NASH Cirrhosis:

(When) To operate or (Better) Not to Operate

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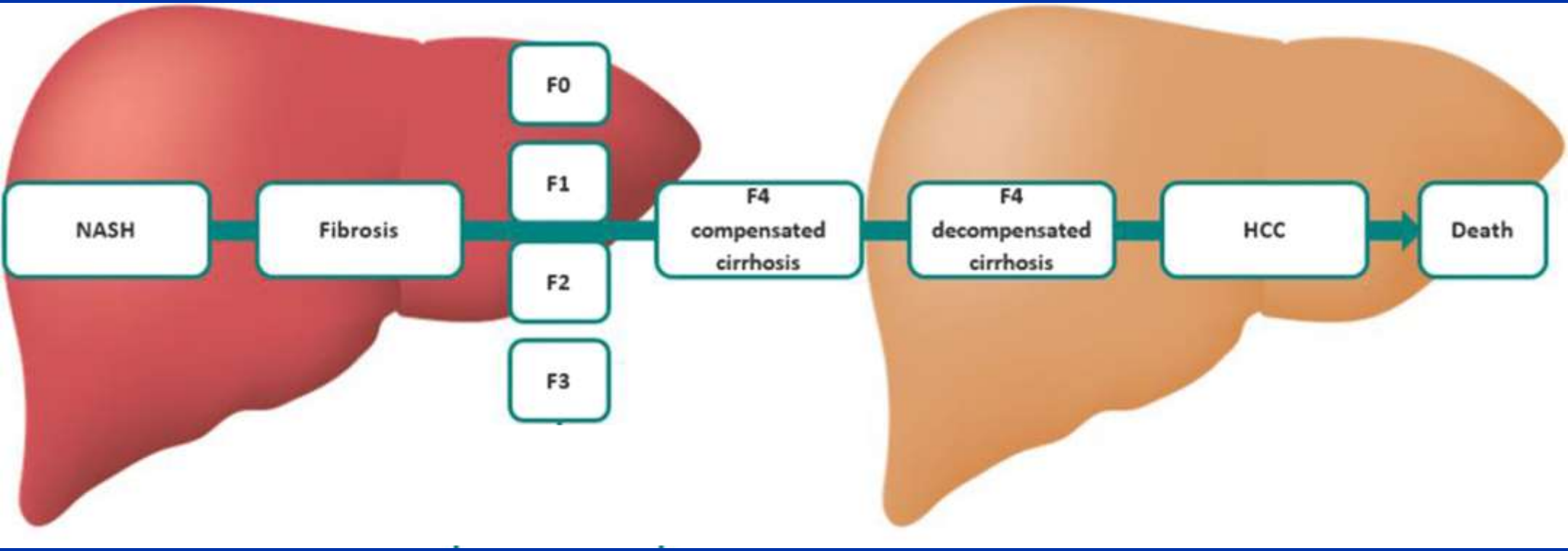
Disclosures

- Medtronic (research grant and honorarium)
- Ethicon (research grant and honorarium)
- NIH (research grant)

NASH

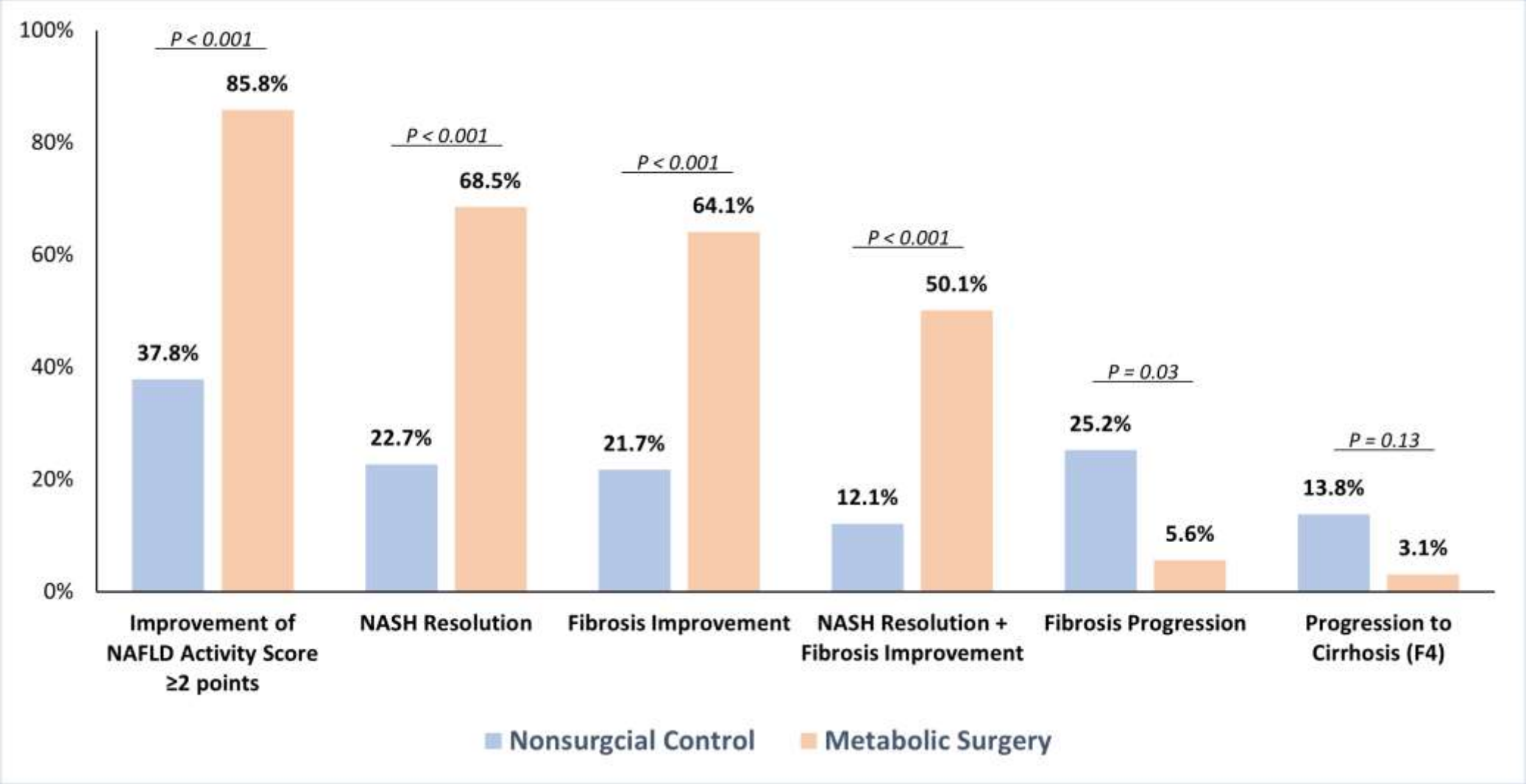
- NASH ⟺ Metabolic Syndrome ⟺ CV Disease
- Obesity is the main pathophysiologic driver of NASH.
- Diagnosis & management of NASH are challenging.
- No approved pharmacotherapies for NASH.
- No therapy to reduce the risk of serious cardiovascular or hepatic clinical outcomes in patients with NASH.

