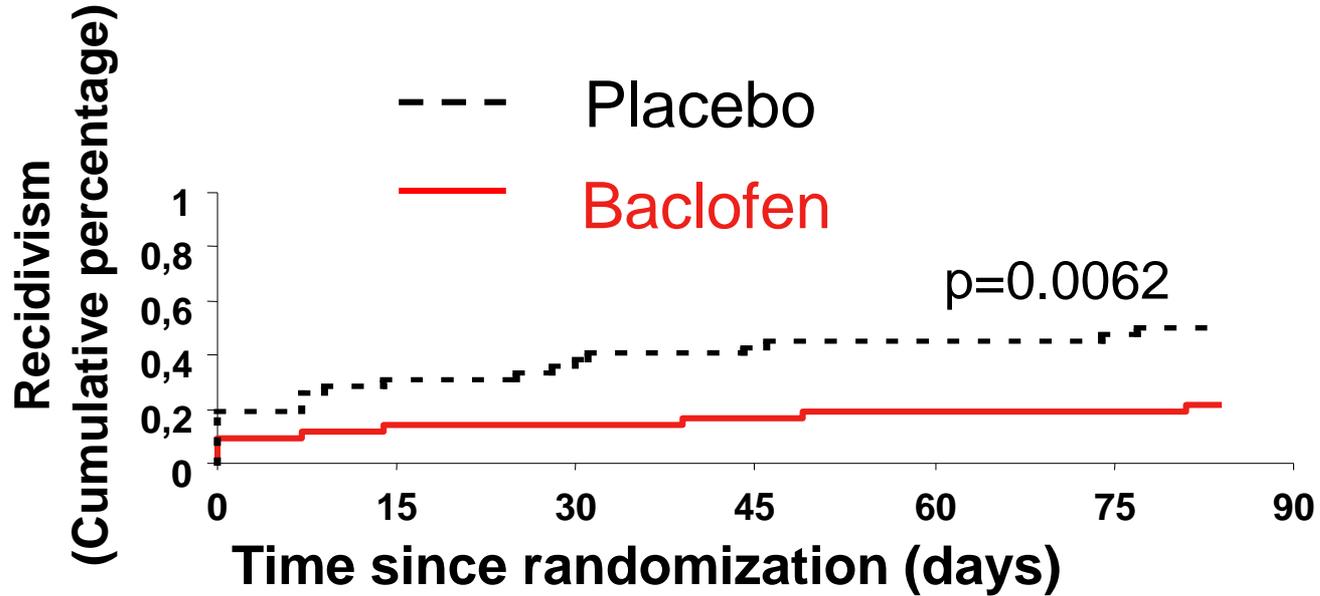
**EASL**  
The Home of Hepatology

**BEST OF EASL**  
Addis Ababa

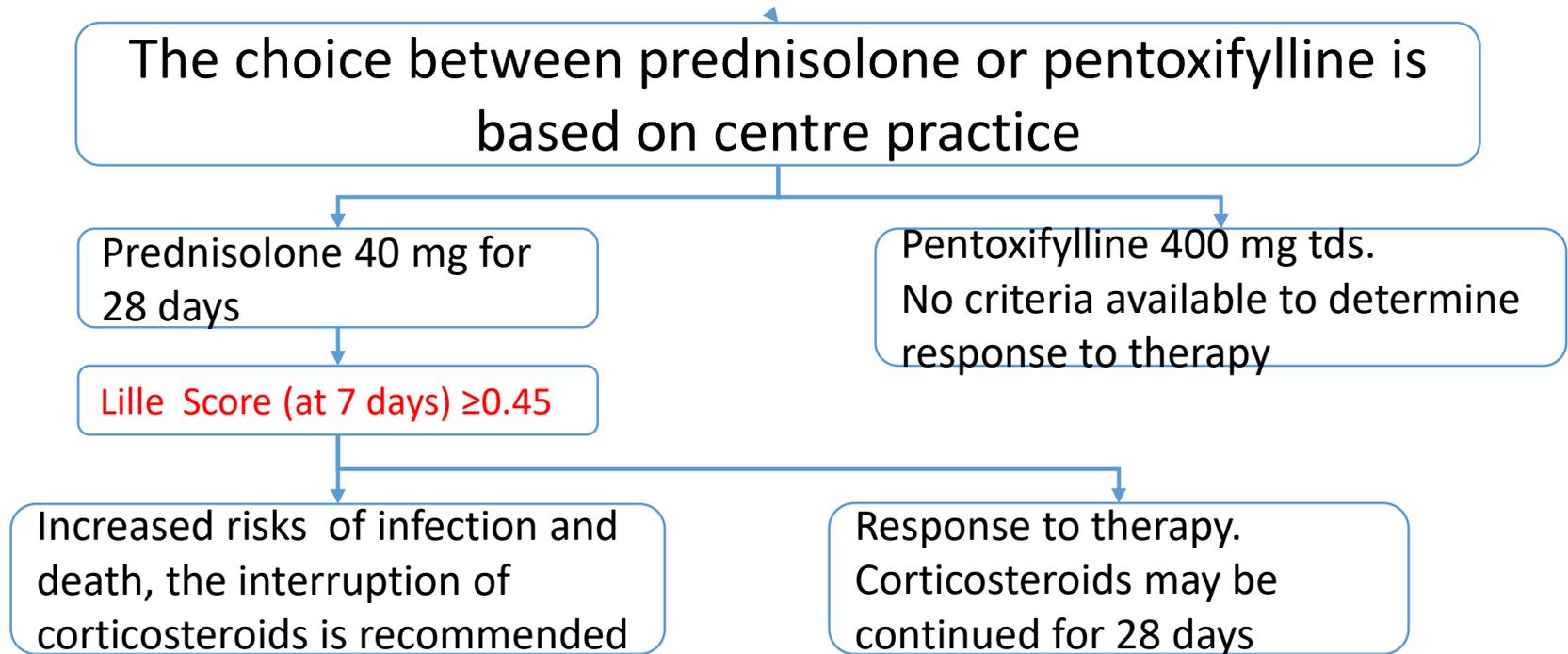
# Oral Naltrexone for Alcohol Dependence



