MAFLD, Cirrhosis, Bariatric Intervention

Benefits, Challenges & Outcomes

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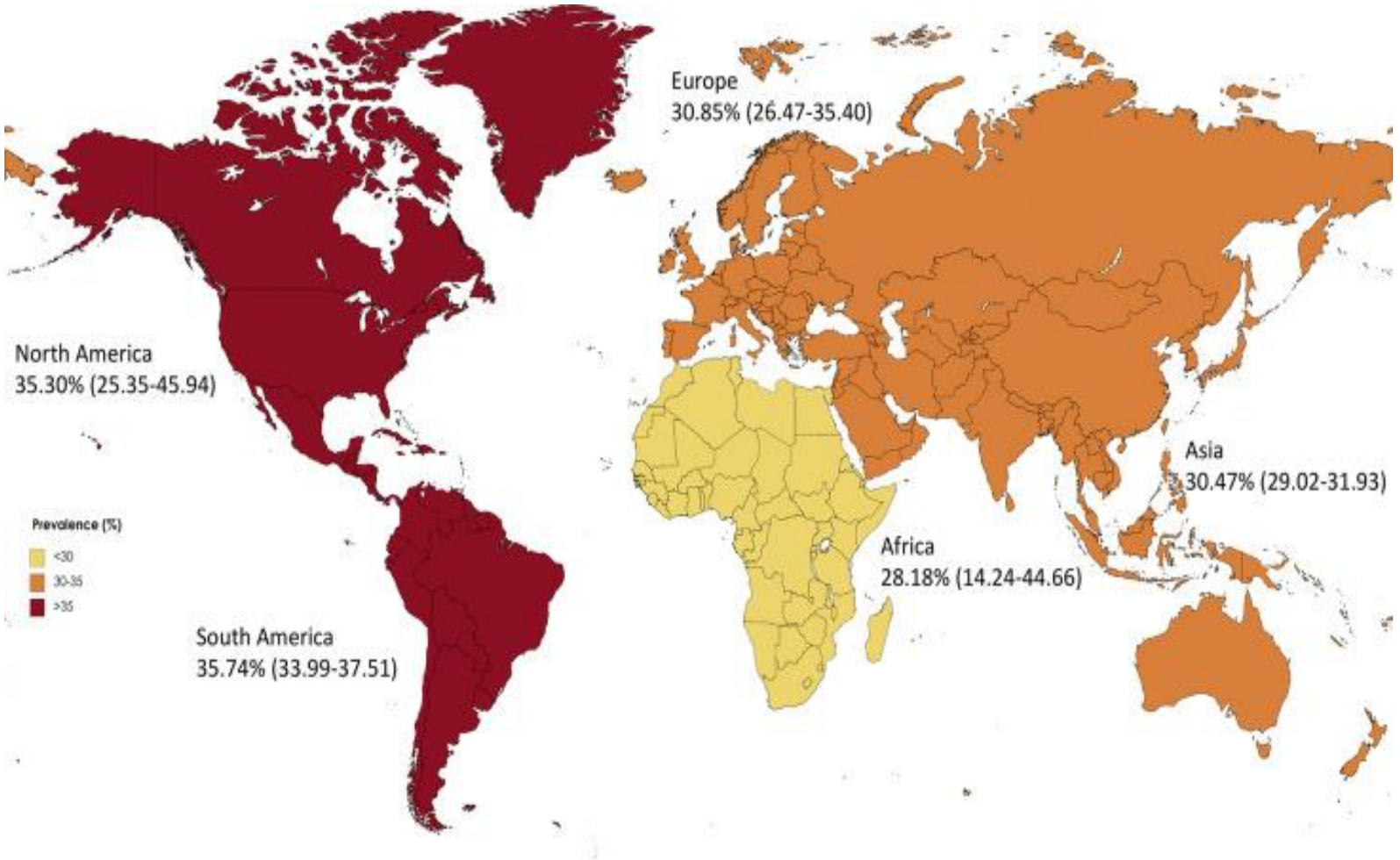
I have no conflicts of interest to disclose

MAFLD

- Epidemiology
- Treatment options
  - Lifestyle modification
  - Medication
  - Endoscopy
  - Surgery
- Cirrhosis
- Transplant

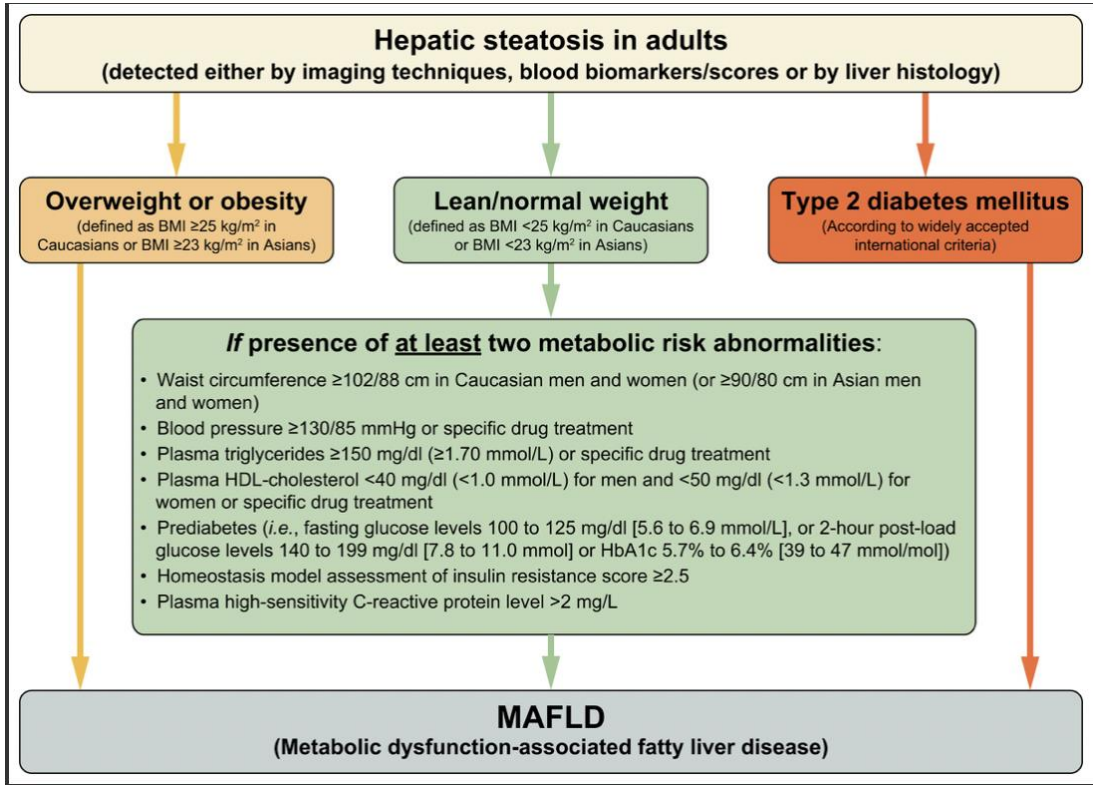
MAFLD



Overall 25-30% worldwide
↑ incidence (0.7% -2.7% per yr)
40% are not obese
COST - $100 billion USD/year