NASH Progression



Traussnigg et al. Dig Dis. 2015

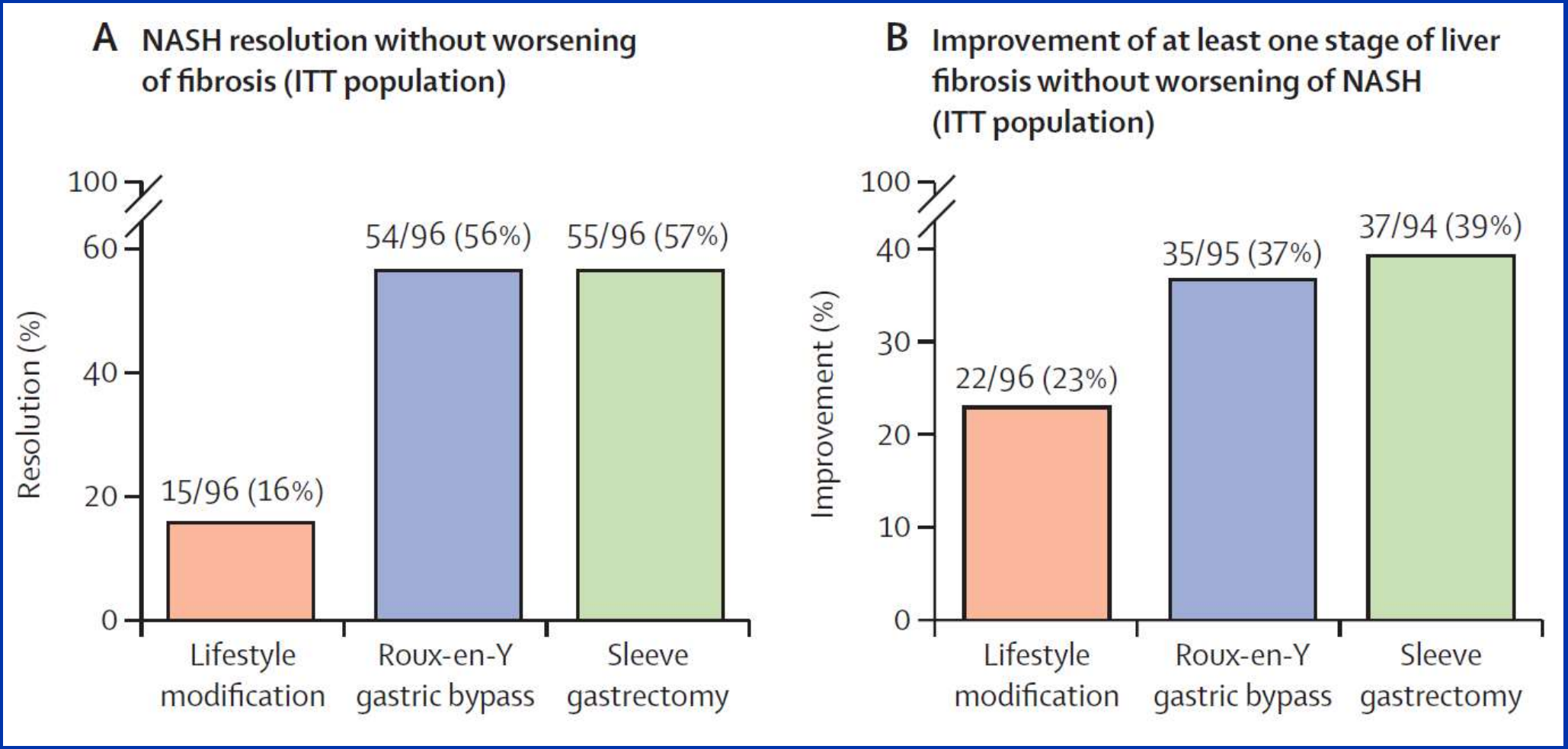
Liver Histological Comparison after Metabolic Surgery vs Usual Care



