



# 非酒精性脂肪肝的診治

## Non-alcoholic fatty liver disease

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# Disclosures

- Advisory board member: AbbVie, Gilead, Janssen, Otsuka, Roche
- Consultancy: Merck, Novomedica
- Speaker: Abbott, AbbVie, Echosens, Gilead, Novartis, Roche

# Fatty liver



Less common causes:

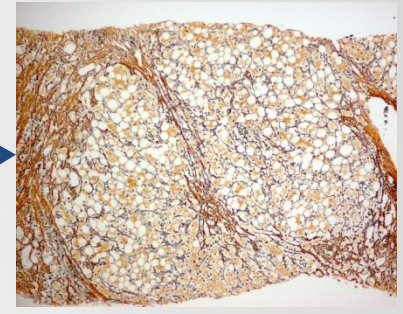
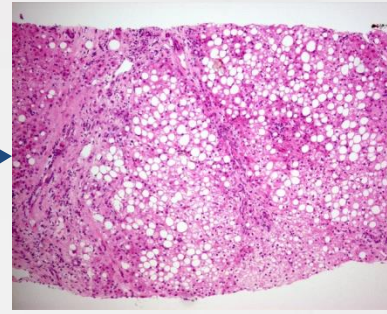
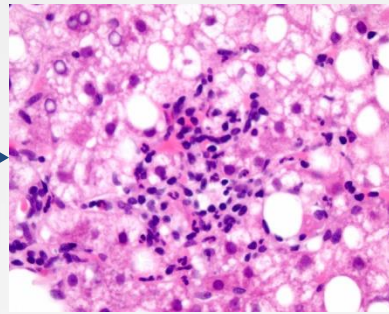
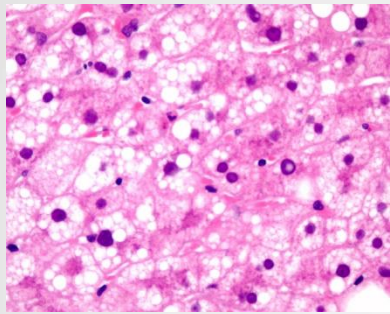
Drugs (e.g. methotrexate, steroids)

Rapid weight loss

Acute fatty liver of pregnancy

# Non-alcoholic fatty liver disease (NAFLD)

## The spectrum of disease



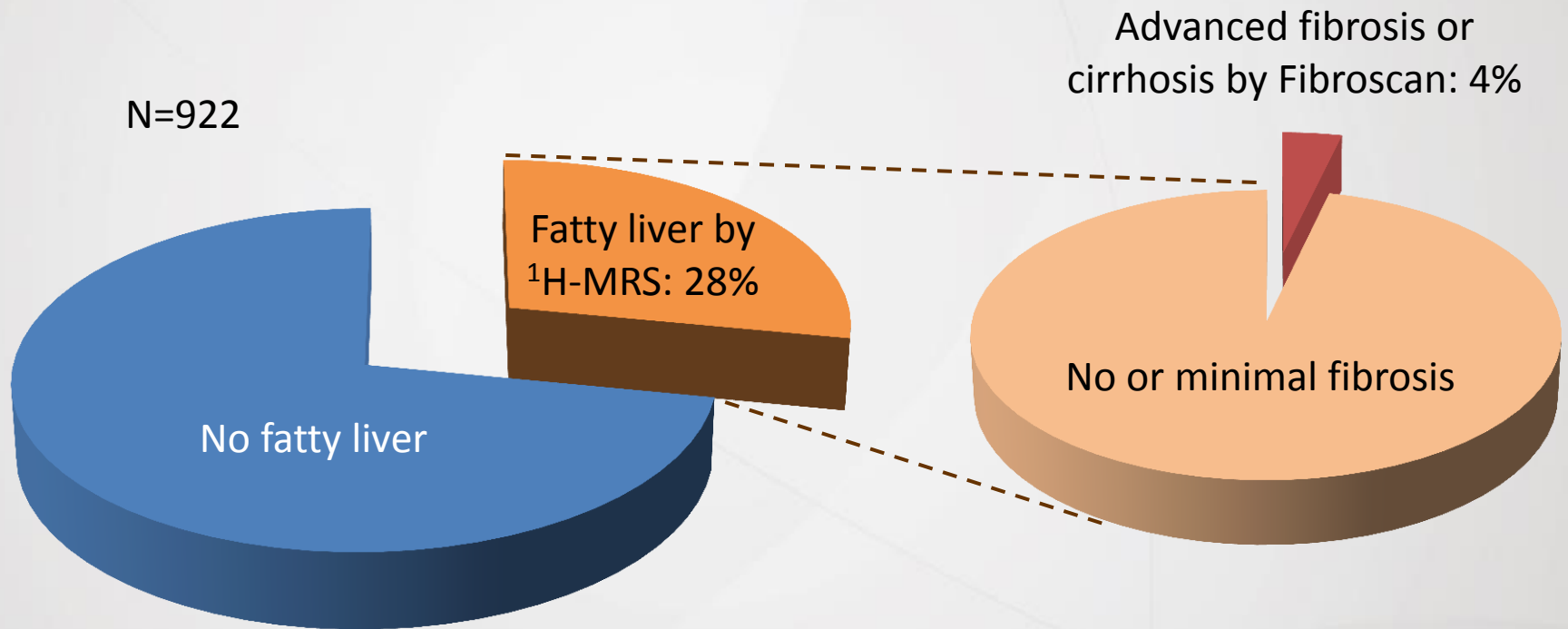
Non-alcoholic  
fatty liver  
(NAFL)

Non-alcoholic  
steatohepatitis  
(NASH)

Progressive  
liver fibrosis

Cirrhosis

# The HK-MRS Study



Wong VW et al. Gut 2012;61:409

# Public health implications

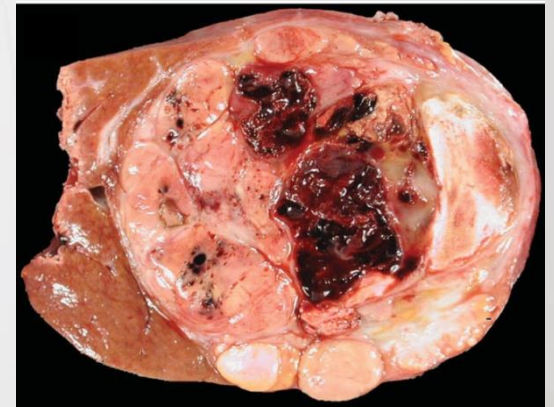
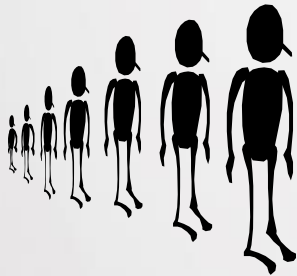
>1,000,000  
adult NAFLD  
patients in HK



