Diagnostic et prise en charge de la MASLD

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MCU-PH en physiologie

Equipe EPICAD - INSERM LNC-UMR 1231

FORUM NATIONAL 26e ÉDITION

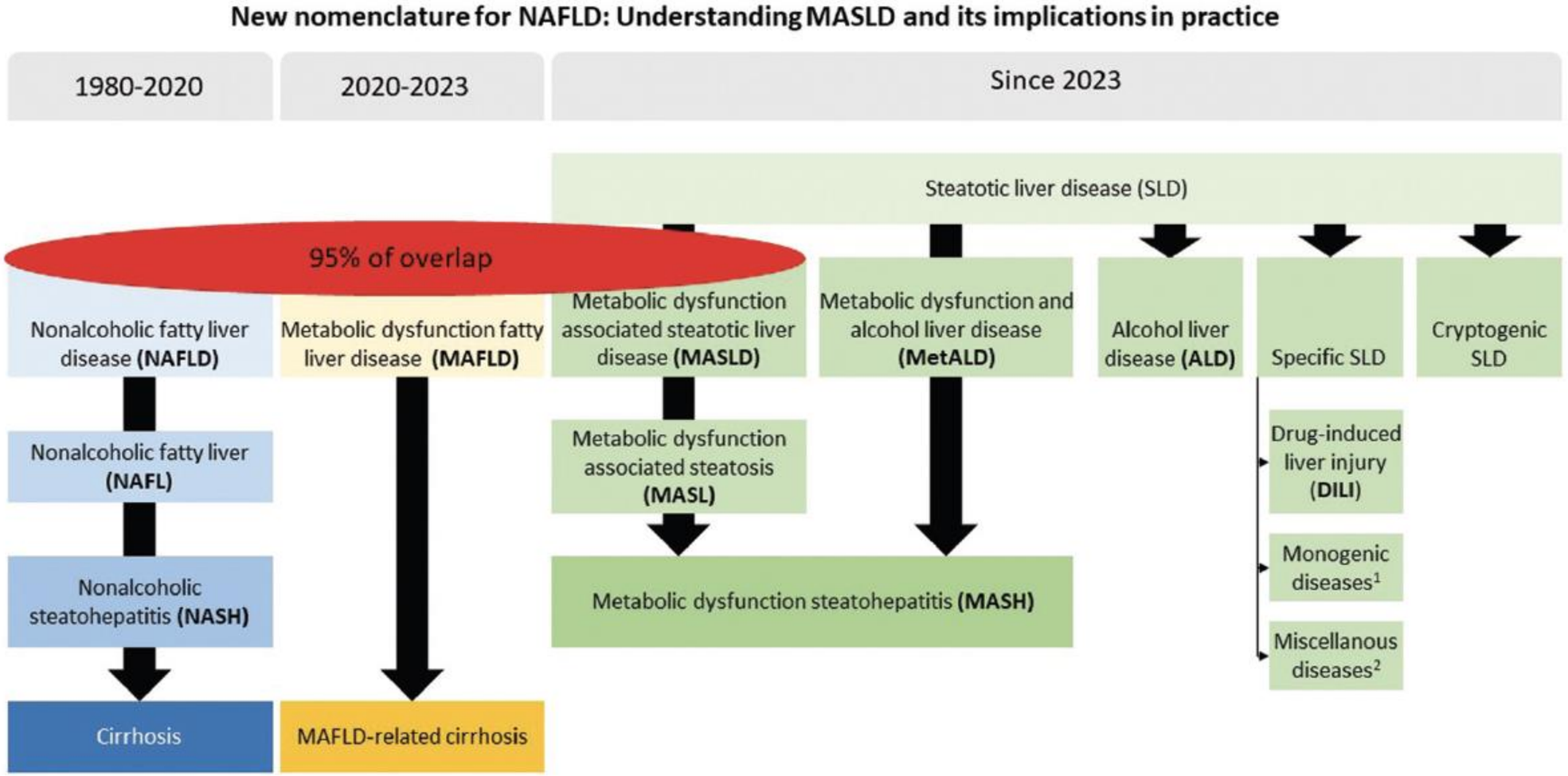
20 NOVEMBRE 2025
100 % VIRTUEL

SOS hépatites Fédération
Hépatites & Maladies du foie

Déclaration de conflits d’intérêt

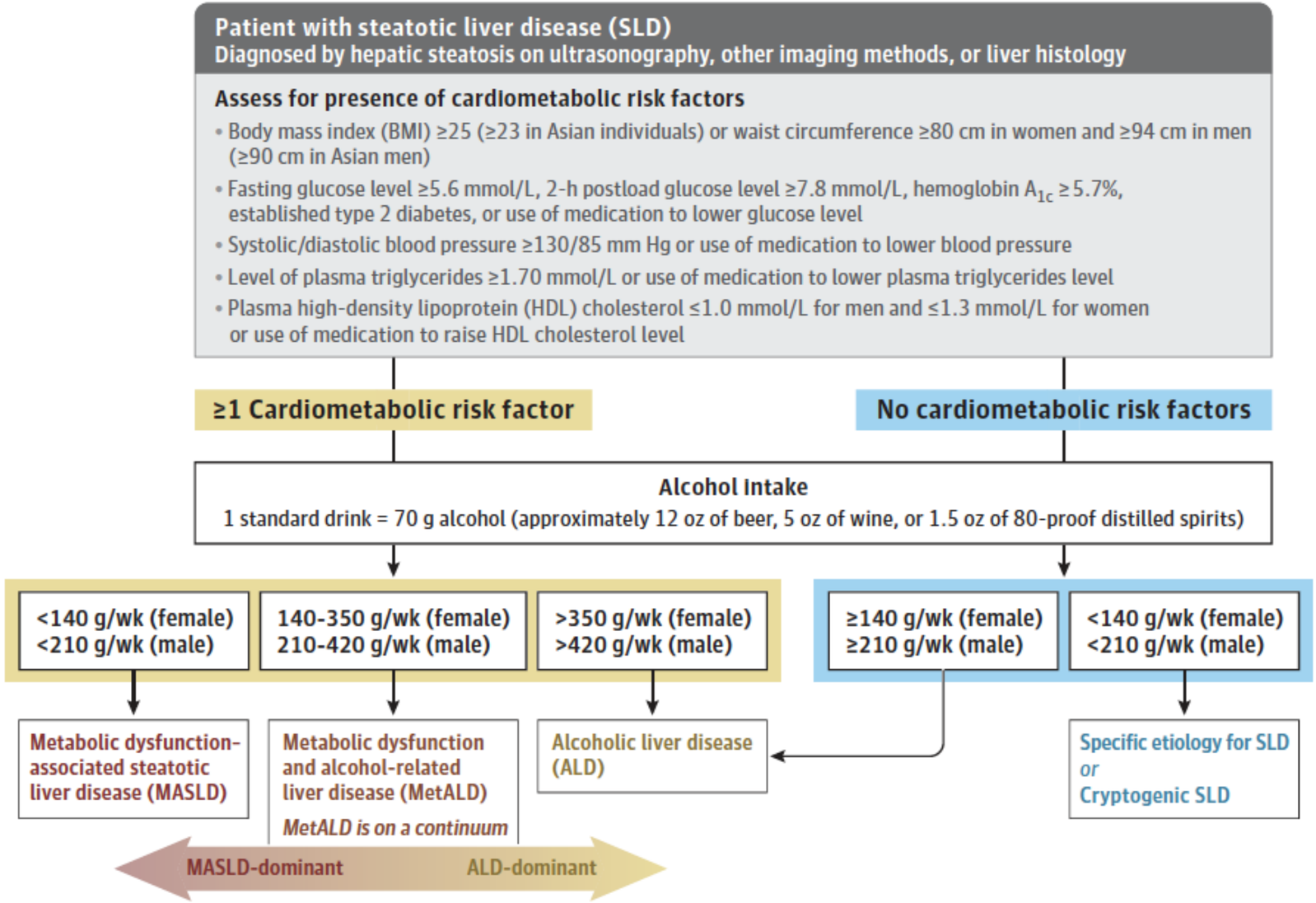
- Invitations à des congrès : FRESENIUS KABI, ELIVIE, ASTEN SANTE, NOVO NORDISK, LILLY
- Interventions et séminaires : NOVO NORDISK, GILEAD, MSD, SIEMENS HEALTHINEERS

Anciennes et nouvelles nomenclatures



Canivet CM, et al. Semin Liver Dis. 2024 Feb;44(1):35-42

Définition de la MASLD



Tilg H, et al. JAMA. 2025 Nov 10

EASL-EASD-EASO Clinical Practice Guidelines. J Hepatol. 2024 Sep;81(3):492-542

Prévalence de la MASLD

Méta-analyse avec MASLD diagnostiquée soit par imageries, tests sanguins non invasif ou élastométrie (CAP)

92 études incluses soit 9 361 716 sujets (102-8 120 674)

Age moyen de 48,4 ans (38,30-59,1 ans) et IMC moyen de 25,8 kg/m2 (22,3-30,4 kg/m2)]

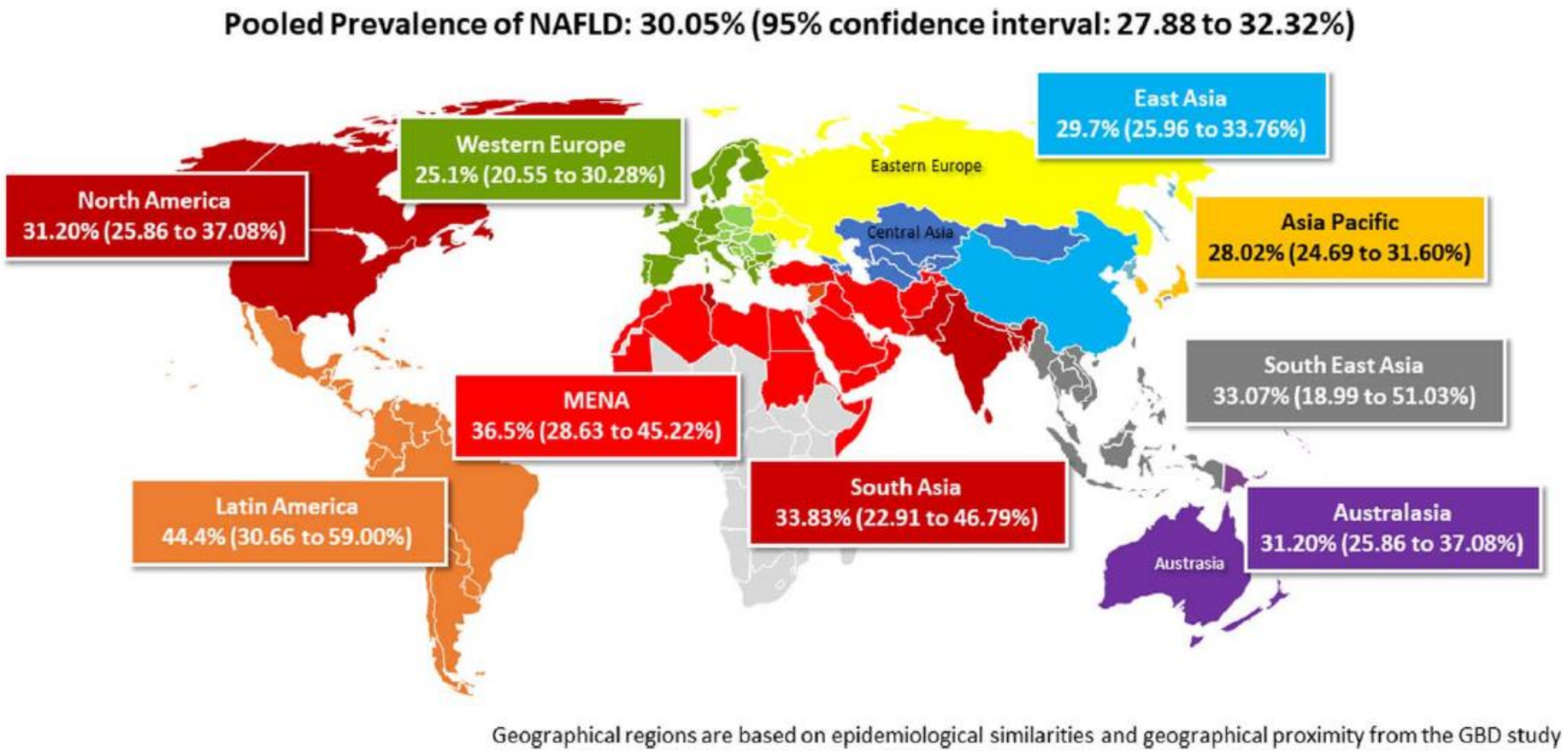


FIGURE 2 Prevalence of NAFLD According to Global Regions Data Collected 1990–2019.