- 42 surgery & 91 nonsurgical controls
- A repeat liver biopsy with a median interval of 2 yrs

Aminian A. Ann Surg 2023

BRAVES RCT



Verrastro….Mingrone, Lancet 2023

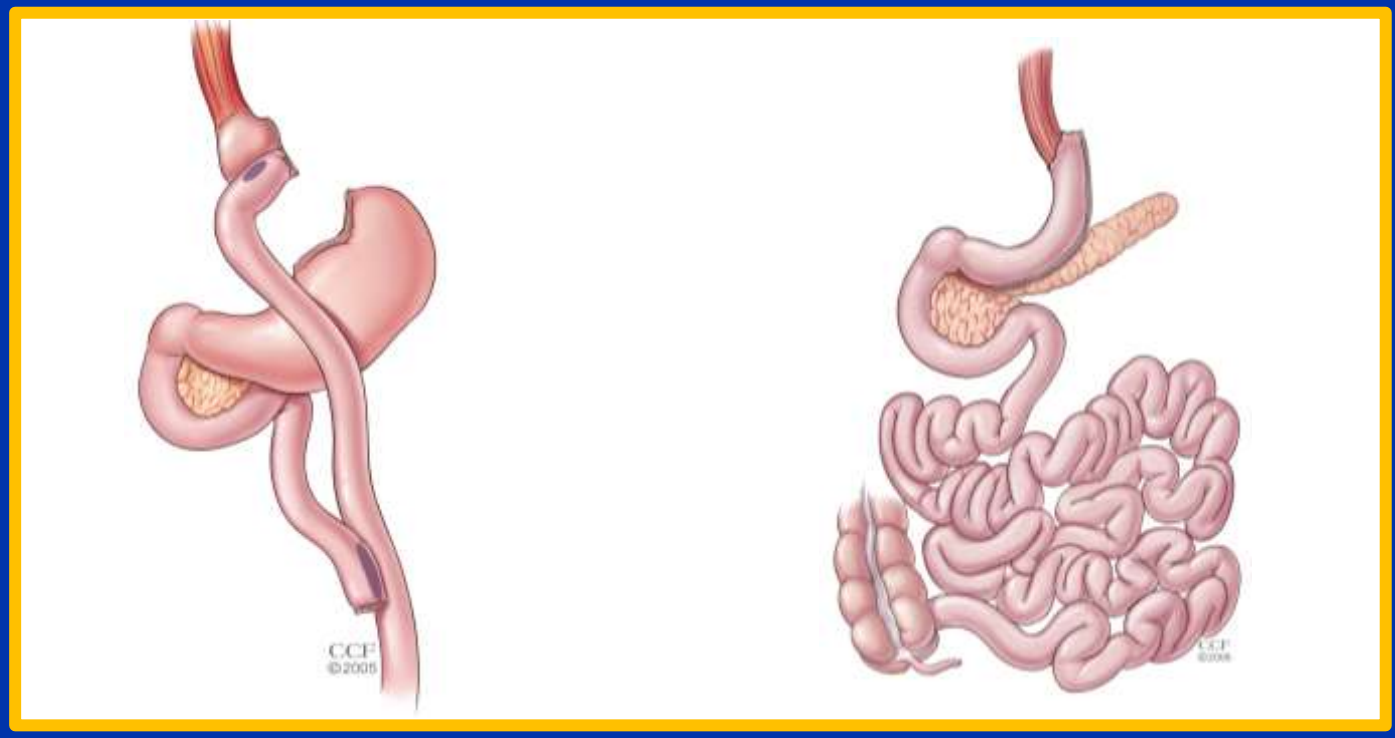
JAMA | Original Investigation

Association of Bariatric Surgery With Major Adverse Liver and Cardiovascular Outcomes in Patients With Biopsy-Proven Nonalcoholic Steatohepatitis

Ali Aminian, MD; Abbas Al-Kurd, MD; Rickesha Wilson, MD; James Bena, MS; Hana Fayazzadeh, MD; Tavankit Singh, MD; Vance L. Albaugh, MD, PhD; Faiz U. Shariff, MD; Noe A. Rodriguez, MD; Jian Jin, MS; Stacy A. Brethauer, MD, MBA; Srinivasan Dasarathy, MD; Naim Alkhouri, MD; Philip R. Schauer, MD; Arthur J. McCullough, MD; Steven E. Nissen, MD

Surgical Procedures and Long-term Effectiveness in NASH Disease and Obesity Risk (SPLENDOR)

Metabolic Surgical Procedures (N=650)



Gastric Bypass

N=537 (83%)

Sleeve Gastrectomy

N=113 (17%)

