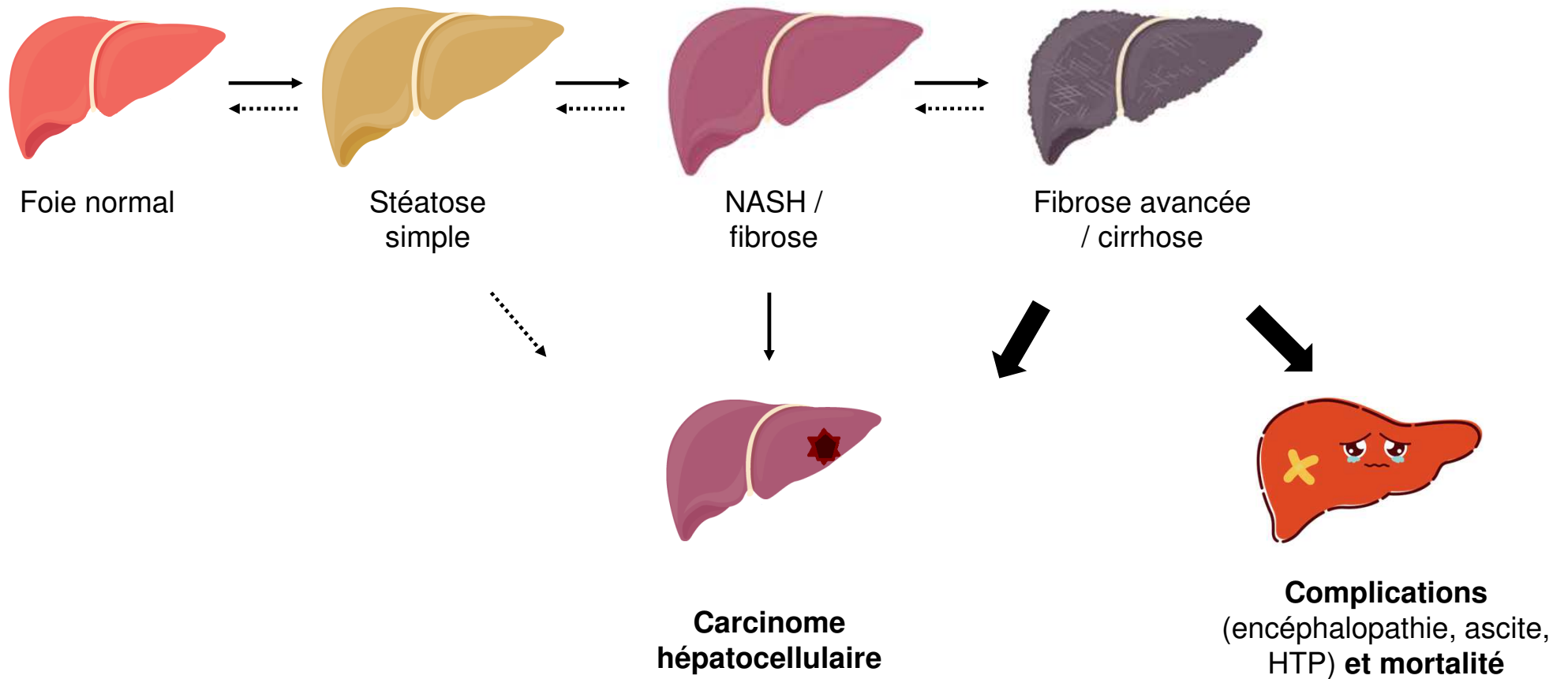


NASH: le rôle du médecin généraliste

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Service de Gastroentérologie & Hépatologie
Service de Transplantation
Hôpitaux Universitaires de Genève

4 mai 2023

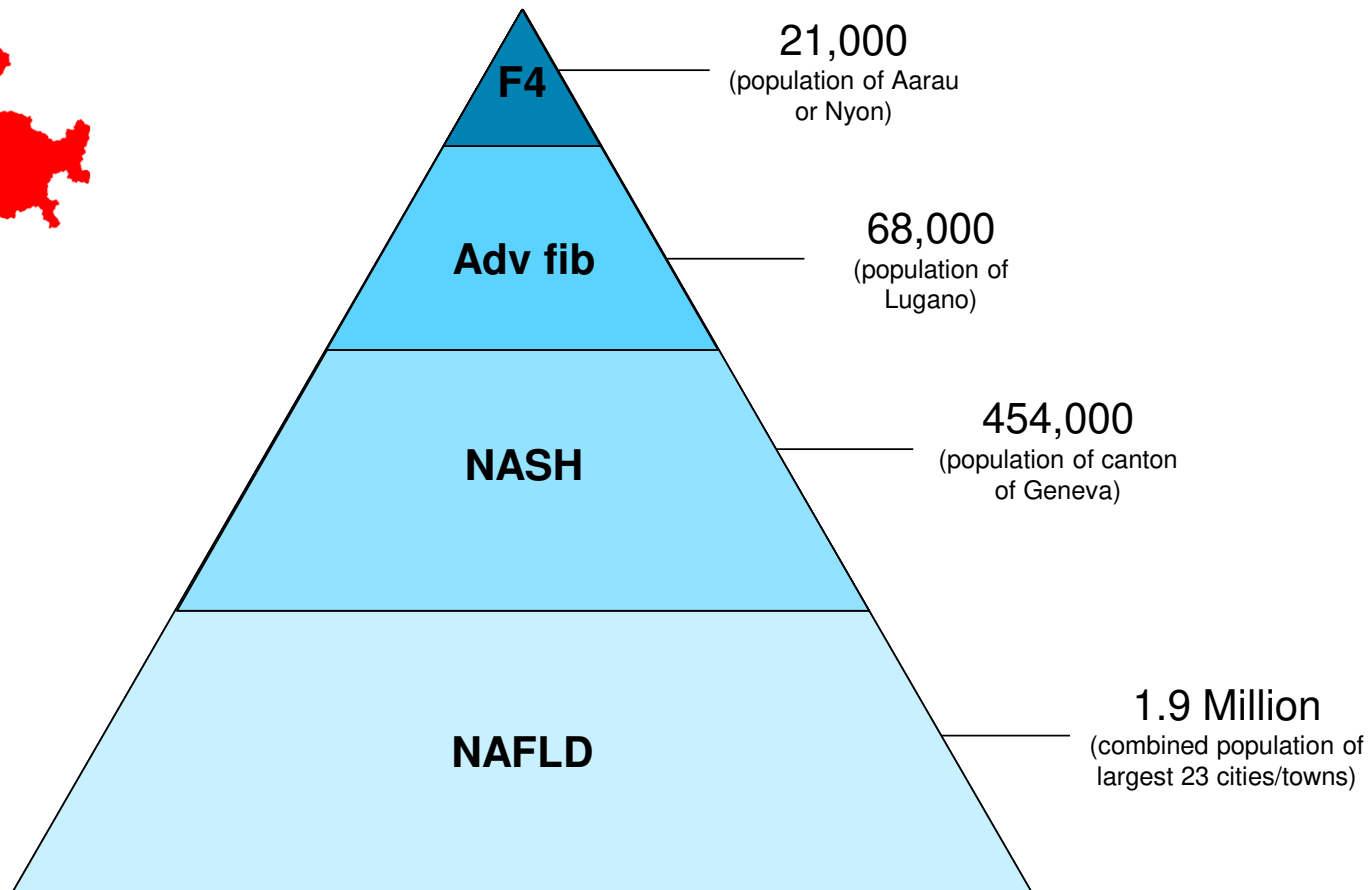
Quelle est l'histoire naturelle de la stéatose dysmétabolique (=NAFLD) ?