Younossi ZM, et al. Hepatology. 2023 Apr 1;77(4):1335-1347

Surpoids, obésité, diabète de type 2 et MASLD

Surpoids : 69,99%

Obésité : 75,27%

DT2 : 65,04%

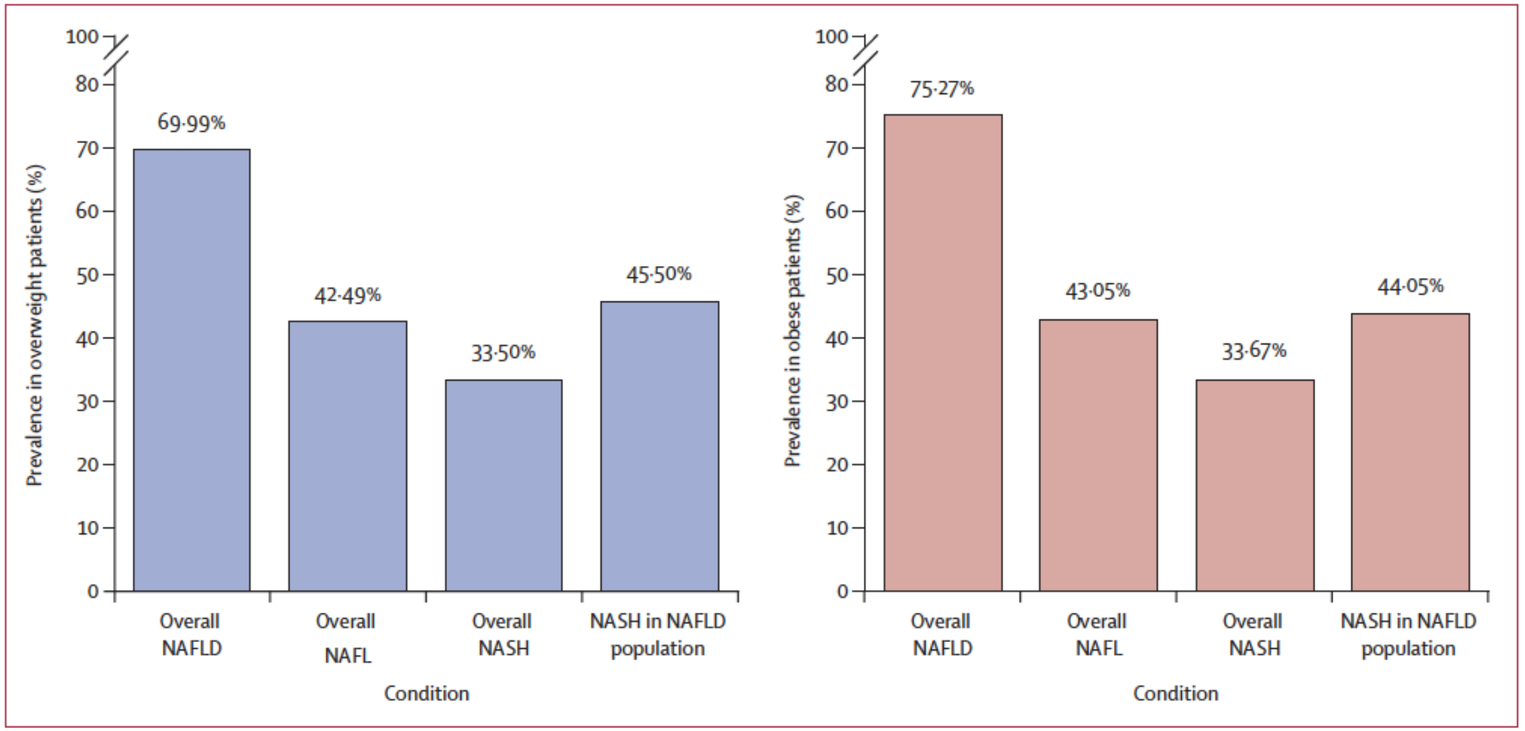
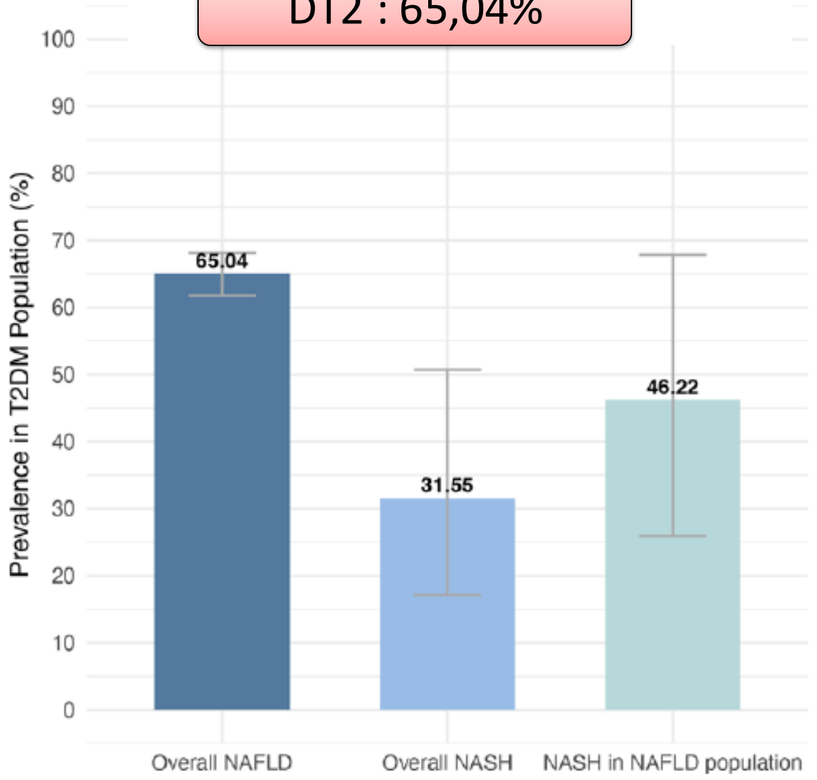


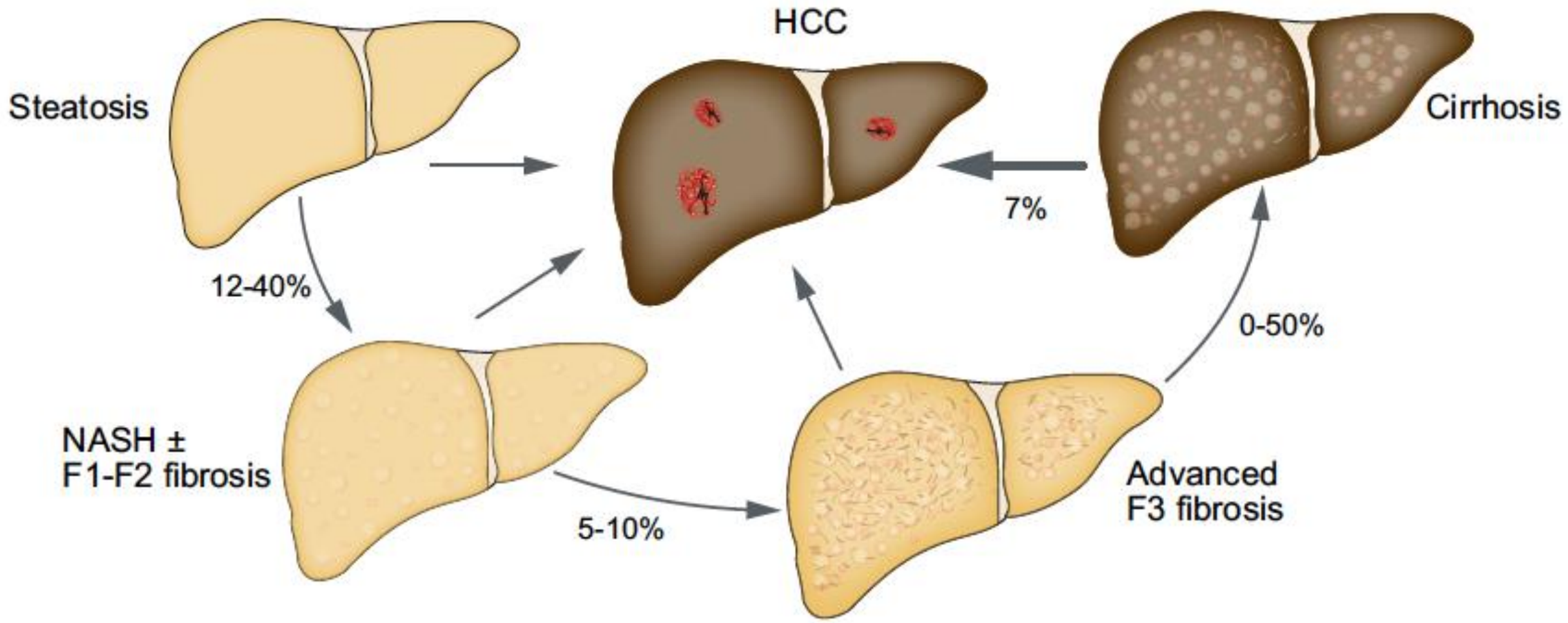
Figure 2: **Prevalence of NAFLD, NAFL, and NASH in overweight and obese populations**
NAFLD=non-alcoholic fatty liver disease. NAFL=non-alcoholic fatty liver. NASH=non-alcoholic steatohepatitis.