Prespecified Composite Endpoints

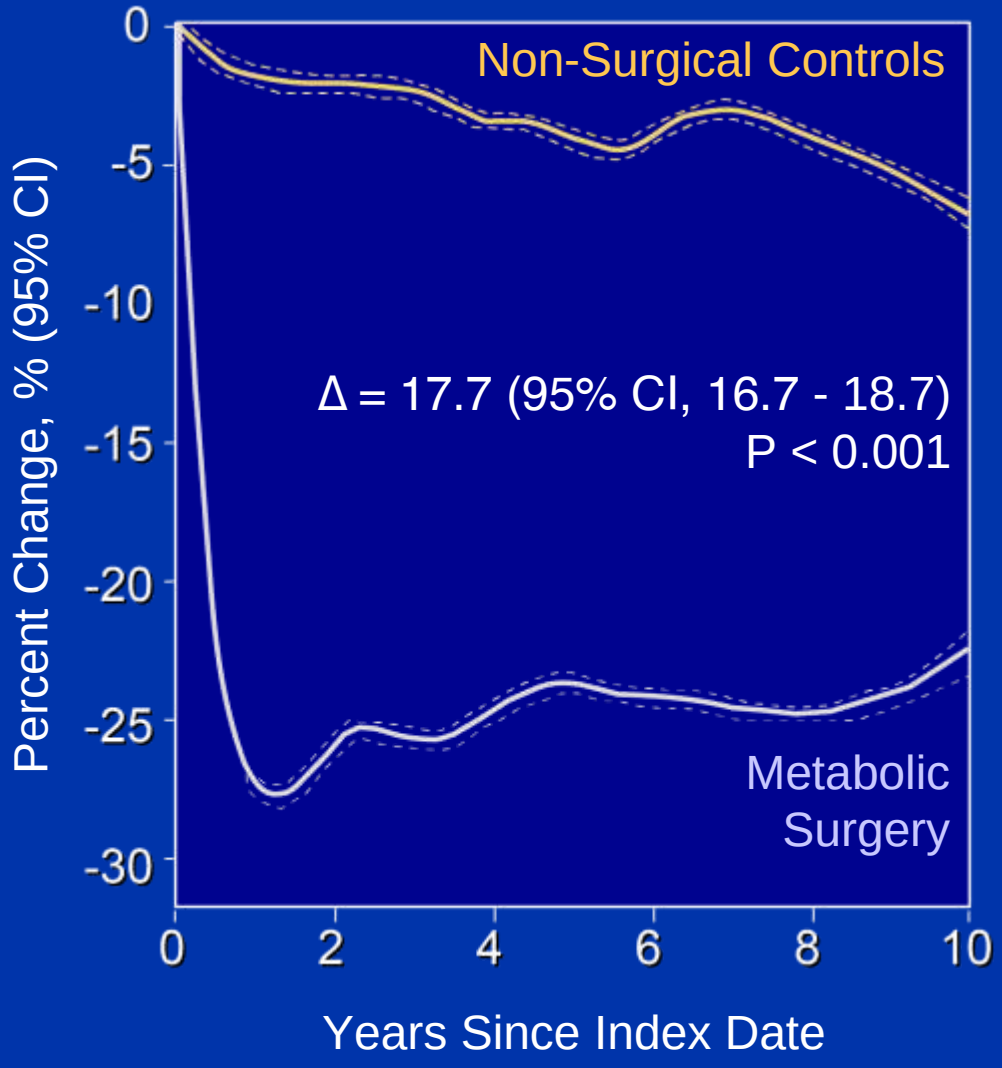
- First occurrence of major adverse liver outcomes (MALO): progression to clinical or histologic (F4 on repeat liver biopsy) cirrhosis, development of hepatocellular carcinoma, liver transplantation, or liver-related mortality.
- First occurrence of major adverse cardiovascular events (MACE): coronary artery events, cerebrovascular events, heart failure, or CV mortality.

Selected Baseline Characteristics After Overlap Weighting

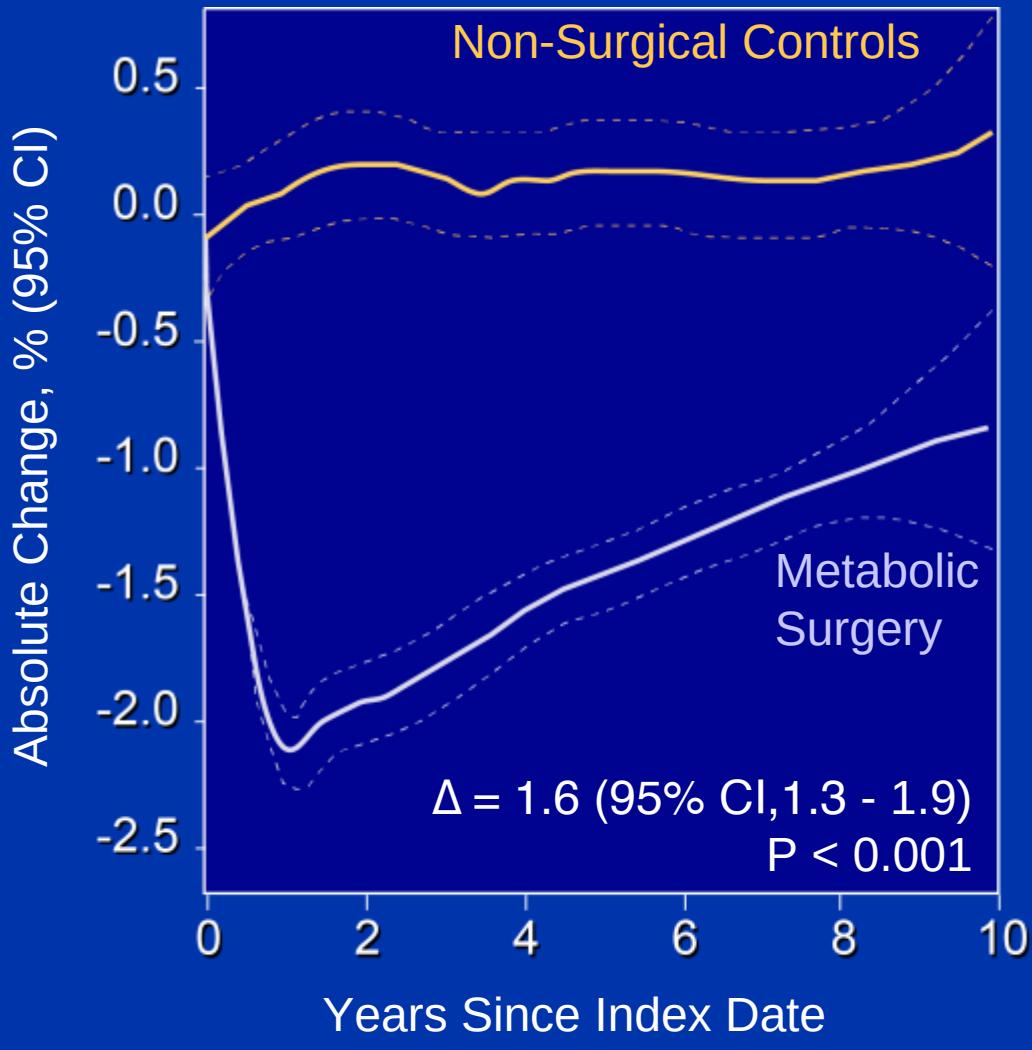
Characteristic	Metabolic Surgery	Non-Surgical Controls
Age (years)	49.0	49.0
Female Gender	62.9%	62.9%
BMI (kg/m^2)	45.7	36.0
Type 2 diabetes	40.6%	40.6%
Smoker	8.4%	8.4%
NAFLD Activity Score 4	30.7%	30.7%
5	29.2%	29.2%
Fibrosis Stage 1	50.8%	50.8%
2	29.2%	29.2%
3	20.0%	20.0%