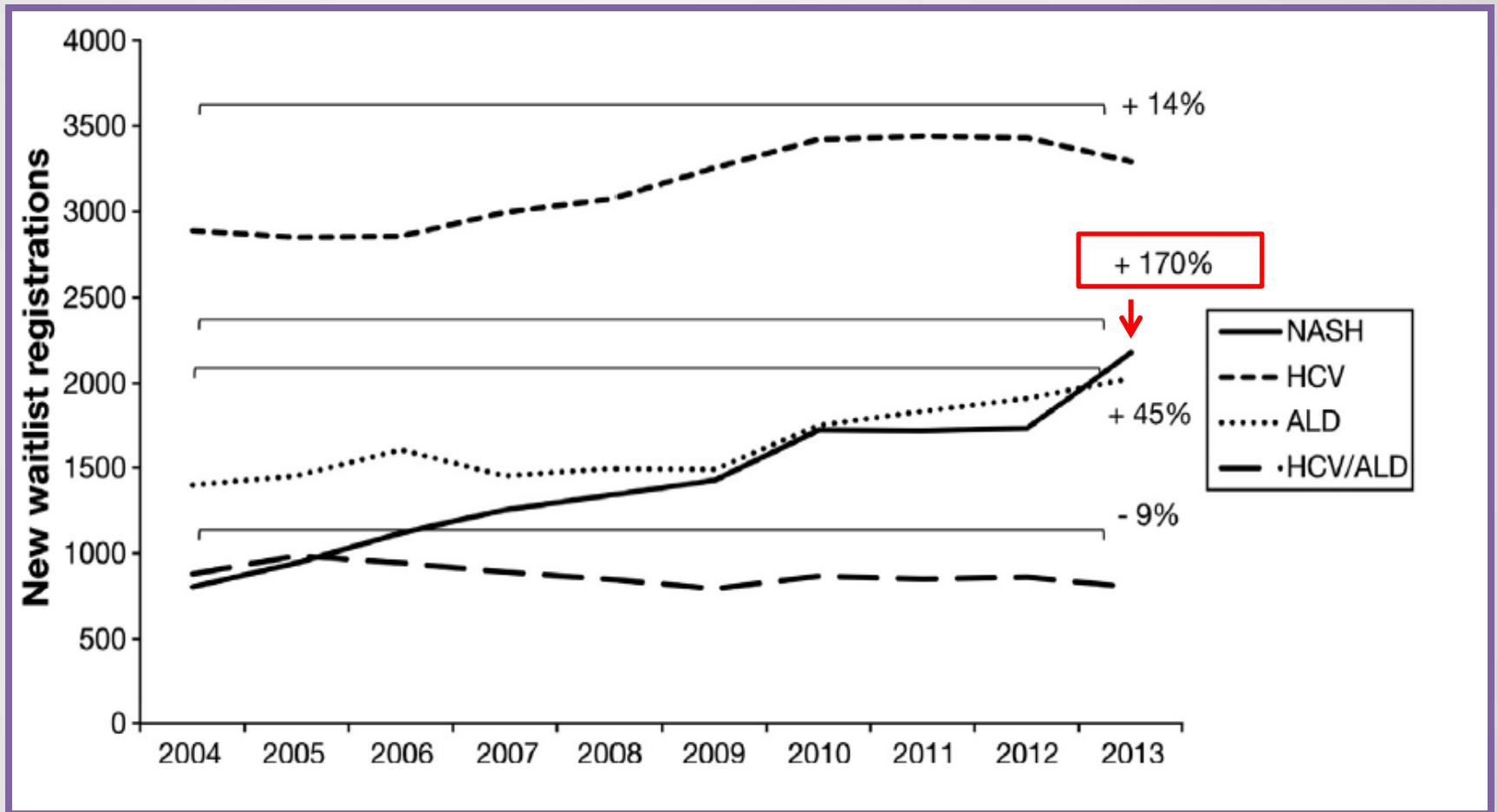
40,000 have  
advanced fibrosis  
or cirrhosis



20-30% will  
develop liver  
cancer and  
cirrhotic  
complications



# Fatty liver has become the 2<sup>nd</sup> leading indication for liver transplantation in USA



# Investigations for suspected NAFLD

- Confirm the diagnosis
- Assess disease severity
- Associated cardiometabolic diseases



# Diagnosis

- Bright liver under ultrasound
- Liver enzymes can be normal in >half of cases
- Exclude other liver diseases (e.g. viral hepatitis)