Le et al. Clinical Gastroenterology and Hepatology 2022

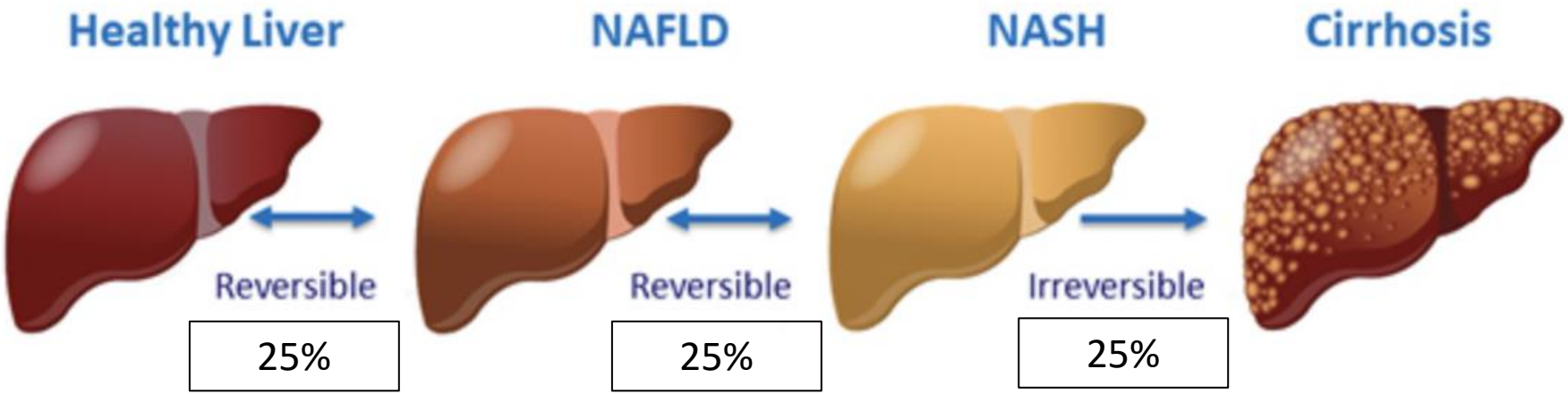
NAFLD → MAFLD



- Change in 2020
- Independent of other liver diseases
- Steatosis + one of
  - A) Overweight/obesity
  - B) DM-2
  - C) Metabolic dysregulation

Eslam et al. J Hepatol 2020

Spectrum of MAFLD



Total population	**25%**	**5-6%**	**1-2%**

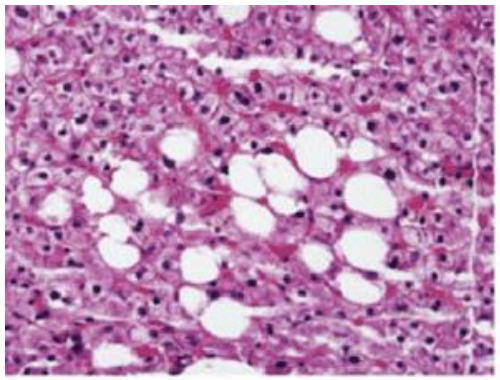
HCC

Diehl et al. NEJM 2017

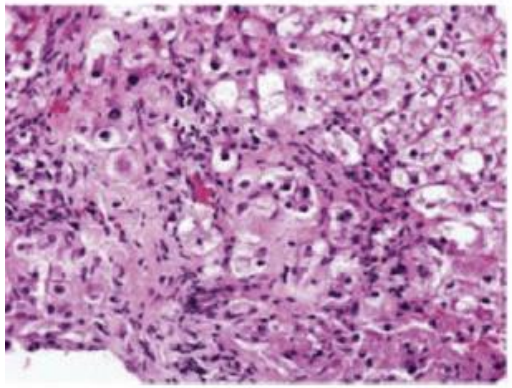
Management of MAFLD

- Modifying components of metabolic syndrome
  - OBESITY, type 2 diabetes mellitus, insulin resistance, dyslipidaemia, and hypertension
- **Mainstay** = Weight loss 7-10%
- No currently FDA/TGA approved medication for MAFLD