Quek J, et al. Lancet Gastroenterol Hepatol. 2023 Jan;8(1):20-30

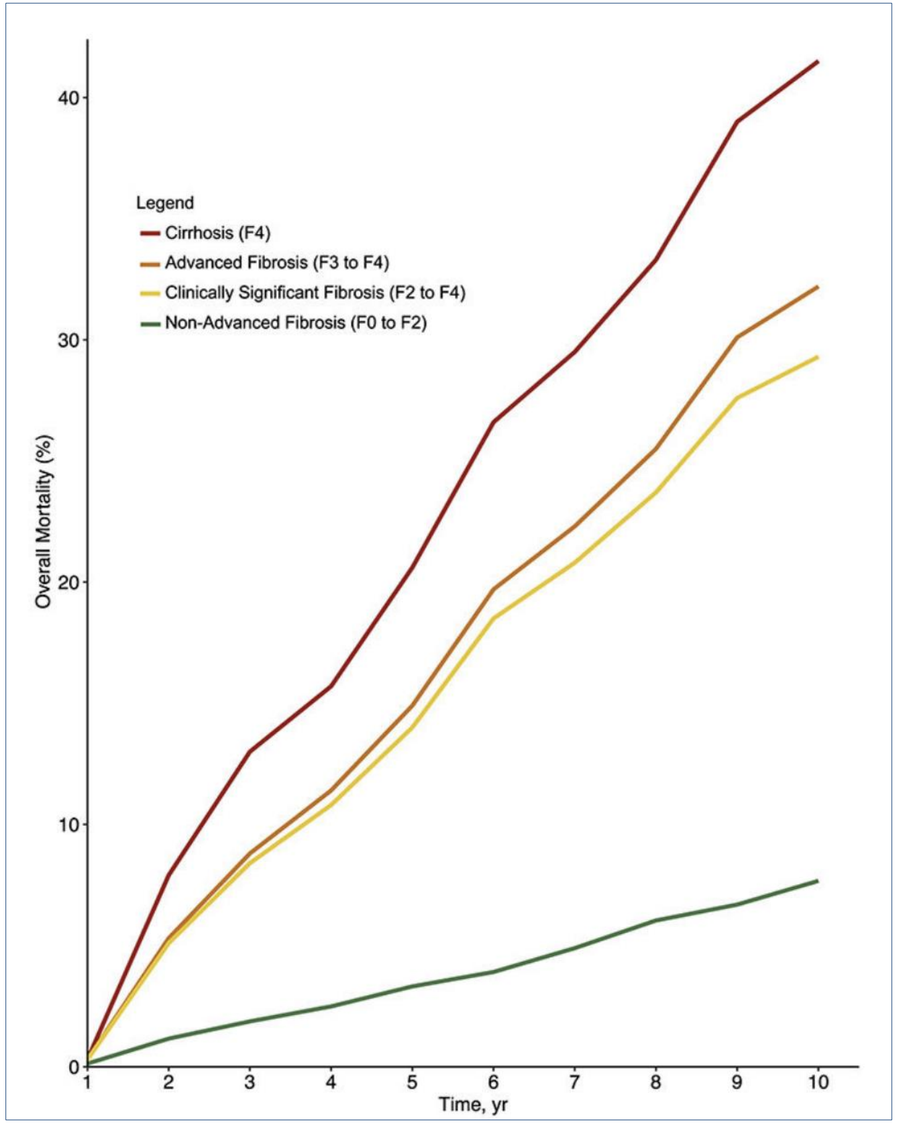
En Li Cho E, et al. Gut. 2023 Nov;72(11):2138-2148

Histoire naturelle de la MASLD / MASH



EASL. JHEP. 2021
EASL–EASD–EASO, Journal of Hepatology, 2024

Valeur pronostic de la fibrose dans la MASLD



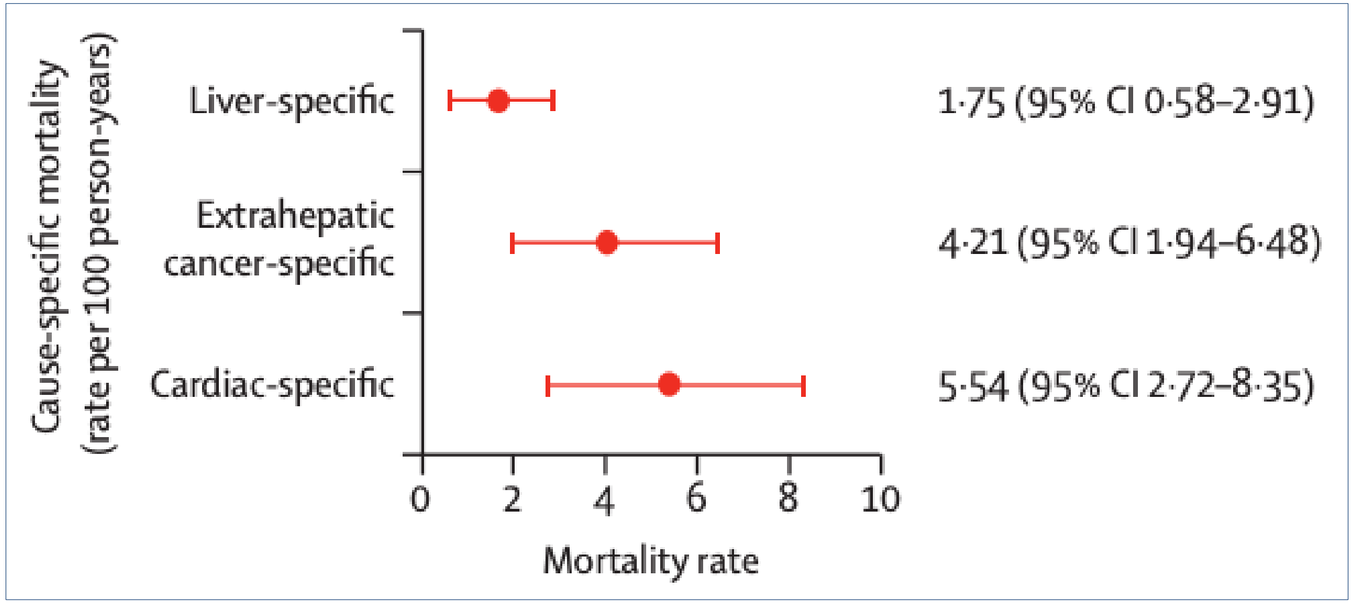
Résultats cliniques comparatifs selon le stade de fibrose

Fibrosis stage	HR	95% CI	Cochran Q	I^2	*P*-value
All-cause mortality					
F1 vs F0	1.24	0.85–1.81	0.23	28.0%	.27
F2 vs F0	1.46	1.08–1.98	0.60	0.00%	**.01**
F3 vs F0	1.96	1.41–2.72	0.86	0.00%	**< .01**
F4 vs F0	3.66	2.65–5.05	0.06	31.0%	**< .01**
Liver-related mortality					
F1 vs F0	1.69	0.56–5.14	0.87	0.00%	.35
F2 vs F0	4.07	1.44–11.5	0.94	0.00%	**< .01**
F3 vs F0	7.59	2.80–20.5	0.69	0.00%	**< .01**
F4 vs F0	15.1	5.27–43.4	0.81	0.00%	**< .01**

Note: Boldface *P*-value (< .05) denotes statistical significance.
CI, Confidence interval; F0, stage 0 fibrosis; F1, stage 1 fibrosis; F2, stage 2 fibrosis; F3, stage 3 fibrosis; F4, stage 4 fibrosis/cirrhosis; HR, hazard ratio.

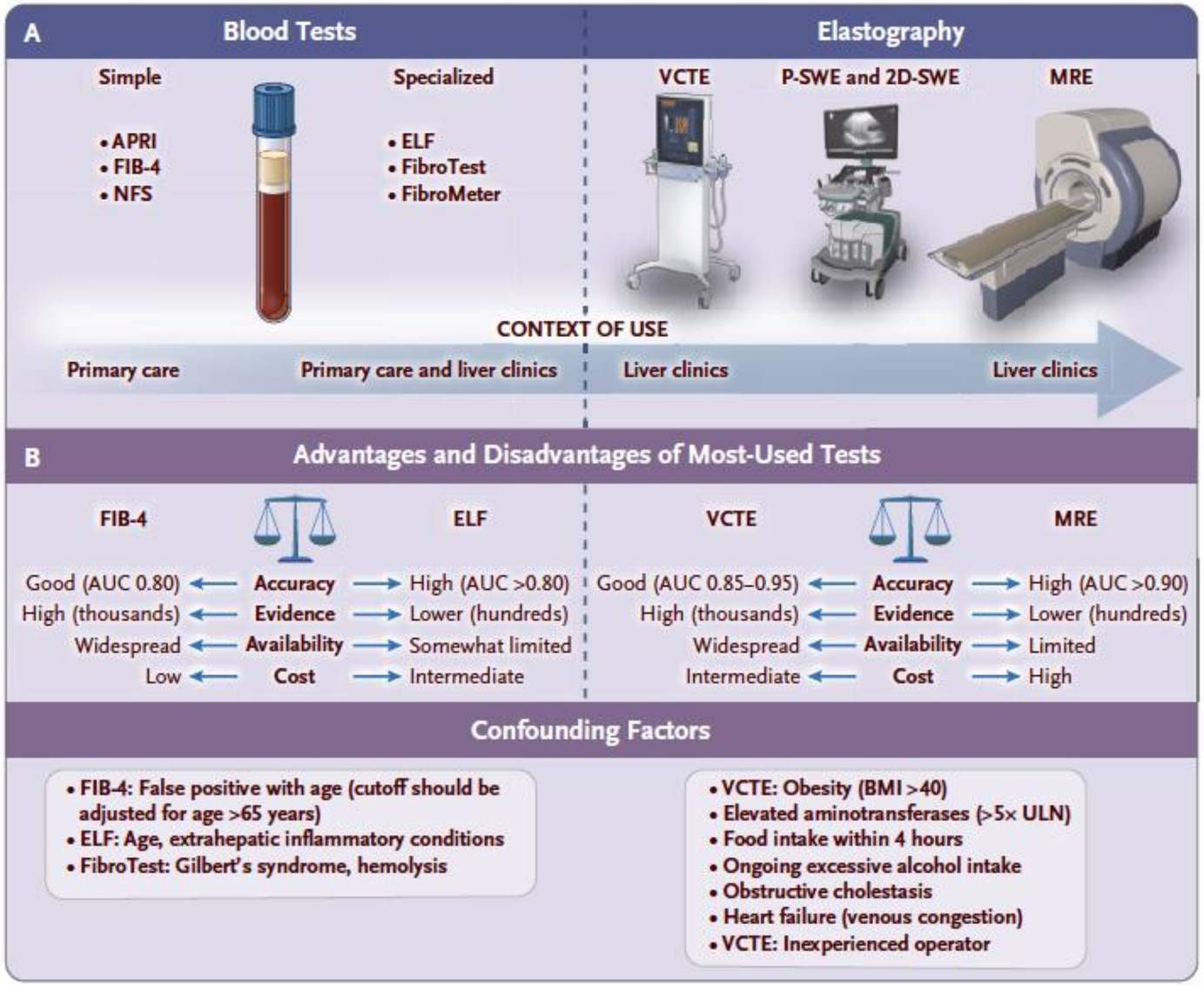
Ng CH, et al. Clin Gastroenterol Hepatol. 2023;21(4):931-9.e5

Mortalité de la MASLD



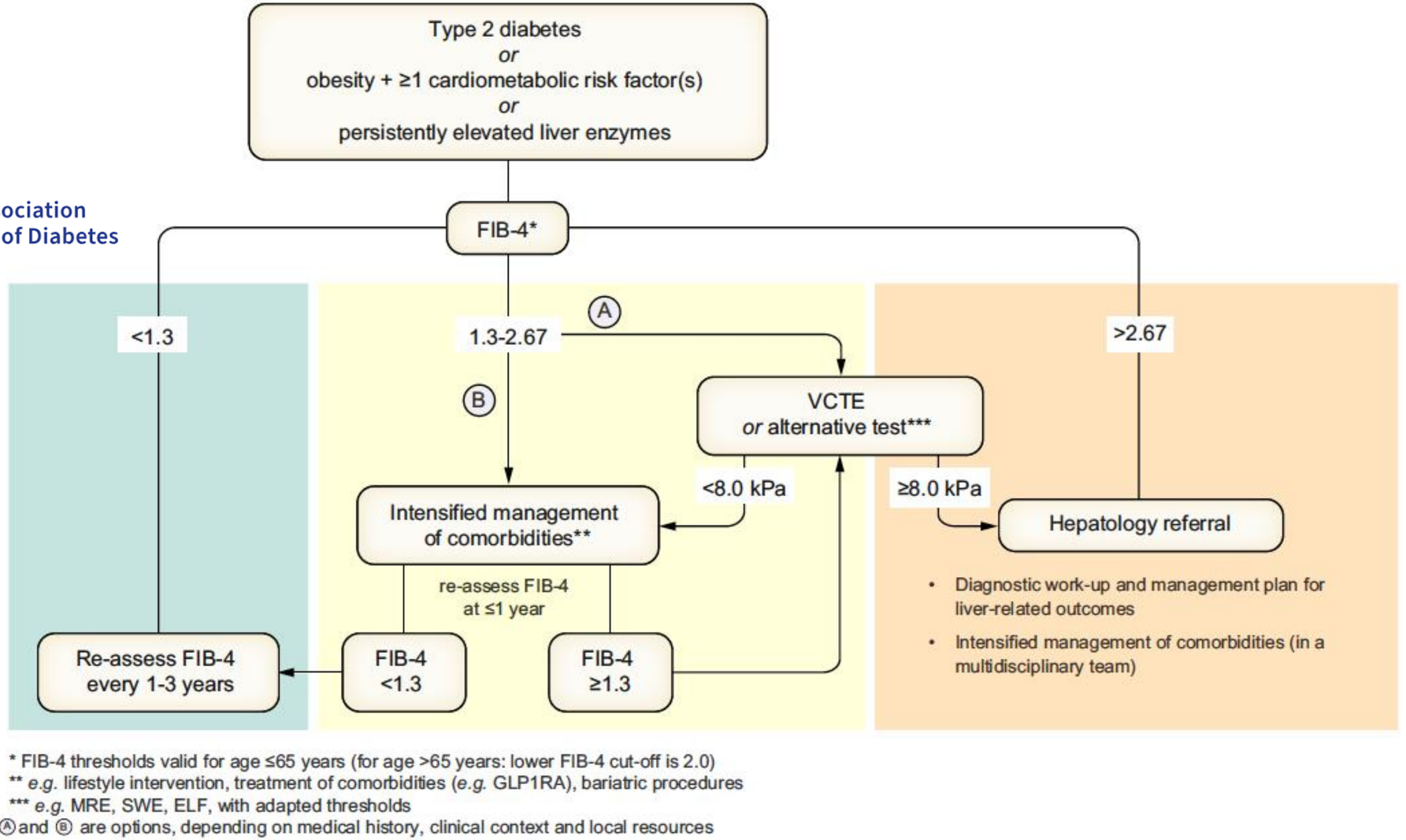
Stefan N, et al. Lancet Diabetes Endocrinol. 2025;13(2):134-48
Younossi ZM, et al. Hepatology. 2023;77(4):1335-47