Epidémiologie en Suisse



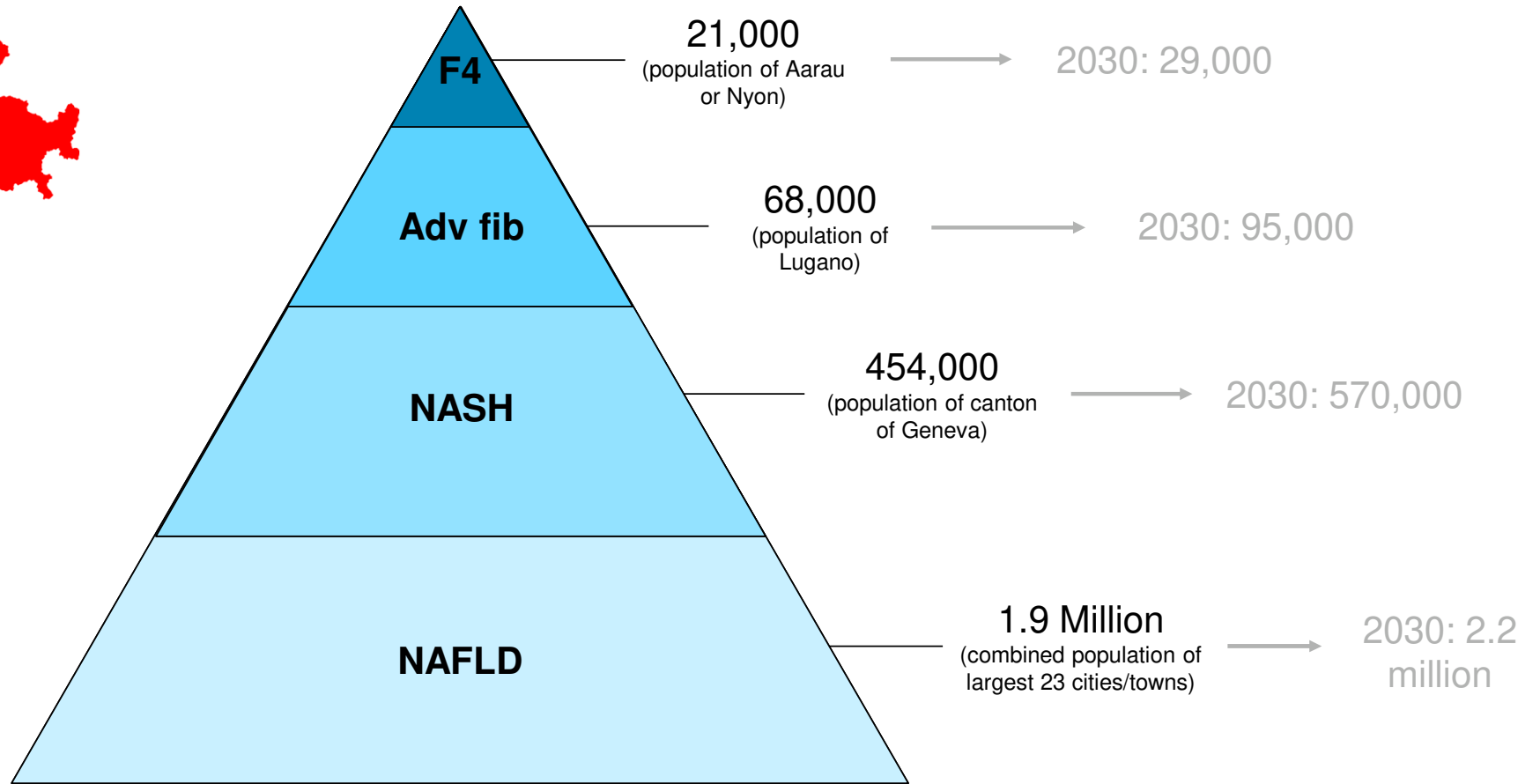
2018 estimates



Epidémiologie en Suisse



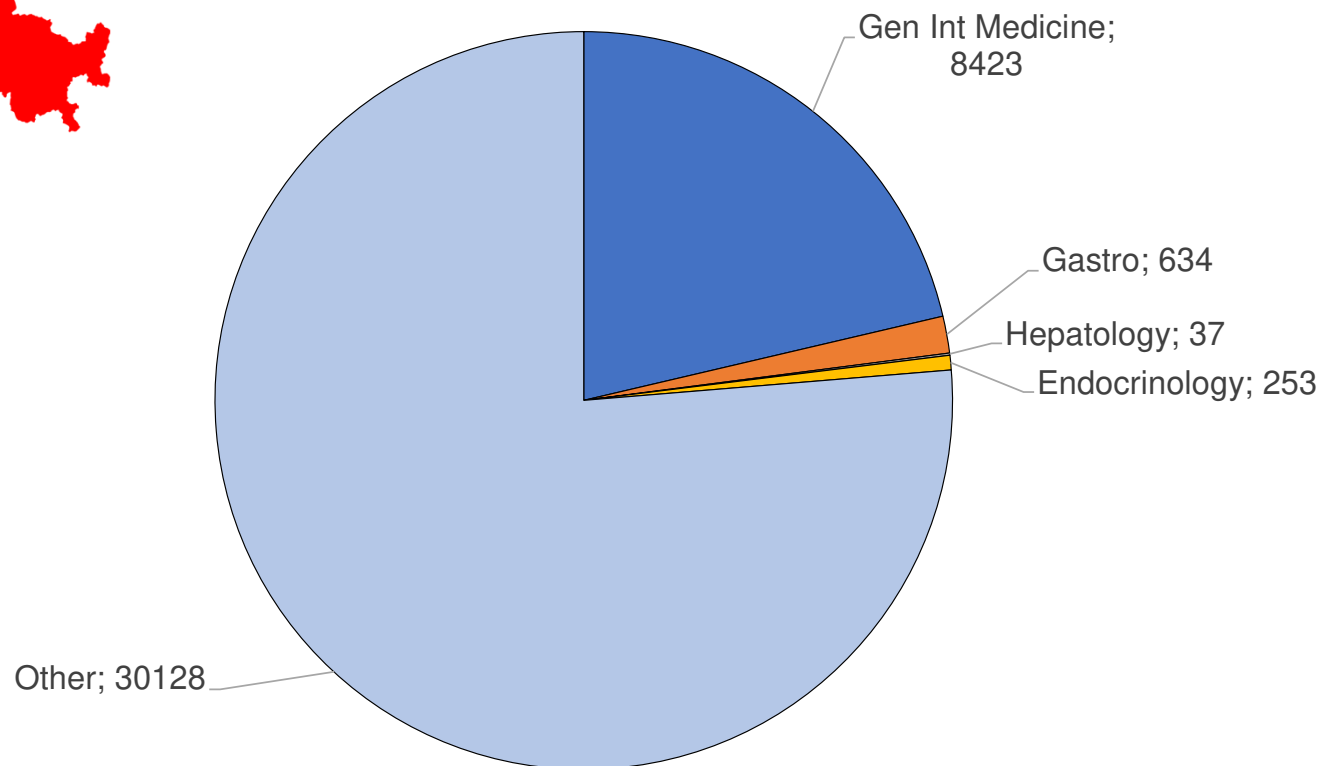
2018 estimates



Ressources médicales limitées



2021



Nouvelle nomenclature: **MAFLD**

Metabolic associated fatty liver disease

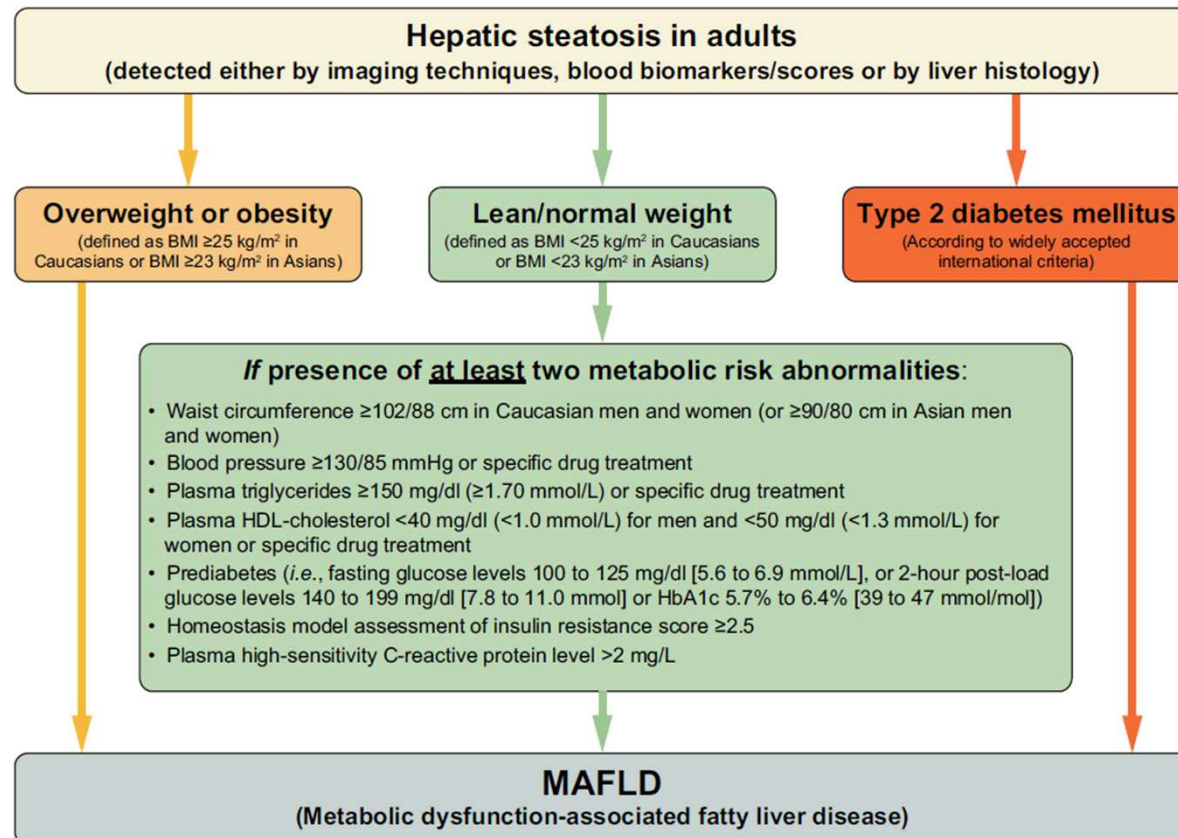


Fig. 1. Flowchart for the proposed “positive” diagnostic criteria for MAFLD.

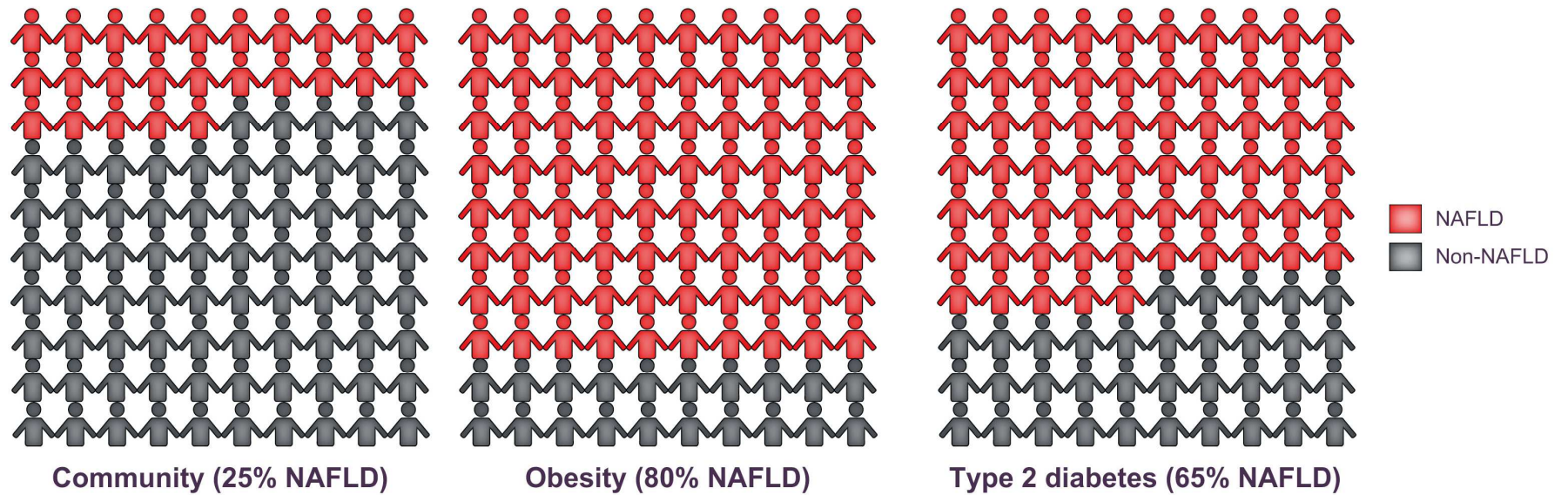
Quels questions poser face à un patient avec une suspicion de stéatose hépatique?

1. Identifier les patients à risque
2. Anamnèse et examens biologiques (étiologie et stade)
3. Mesure de la fibrose hépatique à l'aide d'outils non-invasifs (FIB-4 et/ou elastométrie)
4. Prise en charge

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Facteurs de risque métabolique