Assessment - Histology



Fatty Liver



NASH

Fatty Liver

↓

NASH

↓

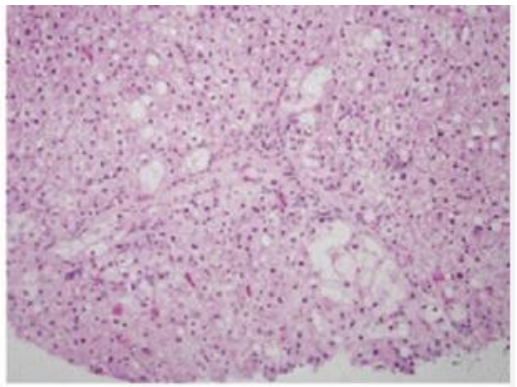
NASH
with Fibrosis

↓

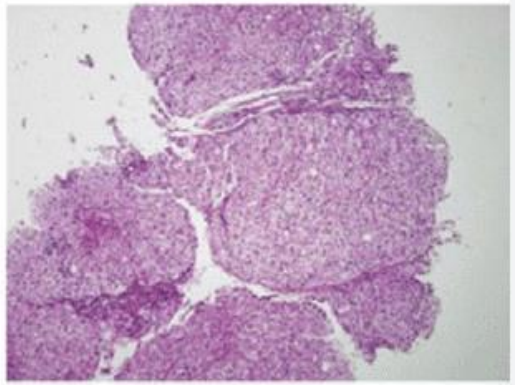
Cirrhosis

↓

Decompensated
Cirrhosis



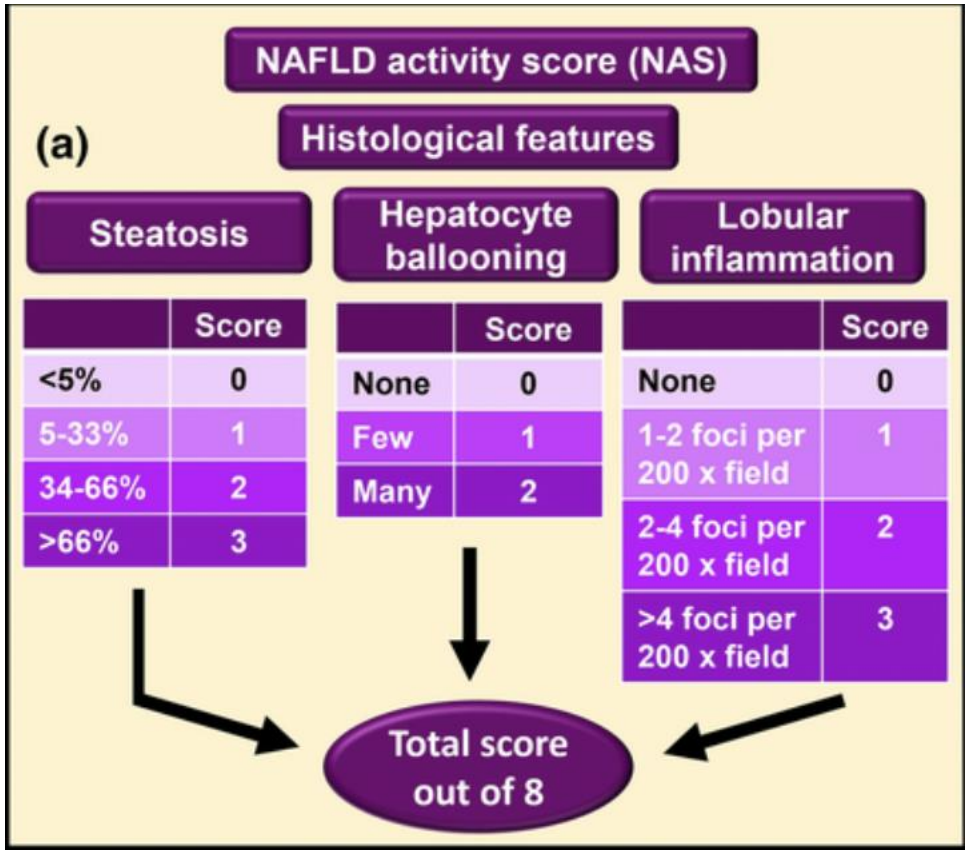
NASH with Fibrosis



Cirrhosis

Coppel at al. Am J Gastro 2006

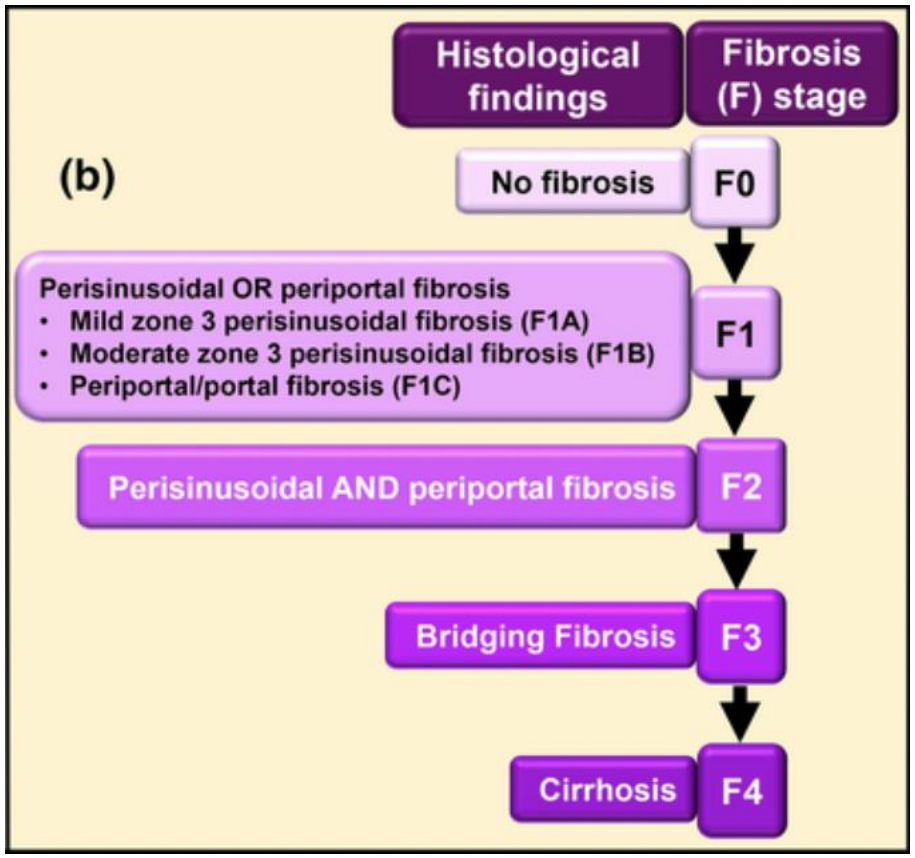
Assessment - NAFLD activity score (NAS)



- Unweighted score out of 8
- Validated measure of disease activity for liver biopsy sections
- ↑ NAS correlates ↑ fibrosis
- ↓ NAS correlates ↓ fibrosis
- NOT for NASH Dx
- BETTER for change assessment