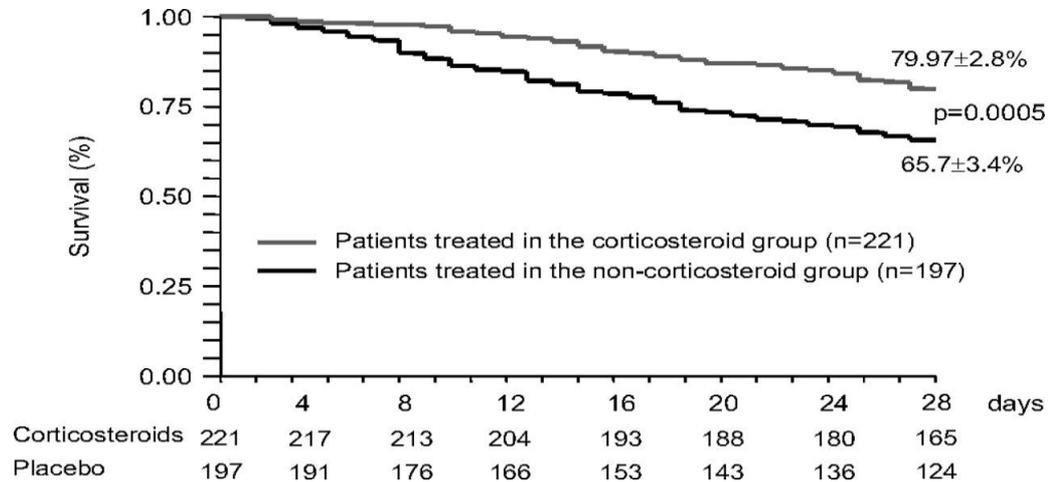
# Baclofen in alcoholic cirrhosis



# Treatment - EASL Guidelines

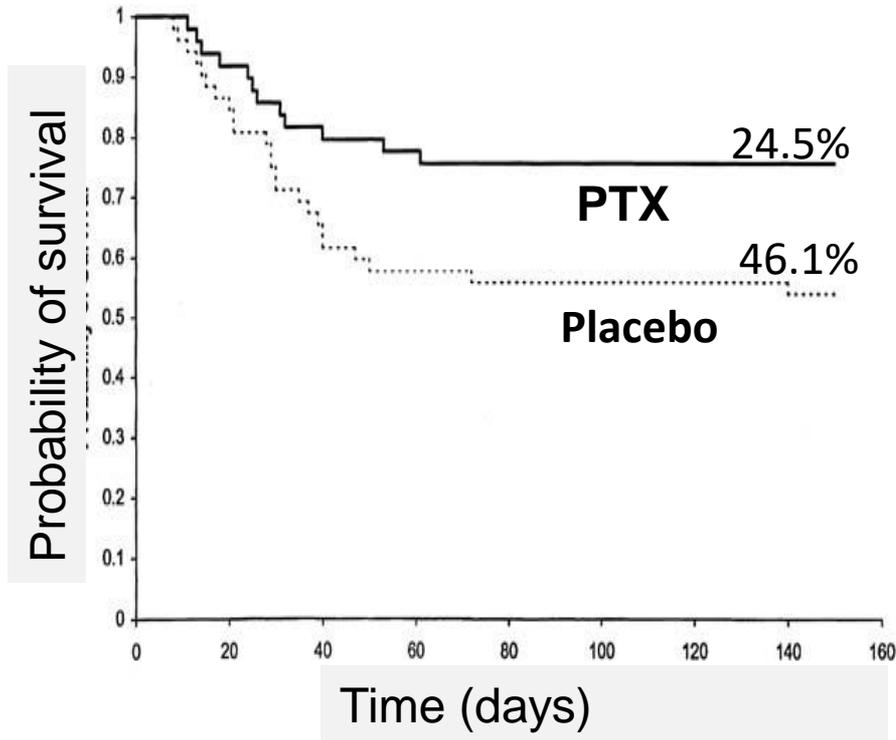


# Steroids: meta-analysis



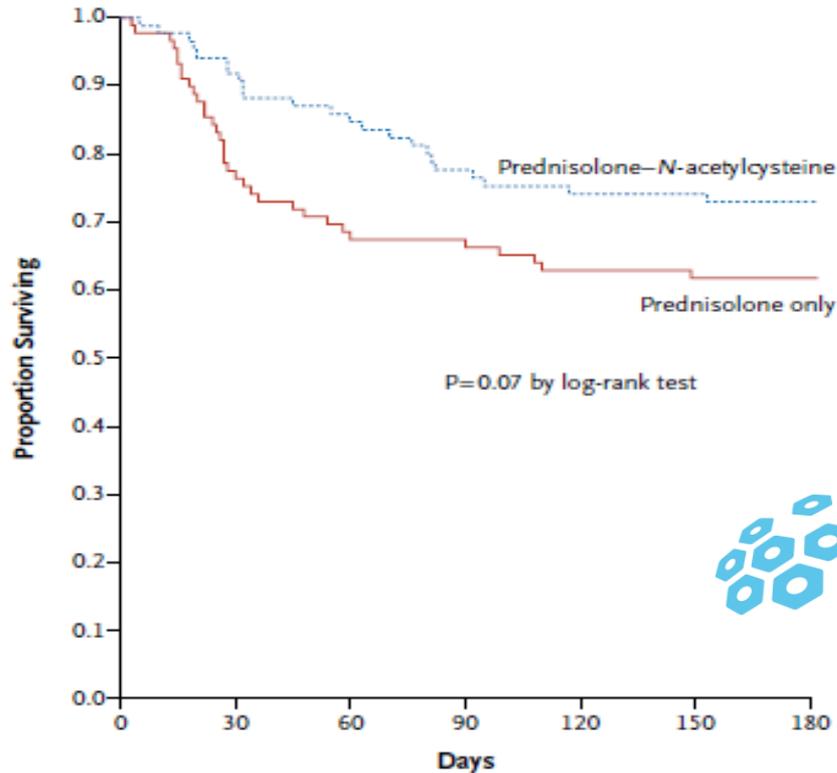
- Individual patient data from largest 5 RCTs
- 197 on placebo, 221 steroids
- All: mDF >32,
- 28 day survival 80 vs 66% (p=0.0005)

# Pentoxifylline



- 101 patients with mDF >32
- 4/52 PTX 400<sup>3</sup> vs placebo
- RR 0.59[0.35-0.97]
- Improved mortality due 1<sup>o</sup> to ↓ HRS deaths

# N-Acetyl-Cysteine + Steroids for Alcoholic Hepatitis



## No. at Risk

Prednisolone only	89	69	61	60	56	55	46
Prednisolone– N-acetylcysteine	85	78	73	66	63	63	48