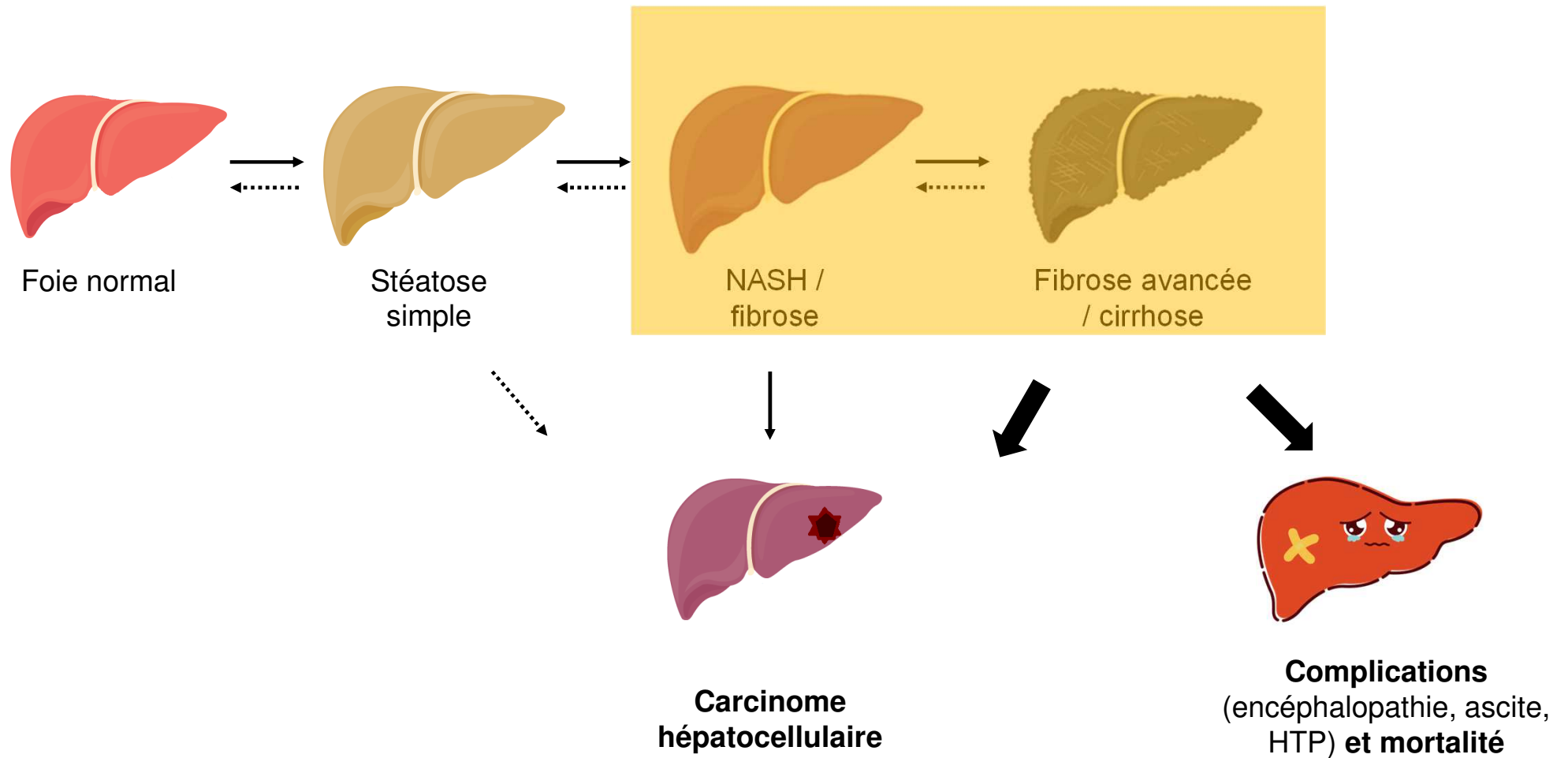
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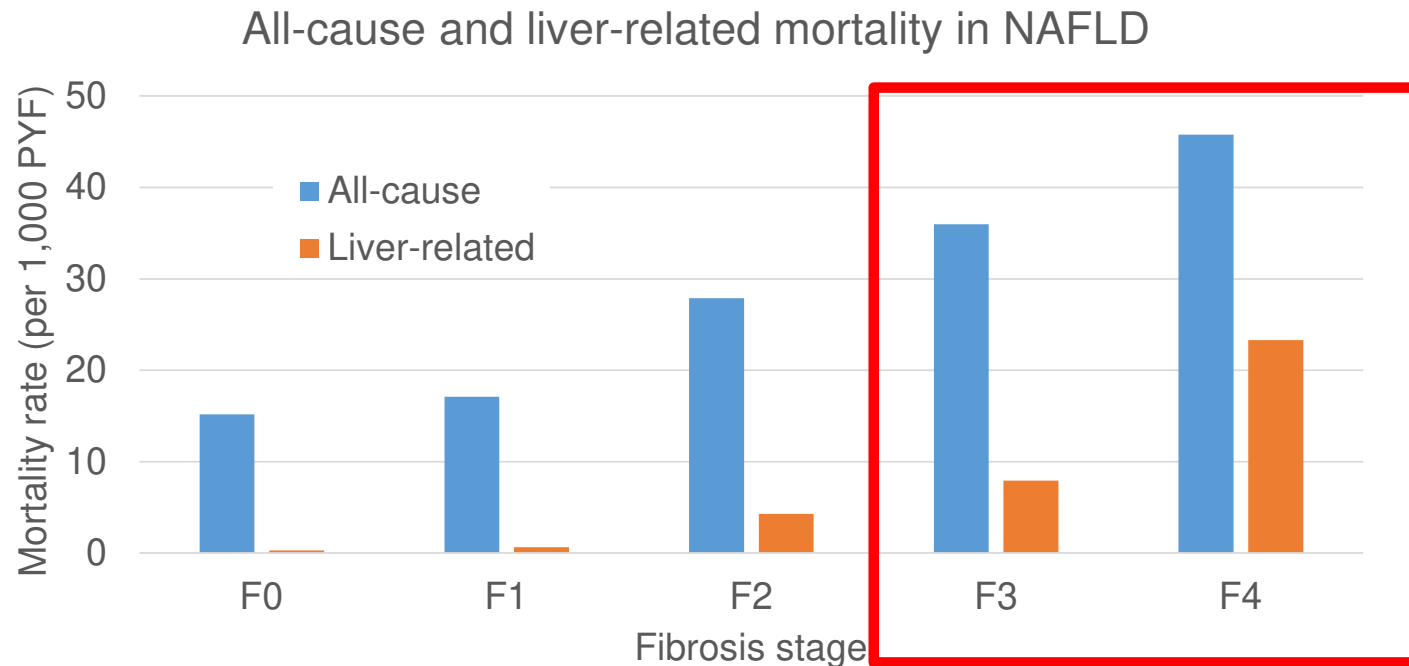
Exclure les co-facteurs et autres étiologies de pathologie hépatique

Toujours ++	Au cas par cas
<ul style="list-style-type: none">• Hépatite B, C• Alcool	<ul style="list-style-type: none">• Hémochromatose• Auto-immune• Déficit en α1-antitrypsine• Médics (MTX, amiodarone, corticoïdes etc..) <p>Mais encore....</p> <ul style="list-style-type: none">• Maladie de Wilson• Maladie coeliaque• Déficience LAL• Hypobétalipoprotéïnémie

Identifier les patients à risque



NASH – le rôle pronostic de la fibrose hépatique



Systematic review of 1,495 NAFLD patients with 17,452 patient years of follow-up.
No adjustment for confounders

Comment identifier les sujets à risque de maladie hépatique avancée ?

Paramètres simples!

- Age
- ASAT
- ALAT
- Thrombocytes

Calcul du score **FIB-4**

Pour le calcul rechercher "FIB-4" sur votre moteur de recherche préféré

Comment identifier les sujets à risque de maladie hépatique avancée ?

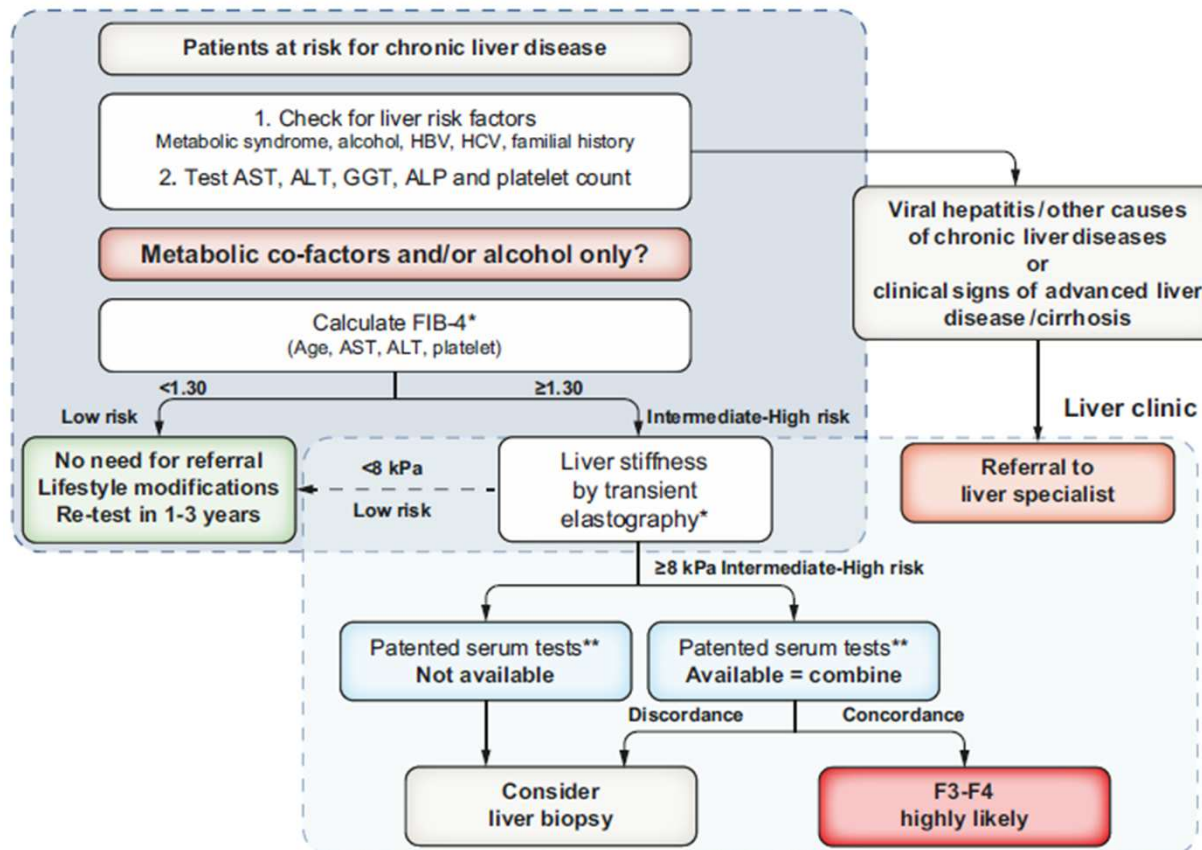
Paramètres simples!

- Age
- ASAT
- ALAT
- Thrombocytes

Calcul du score **FIB-4 \geq 1.3**

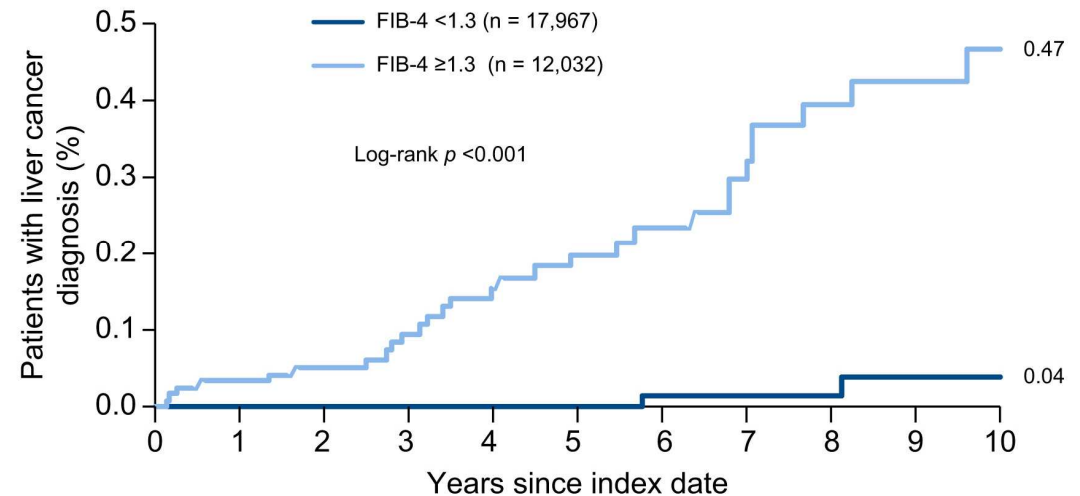
Pour le calcul rechercher "FIB-4" sur votre moteur de recherche préféré

Comment identifier les sujets à risque de maladie hépatique avancée ?



FIB4 is associated with HCC development

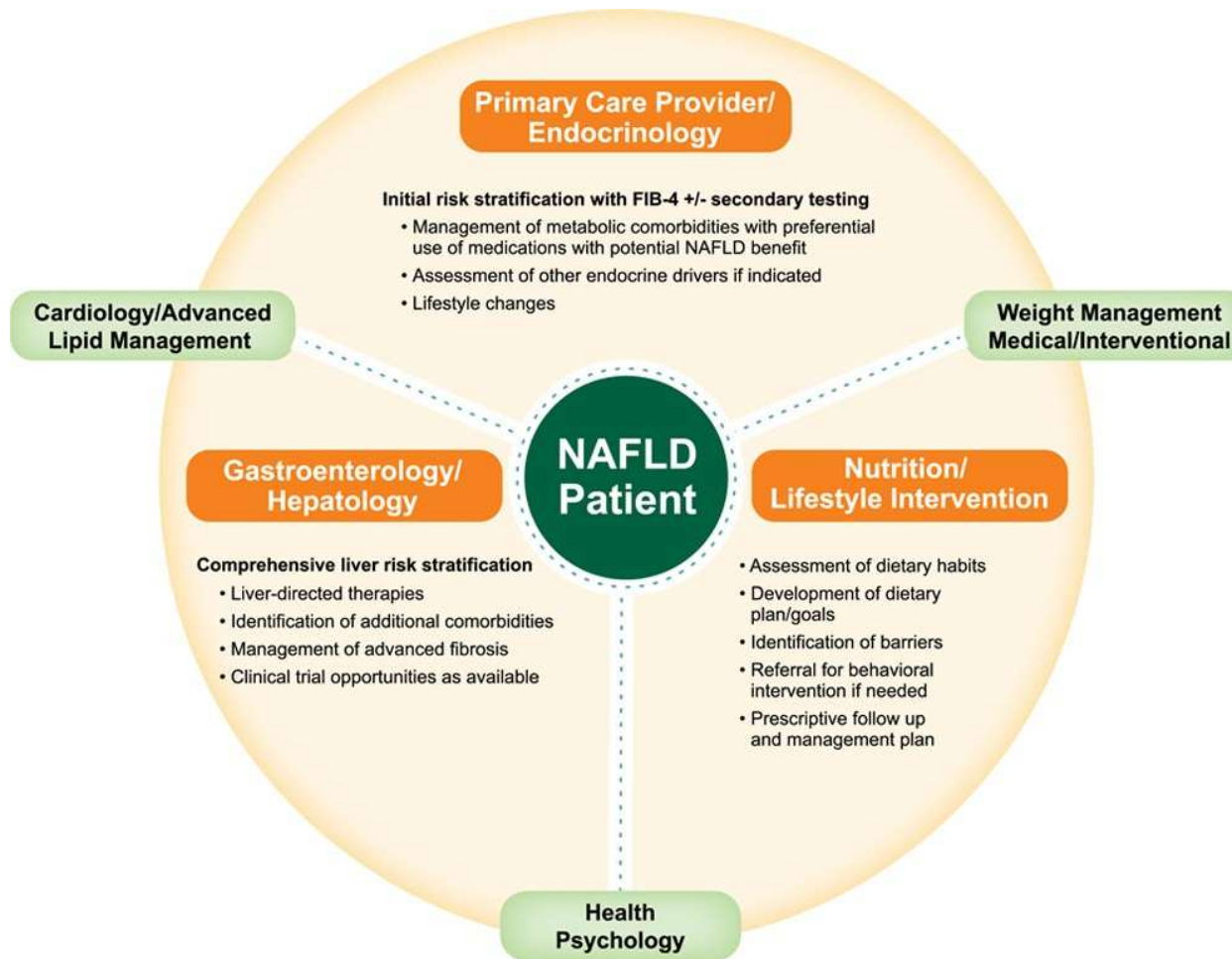
- Retrospective cohort of 30,000 NAFLD patients in Germany
- FIB-4 ≥ 1.3 was a strong predictor of HCC in 10y follow-up (HR 12.85; 95% CI 3.58-46.16; $p < 0.001$)
- FIB-4 was not associated with non-liver cancer



