# Is There a Role for Primary Care Providers to Manage Patients with MASH?

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# Disclosure

Advisory Board: Boehringer-Ingelheim; Madrigal; Novo Nordisk

Consultant: Boehringer-Ingelheim; Novo Nordisk

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# Learning Objectives

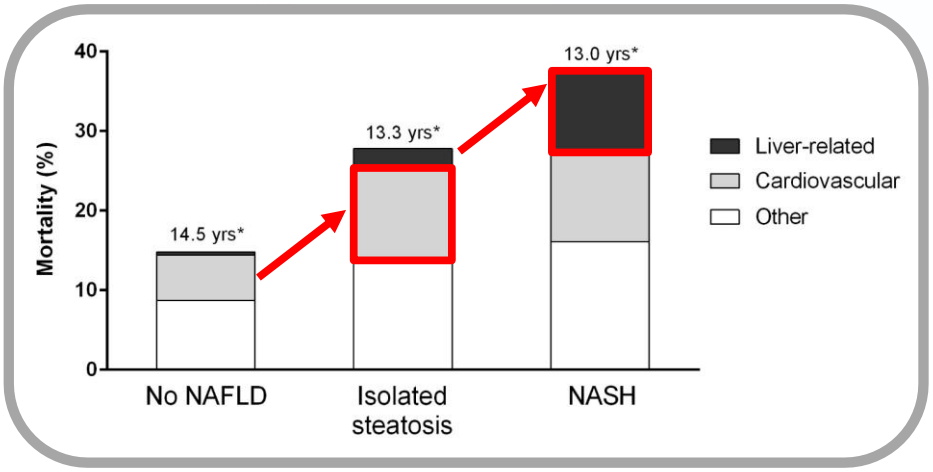
1. Discuss lifestyle interventions and bariatric surgery as therapeutic options for MASH
2. Discuss how to manage diabetes in patients with MASH
3. Describe pharmacological options to treat MASH



# Outline

1. Lifestyle changes and bariatric surgery
2. Medications for T2D
3. Pharmacological options for MASH

# Why Treating?




Bril F & Cusi K. Endocrinol Metab Clin N Am 2016;45:765-781.

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# Addressing CMRFs


Weight loss


Healthy habits


Exercise


Glycemic control


Lipid management


BP control


Cardioprotection


OSA/Sleep


Nephroprotection

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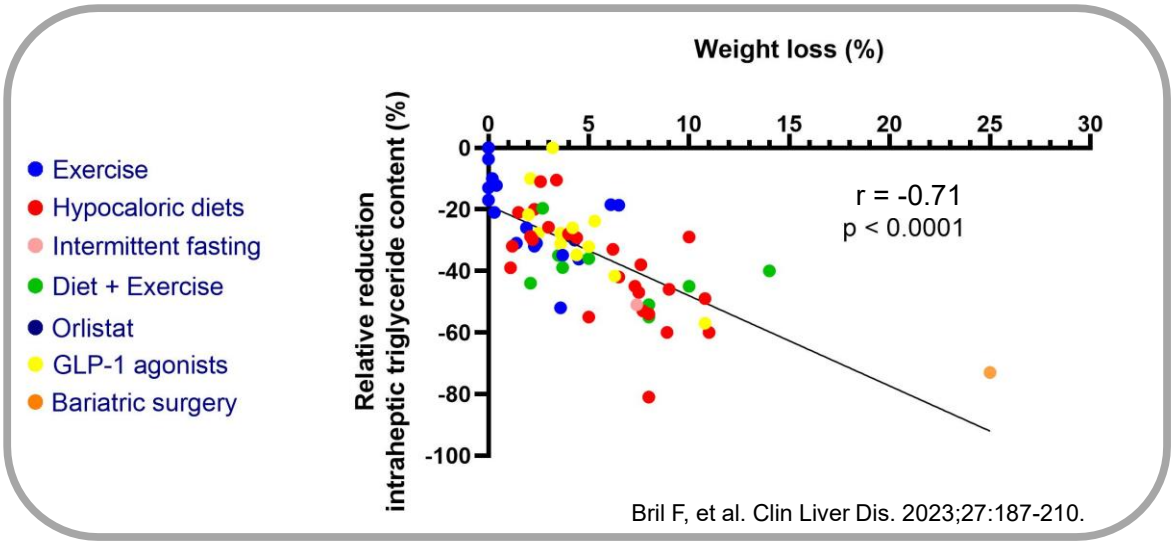
# Lifestyle




Bril F, et al. Clin Liver Dis. 2023;27:187-210.

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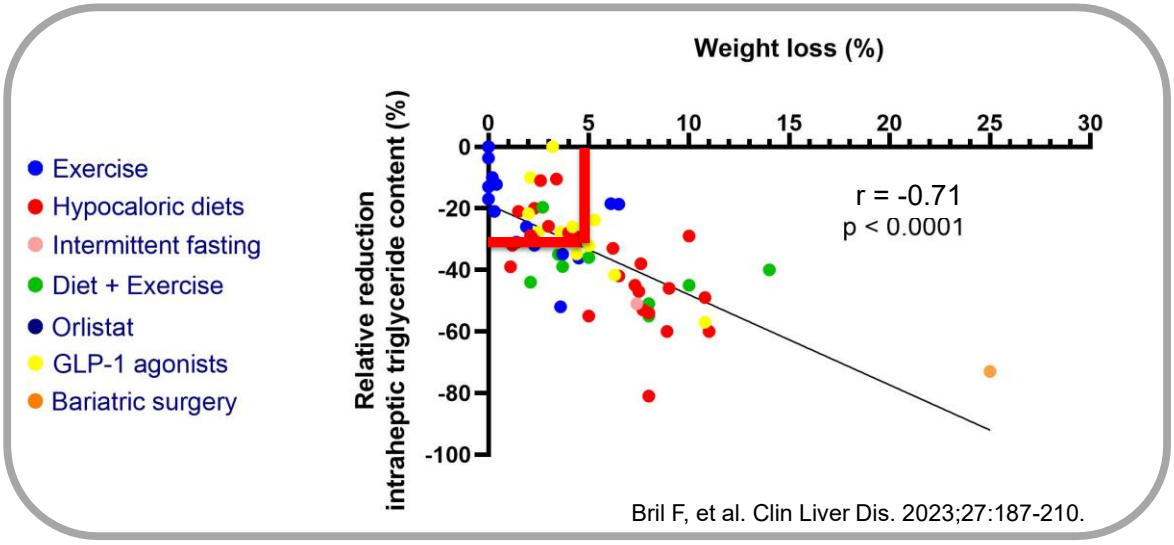
# Lifestyle




Bril F, et al. Clin Liver Dis. 2023;27:187-210.