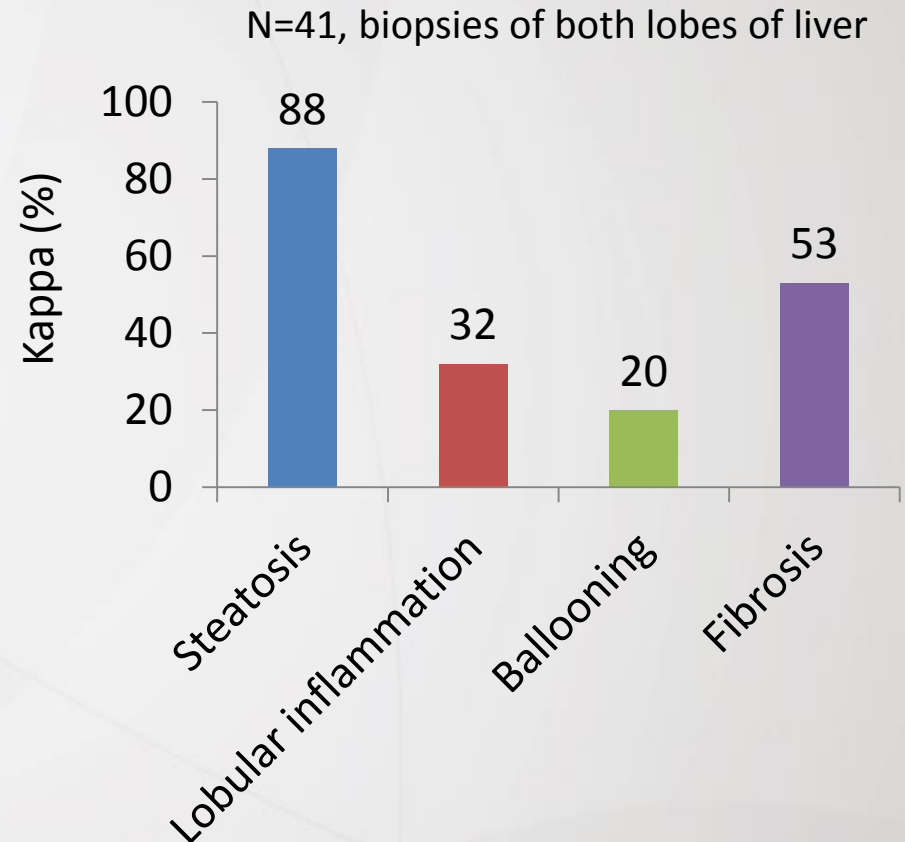


# Diagnostic workup

- Minimal workup: HBsAg, anti-HCV
- Alcohol and drug history
- Less common liver diseases according to clinical presentation and local epidemiology

# Problems of liver biopsy for the evaluation of NAFLD

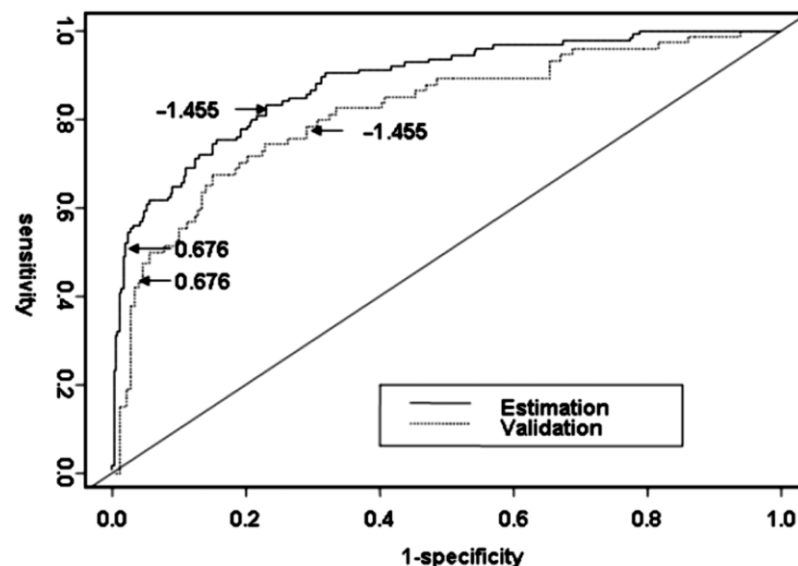
- Contraindications
  - Bleeding tendency
  - Ascites
- Complications
  - Pain
  - Bleeding
- Sampling error



# NAFLD fibrosis score

- Derivation and validation in 733 NAFLD patients
- 6 parameters: age, hyperglycemia, BMI, platelet, albumin, AST/ALT ratio

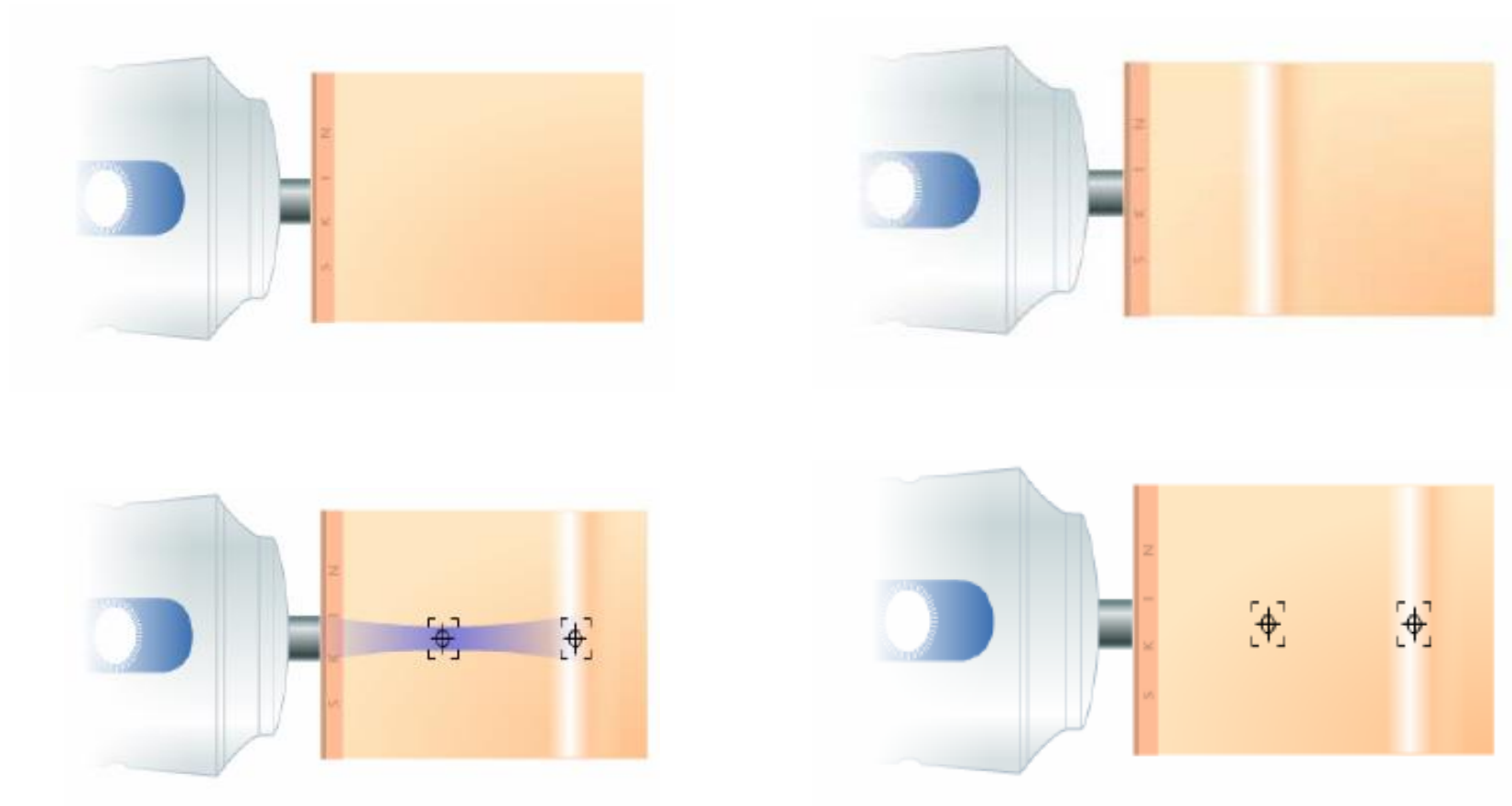
AUROC for F3 disease:  
0.88 in estimation group  
0.82 in validation group