Tests non invasifs dans la MASLD



Castera L, et al. Noninvasive Assessment of Liver Fibrosis. N Engl J Med. 2025 Oct 30;393(17):1715-1729

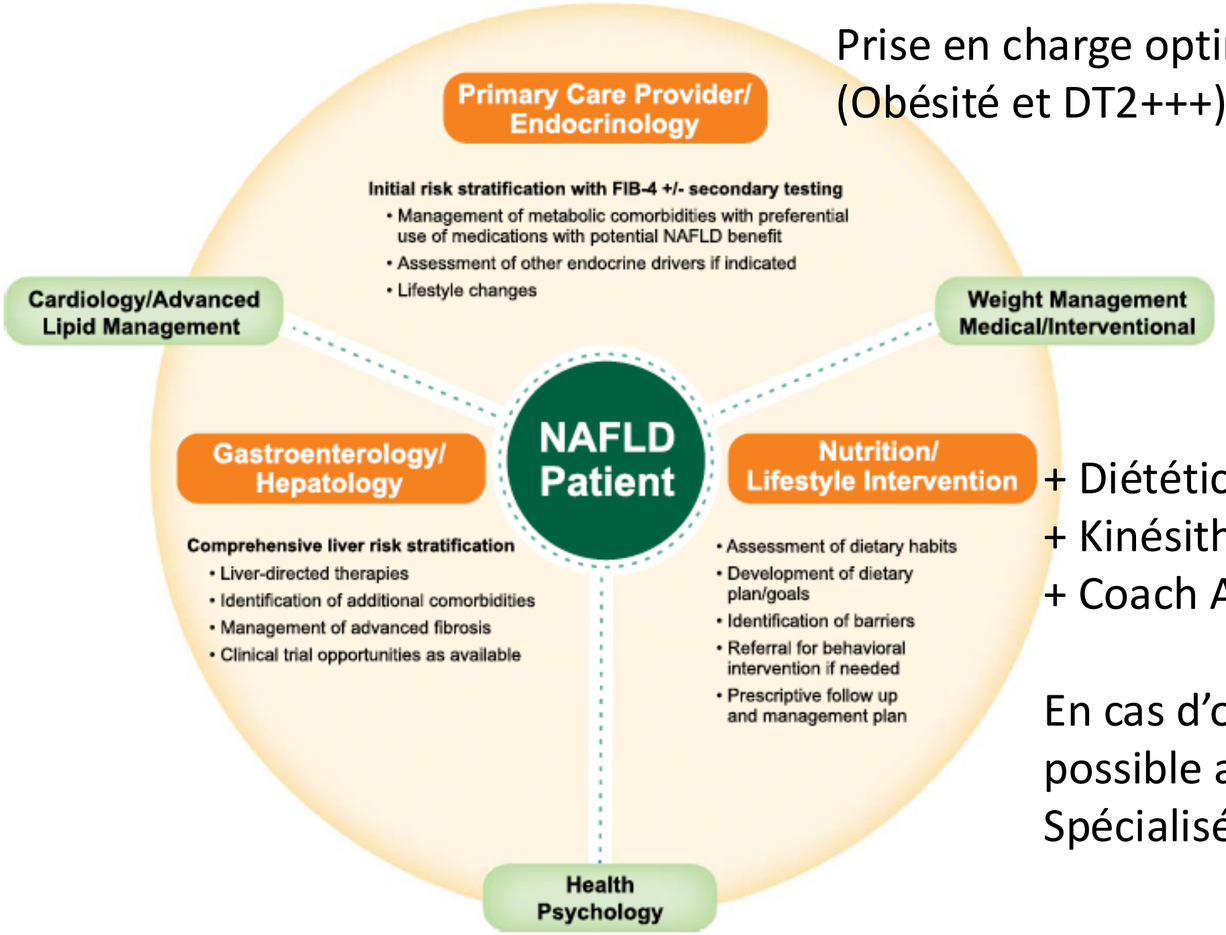
Evaluation non invasive de la fibrose hépatique



* FIB-4 thresholds valid for age ≤65 years (for age >65 years: lower FIB-4 cut-off is 2.0)
** *e.g.* lifestyle intervention, treatment of comorbidities (*e.g.* GLP1RA), bariatric procedures
*** *e.g.* MRE, SWE, ELF, with adapted thresholds
Ⓐ and Ⓑ are options, depending on medical history, clinical context and local resources

EASL-EASD-EASO. J Hepatol. 2024 Sep;81(3):492-542

Prise en charge multidisciplinaire



Prise en charge optimale des comorbidités (Obésité et DT2+++)

+ Diététicien(ne)
+ Kinésithérapeute
+ Coach APA…

En cas d'obésité, prise en charge possible au sein des Centres Spécialisés de l'Obésité (CSO)

Rinella ME, et al. AASLD Practice Guidance. Hepatology. 2023 May 1;77(5):1797-1835

Objectifs de perte de poids

Etude prospective unicentrique cubaine

n = 293 patients avec MASH prouvée par biopsie hépatique

Conseils hygiéno-diététiques

Suivi de 52 semaines

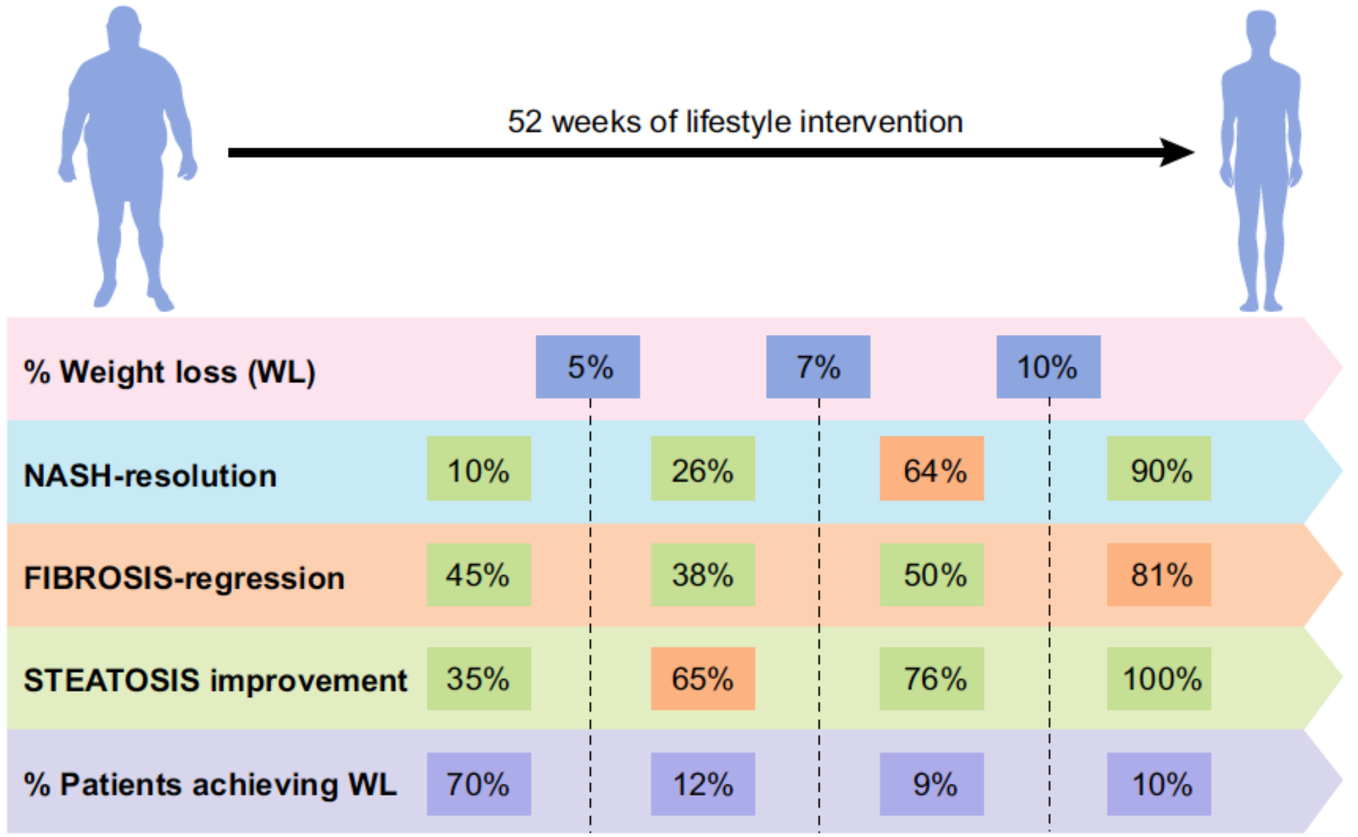


Fig. 3. Probability of reaching NASH resolution, fibrosis regression (at least one stage) and steatosis improvement in patients with NASH under lifestyle intervention according to percentage of weight loss (modified from Vilar-Gomez *et al.*[12]).