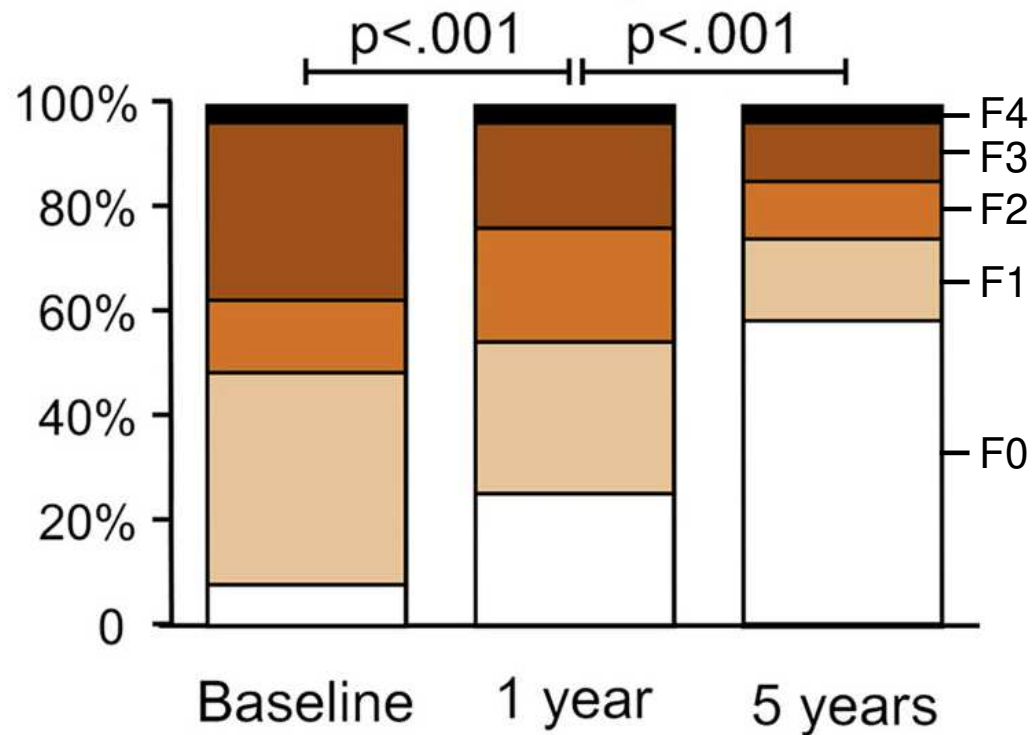
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Approche multidisciplinaire de la prise en charge de la NASH



Reversibility of NASH and fibrosis



Bariatric surgery in 180 obese subjects with biopsy-proven NASH

Résumé des mesures hygiéno-diététiques pour les patients

Overweight/obesity NAFLD

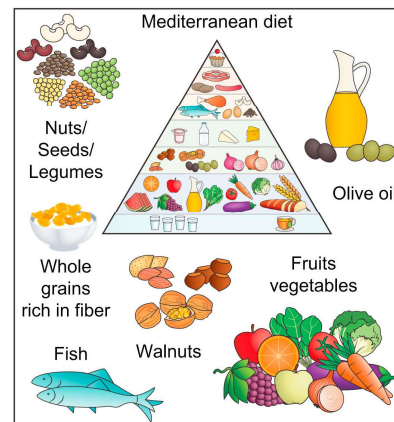
- Weight reduction
- The more severe the liver disease is, the higher the goals are in terms of weight loss
 - Healthy diet with caloric restriction tailored for your preferences

Non-obesity NAFLD

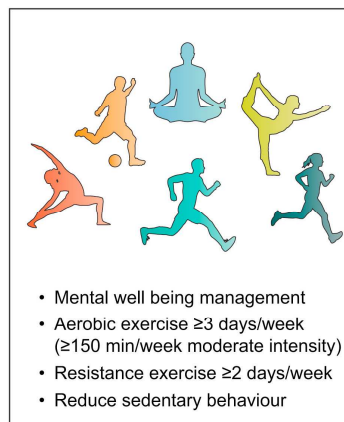
- 3-5% reduction of weight even within the normal BMI range (especially if recent weight gain occurred or if abdominal obesity is present)

Lifestyle advice for ALL patients with NAFLD

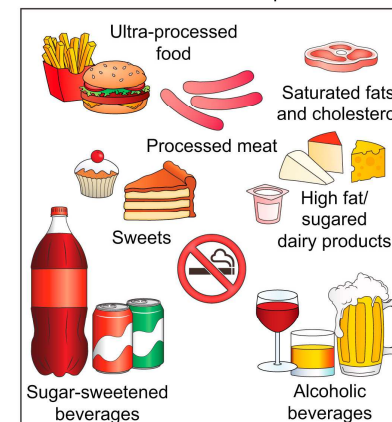
Recommended foods



Recommended activity

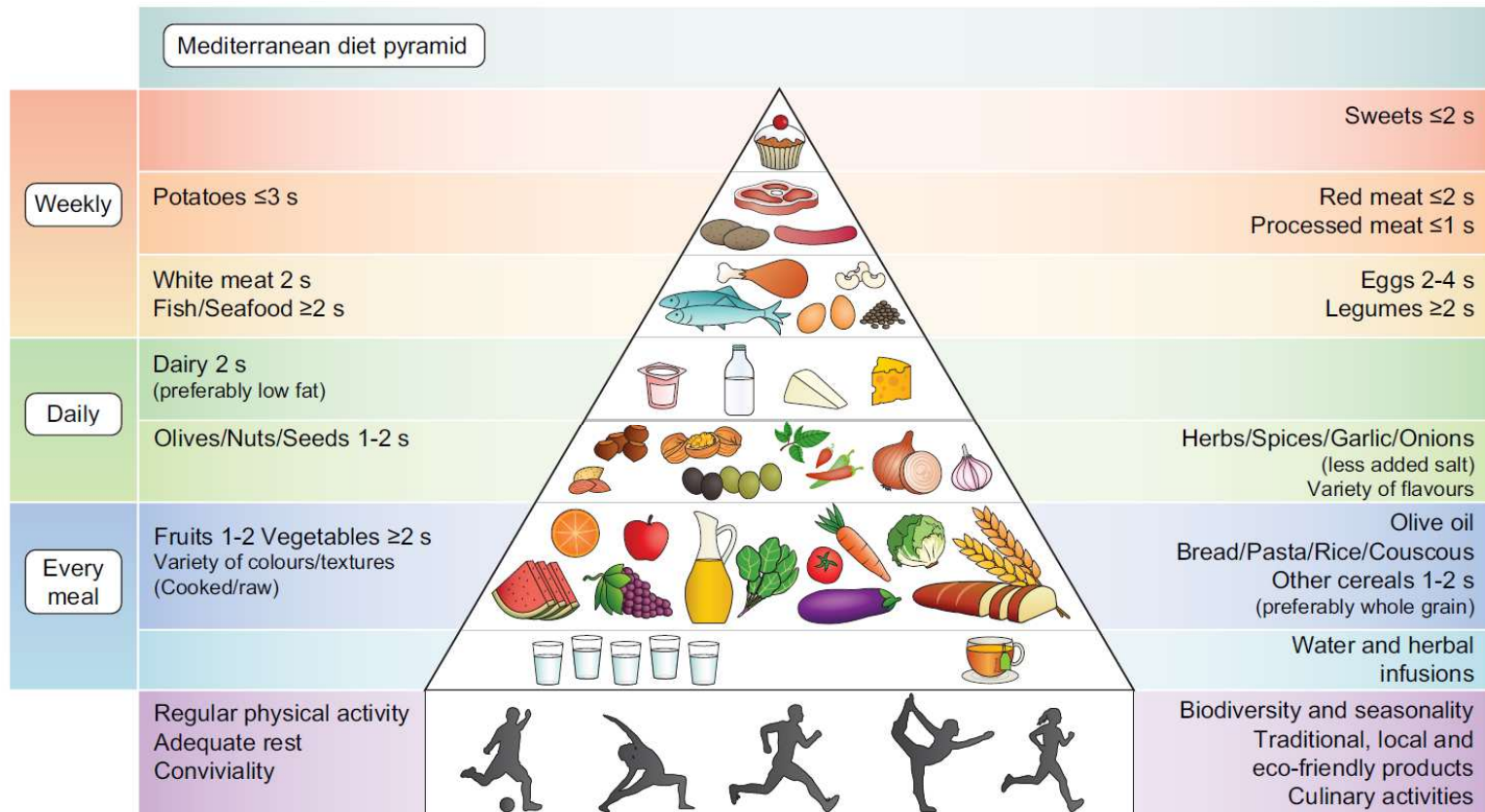


Non-recommended foods/ Minimize consumption



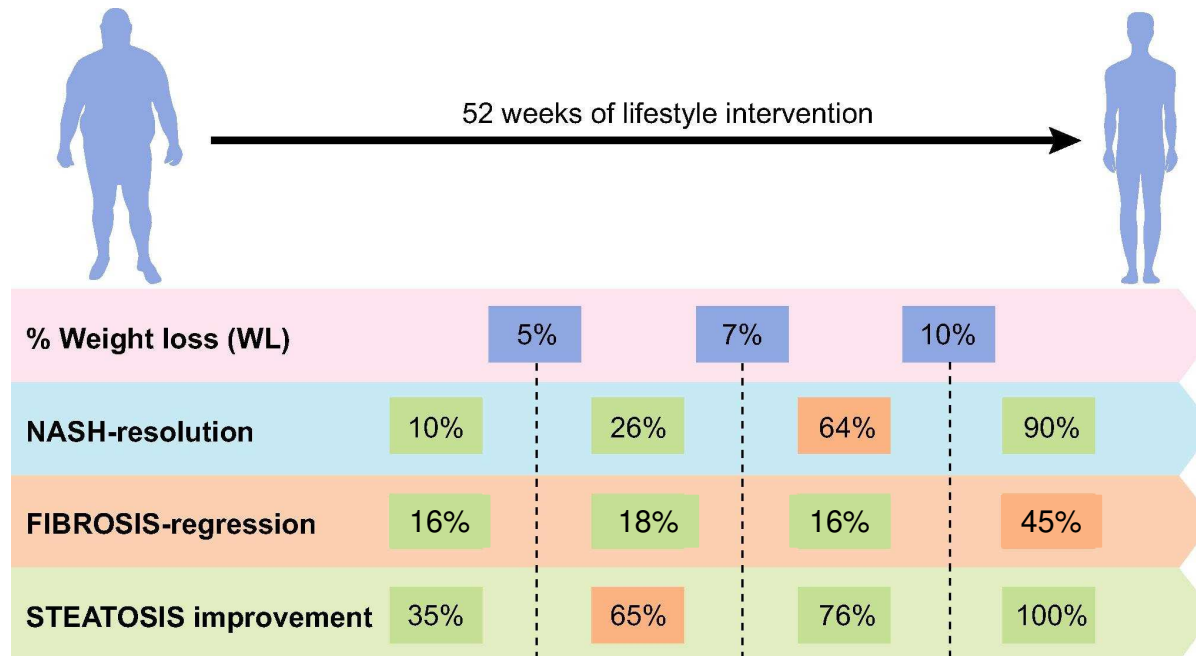
- Reduce added sugar (e.g. by reducing sweets, processed foods, sugared dairy products, etc.)
- Avoid sugar-sweetened beverages
- Reduce saturated fat and cholesterol (e.g. by eating low fat meat and low fat dairy products)
- Increase n-3 fatty acids found in fish, and walnuts; utilize olive oil over other oils more often
- Minimize "fast food" and ultra-processed food
- Home-cooked meals are preferable
- Try to follow the Mediterranean dietary pattern