Metabolic Surgery: Effect on Weight and HbA1c

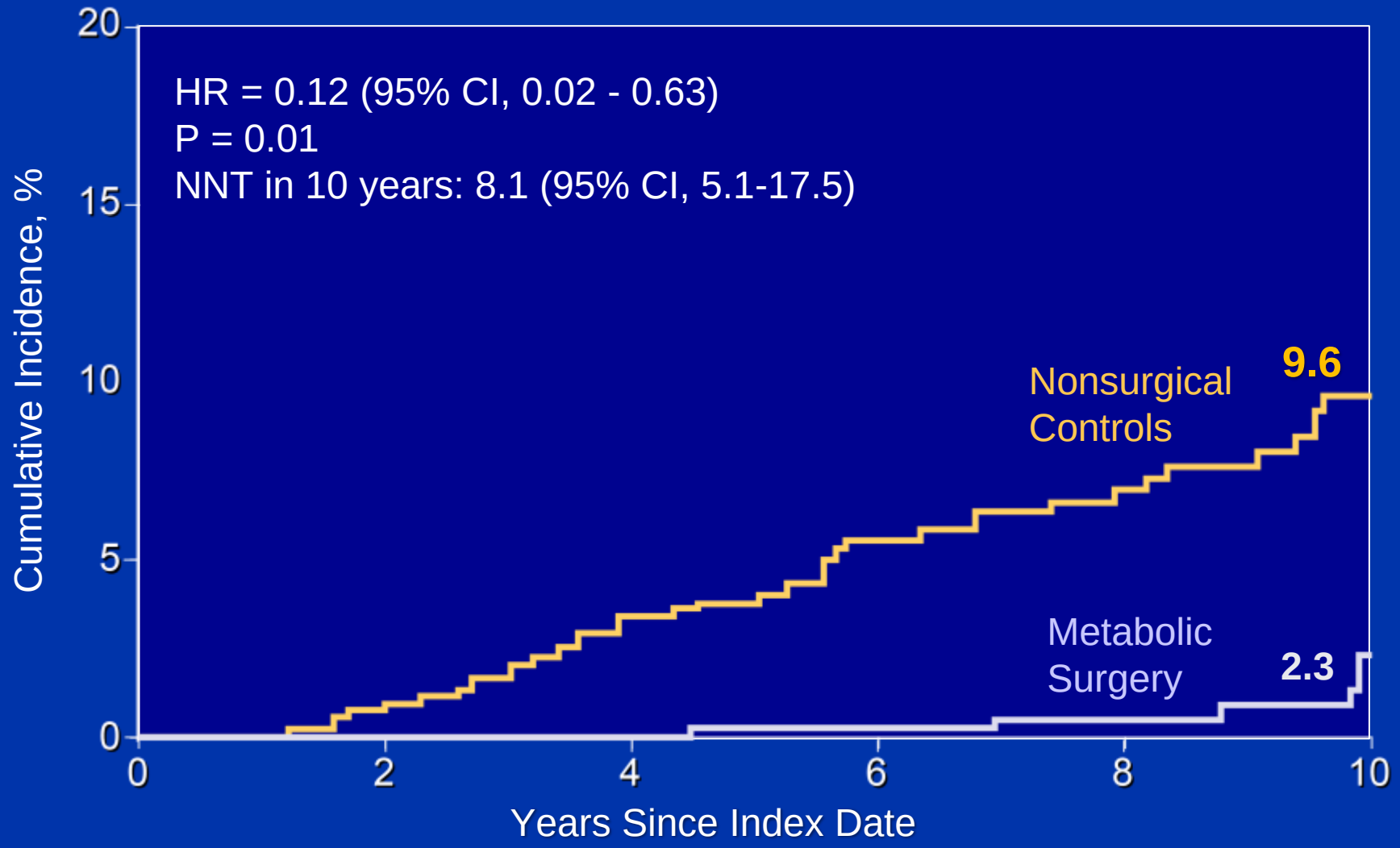
Total Weight Loss (%)