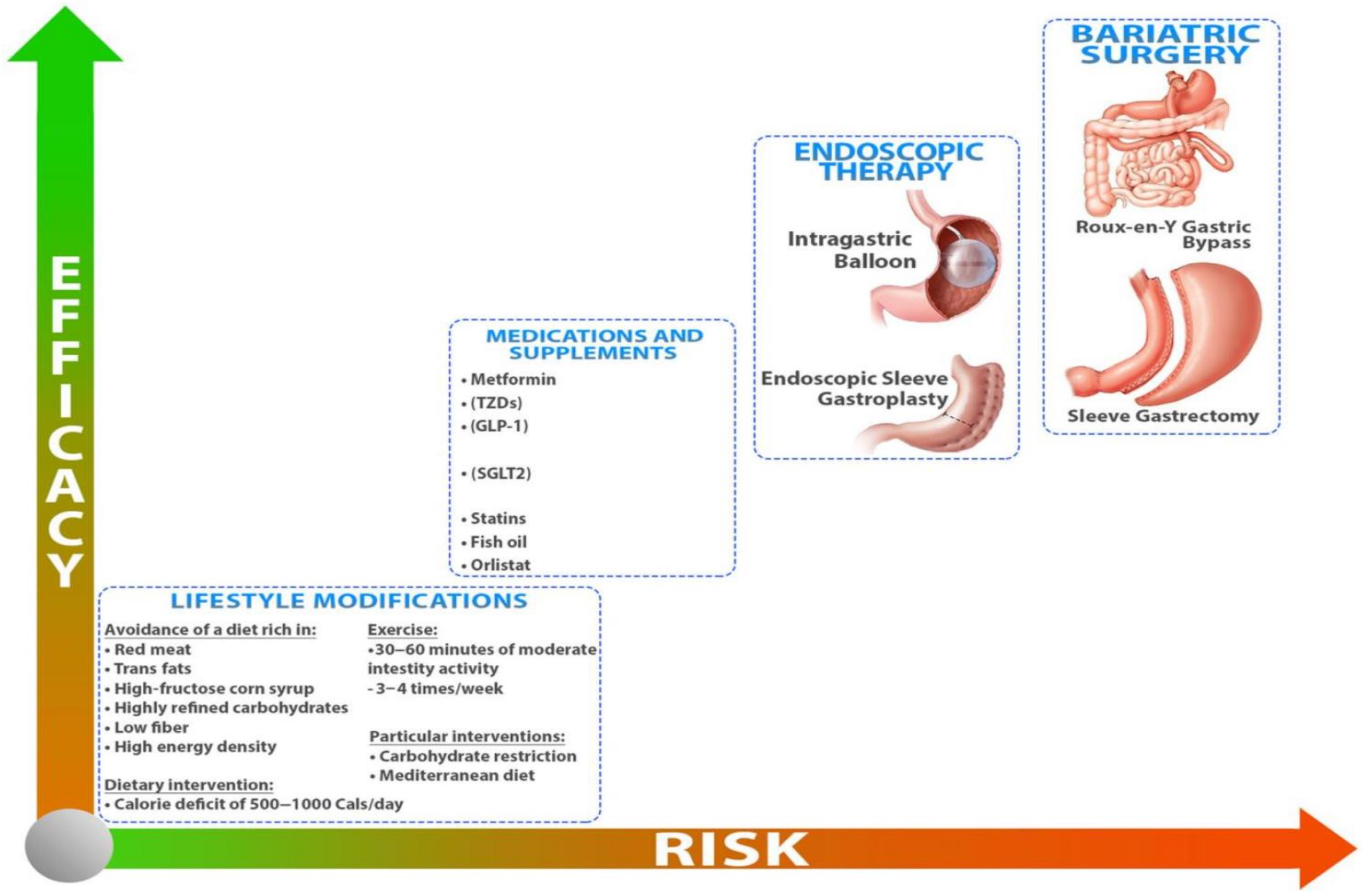
Brunt et al. Hepatology 2021

Assessment - FIBROSIS SCORE



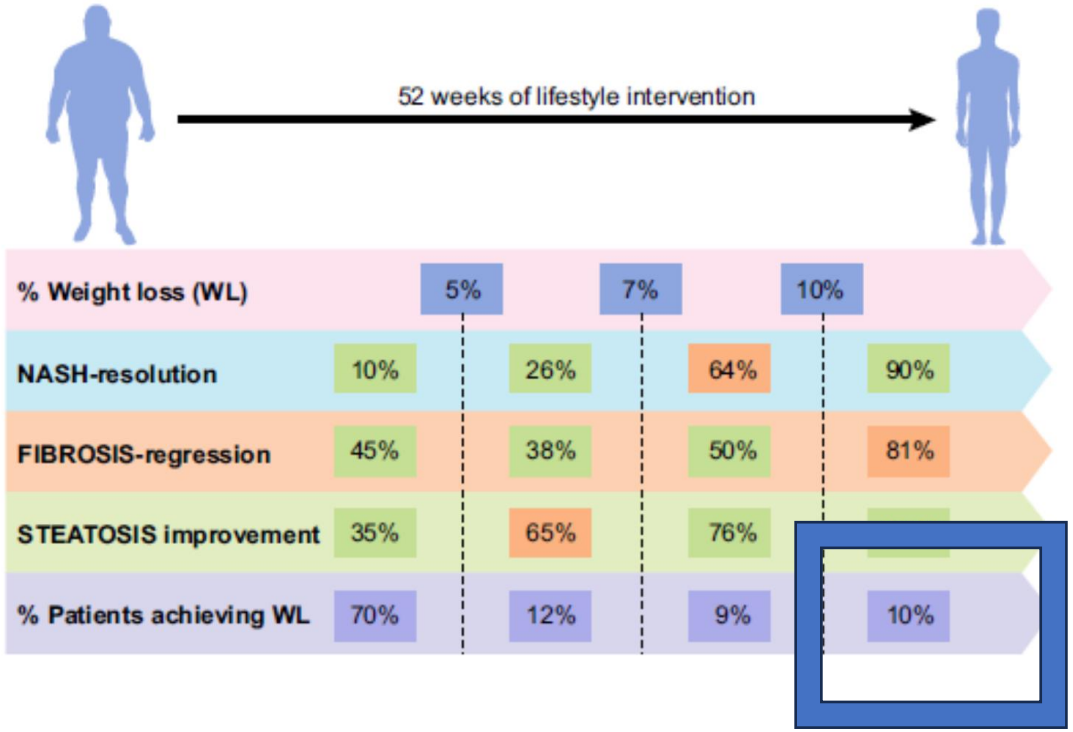
- Often assoc with NASH
- Main predictor of
  - Liver complications
  - Cardiovascular M&M

Bariatric intervention



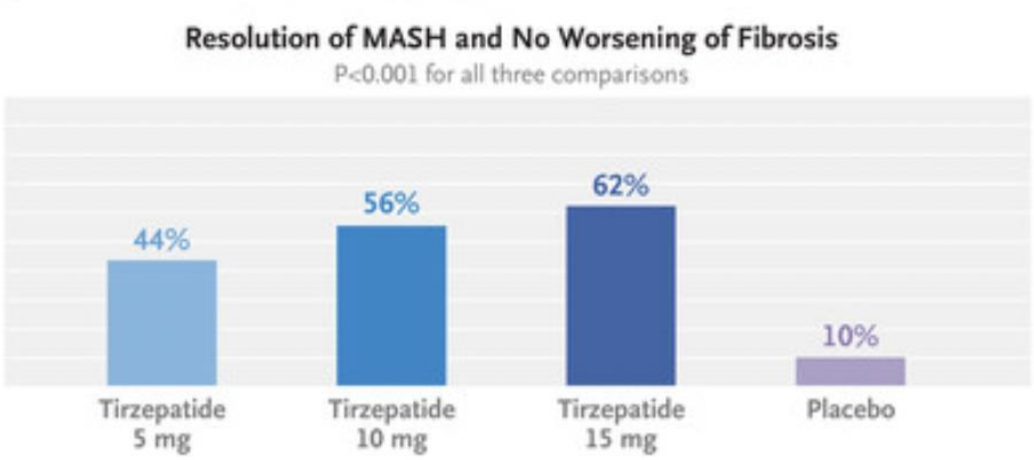
IFSO 2022

MAFLD - Lifestyle modification



Romero Gomez. et al. J Hepatol 2017

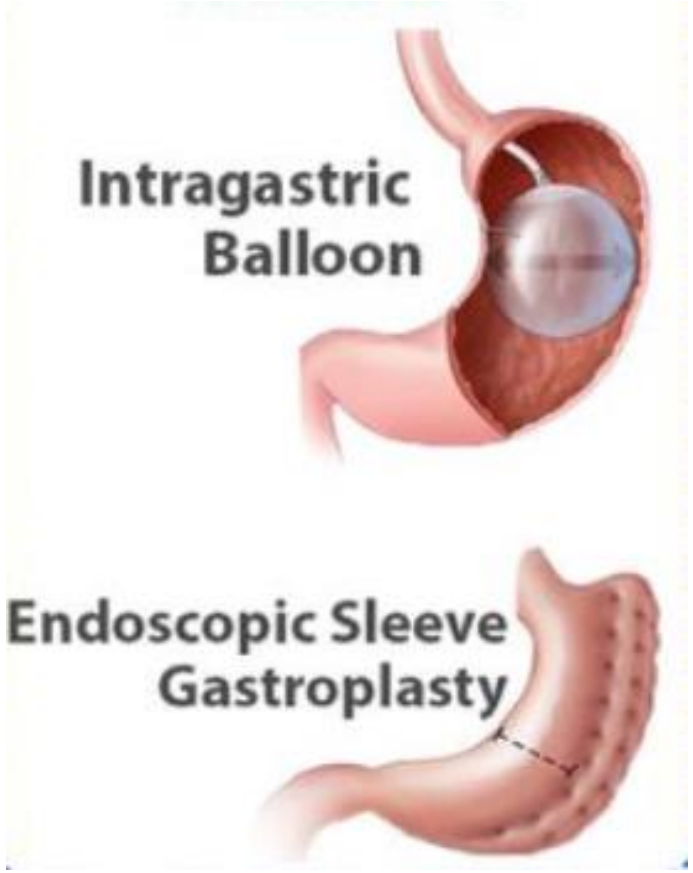
MAFLD - Medications



- Tirzepatide (GLP-1) vs placebo
- RCT, n=152
- 12month follow-up
- Resolution of MASH with no worsening fibrosis 44-62%
- Not powered to assess fibrosis