Mediterranean diet



s, servings

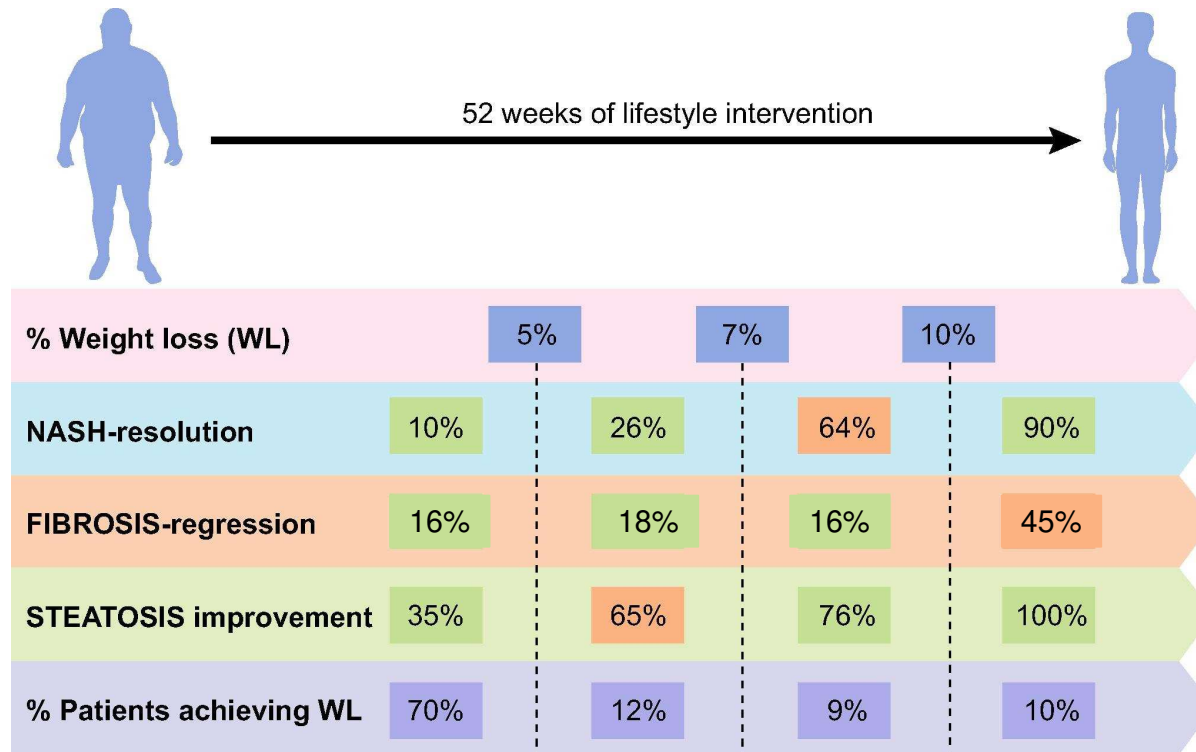
Efficacité mesures hygiéno-diététiques



N=293 patients with biopsy-proven NASH.
52 weeks of lifestyle interventions (low-fat hypocaloric diet, walk 200 mins/week, behavioral sessions every week). 2nd liver biopsy at 52 weeks (n=261/293)

Vilar-Gomez et al, *Gastroenterology*, 2015
Romero-Gomez et al, *J Hep*, 2017

Efficacité mesures hygiéno-diététiques

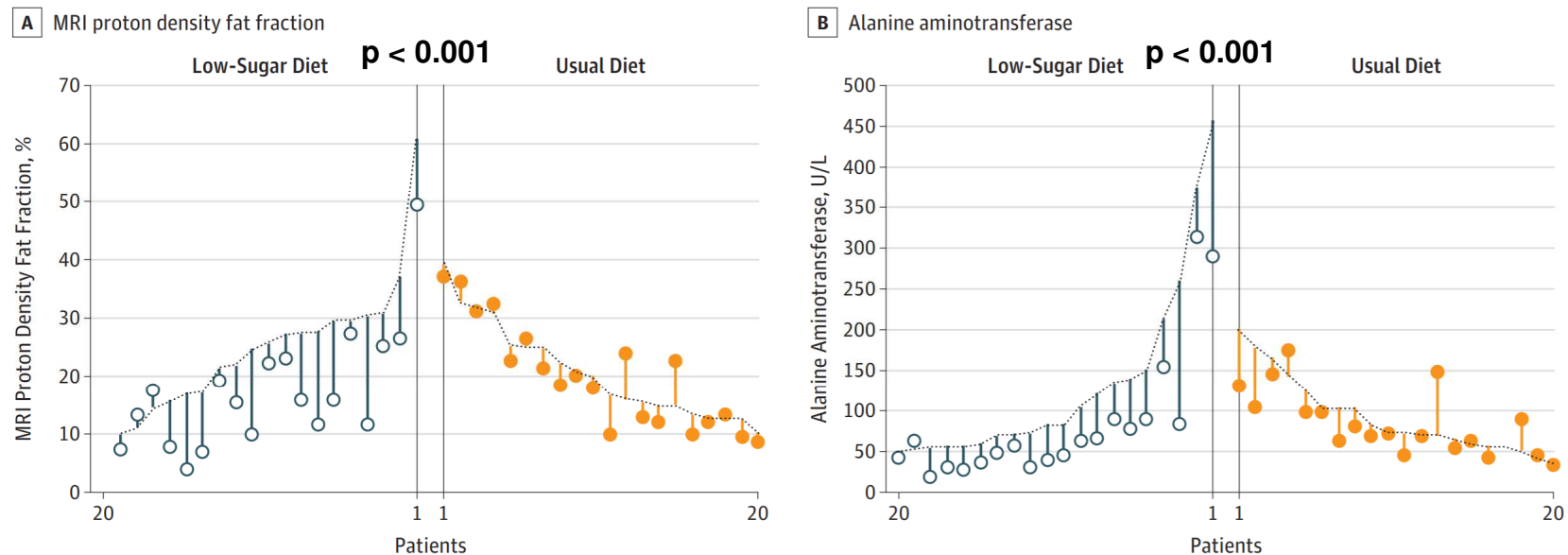


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Low free sugar diet leads to reduced steatosis in adolescent boys with NAFLD

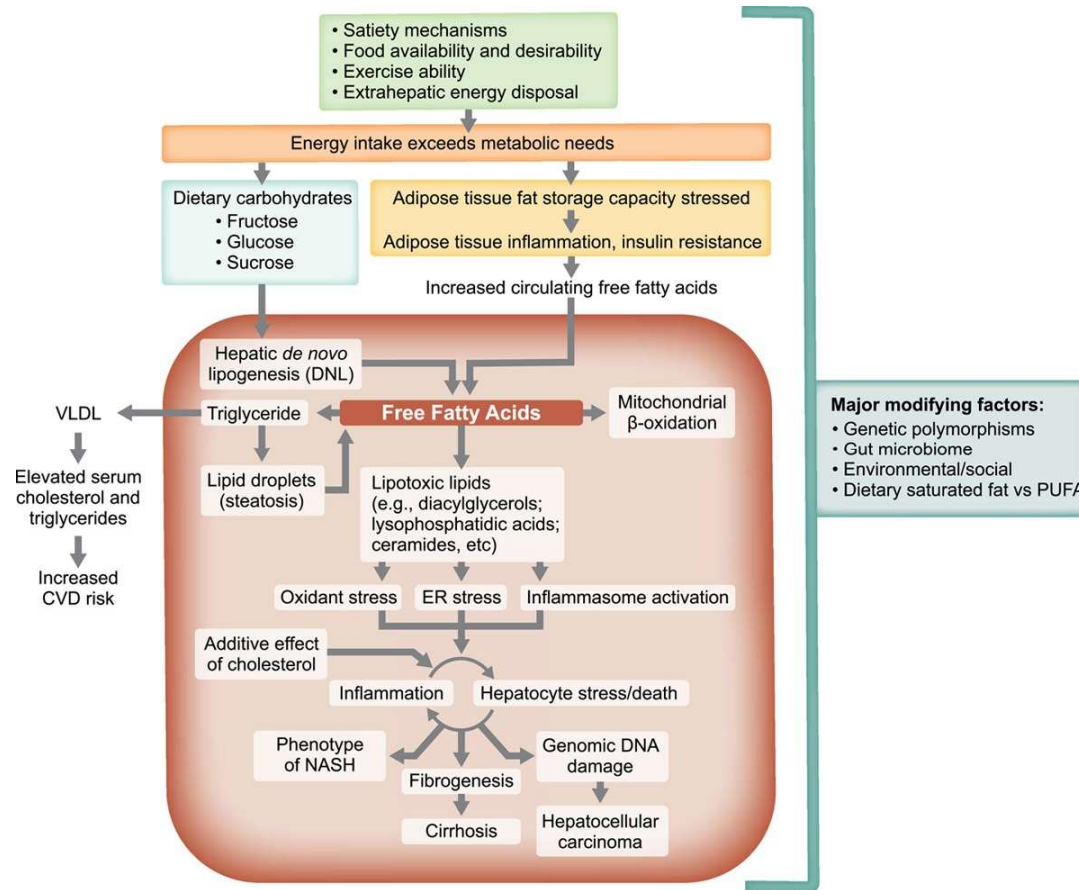


N=40 adolescent boys aged 11-16 years old with NAFLD (MRI-PDFF > 10% and ALT \geq 45)