HbA1c Change (%)



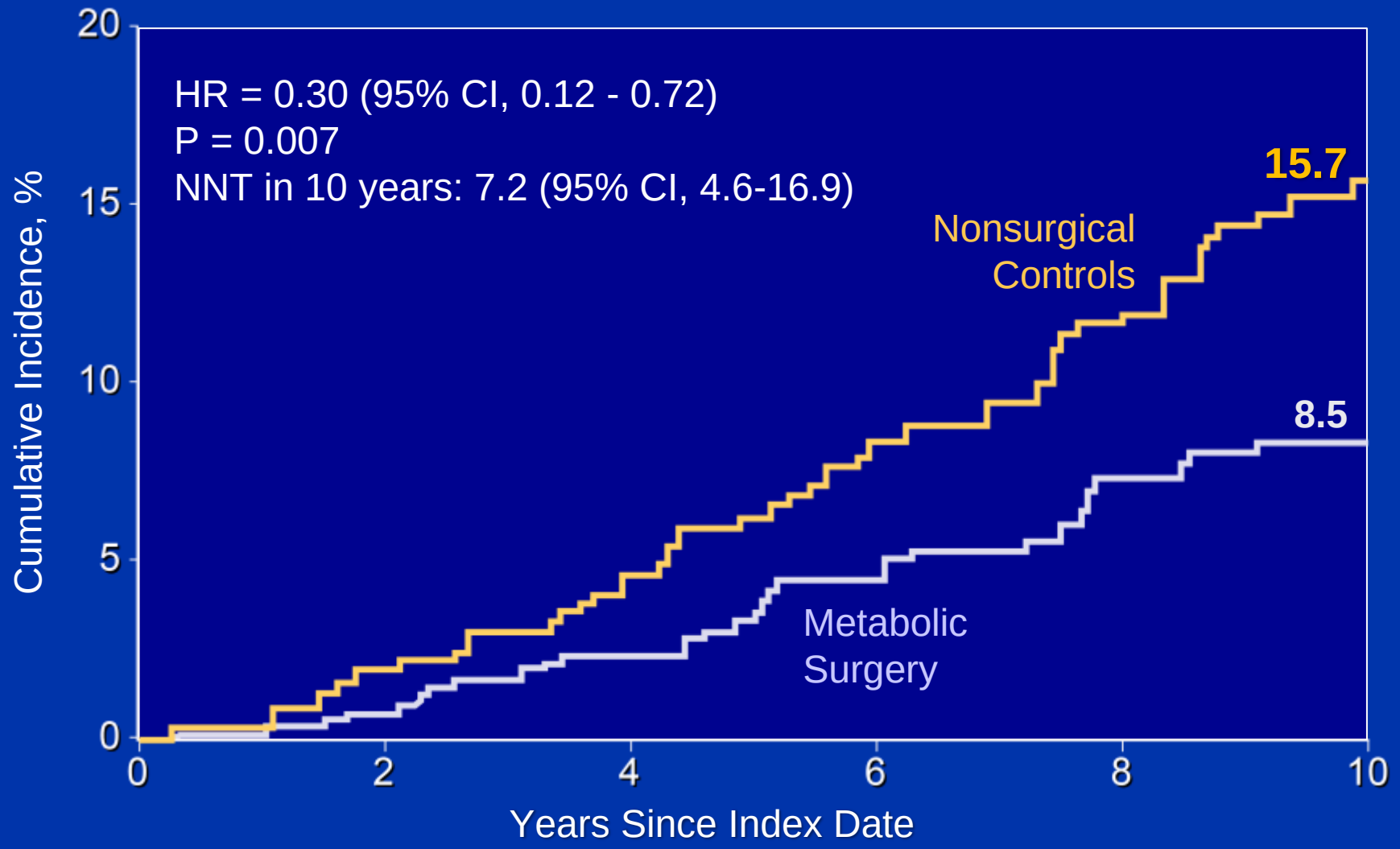
Major Adverse Liver Outcomes (MALO)



N at risk

Nonsurgical Controls	508	422	376	283	211	146
Metabolic Surgery	650	525	463	381	252	153

Major Adverse Cardiovascular Endpoints (MACE)



N at risk

Nonsurgical Controls	508	417	370	270	202	136
Metabolic Surgery	650	523	455	365	234	141

Indications of Bariatric Surgery in NASH

- Patients with BMI >30 and F0-F3

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- Patients with BMI >30, F4 (cirrhosis), compensated, without portal hypertension