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# Lifestyle

| Histologic outcomes | Weight loss <5.0% | Weight loss 5.0 a 6.9% | Weight loss 7.0 a 9.9% | Weight loss ≥10% |
|---|---|---|---|---|
| Resolution of NASH | 10% | 26% | 64% | 90% |
| NAS score reduction | 32% | 62% | 88% | 100% |
| Steatosis improvement | 35% | 65% | 76% | 100% |
| Inflammation improvement | 35% | 71% | 88% | 100% |
| Ballooning improvement | 26% | 41% | 84% | 90% |
| Fibrosis improvement | 16% | 18% | 16% | 45% |

Vilar-Gomez, et al. Gastroenterology 2015;149:367–378.

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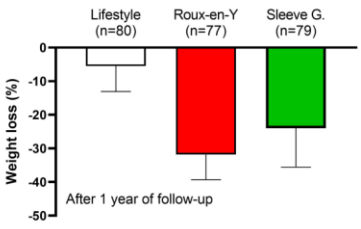
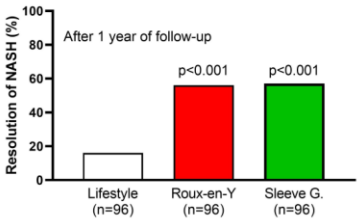
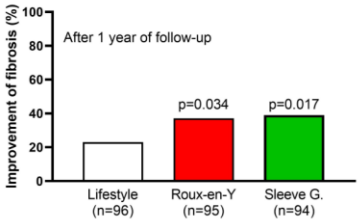
# Bariatric Surgery




Verrastro O, et al. Lancet. 2023;401:1786-1797.

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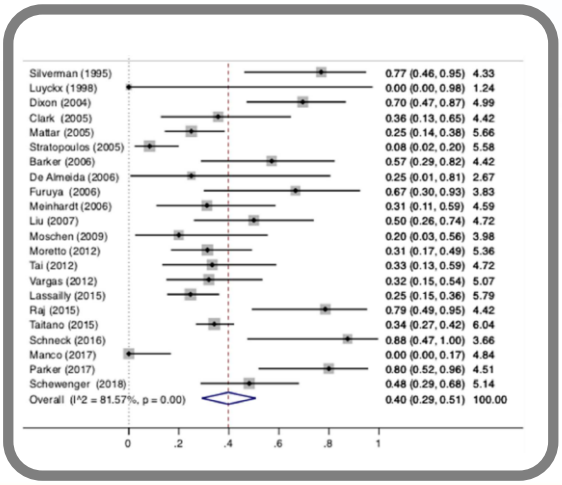
# Bariatric Surgery

Fibrosis stage




**n = 32 studies**
**No RCTs**
**(2,649 paired biopsies)**

Lee, et al. Clin Gastroenterol Hepatol 2019;17:1040-1060.

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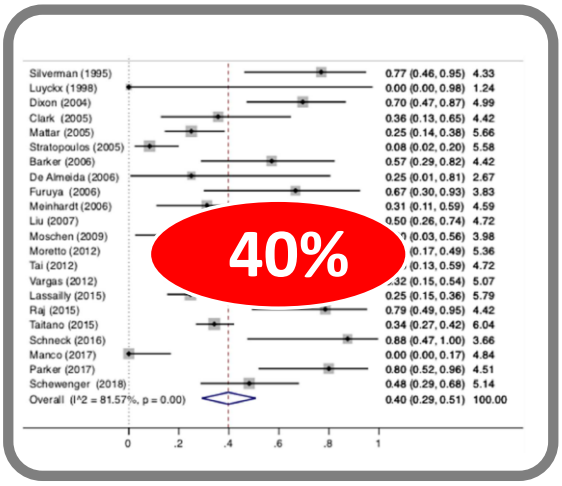
# Bariatric Surgery

Fibrosis stage




40%

**n = 32 studies**
**No RCTs**
**(2,649 paired biopsies)**

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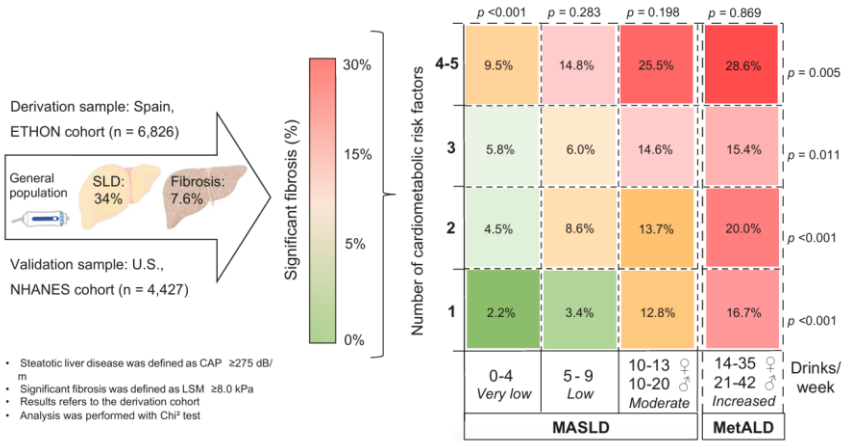
# Alcohol Cessation




Marti-Aguado D, et al. J Hepatol. 2024;81(6):930-940.

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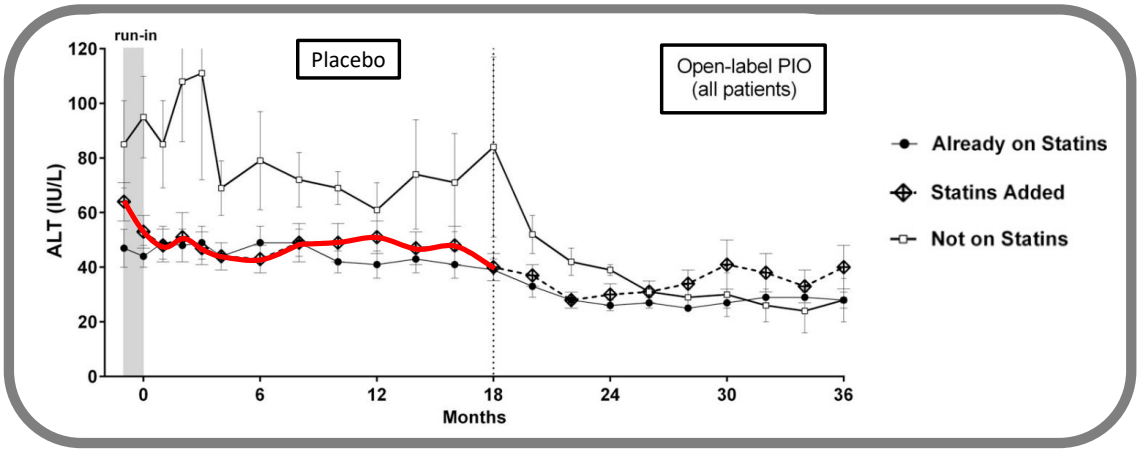
# Addressing CMRFs