Loomba et al. NEJM 2024

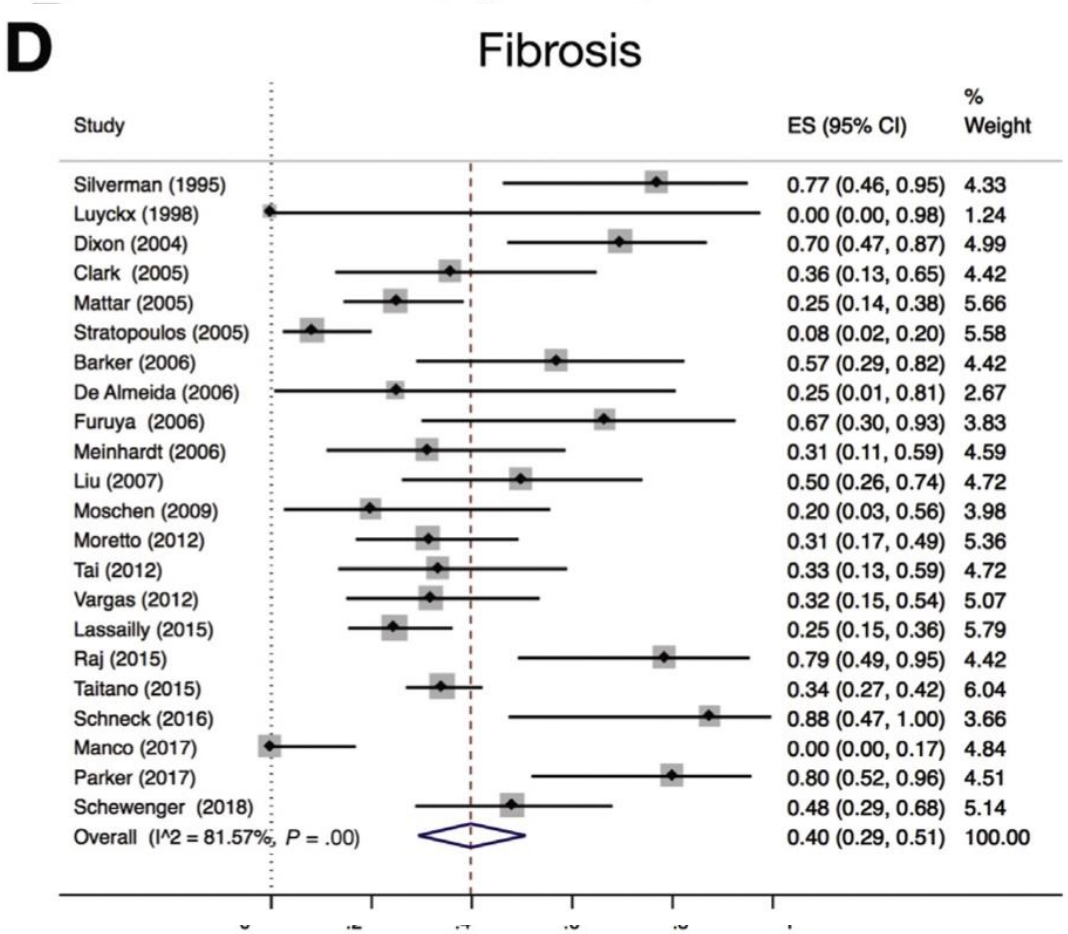
MAFLD - Endoscopic metabolic therapy



- SR, 18 studies EMT
- Improved liver fibrosis (mean difference 0.7)
- Improved NAFLD surrogates (Steatosis, NAS score, LFTs)

Jirapinyo et al. Clin Gastroenterol Hepatology 2022

Bariatric surgery - MAFLD

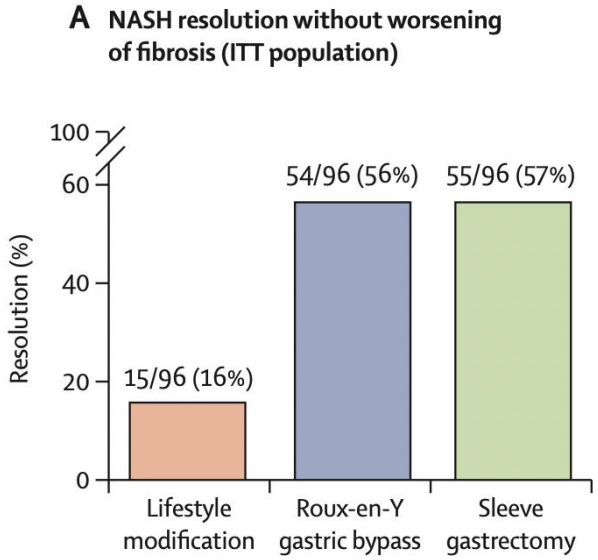


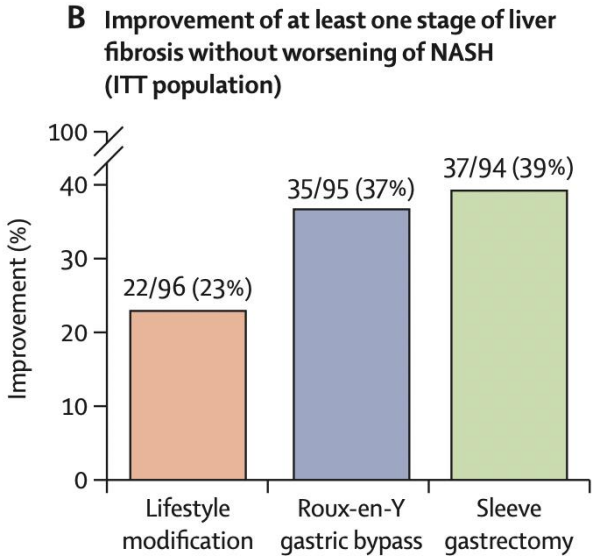
- **Cochrane** review
  - Steatosis – 60-91.7% improvement
  - Inflammation – 50-91.8%
  - Ballooning – 75-77%
  - Fibrosis
    - 40% improvement
    - 12% worsening liver fibrosis
      - Rapid weight loss
      - Malabsorptive/SB bypass procedures (jejuno-ileal bypass)

Mummadi et al. Clin Gastroenterol Hepatol 2008
Lee et al. Clin Gastroenterol Hepatol 2019

BRAVES - RCT

- RYGB vs SG vs lifestyle /medical
- N=288, RCT 1:1:1, 12months
- Endpoints
  - Primary - histo resolution of NASH without fibrosis worsening at 1yr
  - Secondary – Fibrosis improvement by 1+ stage
- RESULTS
  - BS better than lifestyle/meds
  - Threshold of 20% weight loss to achieve endpoint
  - SG=RYGB
    - BUT RYGB was better at improving glycaemic control, lipid profile, insulin resistance, and weight loss

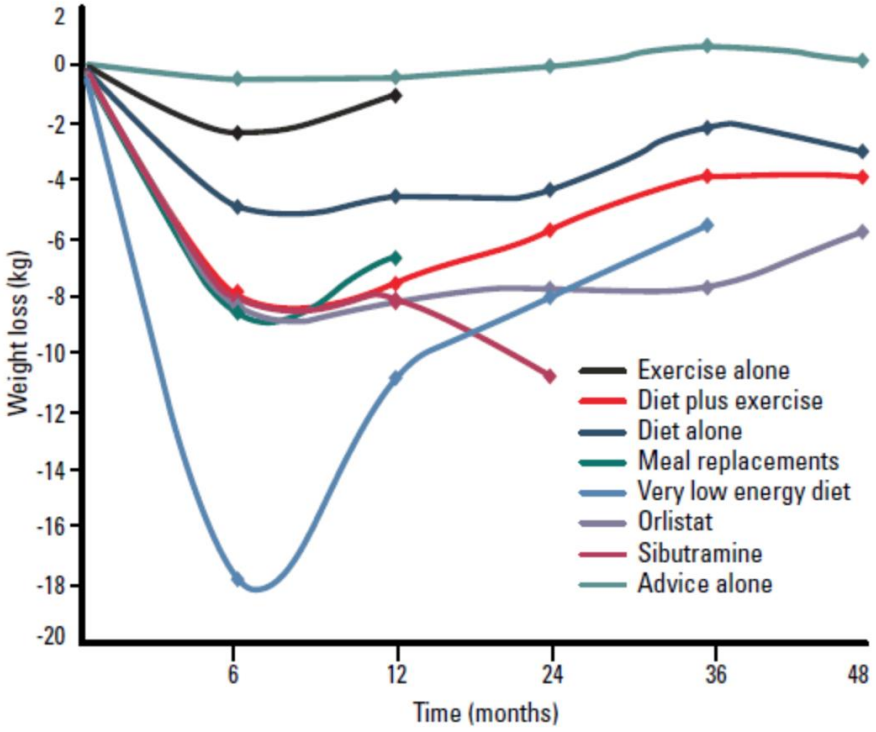




SG and RYGB 3.6 x more likely to achieve resolution vs Lifestyle

Verrastro et al. Lancet 2023

Longevity?