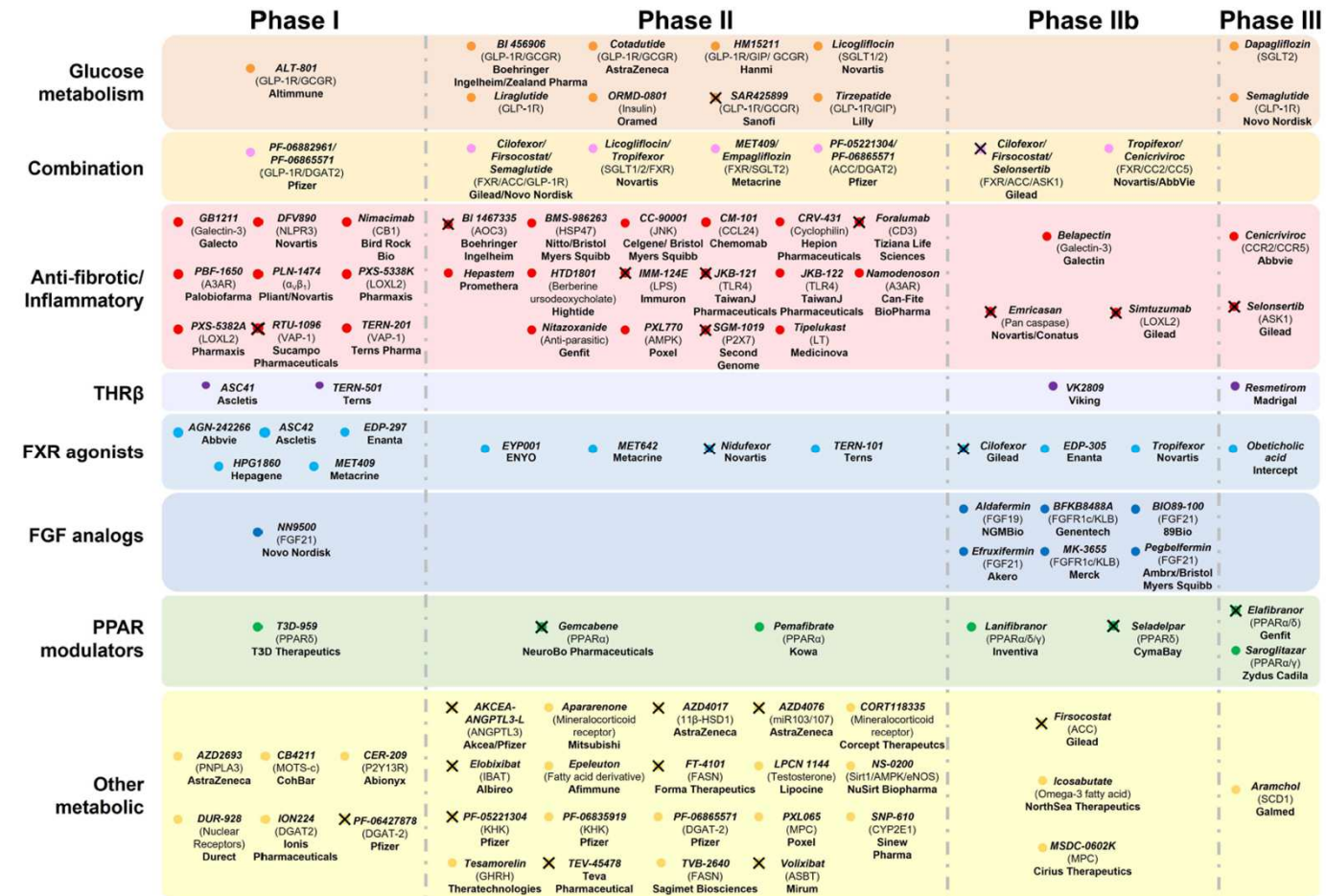
RCT: Restricted free sugar <3% daily calories for 8 weeks vs control (regular diet)

MRI-proton-density fat fraction measurement

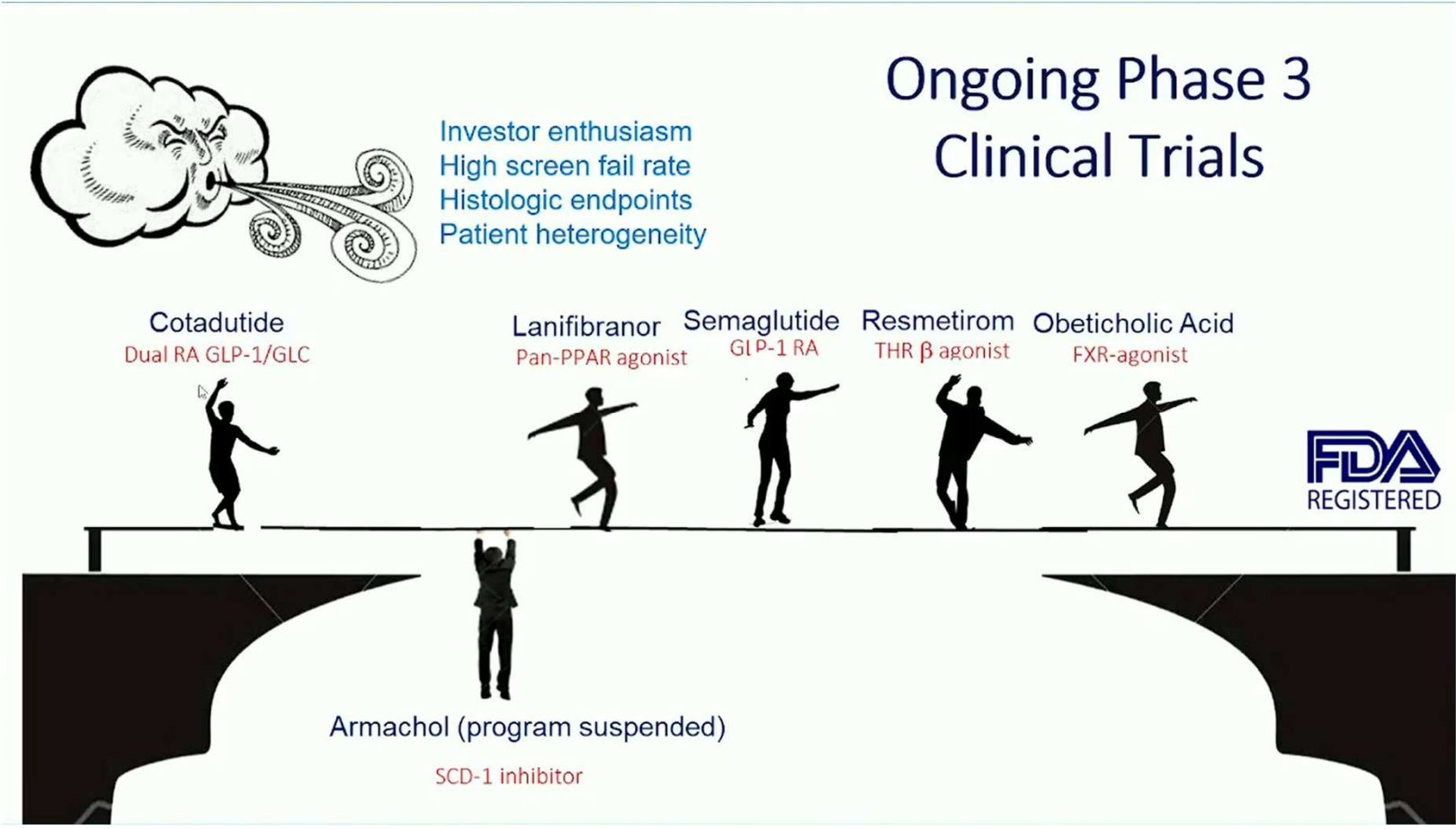
Physiopathologie et cibles thérapeutiques potentielles



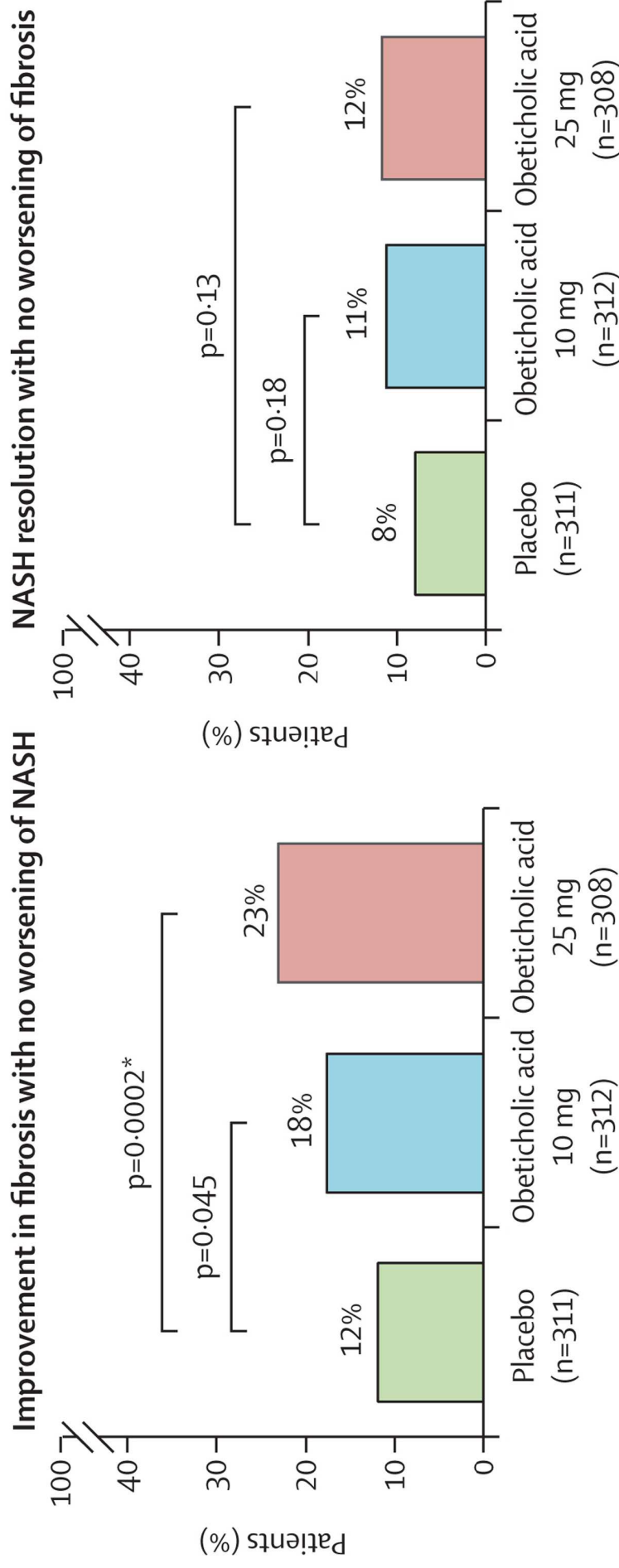
Landscape of therapeutic trials in NAFLD