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# Addressing CMRFs

| Drugs | Improves steatosis | Improves MASH | Delays fibrosis progression | Reduces CV events | TG | LDL-C | HDL-C |
|---|---|---|---|---|---|---|---|
| Statins | ?* | – | – | + | ↓ | ↓↓ | ↑ |
| Fibrates | – | – | – | – | ↓↓ | ↓ | ↑ |
| EPA-ethyl ester | ?* | – | – | + | ↓ | ↓ | ↑ |
| Ezetimibe | – | – | – | + | ↓ | ↓ | ↑ |
| PCSK9-inh | – | – | – | + | ↓ | ↓↓ | ↑ |

* Conflicting data

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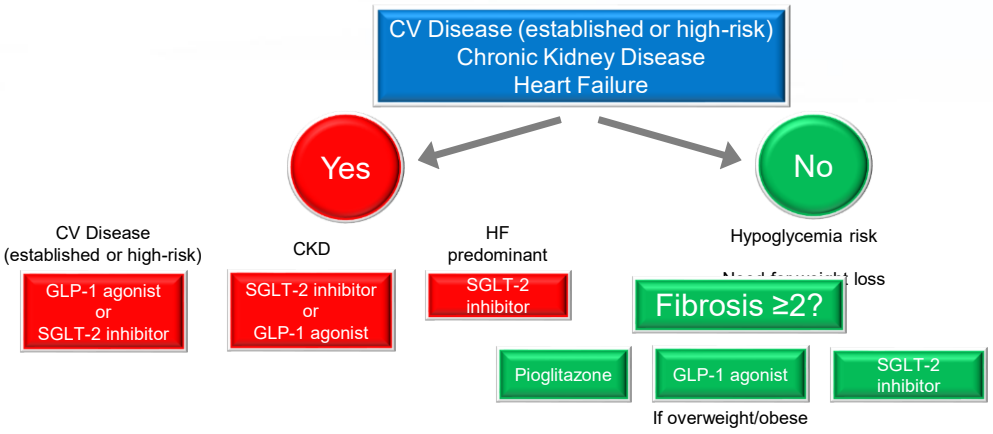
# Managing Diabetes

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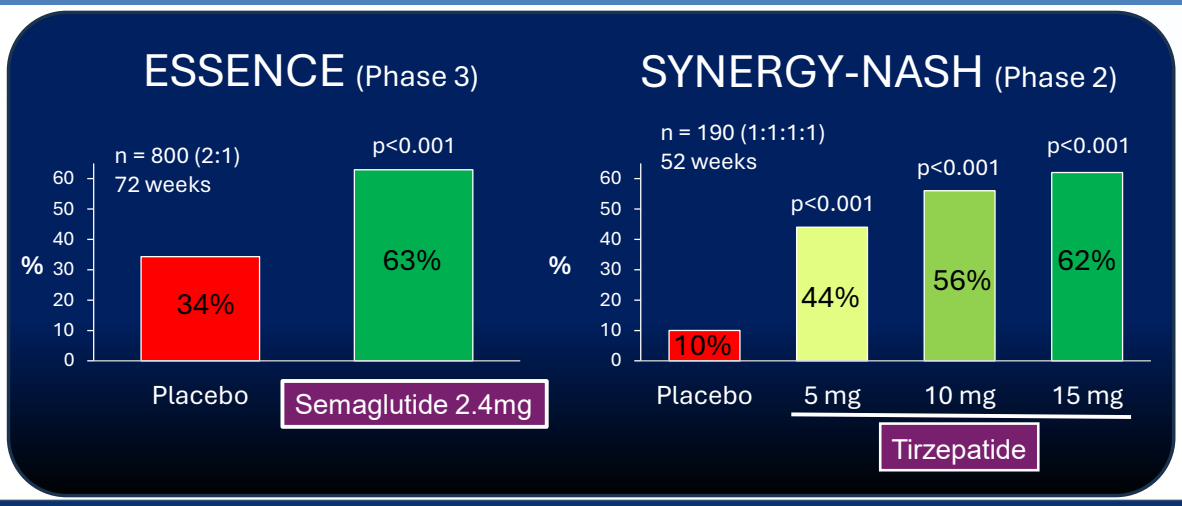
# Managing Diabetes




Sanyal et al. NEJM 2025;392:2089-2099; Loomba et al. NEJM 2024;391:299-310.

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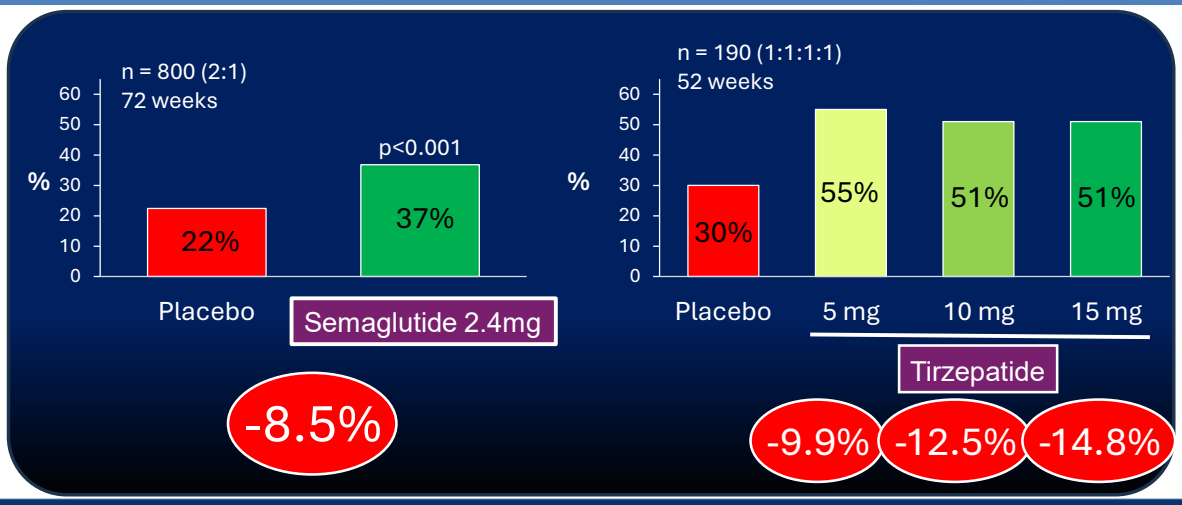
# Managing Diabetes




Sanyal et al. NEJM 2025;392:2089-2099; Loomba et al. NEJM 2024;391:299-310.