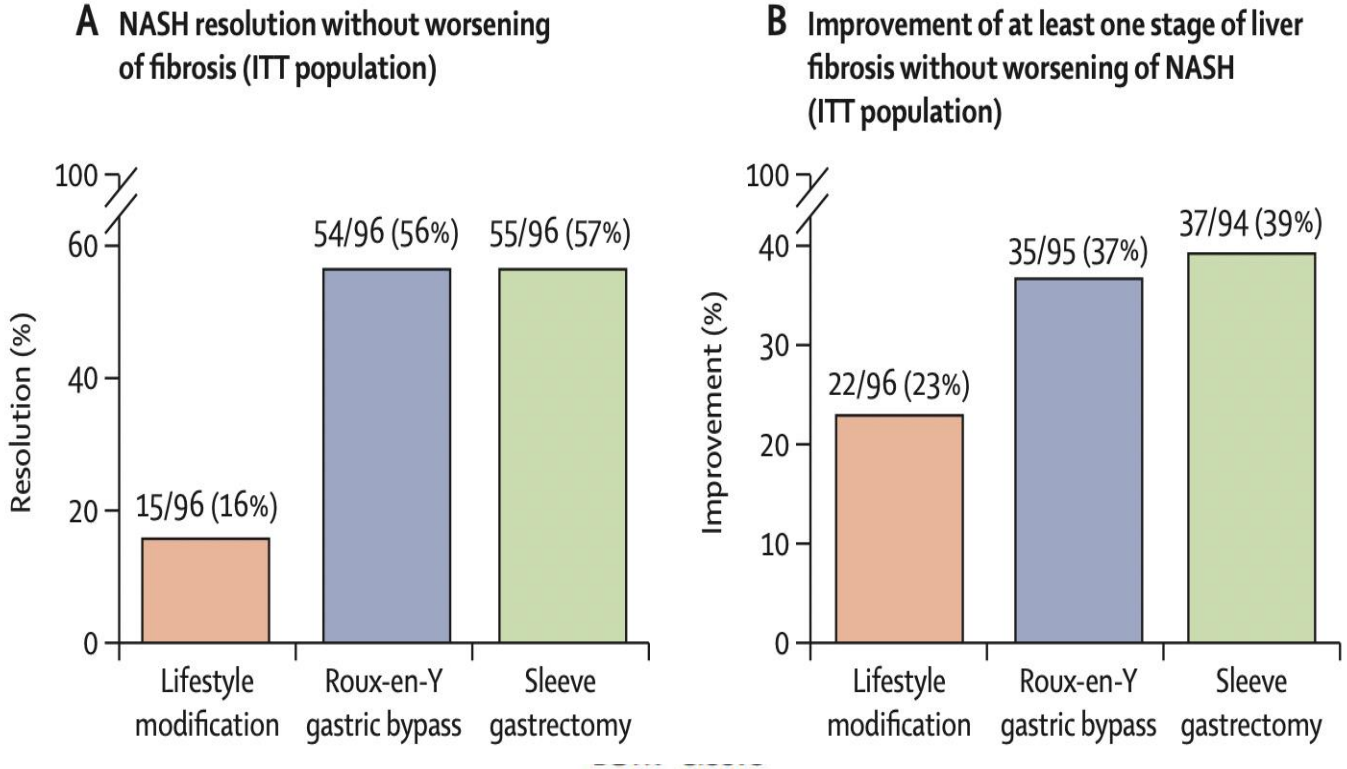


- Bariatric surgery
- 5yr data, n-381 (99 with NASH)
  - ↓NASH prevalence
  - ↓ severity steatosis, ballooning, NAS score
  - Histological benefits seen up to 1yr
  - Fibrosis worsened at 5yrs

Mathurin et al. Gastroenterology 2009

Ok so BS works – which operation?

- Meta-analysis, observational studies & RCT
- SG vs RYGB equivalent
  - Histological changes
  - NAS score
  - Fibrosis

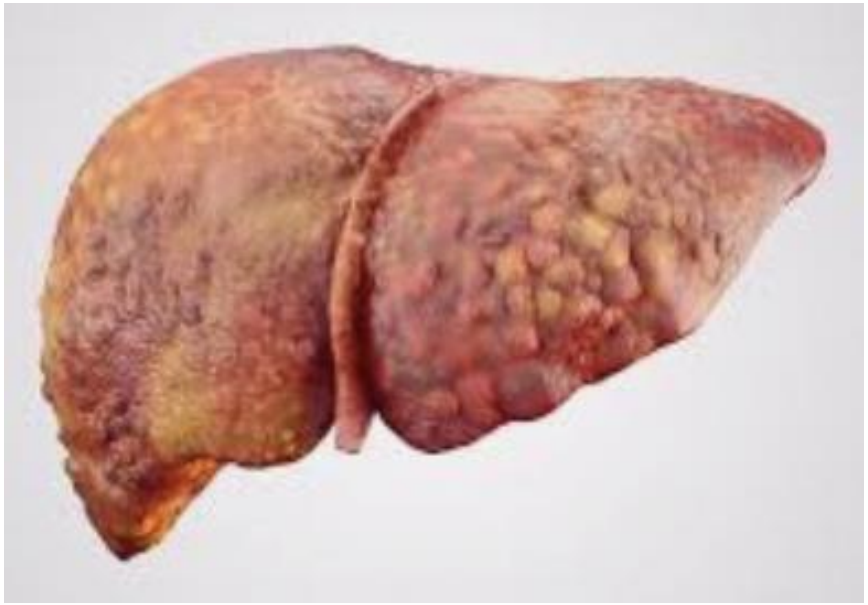


Verrastro et al. Lancet 2023

Barreto de Brito e Silva et al. Obesity Surgery 20213

CIRRHOSIS

Safety – BS in Cirrhosis



- M&M higher (SR)
  - Often incidental cirrhosis (50%)
  - 21.3% morbidity
  - 1.6% periop mortality
  - 2.4-2.8% late onset (1yr) mortality
- Nationwide Inpatient Sample (NIS)
  - Portal HTN extra risk factor (even if CPA)
  - Non-restrictive Sx worse (SG safer)
  - Low volume centres (<50per yr) ↑ M&M
  - Compensated vs decompensated
    - Mortality: Decompensated (16.3%) vs compensated (0.9%)