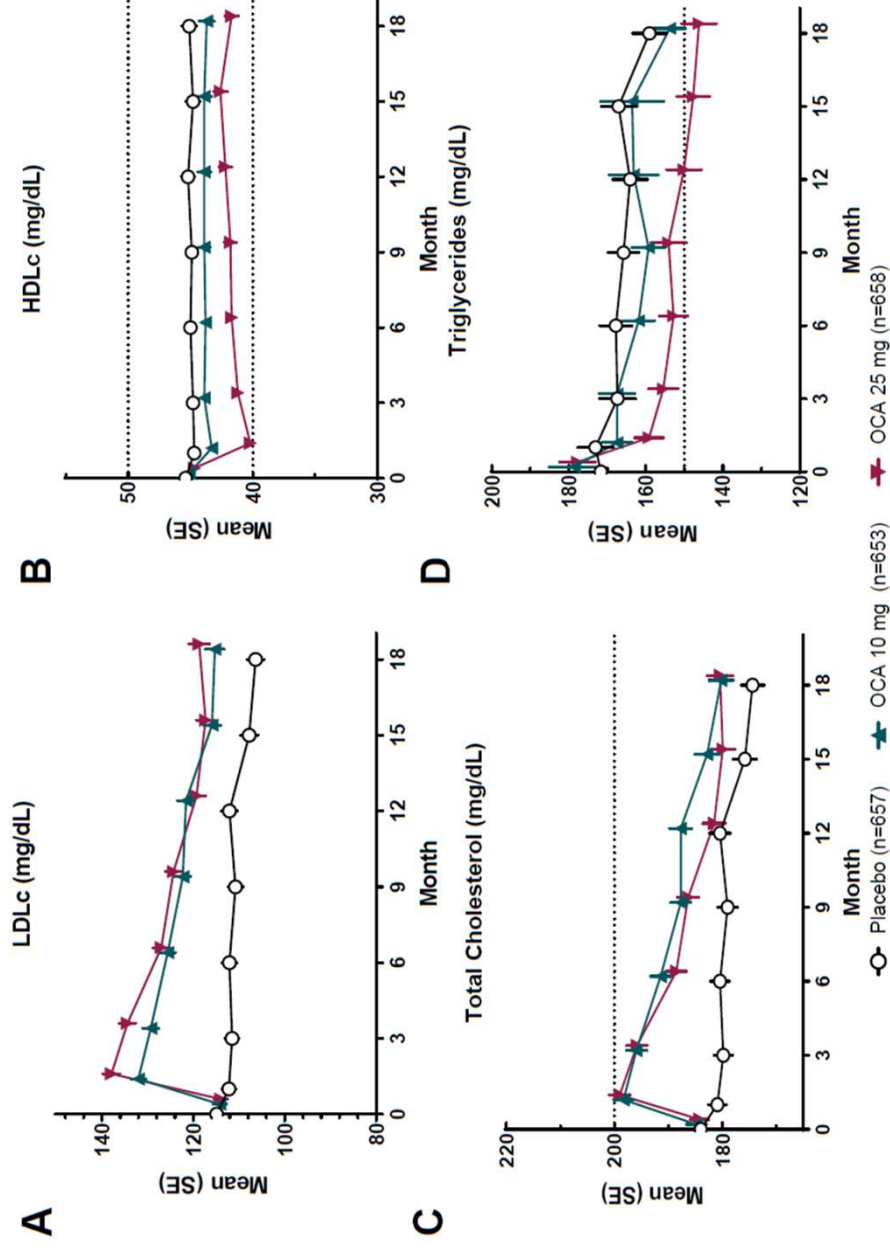
Etudes de phase 3



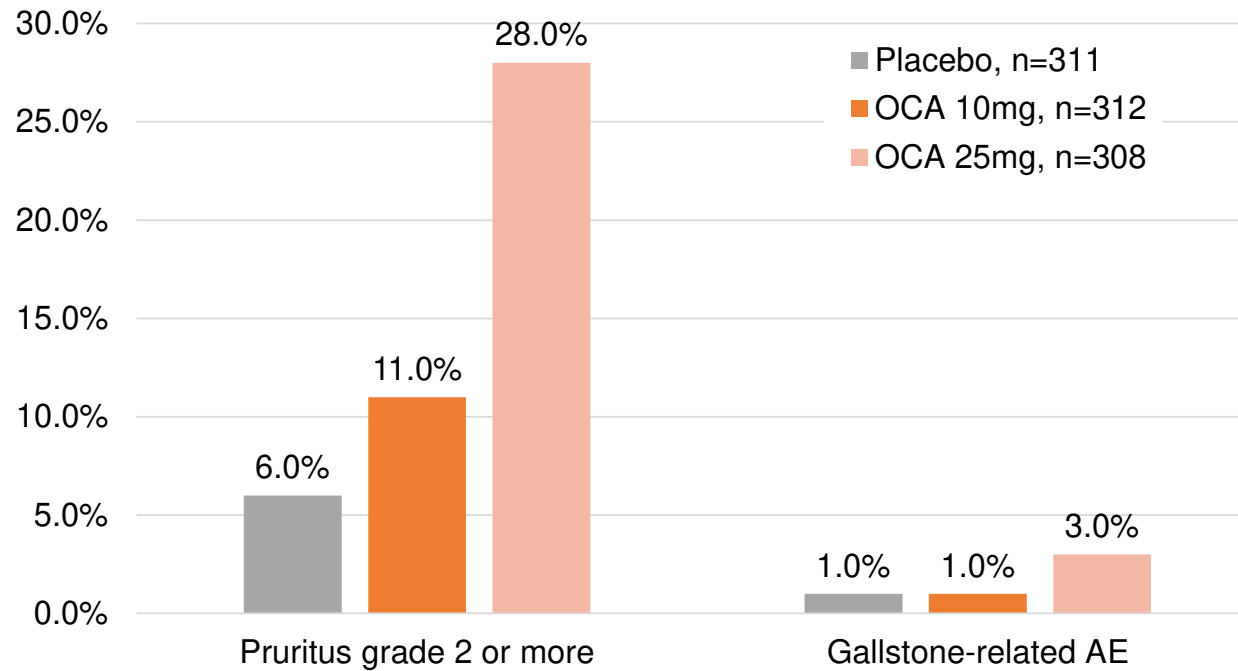
Obeticholic acid for the treatment of non-alcoholic steatohepatitis: interim analysis from a multicentre, randomised, placebo-controlled phase 3 trial



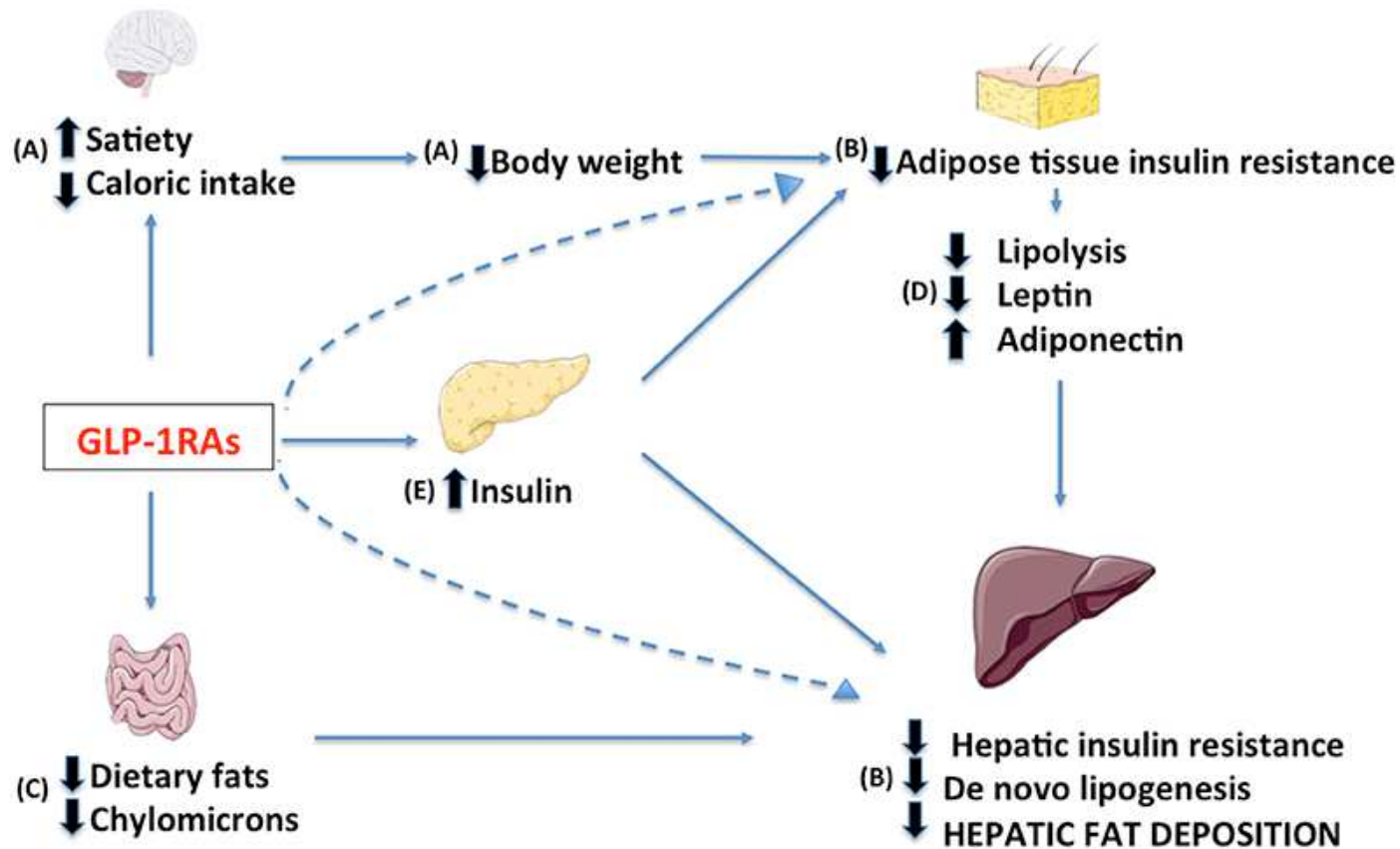
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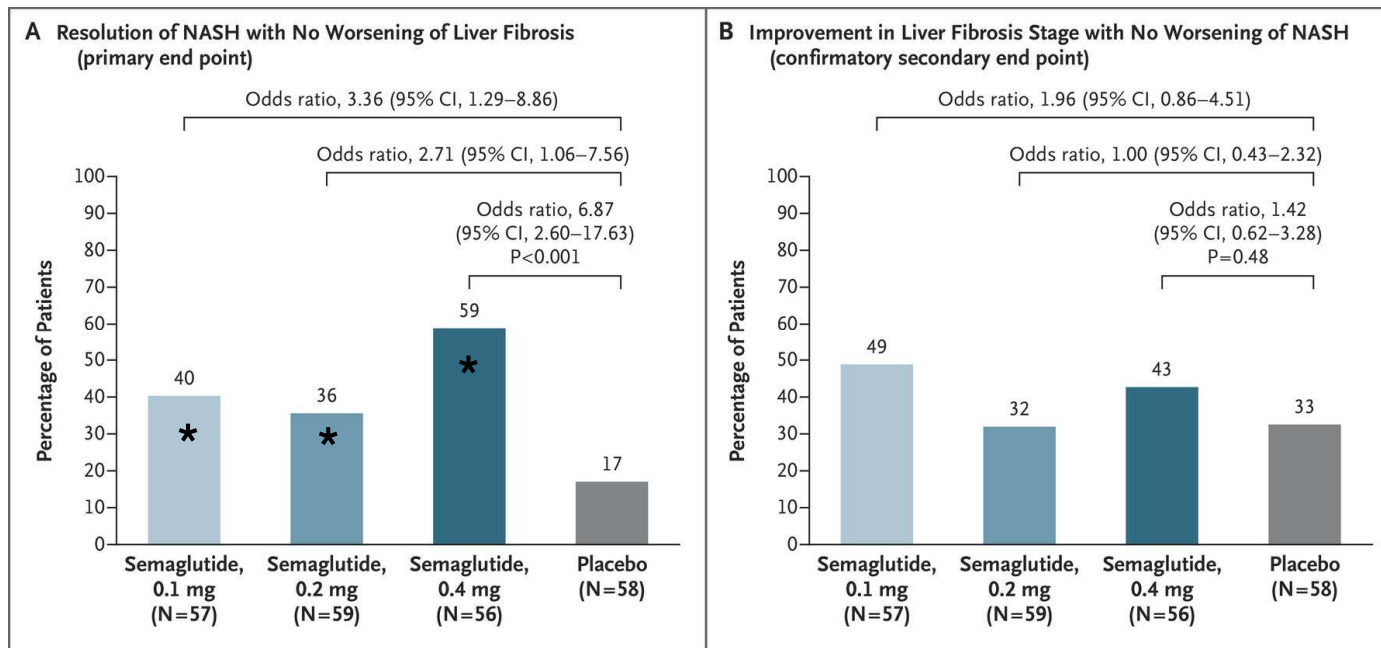


Role of GLP-1 analogues in NASH



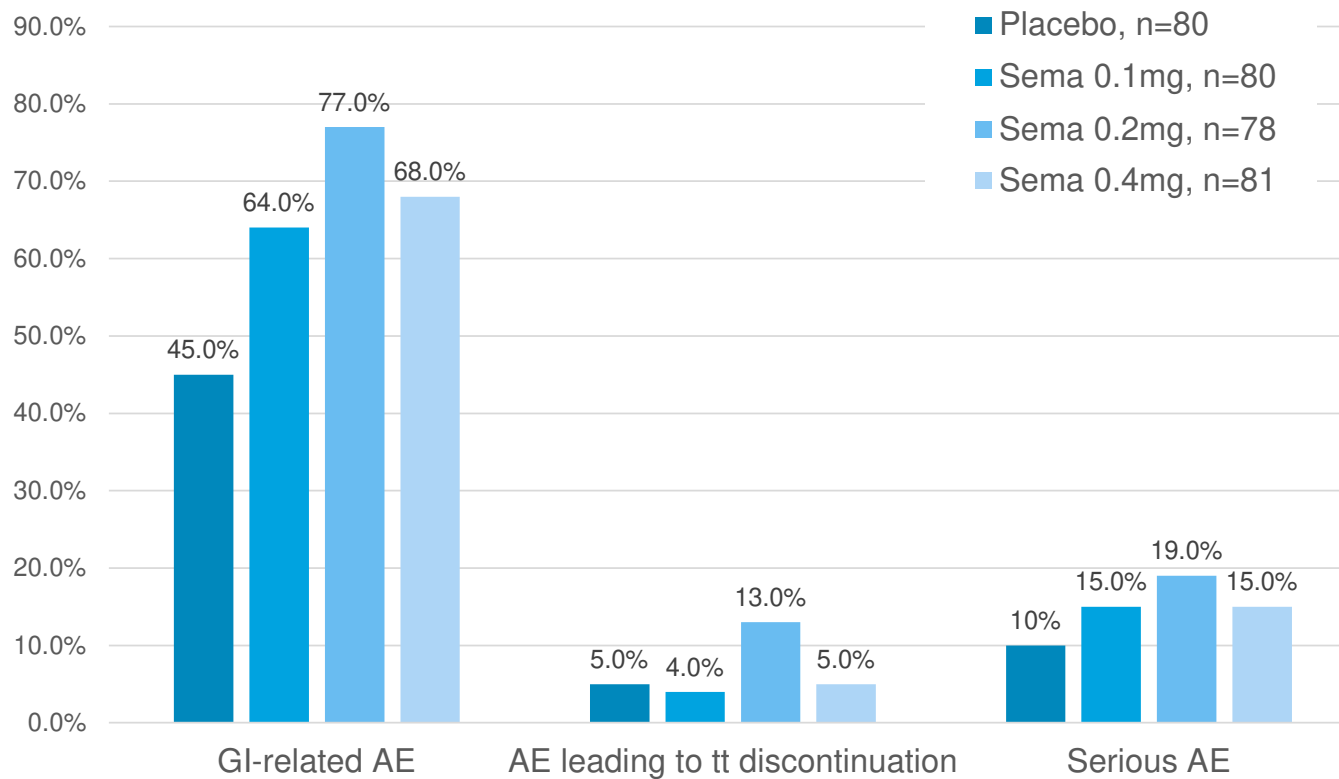
Phase 2 trial of **semaglutide** (GLP-1 analogue) – 72 week results