Romero-Gómez M, et al. J Hepatol. 2017 Oct;67(4):829-846

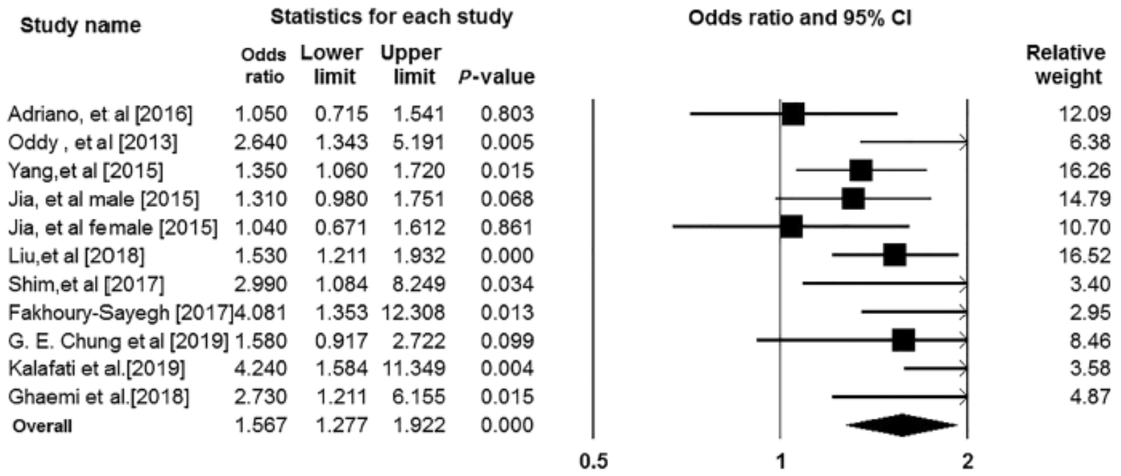
Vilar-Gomez E, et al. Gastroenterology. 2015 Aug;149(2):367-78.e5; quiz e14-5

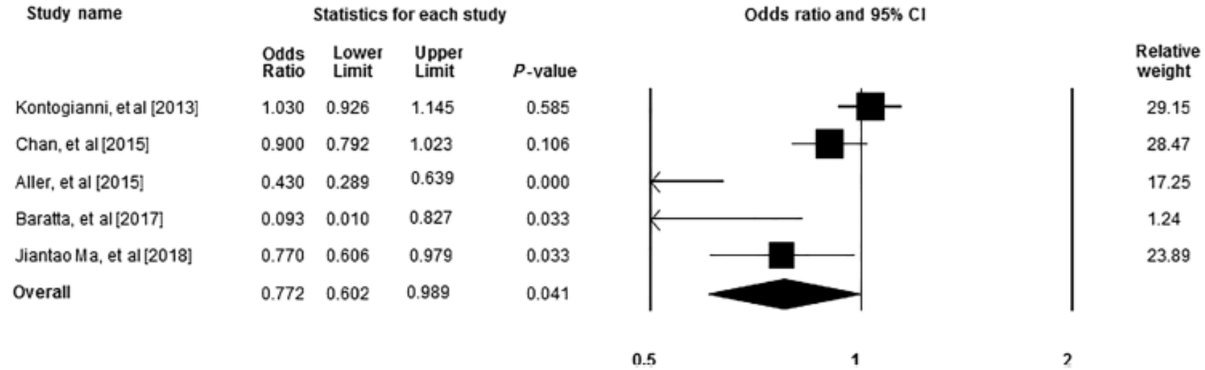
Régime méditerranéen et MASLD

Méta-analyse jusqu'à 2019 : 18 études incluses (n = 24867 participants)
MASLD : diagnostiquée par échographie ou biopsie
3 régimes étudiés : occidental, méditerranéen et prudent

Régime occidental (Western Diet)
n = 8787
OR = 1,56, CI = 1,27 à 1,92 ; p≤0,001

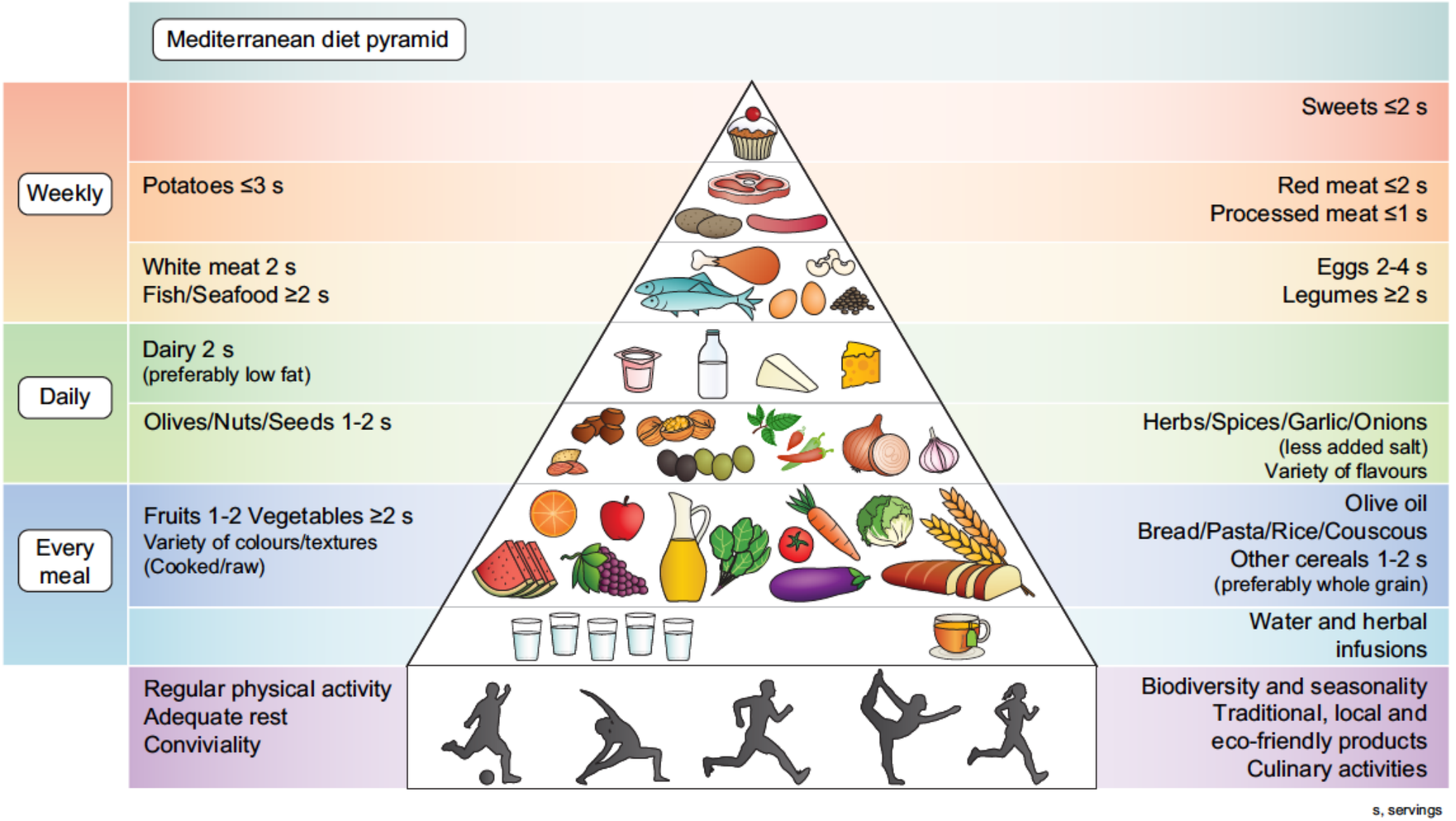
Régime Méditerranéen
n = 3057
OR = 0,77, CI = 0,60 à 0,98 ; p=0,041





Hassani Zadeh S, et al. J Gastroenterol Hepatol. 2021 Jun;36(6):1470-1478

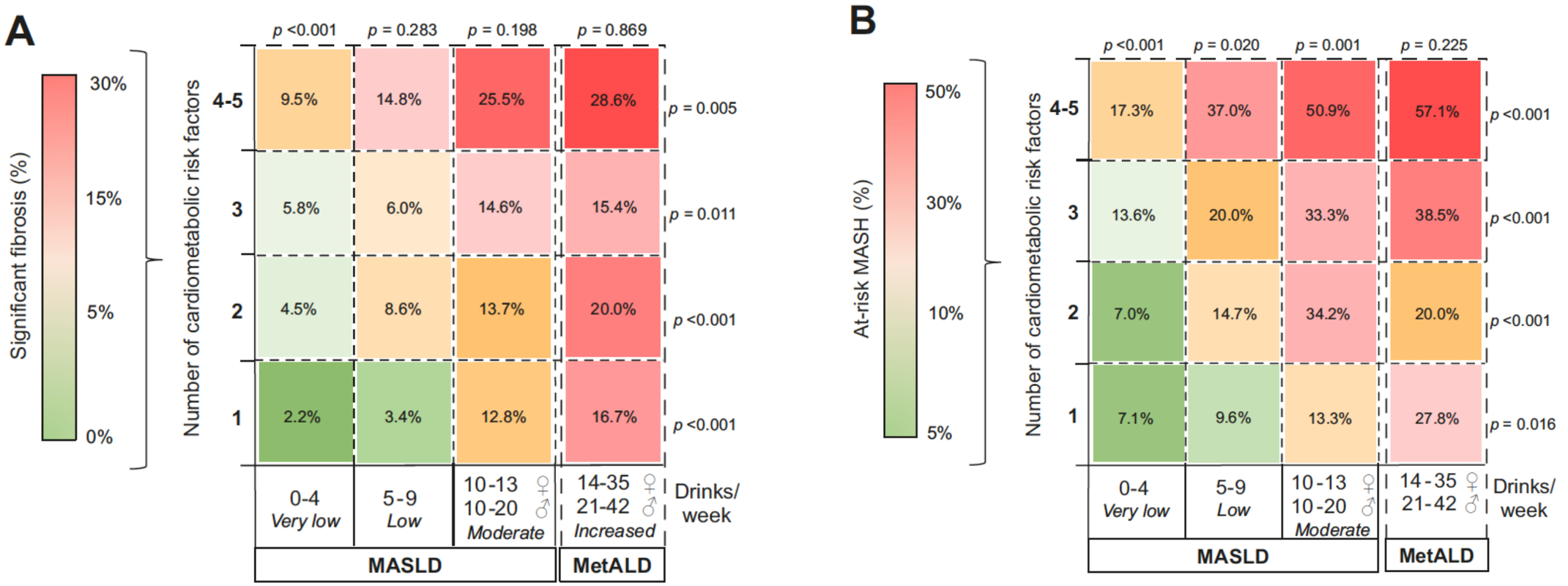
Régime méditerranéen



Francque SM, et al. JHEP Rep. 2021 Sep 17;3(5):100322

Alcool dans la MASLD

Cohorte de dérivation espagnol (n = 6826) et cohorte de validation américaine (n = 4427)
Patients avec MASLD : stéatose si CAP ≥ 275 dB/m ; MASH si FAST ≥ 0,35 ; fibrose significative ≥ 8 kPa
Evaluation par questionnaire de la consommation d'alcool par semaine



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

Effets de l'exercice physique dans la MASLD

Méta-analyse d'études randomisés contrôlées: n = 551 patients (14 études)
Critère de jugement principal : réduction relative de >30 % de la graisse du foie mesurée par IRM

	Exercise training		Control			Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
Hallsworth et al (2011)	4	11	1	8	12.4%	4.00 [0.35, 45.38]	2011
Sullivan et al	1	12	0	6	6.5%	1.70 [0.06, 47.95]	2012
Pugh et al (2013)	2	6	0	5	6.8%	6.11 [0.23, 162.73]	2013
Pugh et al (2014)	2	13	0	8	7.3%	3.70 [0.16, 87.38]	2014
Hallsworth et al (2015)	4	12	1	8	12.5%	3.50 [0.31, 39.15]	2015
Cheng et al	12	22	5	18	41.2%	3.12 [0.83, 11.79]	2017
Stine et al	6	15	1	8	13.4%	4.67 [0.45, 48.26]	2021
Total (95% CI)		**91**		**61**	**100.0%**	**3.51 [1.49, 8.23]**	
Total events	31		8				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.39$, df = 6 (P = 1.00); $I^2 = 0\%$
Test for overall effect: Z = 2.88 (P = 0.004)

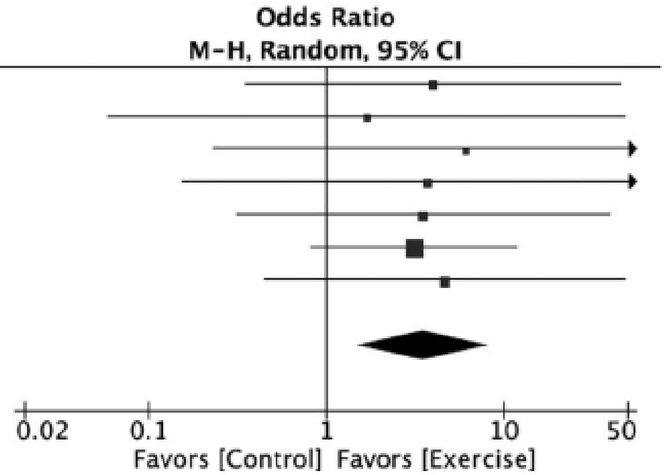


Figure 2. Exercise training achieves threshold of MRI-measured liver fat reduction that predicts histologic treatment response. Exercise training subjects had higher odds of achieving ≥30% relative reduction in MRI-measured liver fat (pooled OR 3.51, 95% CI 1.49–8.23, $P = 0.004$) when compared with standard-of-care controls. CI, confidence interval; OR, odds ratio.