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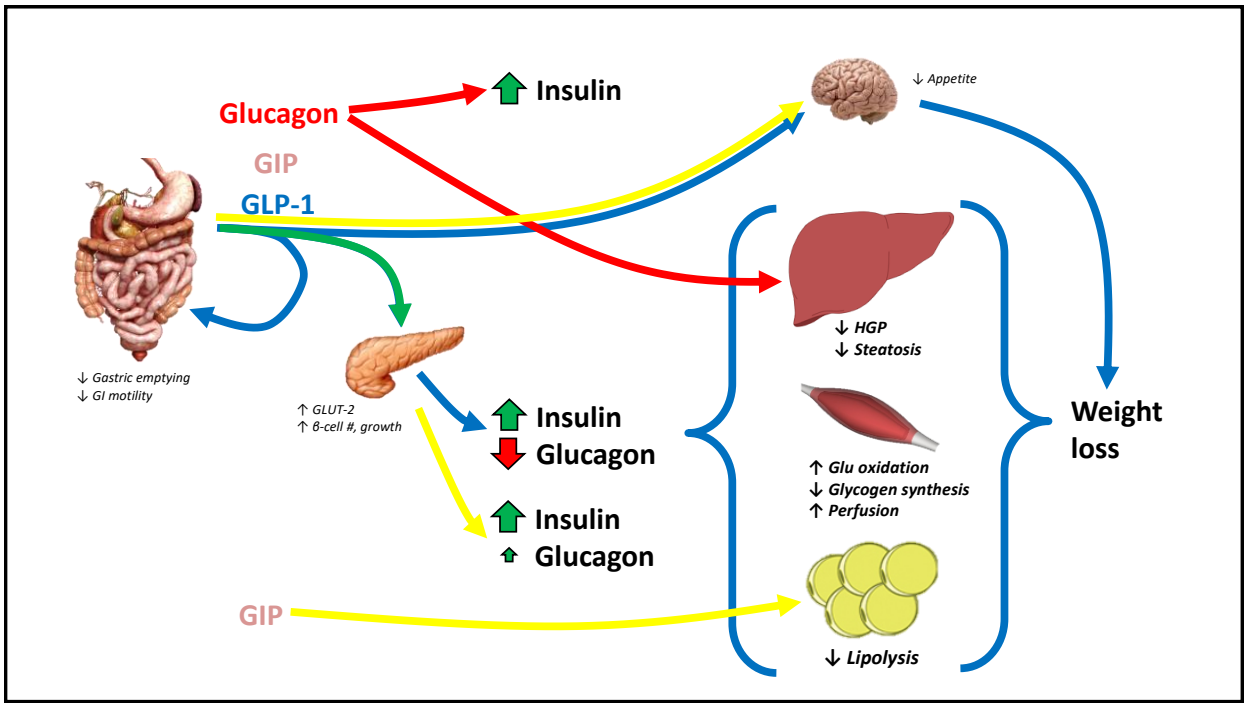


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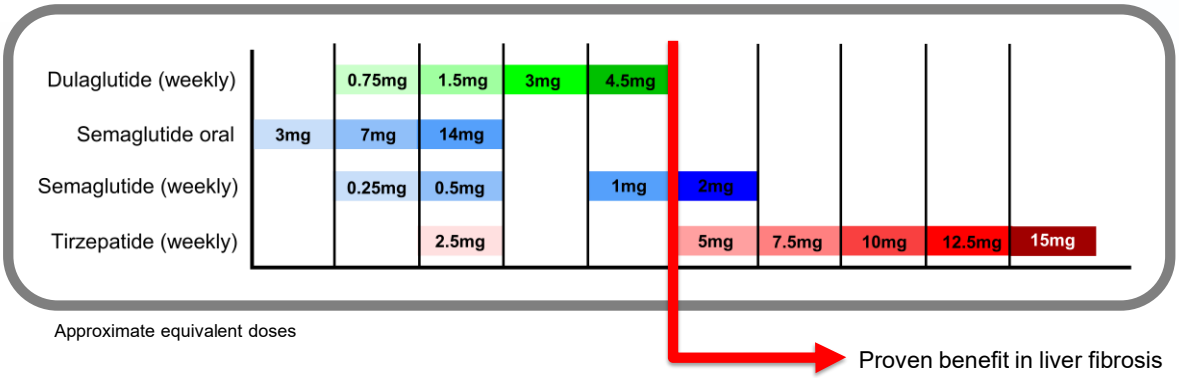
# Managing Diabetes




Whitley HP, et al. Clin Diabetes. 2023;41:467-473.

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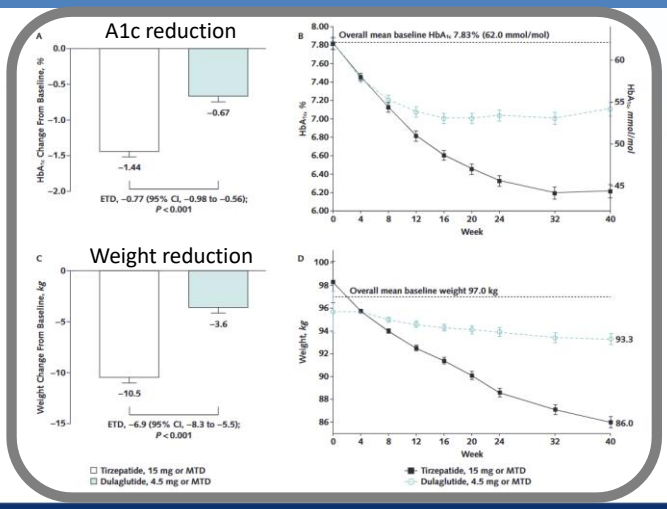
# Managing Diabetes




Billings LK, et al. Ann Intern Med.2025;178:609-619.

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# Managing Diabetes

- GI symptoms. Usually well tolerated.
  - Malik ME, et al. Lancet Reg Health Eur. 2023;29:100617.
    "45% discontinuation at 5 years". However, 56% discontinued SGLT-2 inhibitors, which are also well tolerated.
  - Rodriguez JP, et al. JAMA Netw Open. 2025;8:e2457349.
    "46.5% of patients with T2D discontinued medications at 1 year". However, a minority of these were due to side effects. And ~50% were reinitiated on these medications
  - Do D, et al. JAMA Netw Open. 2024;7:e2413172.
    "35.8% of patients with T2D discontinued medications at 1 year". OOP costs was associated with discontinuation.
- Pancreatitis? No association vs. small risk.
- Thyroid cancer. In rodents GLP-1RA are associated with medullary thyroid cancer (very rare).
- Bone turnover/Sarcopenia
- Retinopathy 2/2 A1c reduction. Nonarteritic anterior ischemic optic neuropathy (Cai CX, et al. JAMA Ophthalmol. 2025).