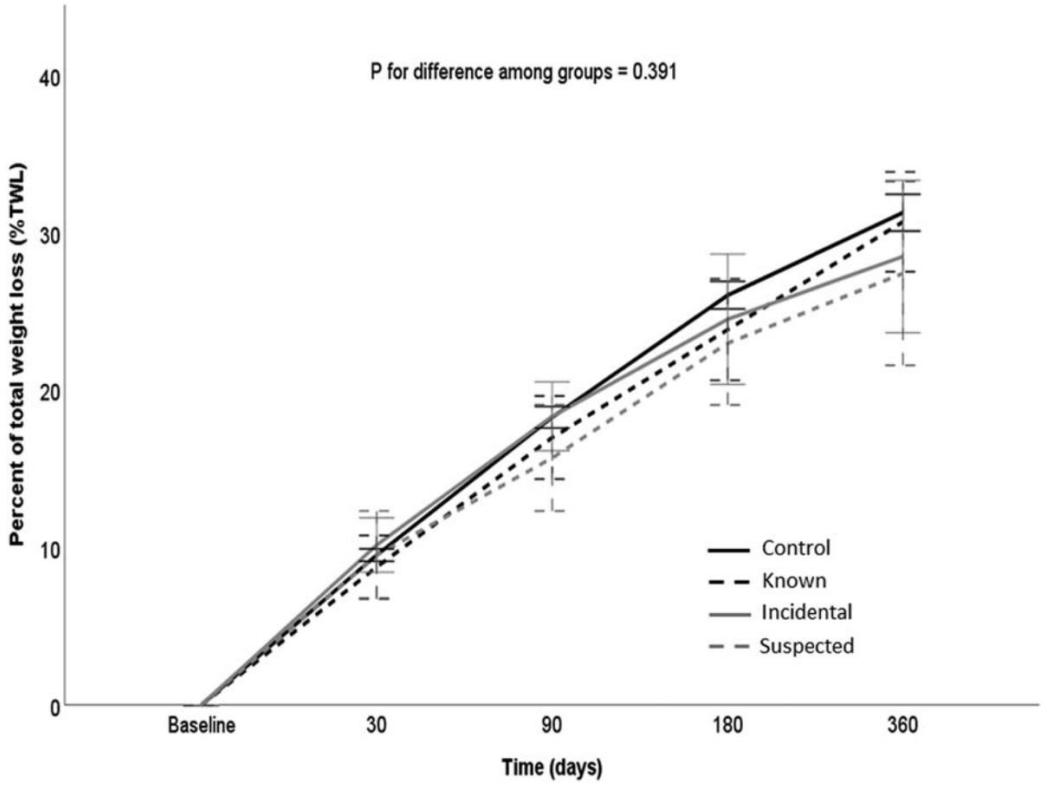
CONTRAINDICATIONS

Childs Pugh B/C (i.e.>7)

Portal HTN – varices, HVWP>10mmHg, CT

Jan et al. Obesity Surg 2015
Mosko et al. Clin Gastroenterol Hepatol 2011

Efficacy – BS in Cirrhosis

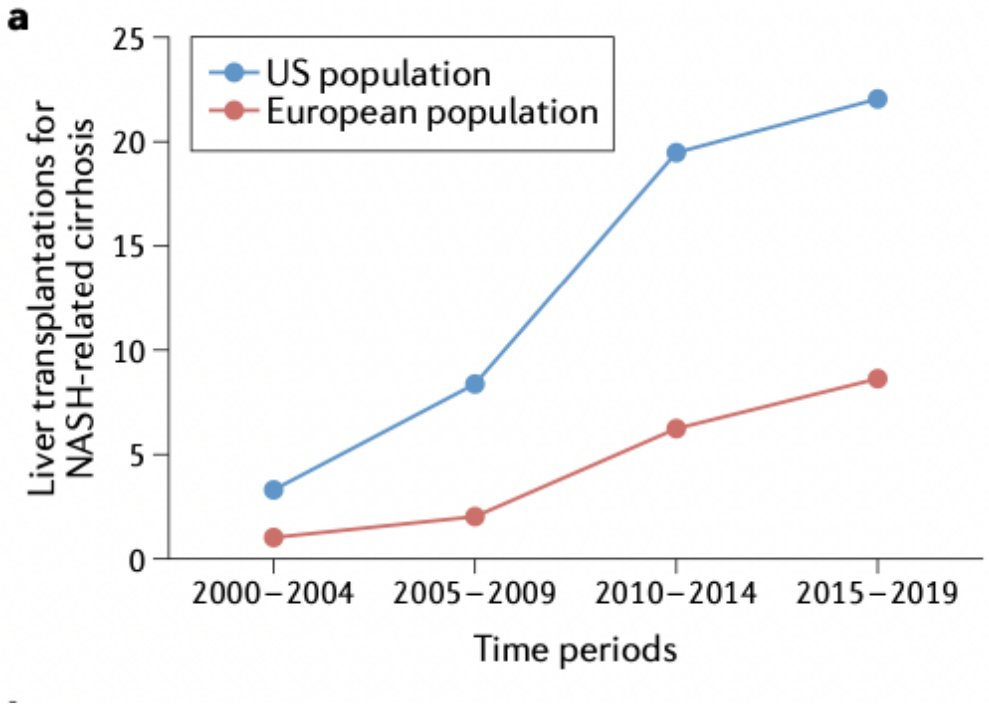


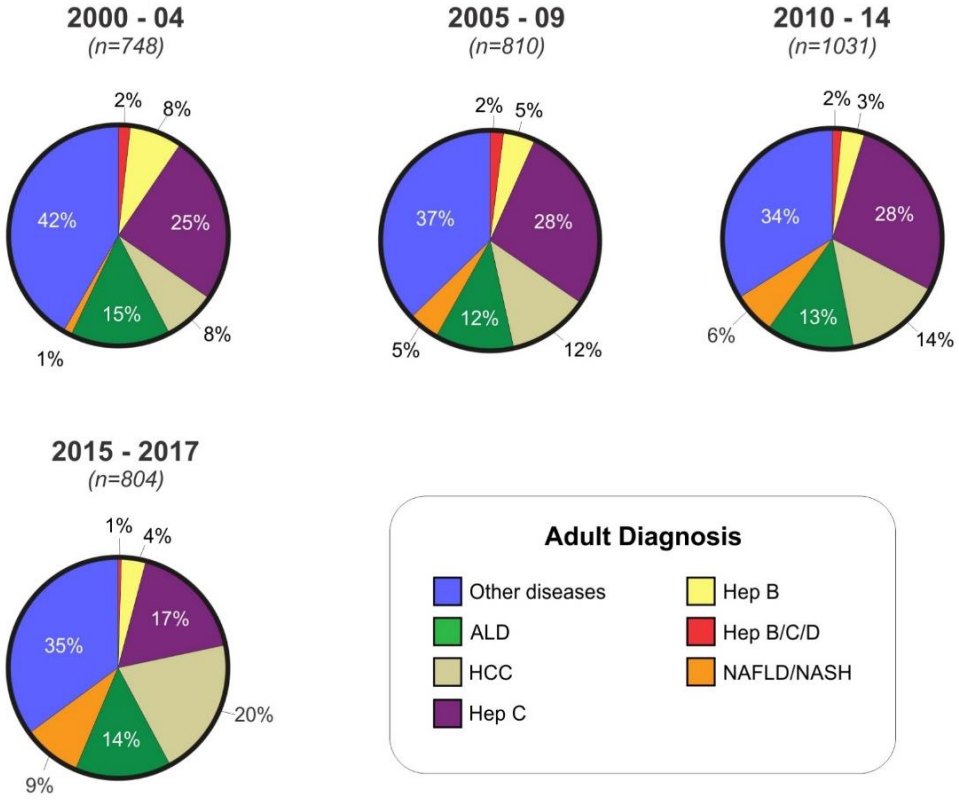
- Case control study
  - 97% CPS-A
  - Cirrhosis Dx 46% preop
  - Weight loss was **equivalent** to non-cirrhotic patients up to 1yr