OR : 3,51, IC à 95 % 1,49-8,23, p=0,004

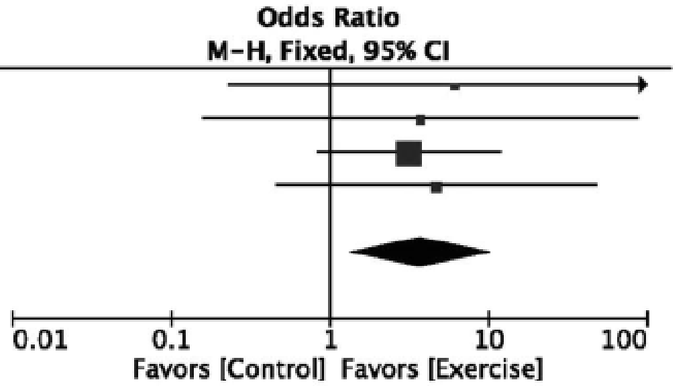
Stine JG, et al. Am J Gastroenterol. 2023 Jul 1;118(7):1204-1213

Effets de l'exercice physique dans la MASLD

a

Study or Subgroup	Exercise training Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Pugh et al (2013)	2	6	0	5	8.4%	6.11 [0.23, 162.73]	2013
Pugh et al (2014)	2	13	0	8	12.1%	3.70 [0.16, 87.38]	2014
Cheng et al	12	22	5	18	60.6%	3.12 [0.83, 11.79]	2017
Stine et al	6	15	1	8	19.0%	4.67 [0.45, 48.26]	2021
Total (95% CI)		**56**		**39**	**100.0%**	**3.73 [1.34, 10.41]**	
Total events	22		6				

Heterogeneity: $Chi^2 = 0.19$, df = 3 (P = 0.98); $I^2 = 0\%$
Test for overall effect: Z = 2.52 (P = 0.01)



b

Study or Subgroup	Exercise training Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Hallsworth et al (2011)	4	11	1	8	39.4%	4.00 [0.35, 45.38]	2011
Sullivan et al	1	12	0	6	20.8%	1.70 [0.06, 47.95]	2012
Hallsworth et al (2015)	4	12	1	8	39.8%	3.50 [0.31, 39.15]	2015
Total (95% CI)		**35**		**22**	**100.0%**	**3.17 [0.69, 14.57]**	
Total events	9		2				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.18$, df = 2 (P = 0.92); $I^2 = 0\%$
Test for overall effect: Z = 1.48 (P = 0.14)

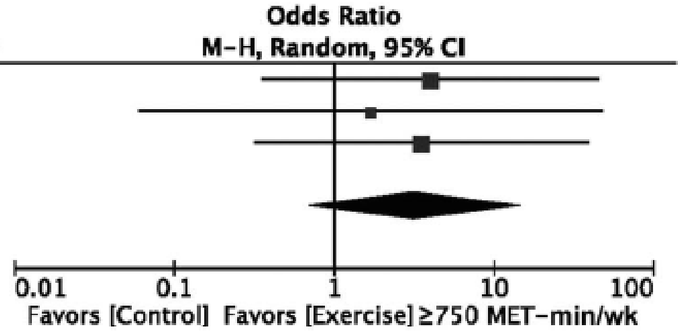
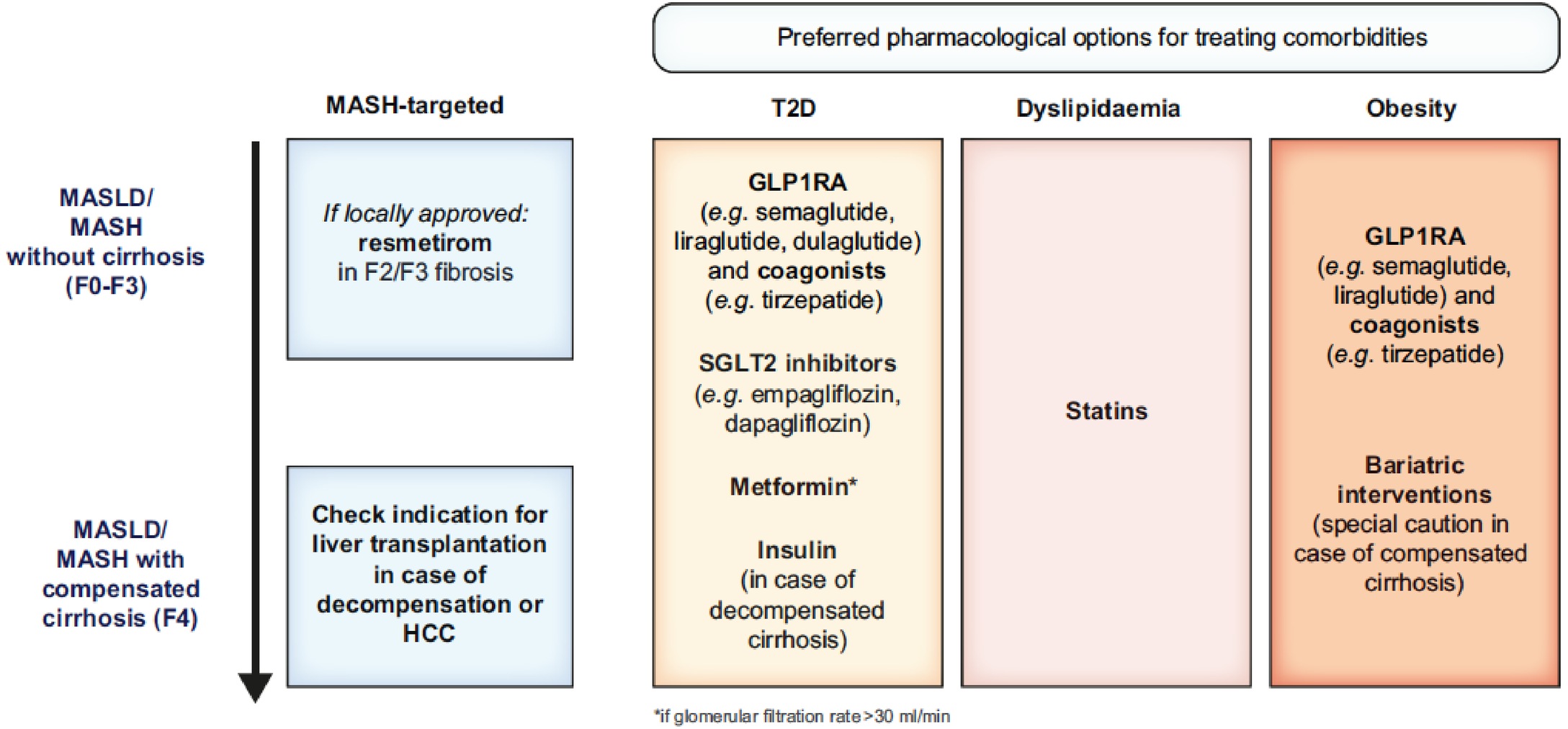


Figure 5. Exercise dose of ≥750 MET-min/wk leads to greater achievement of MRI-measured liver fat reduction threshold for histologic treatment response. (**a**) Meta-analysis showed exercise training subjects prescribed an exercise dose ≥750 MET-min/wk had higher odds of achieving ≥30% relative reduction in MRI-measured liver fat (pooled OR 3.73, 95% CI 1.34–10.31, $P = 0.010$). (**b**) Those prescribed <750 MET-min/wk did not achieve statistically significant rates of ≥30% relative reduction in MRI-measured liver fat (OR 3.17, 95% CI 0.69–14.57, $P = 0.140$). CI, confidence interval; MET, metabolic equivalent of task; OR, odds ratio.

Stine JG, et al. Am J Gastroenterol. 2023 Jul 1;118(7):1204-1213

Prise en charge des comorbidités de la MASLD



EASL-EASD-EASO. J Hepatol. 2024 Sep;81(3):492-542

Prise en charge des comorbidités de la MASLD

Table. Pharmacological Therapies Conditionally Approved by the US Food and Drug Administration for the Treatment of Adults With Noncirrhotic MASH and Moderate to Severe Fibrosis

Phase 3 trial name	Drug name (type)	Population	Group comparison	Primary outcomes	Secondary outcomes	Adverse events and other information
MAESTRO-NASH[66]	Resmetirom (liver-directed, thyroid hormone receptor β-selective agonist)	Patients with biopsy-confirmed MASH and liver fibrosis stage[a] F1b, F2, or F3 (N = 966)	Resmetirom (80 mg/d or 100 mg/d) vs placebo for 52 wk	MASH resolution with stable or improving fibrosis: • Resmetirom (80 mg/d): 25.9% (n = 316) • Resmetirom (100 mg/d): 29.2% (n = 321) • Placebo: 9.7% (n = 318) Improvement in fibrosis by ≥1 stage without worsening of MASH: • Resmetirom (80 mg/d): 24.9% • Resmetirom (100 mg/d): 25.9% • Placebo: 14.2% For comparisons with each dose of resmetirom vs placebo, $P < .001$	Change from baseline in plasma LDL cholesterol level: • Resmetirom (80 mg/d): lowered by 13.6% • Resmetirom (100 mg/d): lowered by 16.3% • Placebo: increased by 0.1% For comparisons with each dose of resmetirom vs placebo, $P < .001$	Resmetirom was well tolerated: • Diarrhea: 27%-33% vs 15% with placebo • Nausea: 19%-22% vs 12% with placebo Resmetirom was not associated with serious adverse events or liver toxicity Resmetirom was associated with significant reductions in: • Liver fat content (measured with an MRI) • Liver stiffness • Noninvasive fibrosis biomarkers • Serum ALT levels • Plasma lipid profile (in addition to lowering LDL cholesterol levels) No significant effects of resmetirom on body weight or insulin resistance (estimated by HOMA-IR)
ESSENCE[67]	Semaglutide (GLP-1 receptor agonist)	Patients with biopsy-confirmed MASH and liver fibrosis stage[a] F2 or F3 (N = 1197)	Semaglutide (2.4 mg/wk) vs placebo for 72 wk	MASH resolution without worsening of fibrosis: • Semaglutide: 62.9% (n = 534) • Placebo: 34.3% (n = 266) Improvement in fibrosis by ≥1 stage without worsening of MASH: • Semaglutide: 36.8% • Placebo: 22.4% For comparison of semaglutide vs placebo, $P < .001$	Change in body weight: • Semaglutide: decreased by 10.5% • Placebo: decreased by 2% Percentage of patients with resolution of MASH and reduction in liver fibrosis: • Semaglutide: 32.7% • Placebo: 16.1% For comparison of semaglutide vs placebo, $P < .001$	Semaglutide was well tolerated: • Diarrhea: 27% vs 12% with placebo • Constipation: 22% vs 18% with placebo • Nausea: 36% vs 13% with placebo • Vomiting: 18% vs 5% with placebo Semaglutide was not associated with serious adverse events or liver toxicity Semaglutide was associated with significant reductions in: • Liver stiffness • Noninvasive fibrosis biomarkers • Serum ALT levels • Plasma lipid profile • Insulin resistance (estimated by HOMA-IR) • Hemoglobin A_{1c} level

Abbreviations: ALT, alanine aminotransferase; GLP-1, glucagon-like peptide-1; HOMA-IR, homeostatic model assessment of insulin resistance; LDL, low-density lipoprotein; MASH, metabolic dysfunction–associated steatohepatitis; MRI, magnetic resonance imaging.

[a] The 5-stage scale for liver fibrosis ranges from F0 (absence of fibrosis), F1 (perisinusoidal or portal fibrosis), F1b (moderate fibrosis, pericentral area only), F2 (perisinusoidal and portal or periportal fibrosis), F3 (septal and bridging fibrosis), to F4 (cirrhosis).