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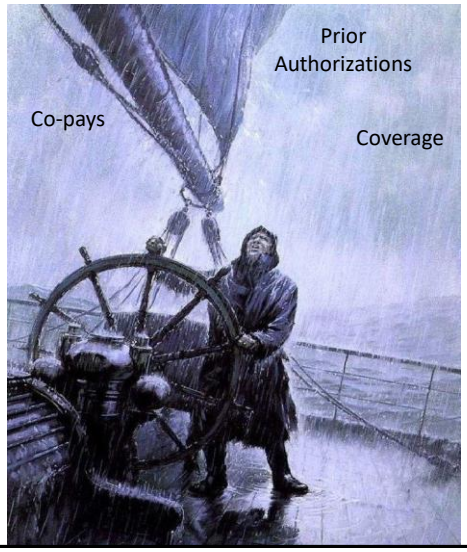
# Managing Diabetes




Navigating the
'Insurance' High Seas

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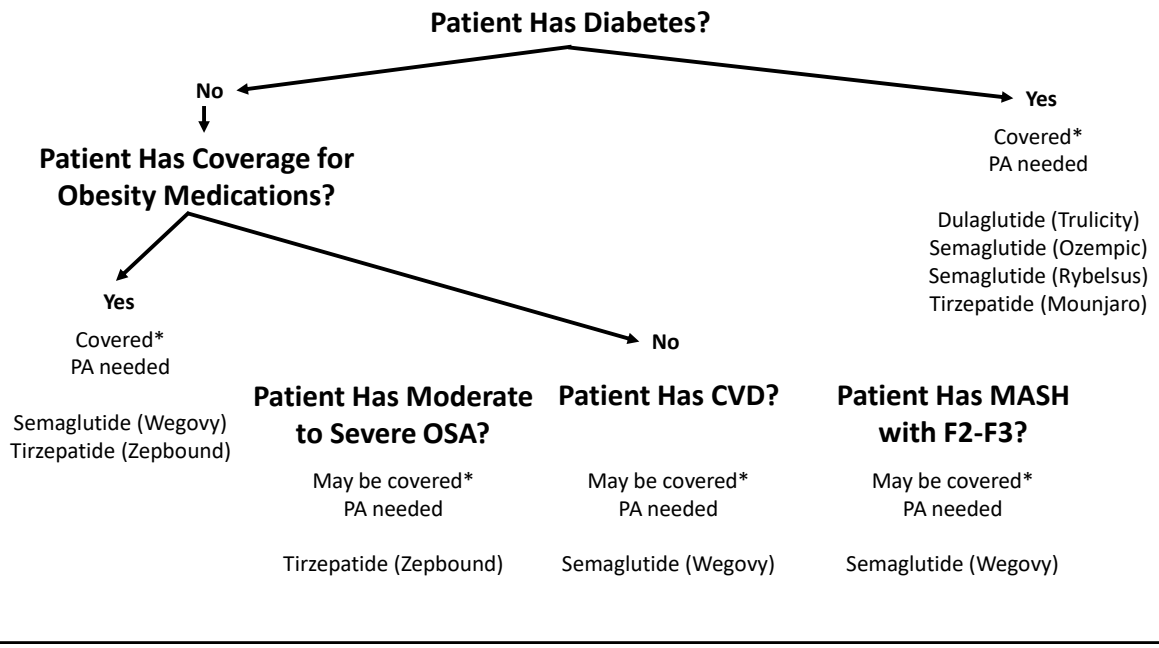


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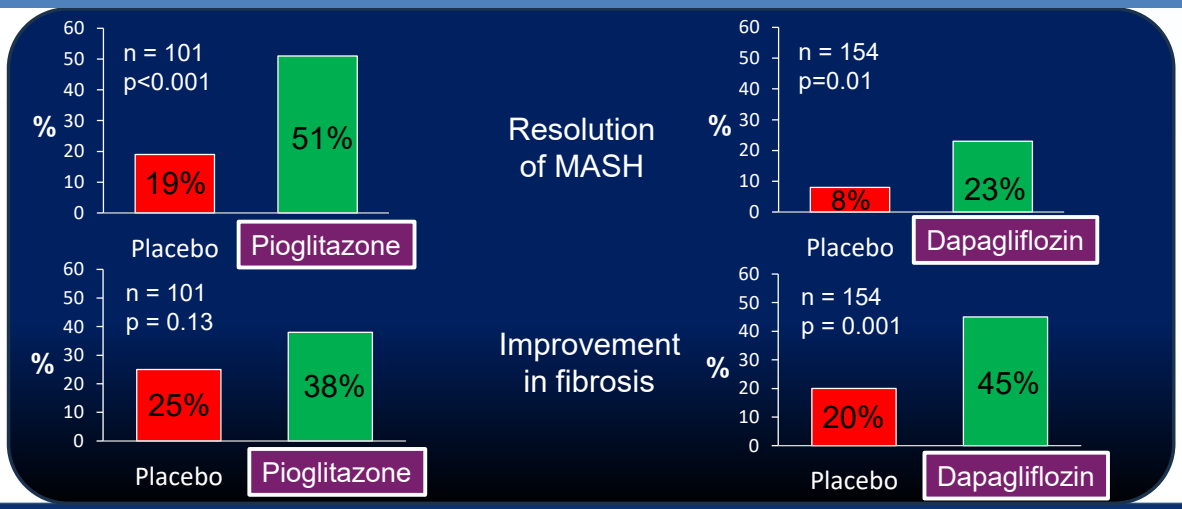
# Managing Diabetes




Cusi et al. Ann Intern Med 2016; Lin et al. BMJ 2025.