# Transient elastography (FibroScan®)



# Liver stiffness measurement (LSM)

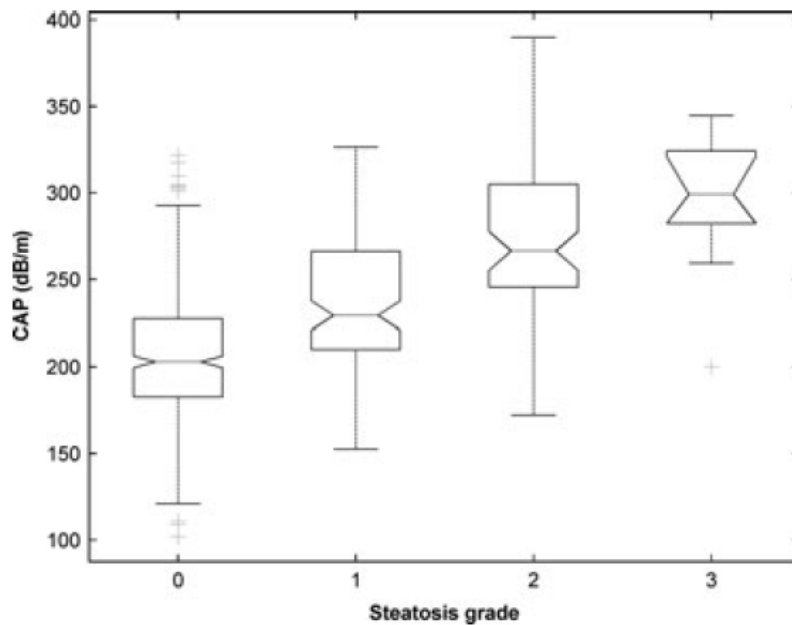
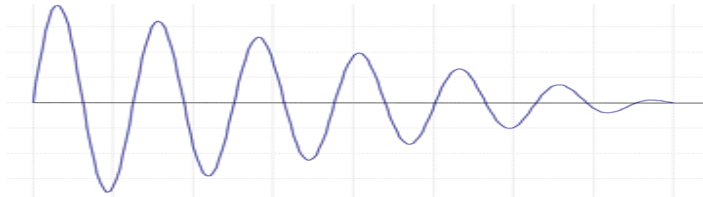


# Detection of advanced fibrosis and cirrhosis by Fibroscan and serum tests

246 NAFLD patients

Tests	AUROC for $\geq$ F3	AUROC for F4
Fibroscan	93%	95%
AST/ALT ratio	66%	66%
APRI	74%	75%
FIB-4	80%	81%
NAFLD fibrosis score	75%	80%
BARD score	69%	62%

# Controlled attenuation parameter (CAP) and liver fat



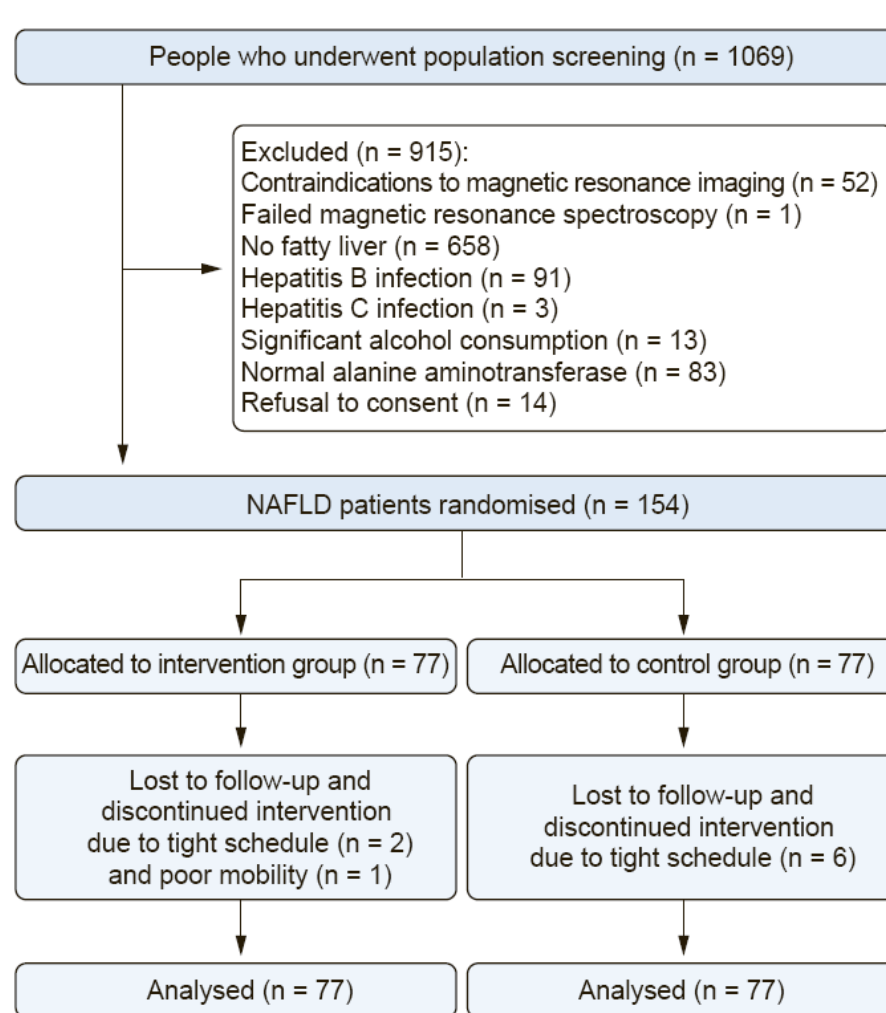
Steatosis	≥10%	≥33%	≥66%
AUROC	0.80	0.86	0.88
Cutoff	222	233	290
Sensitivity	76%	87%	78%
Specificity	71%	74%	93%