320 NASH with BMI $\geq 25\text{kg/m}^2$
28% F1, 22% F2, 49% F3; $\approx 60\%$ T2D



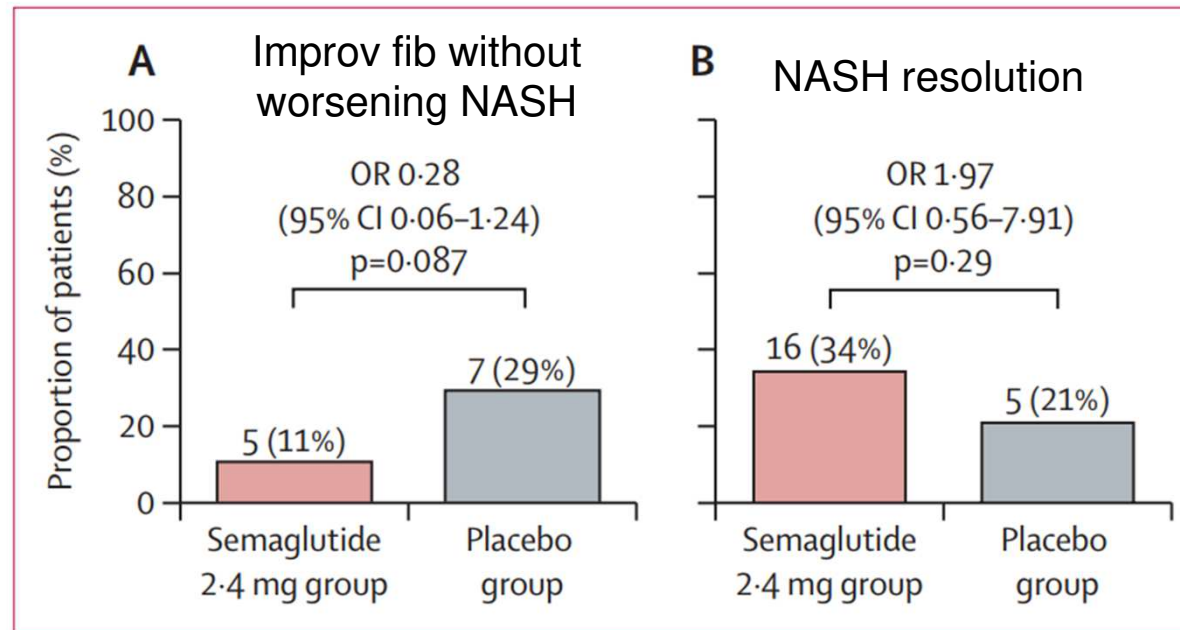
-13% body weight in semaglutide 0.4mg group vs -0.6% in placebo at 72 weeks
Phase 3 ongoing

Phase 2 trial of **semaglutide** (GLP-1 analogue) – 72 week results



Phase 2 trial of semaglutide in cirrhosis— 48 week results

71 NASH with BMI $\geq 27\text{g/m}^2$
BMI 35kg/m^2 , 75% T2D



-8.8% body weight in semaglutide 2.4mg group vs -0.1% in placebo at 48 weeks

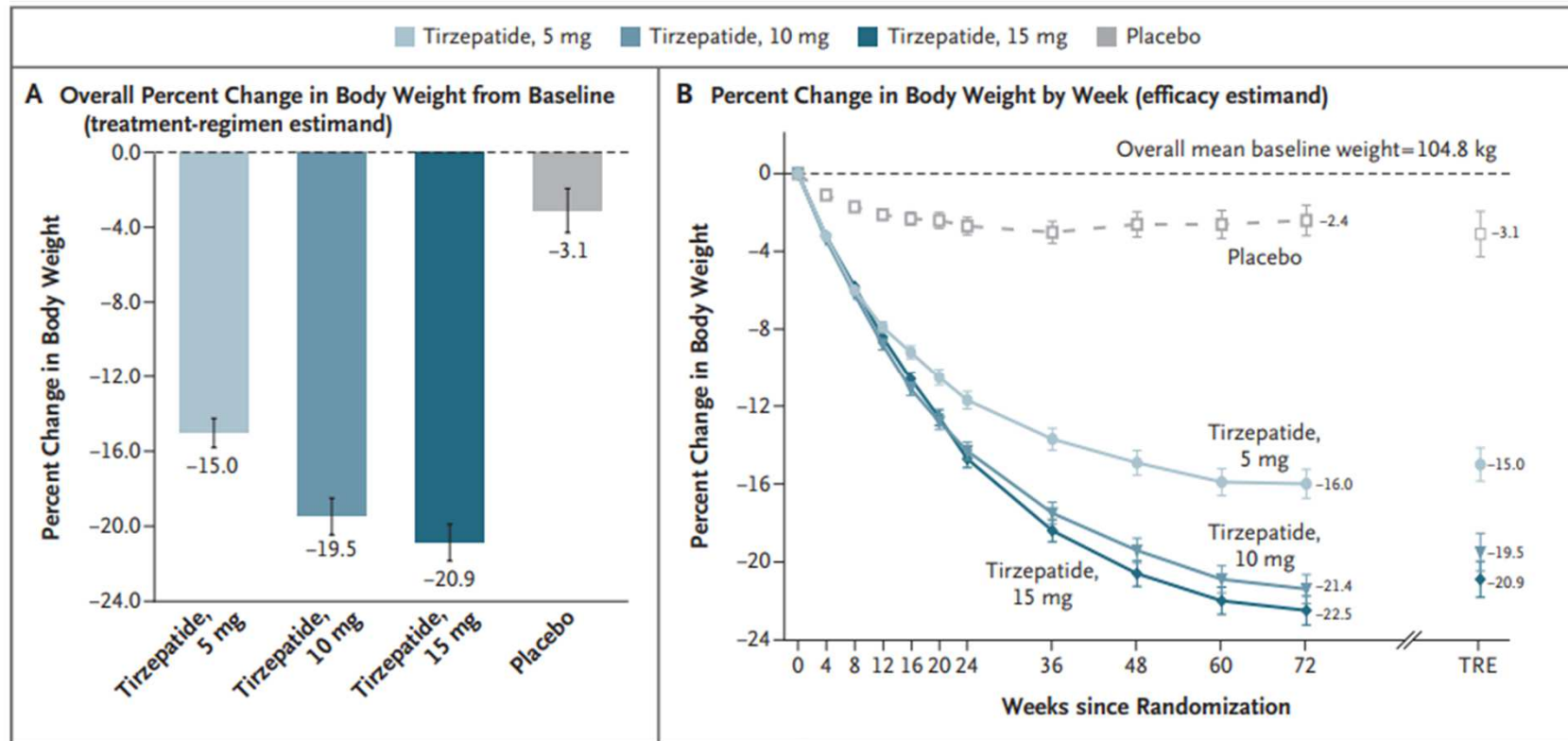
Et après ?

(études de phase 1-2 sélectionnées)

- **Récepteur des sels biliaires:** Agonistes FXR de 2^{ème} génération
- **Régulation métabolisme:** analogues FGF21
- **Inhibition lipogénèse:** FASN ou ACC1 inhibiteurs
- **Incrétines – dual agonistes:** GLP1-GIP, GLP1-glucagon

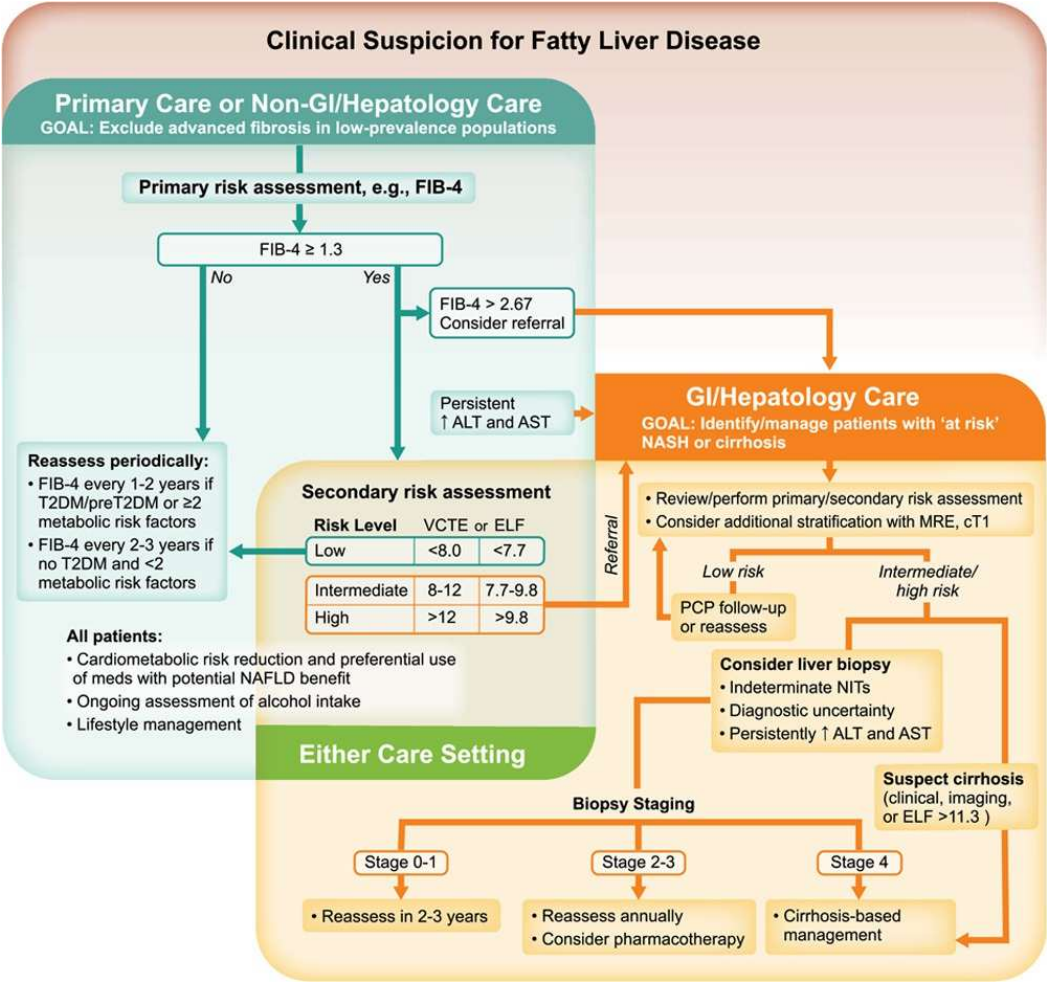
Food for thought ...

Tirzepatide: GLP-1 and GIP analogue



N=2539 adults with BMI > 30 or > 27 and complication
Improvement in all prespecified cardiometabolic measures

Conclusions



Merci pour votre attention!