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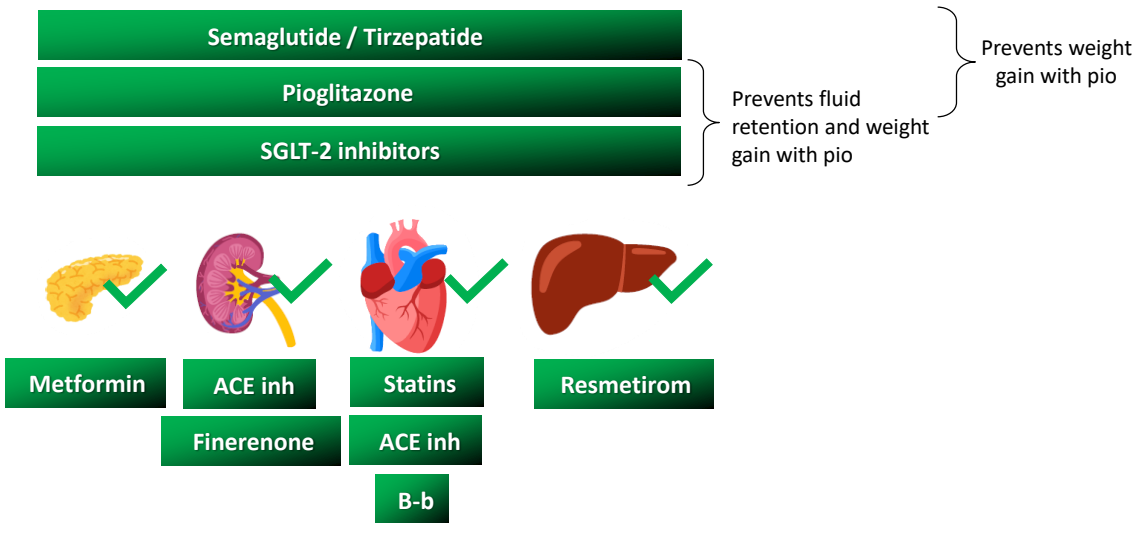
# Combination Therapy

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# Pharmacological Treatment of MASH

## Resmetirom and Semaglutide are approved for MASH with F2-F3

**(F2-F3 on biopsy)**
**(VCTE 8.0-19.9 kPa)***
**(ELF 9.2-11.2)***
**(MRE 3.1-4.9 kPa)***

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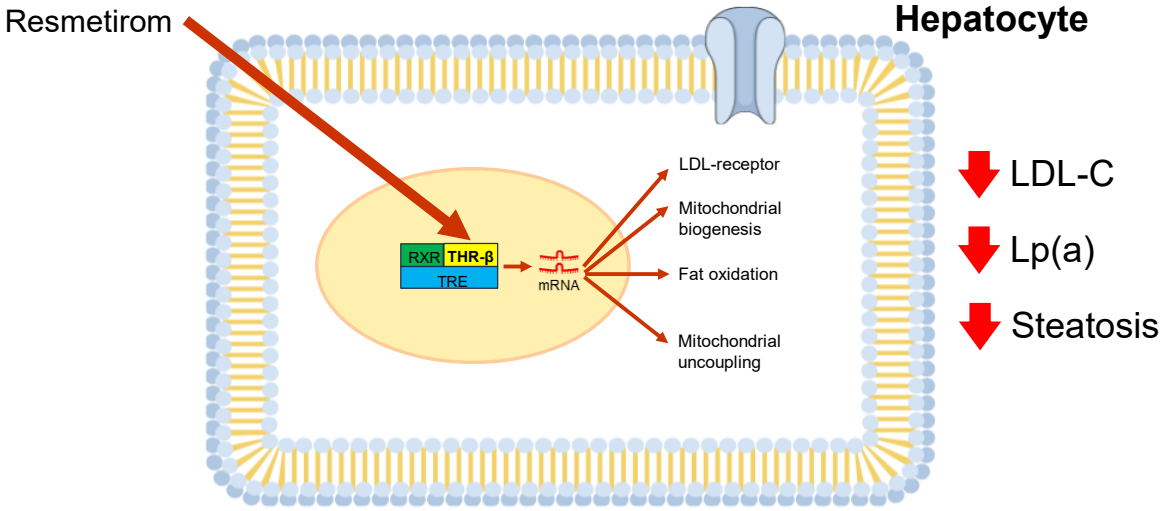
# Pharmacological Treatment of MASH

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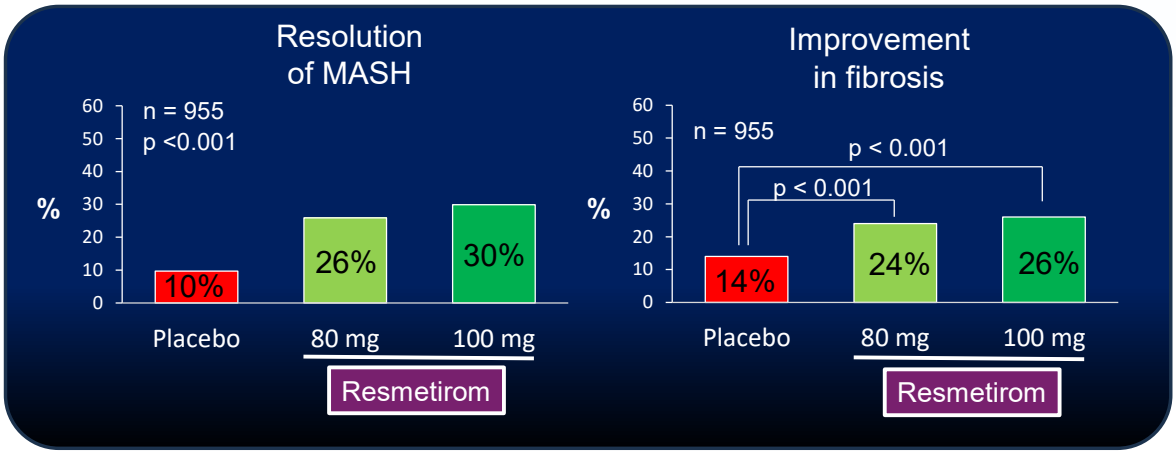
# Pharmacological Treatment of MASH




Harrison et al. NEJM 2024;390:497-509

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# Pharmacological Treatment of MASH

## Side effects - resmetirom

- Mainly GI in origin.
- Resmetirom decreases fT4 ~20% (-22.8 to -18.6%) and TSH ~10% (central inhibition).
- SHBG increases ~200% (> females).
  Leads to ~100% increase in estradiol in females and ~30% in males.
  Leads to ~100% increase in total testosterone. No changes in free?
- No change in DXA in 1 year.
- Dose of statin needs to be adjusted.