**BEST OF EASL**  
Addis Ababa



# STeroids Or Pentoxifylline for Alcoholic Hepatitis

Randomised, Double blind

Placebo controlled

Factorial 2 x 2

Prednisolone efficacy

Pentoxifylline efficacy

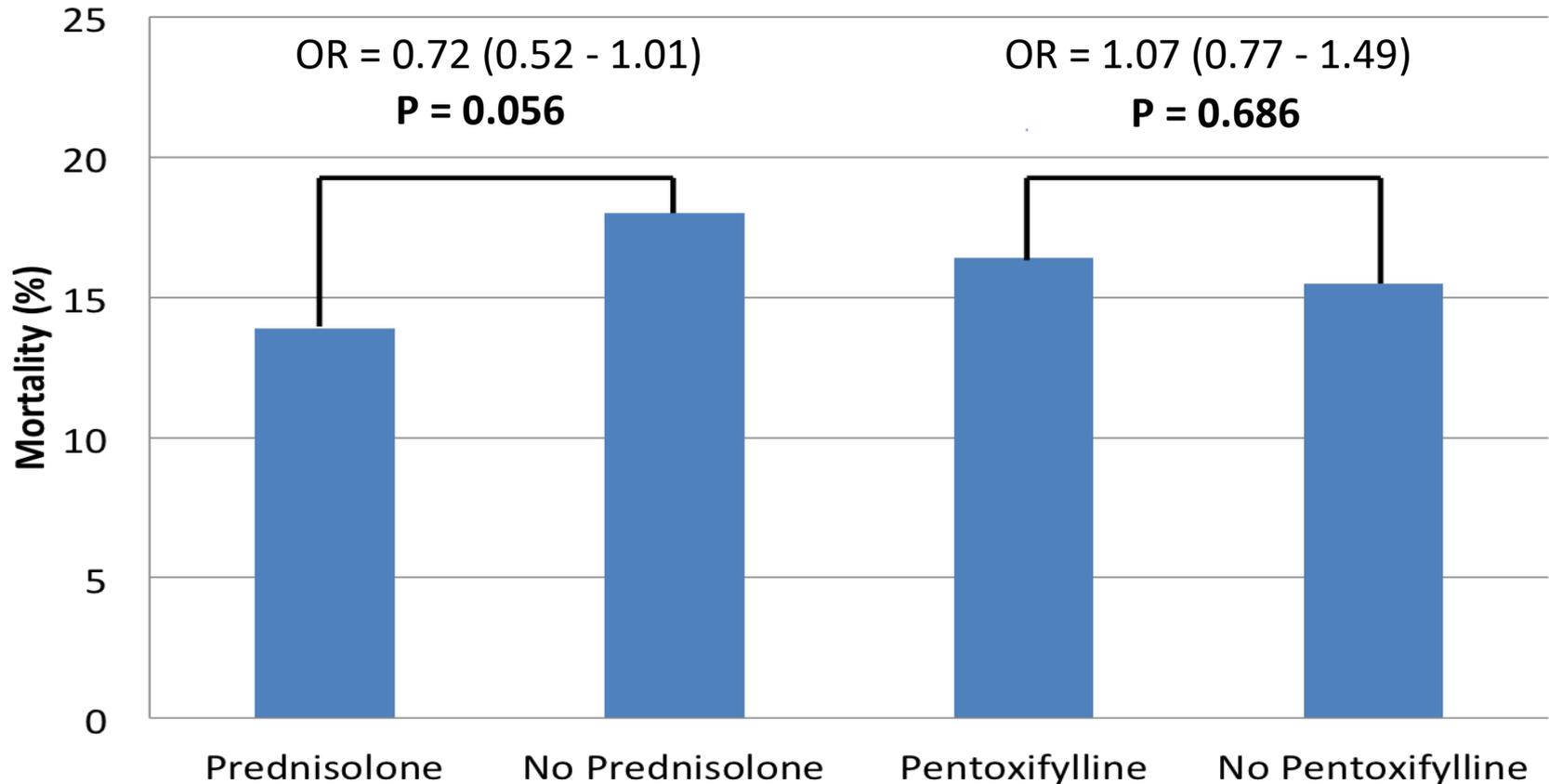
Definitive (power 90%)