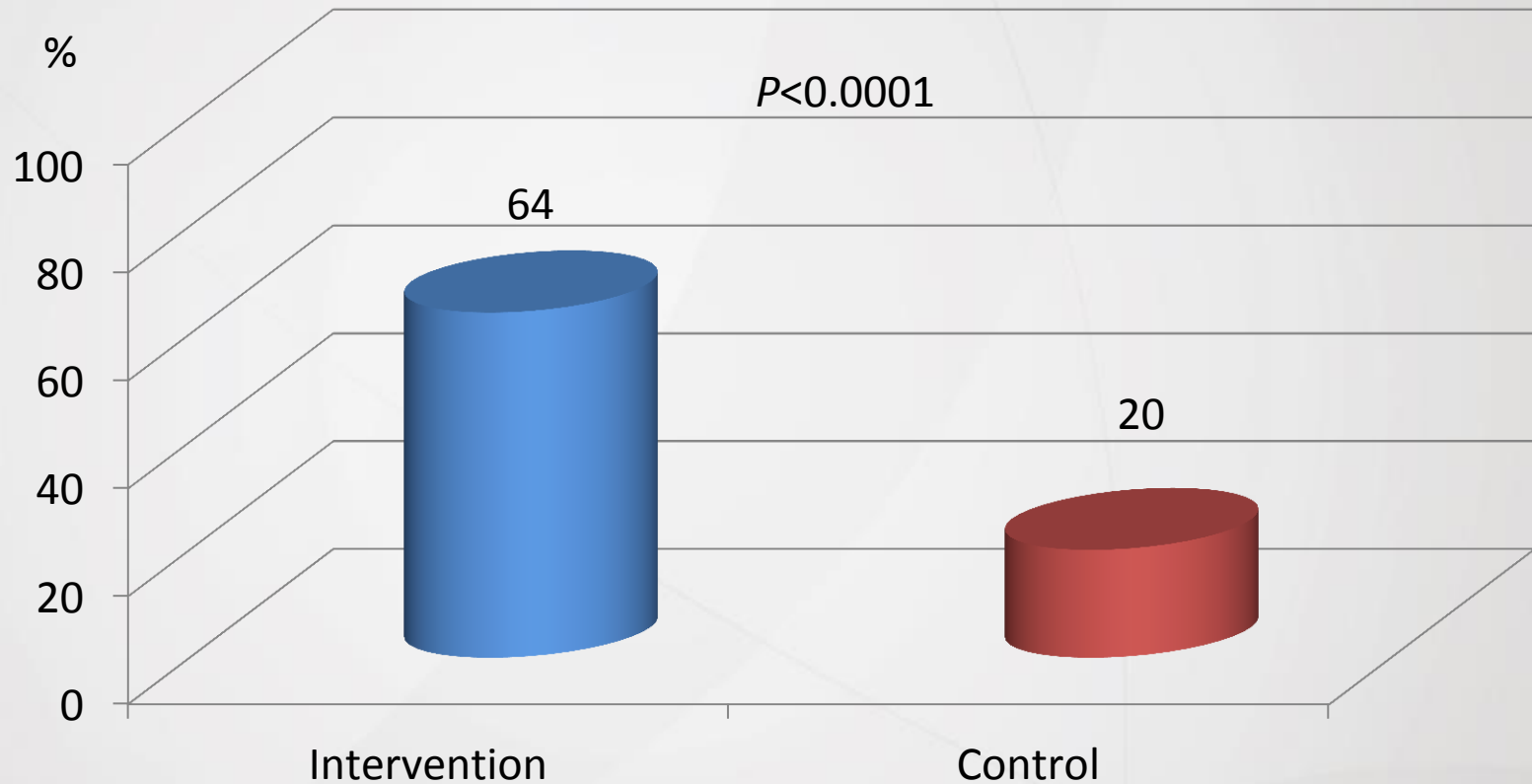
# Treatment of NAFLD

- Lifestyle modification, weight reduction
- Treat associated metabolic disorders (statin is safe)
- Pharmacological treatment for NASH
- Bariatric surgery if morbidly obese