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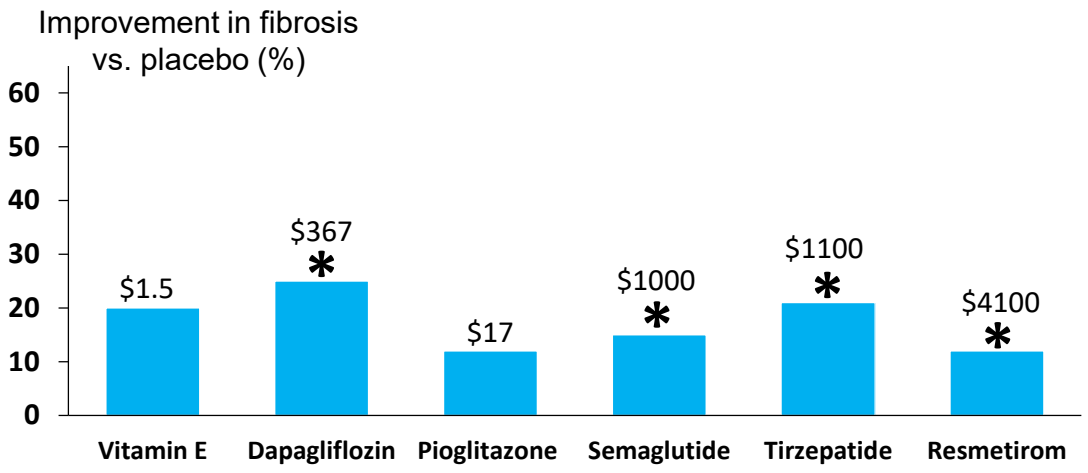
# Pharmacological Treatment of MASH

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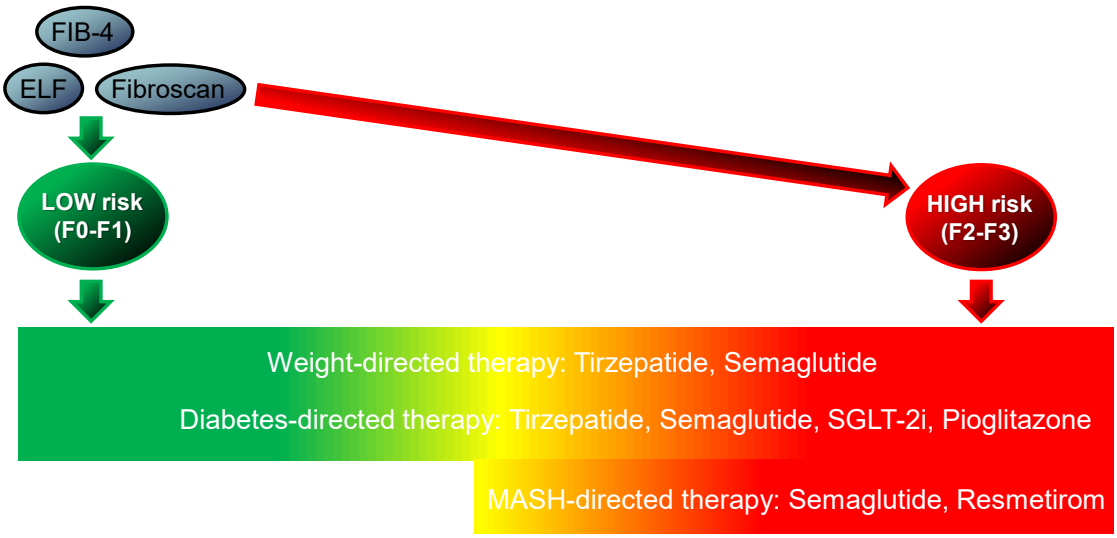
# Pharmacological Treatment of MASH

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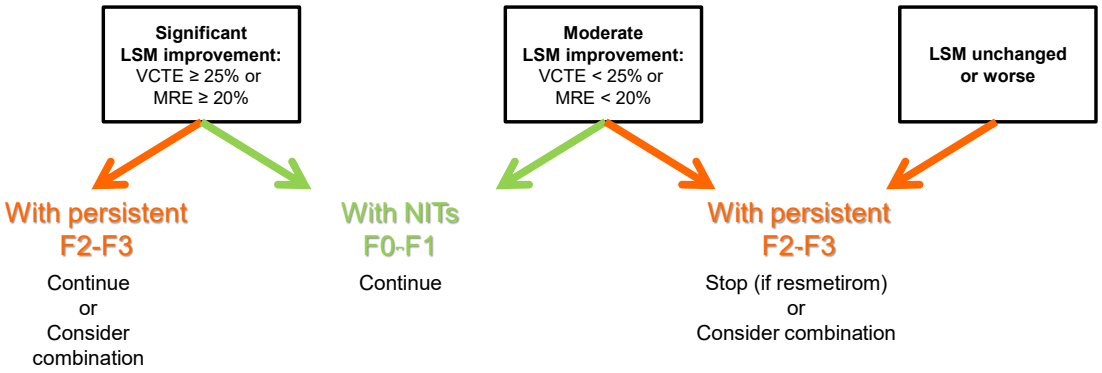
# Monitoring After Therapy

Patient should be monitored with liver enzymes every 3-6 months.

Patient should be reassessed with imaging-based NITs after 12-18 months, depending on baseline availability.

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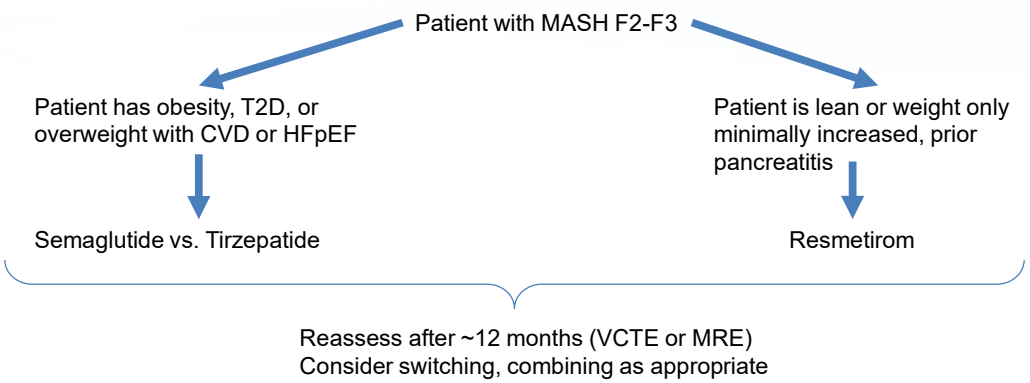
# Pharmacological Treatment of MASH