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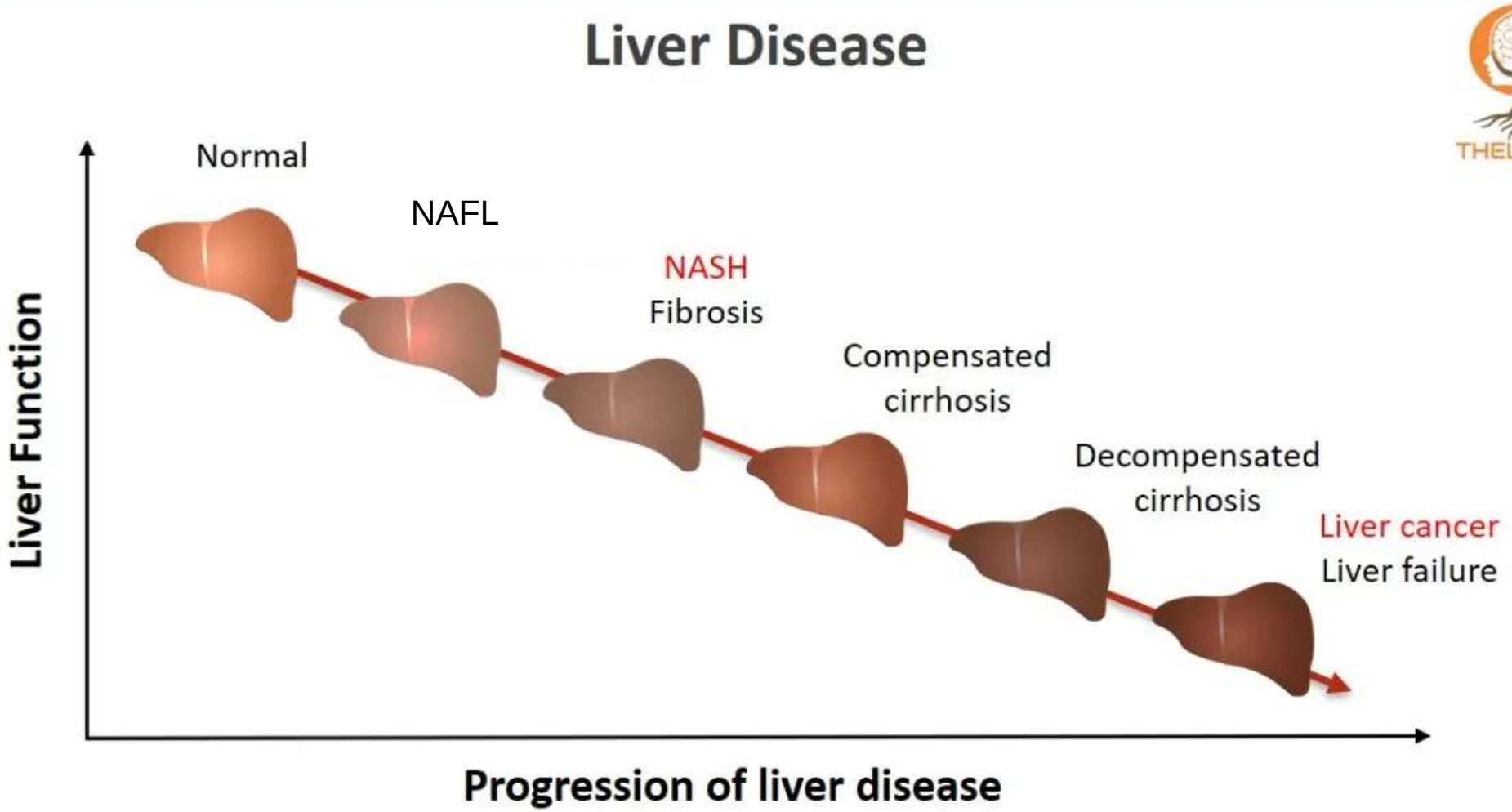
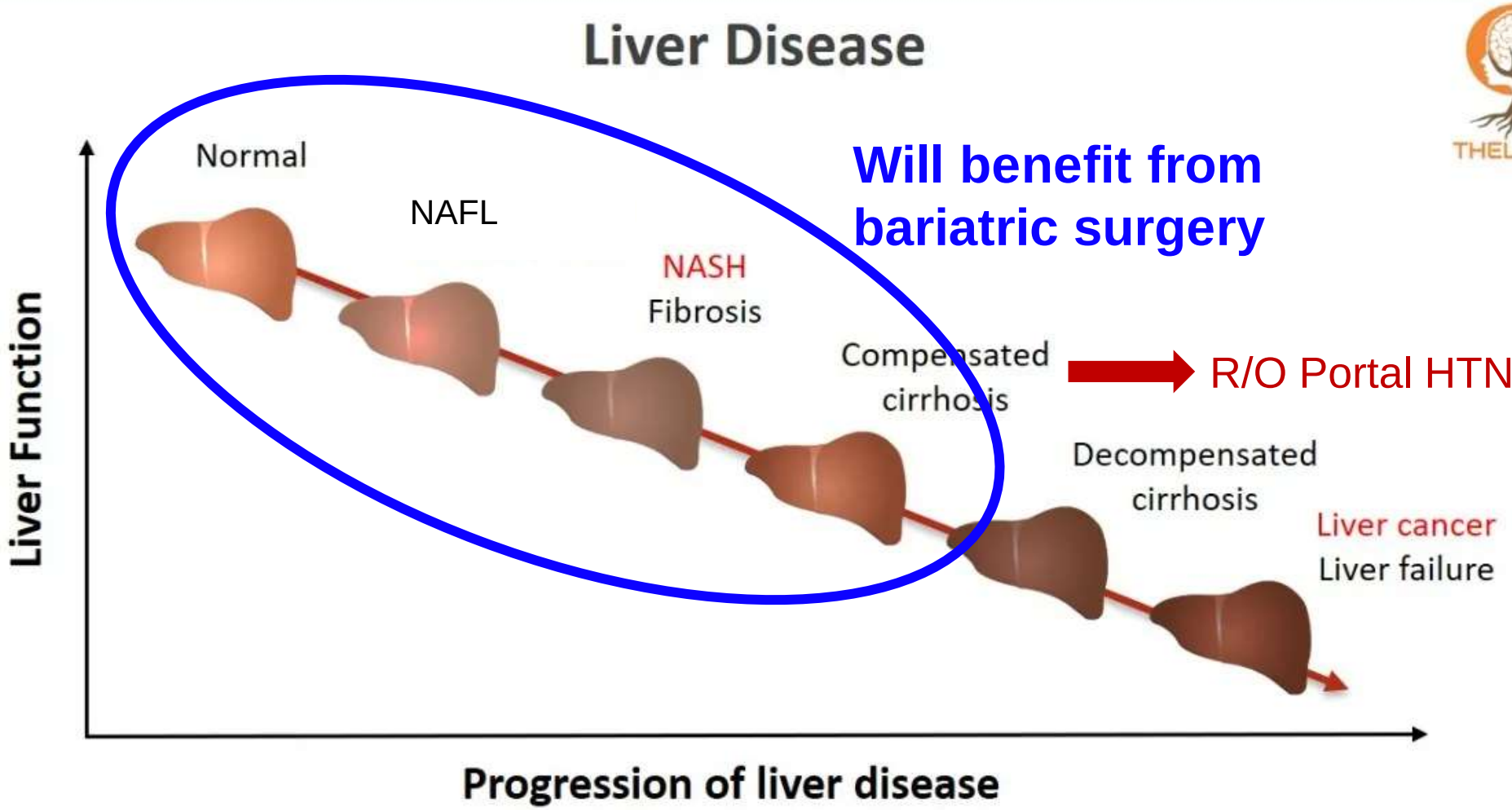