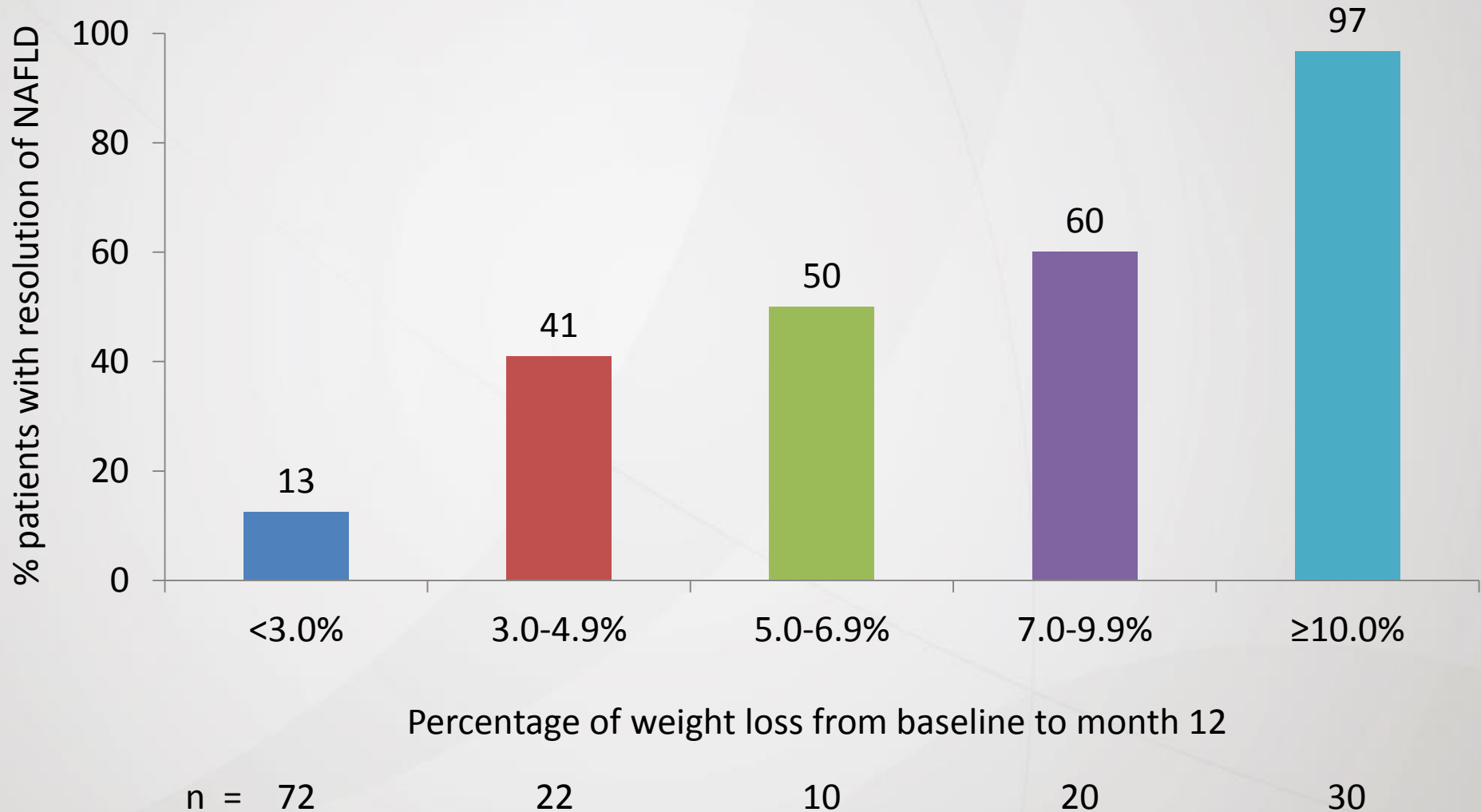
# NAFLD-Diet Study



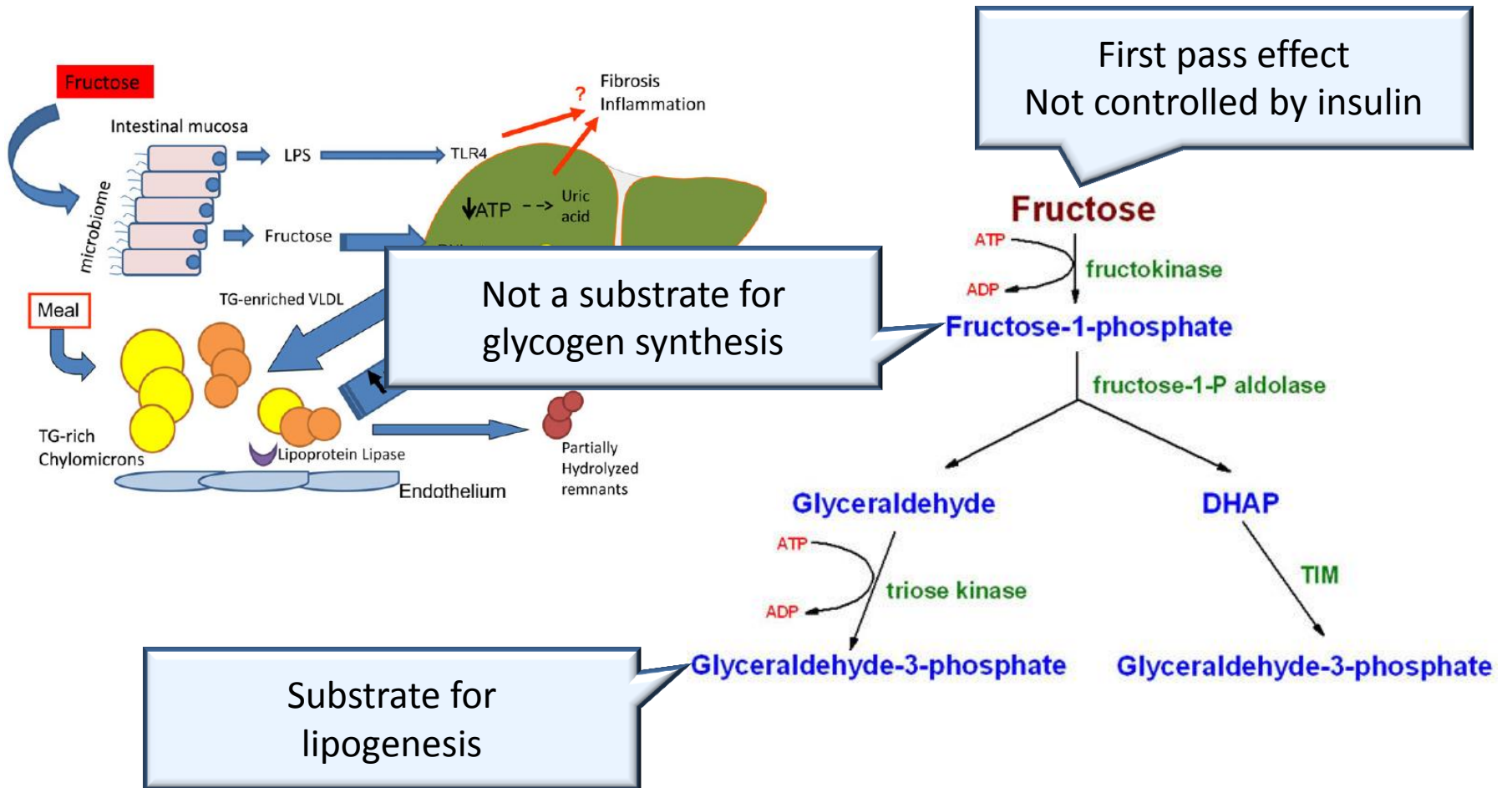
# Proportion of patients with resolved NAFLD



# Degree of weight loss and remission of NAFLD



# Fructose and NAFLD



# Pharmacological treatment of NASH

## Vitamin E

- Anti-oxidant
- Reduces liver fat and inflammation
- Neutral effects on insulin resistance
- Uncertain effects on the cardiovascular system and malignancy

## Pioglitazone

- Insulin sensitizer
- Reduces liver fat and inflammation
- Causes weight gain  $\pm$  fluid retention
- May increase the risk of bladder cancer