Vupalanchi et al. Ann Surg 2022

TRANSPLANT

↑NASH → Liver Transplant



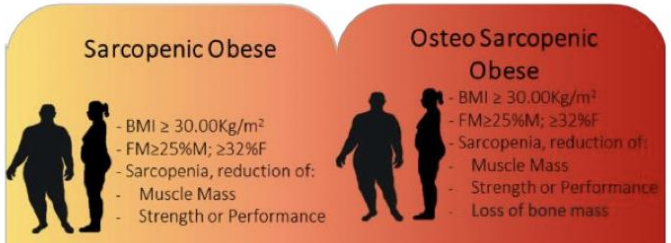


Lonardo et al. Nature Reviews Endo 2022

Transplant patients …

	Frequency of Incidence	Frequency of Incidence	Frequency of Incidence	Frequency of Incidence	Frequency of Incidence
Diabetes Type 2	1.9%	4.6%	8.1%	17.8%	30.5%
Cardiovascular Desease	1.3%	2.7%	6.5%	5.7%	6.3%

Classification of Obesity Phenotypes



	Man	Woman	Man	Woman
ASMMI (kg/m²)	<7.0 kg/m²	<5.5 kg/m²	<7.0 kg/m²	<5.5 kg/m²
Hand Grip (kg)	27<	16<	27<	16<
T-Score (DS)	> -1	> -1	-1 <	-1 <

IFSO guidelines

Bariatric surgery and transplant

- Morbidly obese patients have
  1) ↑ waiting list mortality
     - Disease progression, organ turndown
  2) ↑ post LT mortality
     - Comorbidities, technical difficulty
- **WHY?**
  - To **become** a Tx candidate
  - To **facilitate** surgery
  - To **prevent** recurrent disease

TIMING AROUND TRANSPLANT?

BEFORE

DURING

AFTER

Bariatric surgery **BEFORE** Liver Transplant

- WHO?
  - Careful selection
- CHALLENGES?
  - Sarcopenic, portal HTN, coagulopathy, thrombocytopenia
- SAFE?
  - 3 studies, 73 patients
  - No mortality
  - Morbidity 25%
    - wound infections, staple line leak, bleeding, transient HE, and kidney injury
- EFFECTIVE?
  - 66% weight loss at 2yrs
  - 85-90% meeting criteria for Tx

Chauhun et al. Digestive Diseases Science 2022

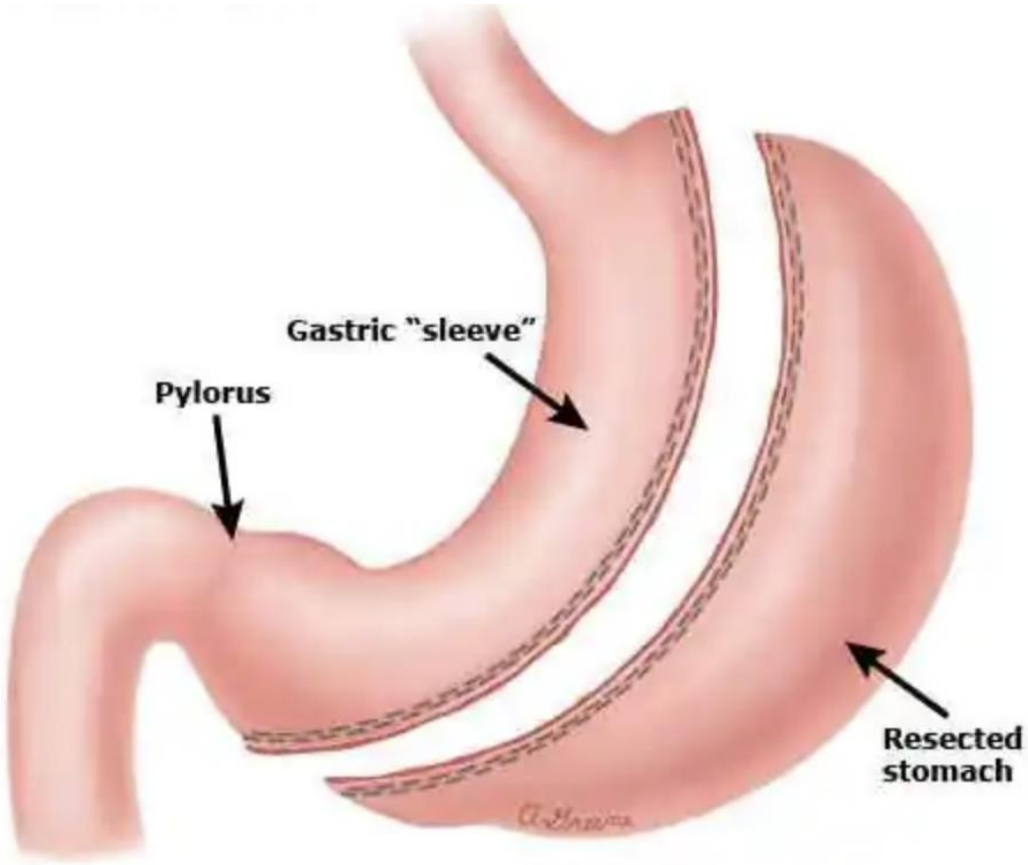
Bariatric surgery **DURING** Transplant

- SAFE
  - Retro cohort 49 combo vs 45000 LT alone
  - No difference in mortality/morbidity/LOS
- EFFECTIVE
  - SR: Better long term weight loss
  - LM/LT vs LT+SG: 100% vs 29% maintain >10%TWL @3yrs
- WHO?
  - OLTx NOT a bloodbath

Zamora-Valdes et al. Hepatology 2018
Wijarnpreecher et al. Transplant international 2020

Bariatric Surgery and Transplant

- Sleeve is best
  - Shorter operating time
  - Anatomy – biliary intervention
  - Predictable absorption immunosuppression



Royal Prince Alfred Hospital protocol

- NASH CIRRHOSIS undergoing Transplant
  - BMI ≥ 40
  - Multiple attempts at weight loss
- MDT assessment (MOS)
- Sleeve gastrectomy
- Nasojejunal feeding for at least 2 weeks <u>after</u> surgery to minimise infection and wound breakdown
- Discretion of the surgeon
- N=2!

Bariatric surgery **AFTER** Liver transplant

- DATA
  - 9 studies, 71 patients
    - 83% SG
    - 16% major post op morbidity
    - 2/71 (1.4%)mortality due to staple line leak/MOF
- CHALLENGES
  - Adhesions, frail, immunosuppression

Chierici et al. J Liver Transplant 2023

Summary

- MAFLD is widespread, increasing and lethal
- Weight loss is the mainstay of treatment
- Lifestyle modification is beneficial if weight loss can be achieved
- Medication (SGLT-2) shows promise in short term studies
- Bariatric surgery can reduce/resolve NAFLD/NASH although fibrosis can progress in up to 15%
- Bariatric surgery is safe and effective in carefully chosen cirrhotics (CPS-A)
- Sleeve vs RYGB is equally safe and effective up to NASH
- Sleeve is preferable in cirrhotics/transplant candidates