EASL-EASD-EASO. J Hepatol. 2024 Sep;81(3):492-542

DIU MASH

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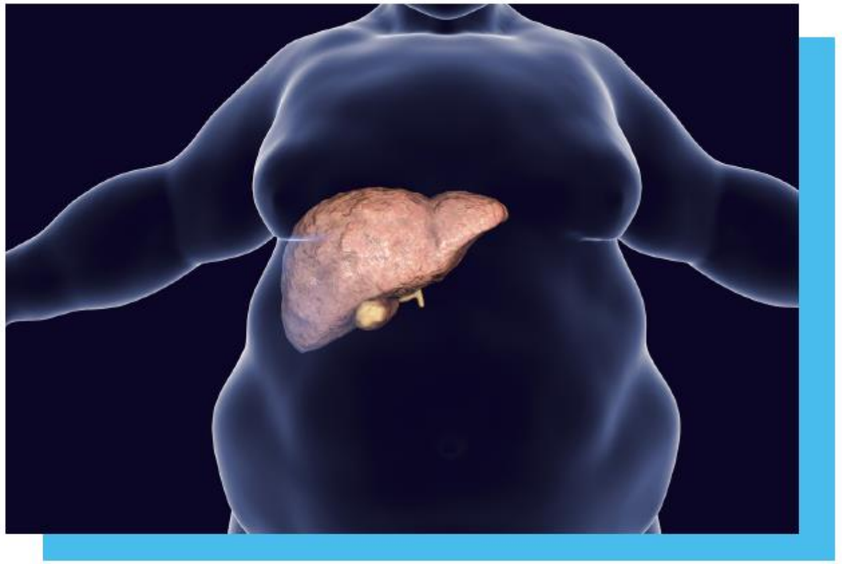
    - valerie.thunot@ube.fr
  - Mme Maéva TROCHERIE, SEFCA-UMDPC, Université Bourgogne Europe

- **Présentation du DIU** :
  - https://sefca-umdpcs.u-bourgogne.fr/nos-formations/pole-hepato-gastro/du-mash.html



D.İ.U. STÉATOHÉPATİTE DYSMÉTABOLİQUE
MASH (METABOLİC DYSFUNCTİON-ASSOCİATED STEATOHEPATİTİS)

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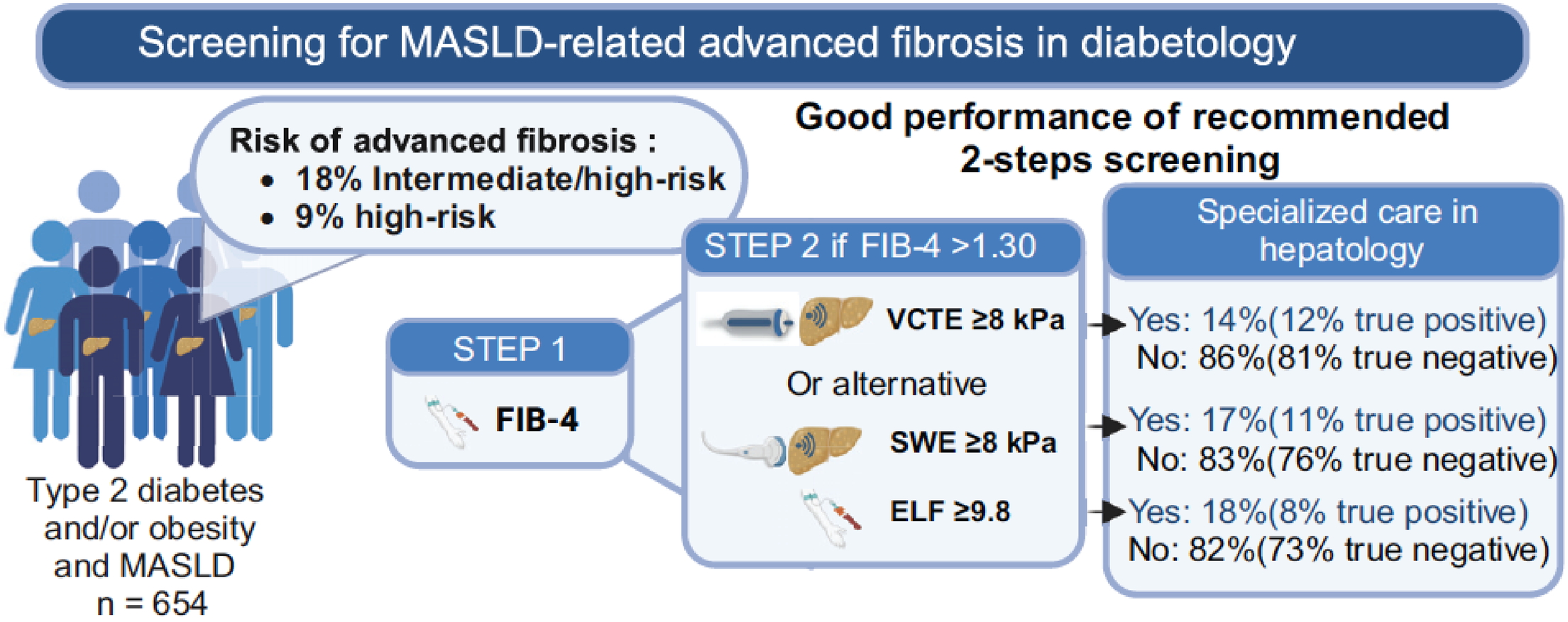
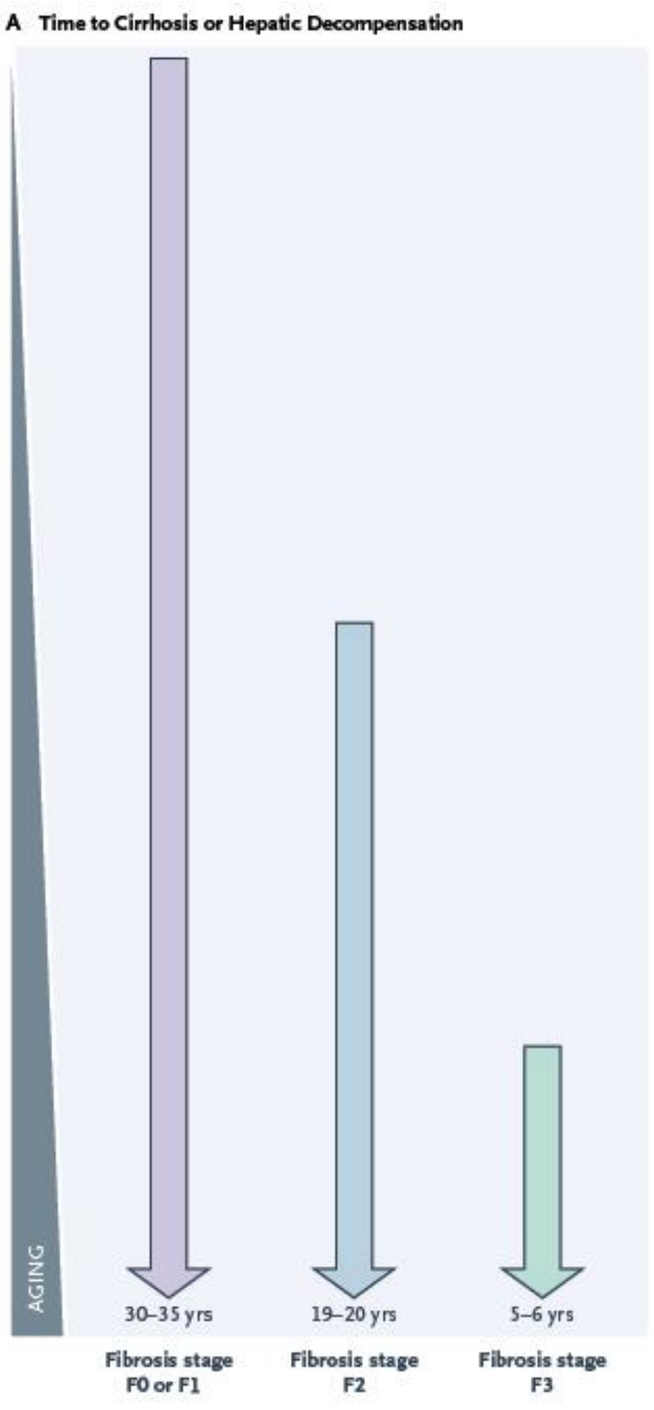
Bourgogne
Europe

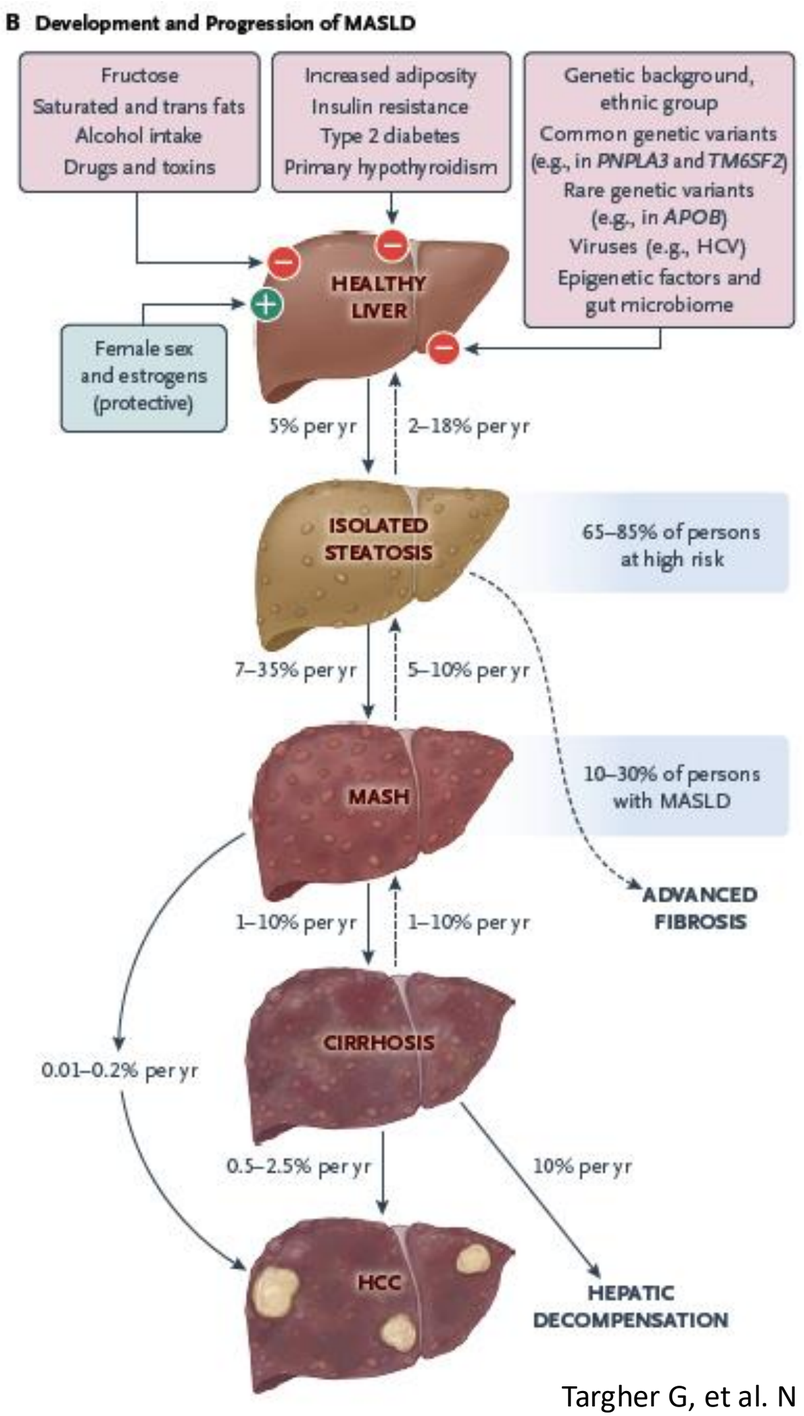
Performances du test ELF



Caussy C, et al. Diabetes Care. 2025 Jun 1;48(6):877-886

Histoire naturelle de la MASLD





Targher G, et al. N Engl J Med. 2025 Aug 14;393(7):683-698

Régimes alimentaires dans la MASLD

	Western Diet	Mediterranean Diet (MD)	Dietary Approach to Stop Hypertension (DASH)
Dietary patterns			
Foods intake	❖ *Processed foods* ❖ *Red meats* ❖ *Processed meats* ❖ *Sugary beverages* ❖ *Snacks* ❖ *cakes and biscuits* ❖ *eggs* ❖ *butter*	❖ *Extra virgin olive oil* ❖ *Vegetables and Fruits* ❖ *Cereals, legumes, nuts* ❖ *Moderate intakes of fish and other meat, dairy products and red wine* ❖ *Low intakes of eggs and sweets.*	❖ *Fruits* and *vegetables* ❖ *whole grains,* ❖ *fish, poultry, nuts,* ❖ *legumes* ❖ *low-fat dairy products* ❖ *reduced sodium* ❖ *Fresh food* ❖ *Minimally processed food*
Nutrients	↑**Energy intake** ↑SFA ↓PUFA ↑protein animal ↑sugar, fructose ↑cholesterol ↑Salt ↓fiber	↓SFA ↑**MUFA** ↑**PUFA** ↑protein vegetables ↓sugar fructose ↓cholesterol ↑**fiber** ↑**polyphenols,** ↑**carotenoids**	↓ **total fat** ↓**Salt** ↑protein vegetables ↓sugar fructose ↓cholesterol ↑fiber ↑polyphenols, ↑carotenoids