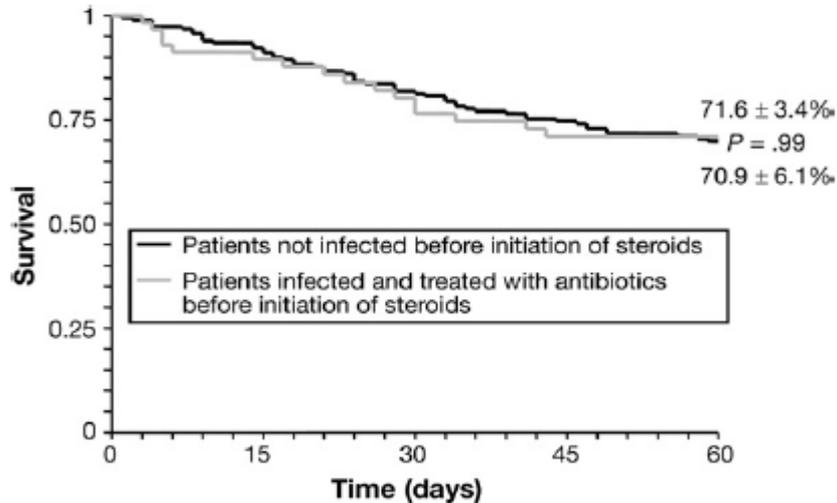
**BEST OF EASL**  
Addis Ababa

# Primary Endpoint

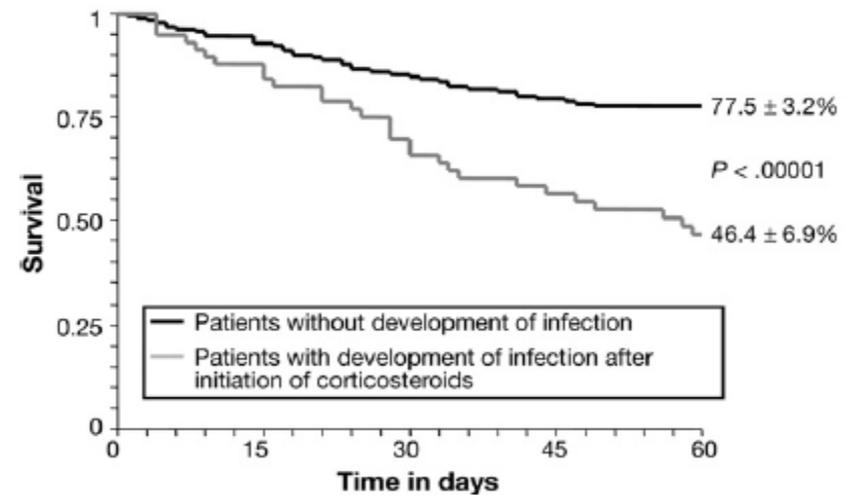
## Mortality at 28 Days



# Infection in Alcoholic Hepatitis

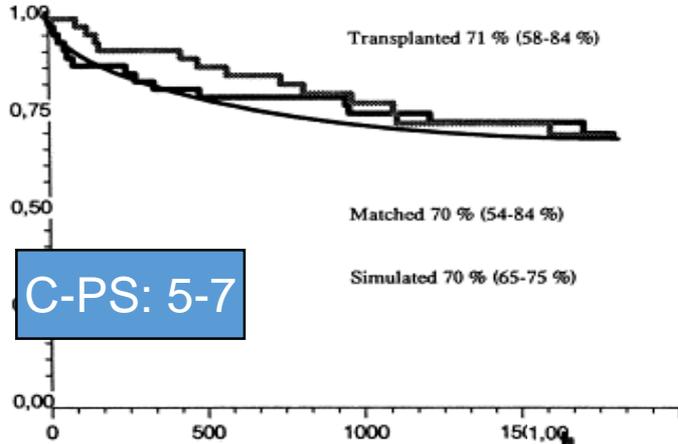


**Figure 1.** Survival impact of infection diagnosed before initiation of corticosteroids.

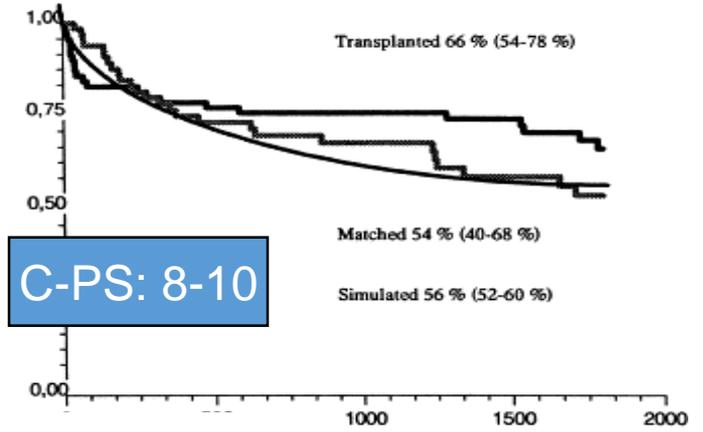


**Figure 2.** Two-month survival according to the development of infection after corticosteroids.

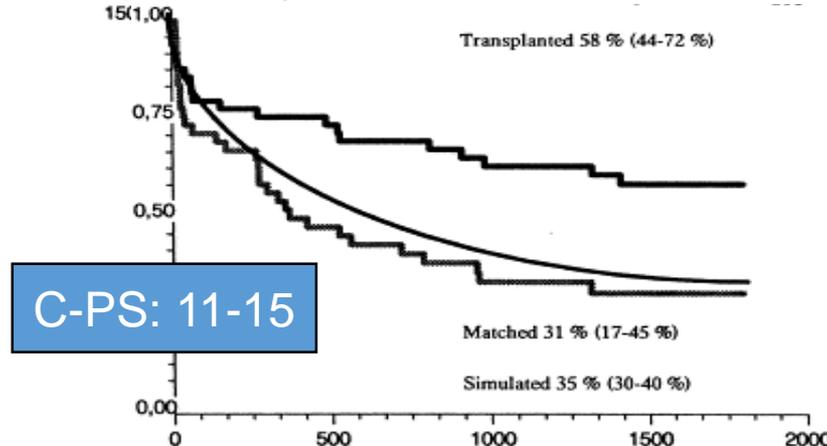
# Transplantation Improves survival in selected patients