ORIGINAL ARTICLE

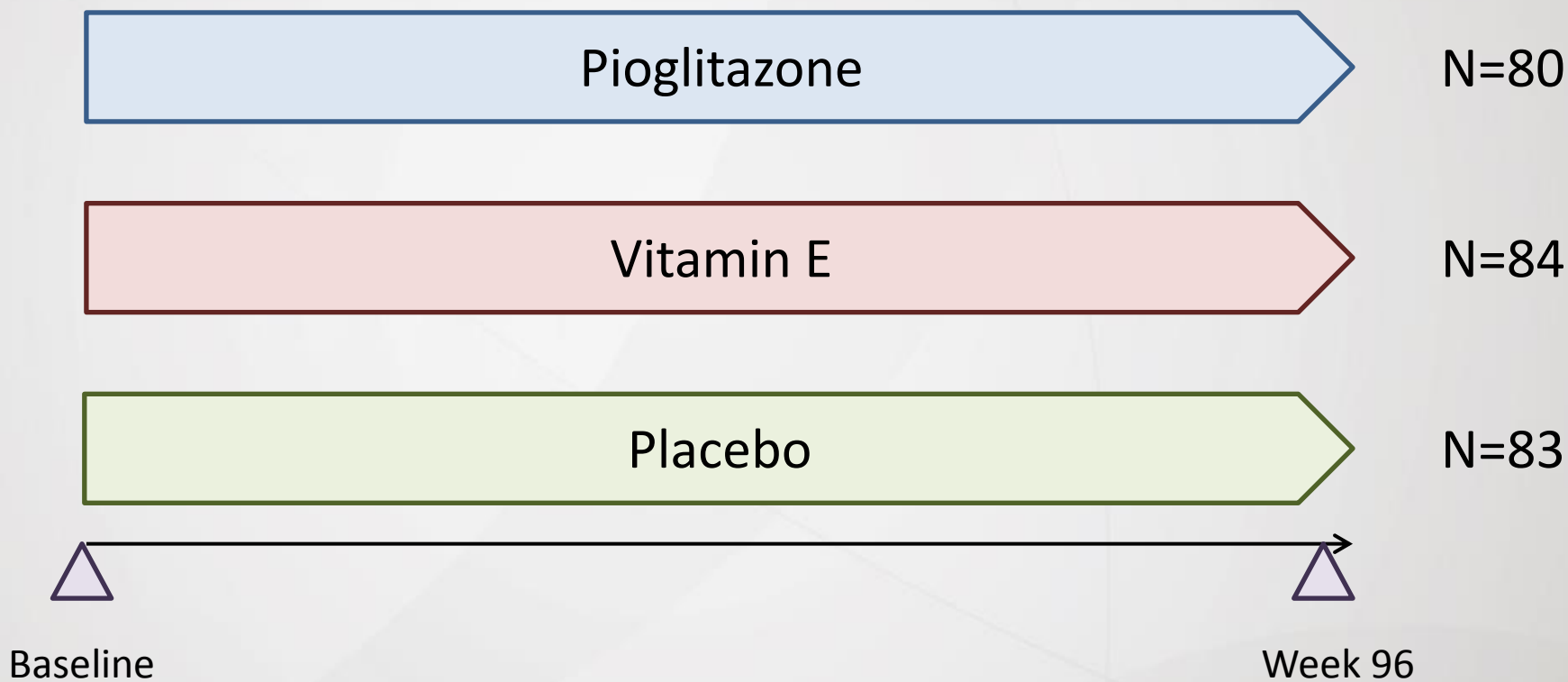
# Pioglitazone, Vitamin E, or Placebo for Nonalcoholic Steatohepatitis

Arun J. Sanyal, M.D., Naga Chalasani, M.B., B.S., Kris V. Kowdley, M.D.,  
Arthur McCullough, M.D., Anna Mae Diehl, M.D., Nathan M. Bass, M.D., Ph.D.,  
Brent A. Neuschwander-Tetri, M.D., Joel E. Lavine, M.D., Ph.D.,  
James Tonascia, Ph.D., Aynur Unalp, M.D., Ph.D., Mark Van Natta, M.H.S.,  
Jeanne Clark, M.D., M.P.H., Elizabeth M. Brunt, M.D.,  
David E. Kleiner, M.D., Ph.D., Jay H. Hoofnagle, M.D.,  
and Patricia R. Robuck, Ph.D., M.P.H., for the NASH CRN\*