Berná G, Romero-Gomez M. Liver Int. 2020 Feb;40 Suppl 1:102-108

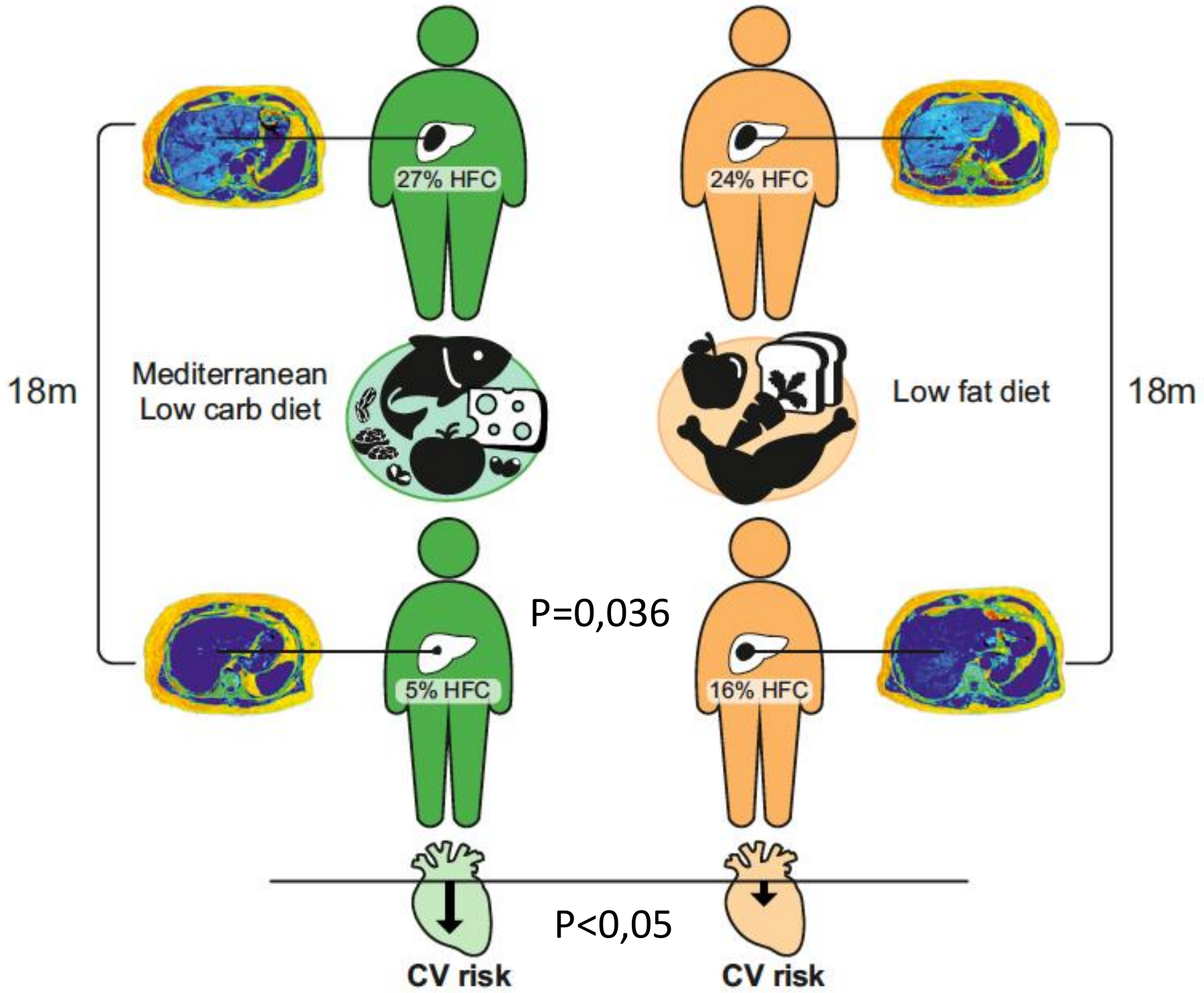
Régime alimentaire et MASLD

Etude randomisée contrôlée sur 18 mois

n = 139 avec régime Méditerranéen/ pauvre en sucre
n = 139 avec régime pauvre en graisse

Evaluation de la stéatose hépatique par IRM

Suivi de 18 mois



Gepner Y, et al. J Hepatol. 2019 Aug;71(2):379-388

Prise en charge de la MASLD en France en 2024

Recommandations hygiéno-diététiques

Nutrition :
- Régime Méditerranéen
- Réduire la consommation de produits ultra-transformés, de viande rouge, de fructose et de boissons sucrées
- Augmenter la consommation de légumes, de fruit et de produits non transformés
- Consommation régulière de café

Activité physique :
- Régulière et adaptée aux préférences et aux capacités de l'individu
- >150 min/semaine d'activité physique d'intensité modérée ou 75 min/semaine d'activité physique d'intensité vigoureuse
- Minimiser le temps sédentaire

Hygiène de vie :
- Sevrage tabagique
- Limiter la consommation d'alcool (sevrage complet en cas de fibrose avancée)

Au stade de cirrhose :
- *Dépistage et prise en charge de la sarcopénie et de dénutrition*
- *Adaptation des apports alimentaires et collation nocturne si besoin*

Prise en charge multidisciplinaire

Surpoids / Obésité

Objectifs :
- ≥ 5% de perte de poids pour une réduction de la stéatose
- ≥ 7-10% de perte de poids pour une réduction de la MASH et de la fibrose

Prise en charge globale :
- Recommandations hygiéno-diététiques (RHD) adaptées
- Thérapies cognitivo-comportementales et psychologiques

Traitements possibles (si échec des RHD et IMC > 35 kg/m^2) :
- Discuter traitement par analogues du GLP-1 et co-agonistes (dans l'AMM)
- Discuter chirurgie bariatrique (sauf si cirrhose décompensée)

Diabète de type 2

Objectif : équilibre du diabète

Prise en charge globale :
- Recommandations hygiéno-diététiques (RHD) adaptées

Traitements possibles (selon sévérité diabète et en accord avec AMM) :
- Metformine (si DFG > 30 mL/min)
- Analogues du GLP-1 et co-agonistes
- Inhibiteurs du SGLT-2
- Insuline (en cas de cirrhose décompensée)

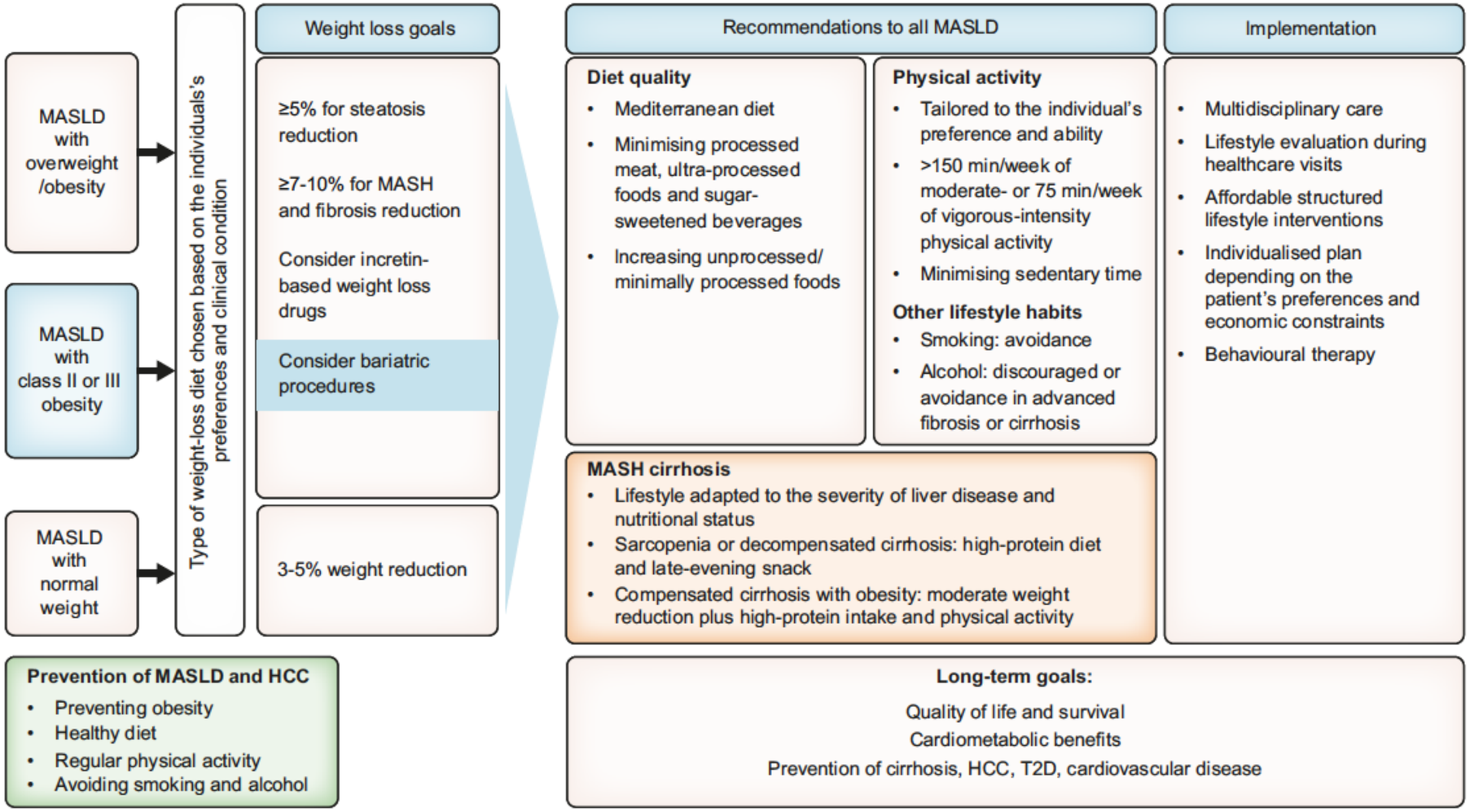
Dyslipidémie

Objectif : amélioration du profil lipidique

Traitement possible : statines

Mouillot T
Post'U 2025

Conseils hygiéno-diététiques dans la MASLD



EASL-EASD-EASO. J Hepatol. 2024 Sep;81(3):492-542