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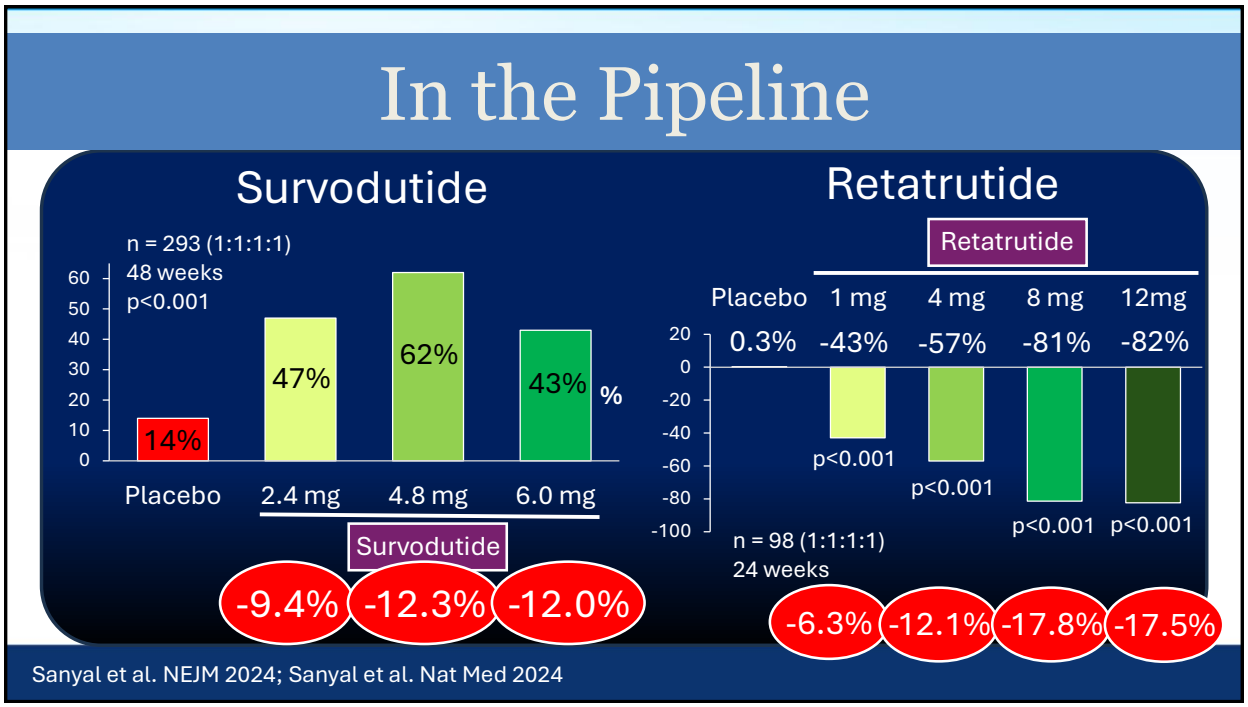
In the Pipeline
Survodutide
n = 293 (1:1:1:1)
48 weeks
p<0.001
14%
47%
62%
43%
%
Placebo
2.4 mg
4.8 mg
6.0 mg
Survodutide
-9.4%
-12.3%
-12.0%
Retatrutide
Retatrutide
Placebo
1 mg
4 mg
8 mg
12mg
0.3%
-43%
-57%
-81%
-82%
p<0.001
p<0.001
p<0.001
p<0.001
n = 98 (1:1:1:1)
24 weeks
-6.3%
-12.1%
-17.8%
-17.5%
Sanyal et al. NEJM 2024; Sanyal et al. Nat Med 2024

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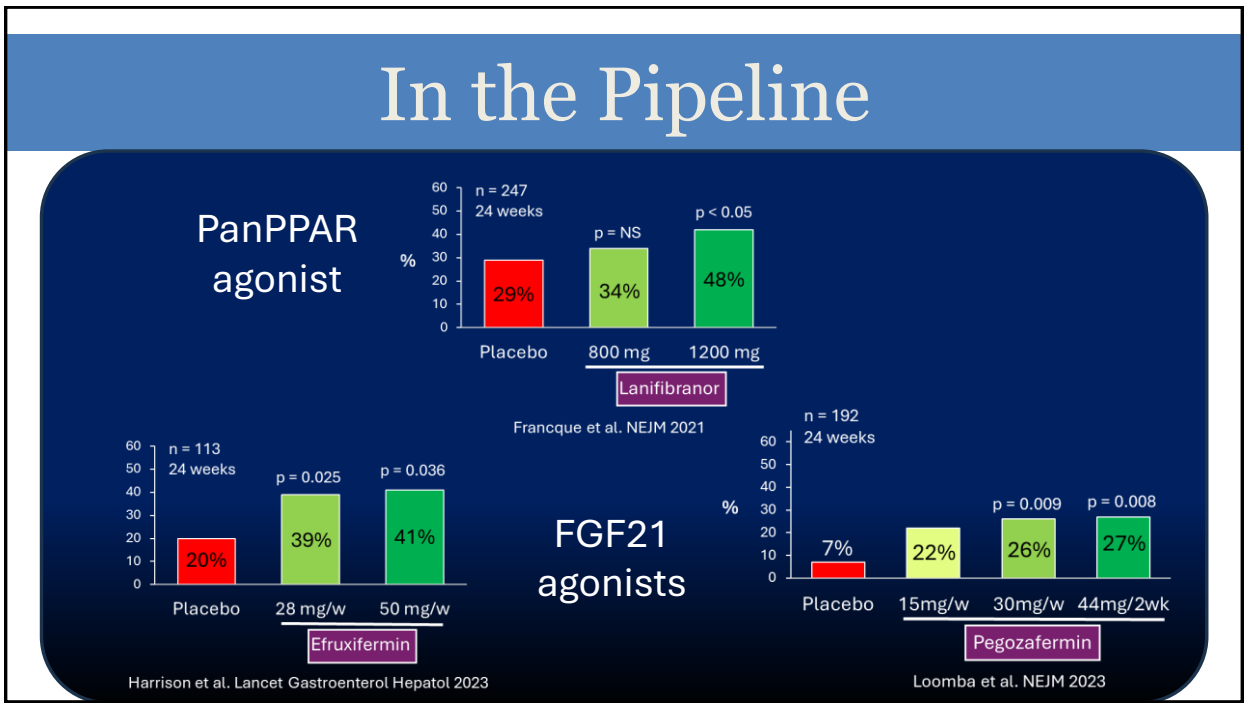
In the Pipeline
PanPPAR agonist
n = 247
24 weeks
p = NS
p < 0.05
29%
34%
48%
%
Placebo
800 mg
1200 mg
Lanifibranor
Francque et al. NEJM 2021
n = 113
24 weeks
p = 0.025
p = 0.036
20%
39%
41%
Placebo
28 mg/w
50 mg/w
Efruxifermin
Harrison et al. Lancet Gastroenterol Hepatol 2023
FGF21 agonists
n = 192
24 weeks
p = 0.009
p = 0.008
7%
22%
26%
27%
%
Placebo
15mg/w
30mg/w
44mg/2wk
Pegozafermin
Loomba et al. NEJM 2023

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# Conclusions

1. Early identification of MASH is essential to introduce effective pharmacological therapy
2. Primary care providers have a central role in managing these patients
3. This includes CV risk management, and introducing medications with known metabolic benefits
4. Combination therapy is likely to play a key role in the management of patients with MASH