NEJM 2010;362:1675

# PIVENS Study

247 patients with biopsy-proven NASH



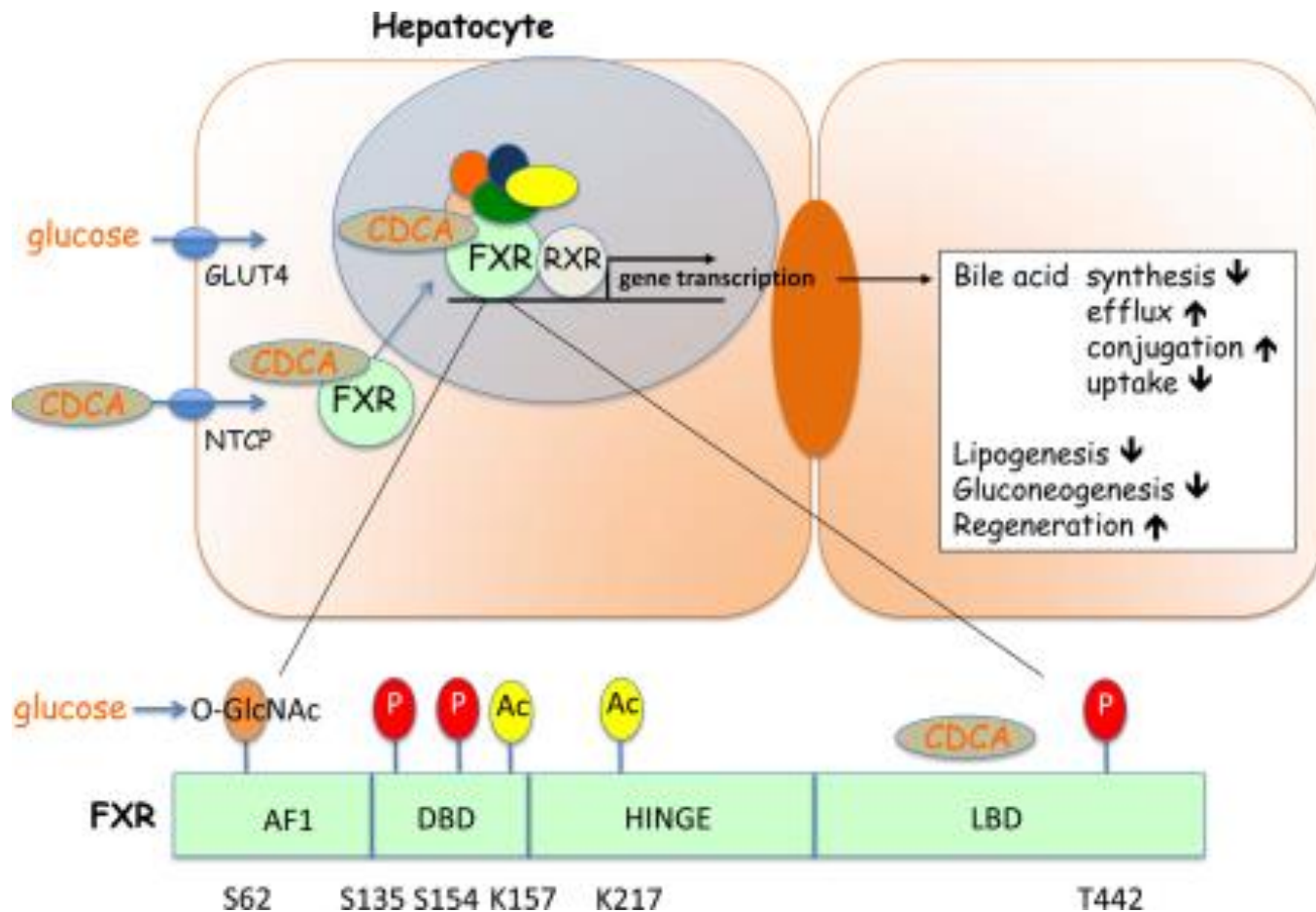


# Histological changes at 96 weeks

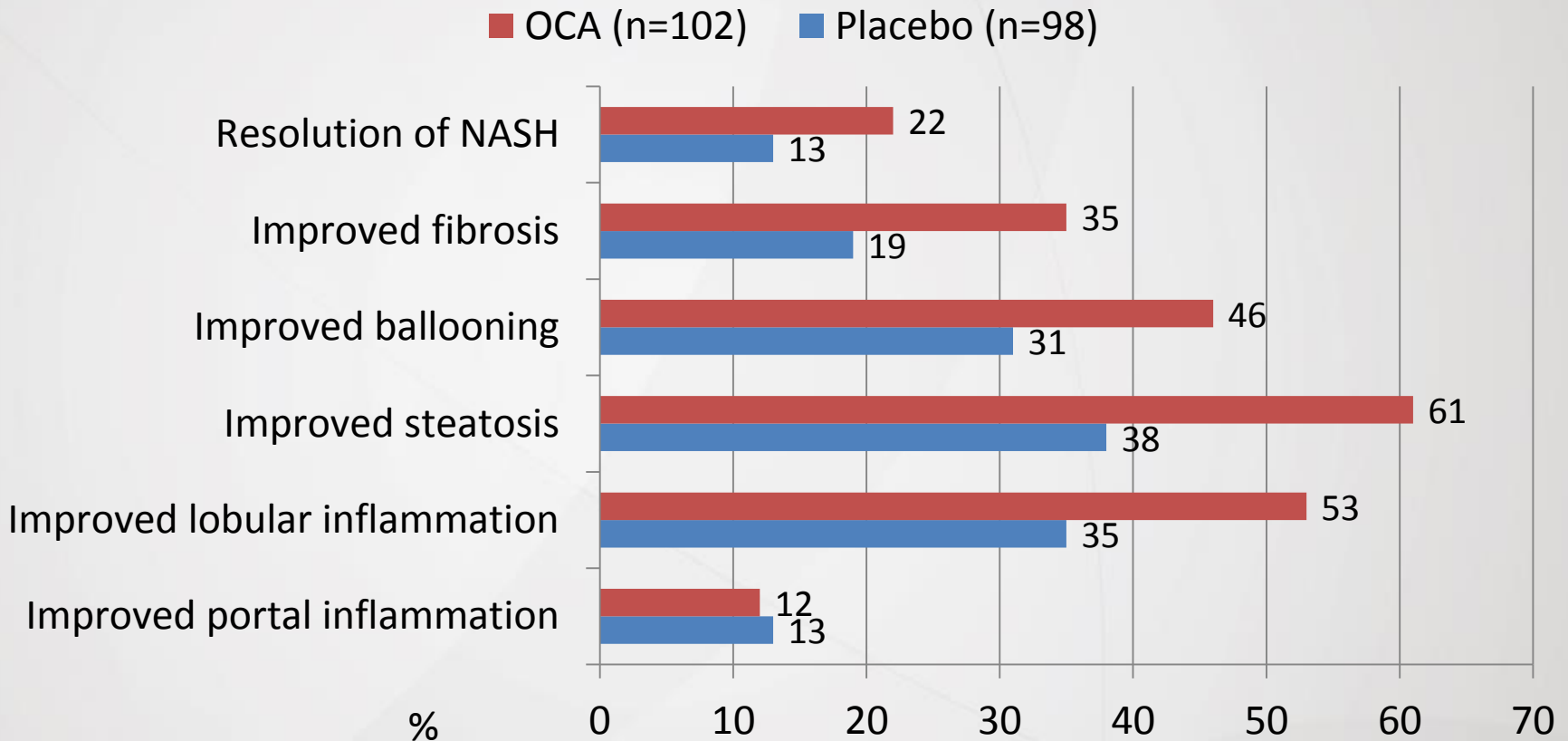
Variable	Placebo	Vitamin E	Pioglitazone	P (Vitamin E vs placebo)	P (Pioglitazone vs placebo)
Primary outcome*	19%	43%	34%	0.001	0.04
Improvement in steatosis	31%	54%	69%	0.005	<0.001
Improvement in lobular inflammation	35%	54%	60%	0.02	0.004
Improvement in ballooning	29%	50%	44%	0.01	0.08
Improvement in fibrosis	31%	41%	44%	0.24	0.12
Resolution of NASH	21%	36%	47%	0.05	0.001

\* Improvement of ballooning by  $\geq 1$  point; no increase in fibrosis; NAFLD activity score declines by  $\geq 2$  points or to  $\leq 3$  points

# Farnesoid X receptor (FXR)



# FLINT Study: Obeticholic acid for NASH



# Take home messages

- NAFLD is the most common chronic liver disease worldwide and is emerging to be an important cause of cirrhosis and liver cancer.
- NAFLD is strongly associated with metabolic syndrome, cardiovascular disease and malignancy.
- Apart from diagnosis and risk stratification, it is important to detect and manage the associated metabolic disorders.
- Vitamin E and pioglitazone may be considered in selected NASH patients.

# Thank you!



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