C-PS: 5-7

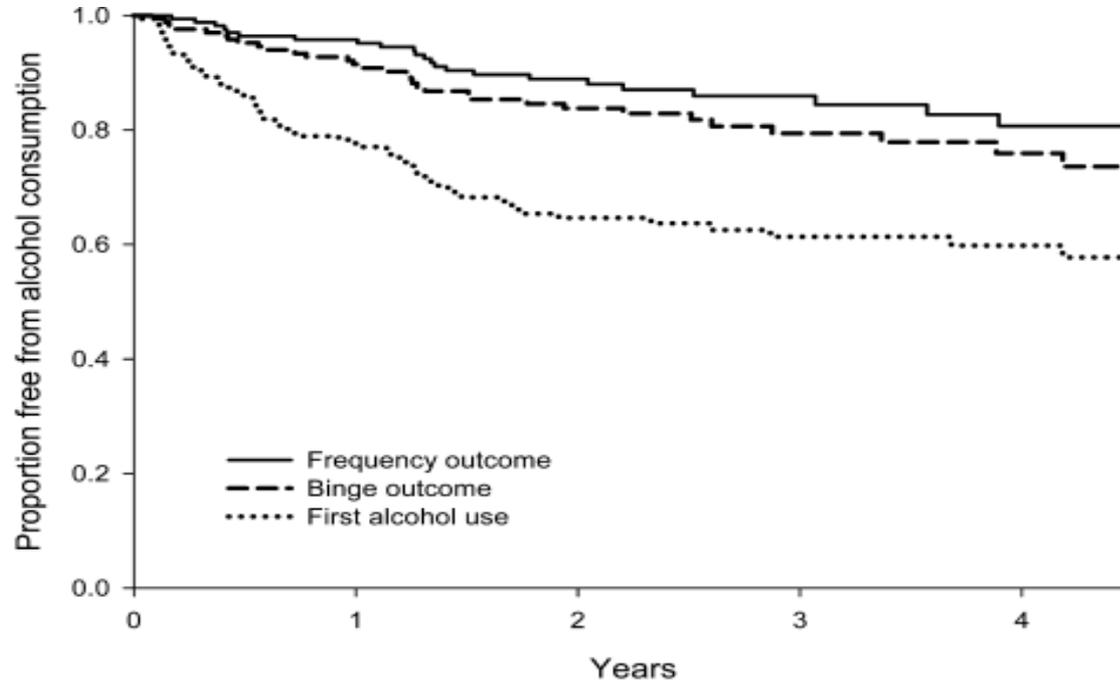


C-PS: 8-10



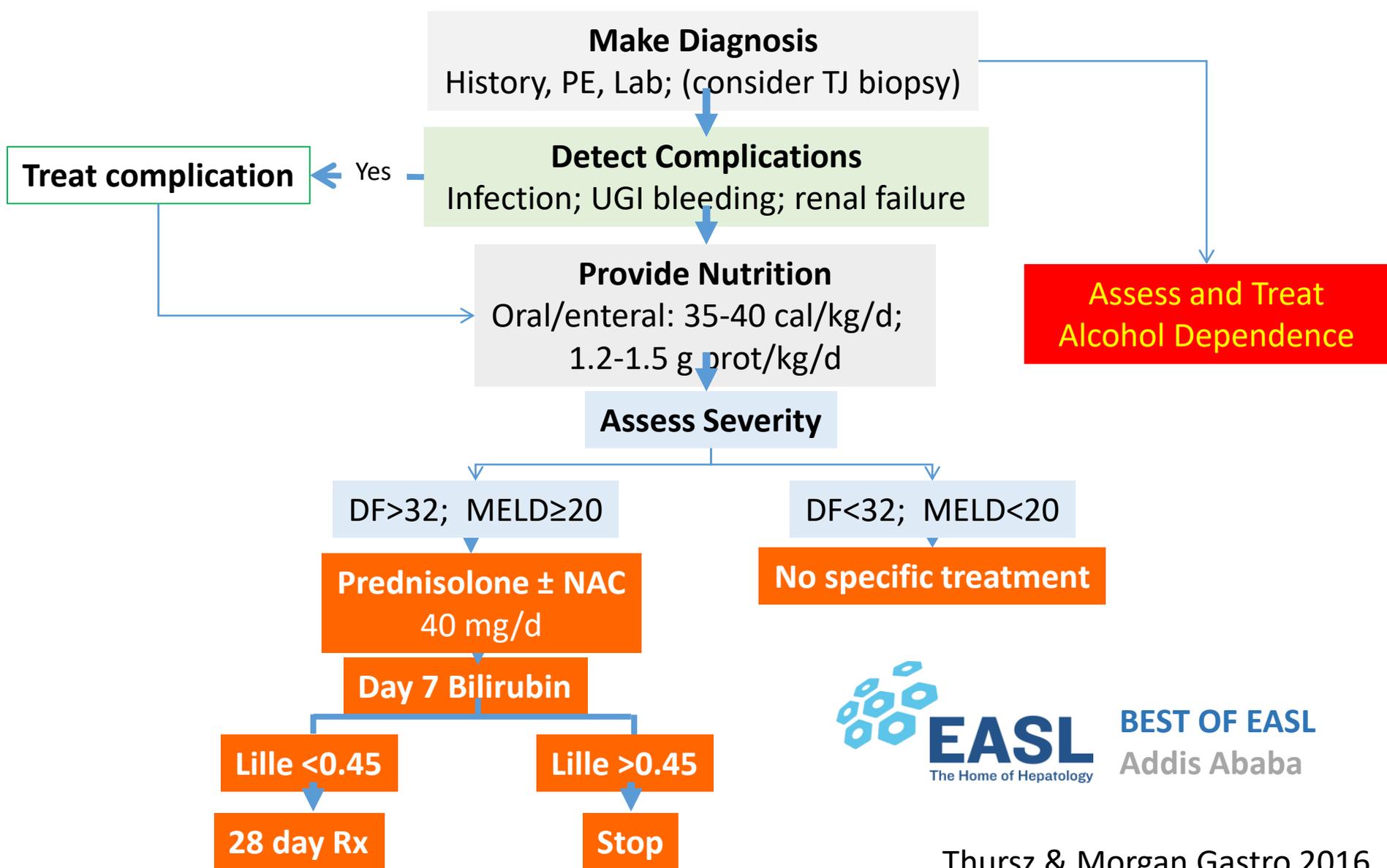
C-PS: 11-15

# Recidivism after Transplantation



Number remaining from 167 at time 0:

First Drink	123	79	46	33
Binge	144	101	56	37
Frequency	151	105	58	38





**BEST OF EASL**  
**Addis Ababa**