*NASH = non-alcoholic steatohepatitis.

NASH Progression



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R/O Portal Hypertension Before Surgery in Patients with **Suspected Cirrhosis**

- EGD
- Liver Vascular Ultrasound

R/O Portal Hypertension Before Surgery in Patients with **Suspected Cirrhosis**

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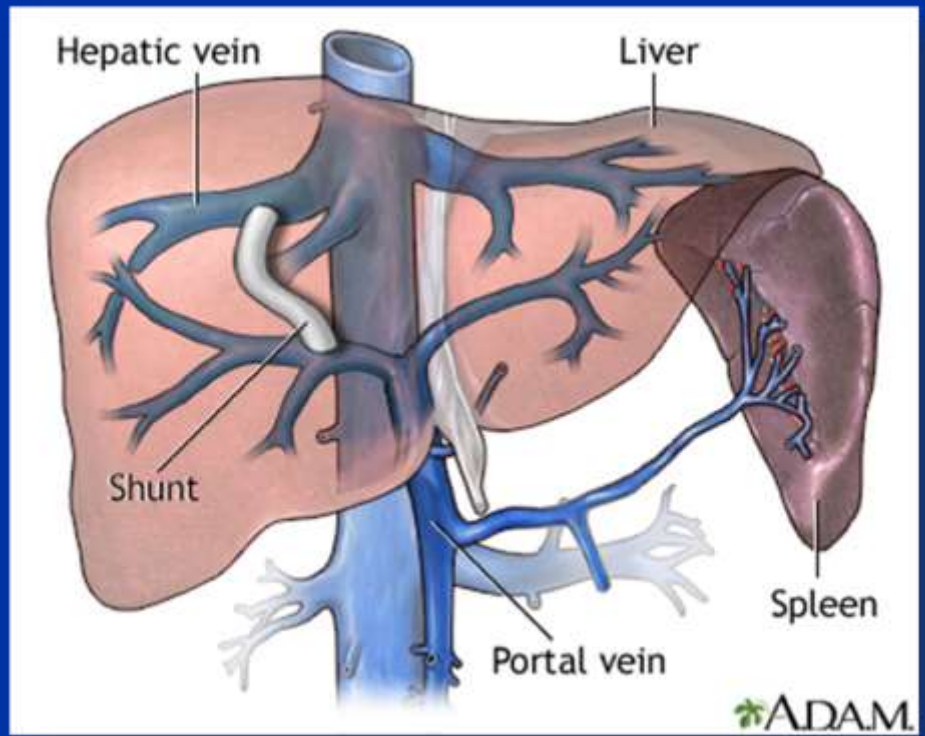
- **Transjugular Intrahepatic**

  Portosystemic Shunt (TIPS)



Contraindications of Bariatric Surgery

- Decompensated Cirrhosis
  - Ascites, Hepatic Encephalopathy, Variceal bleeding
- Portal Hypertension
  - Can be lowered by TIPS
- MELD Score >15 (relative contraindication)
- Severe Coagulopathy

Bariatric Procedure Selection

- In NASH (F0-F3): ALL bariatric procedures

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- In NASH with compensated F4:
  - *Sleeve Gastrectomy* is preferred over the bypass procedures.
  - Need for future liver transplant:
    - Access to biliary tree
    - Medication absorption
    - Roux construction

Conclusion

- Metabolic surgery is safe & effective treatment for obesity & NASH (F0-F3, selected compensated F4) leading to:
  - NASH resolution in over 50% of patients
  - Lowering the risk of MACE & MALO in ~75% of pts

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- Metabolic surgery is safe & effective treatment for obesity & NASH (F0-F3, selected compensated F4) leading to:
  - NASH resolution in over 50% of patients
  - Lowering the risk of MACE & MALO in ~75% of pts
- R/O Portal HTN in patients with suspected cirrhosis before metabolic surgery. Consider TIPS placement.