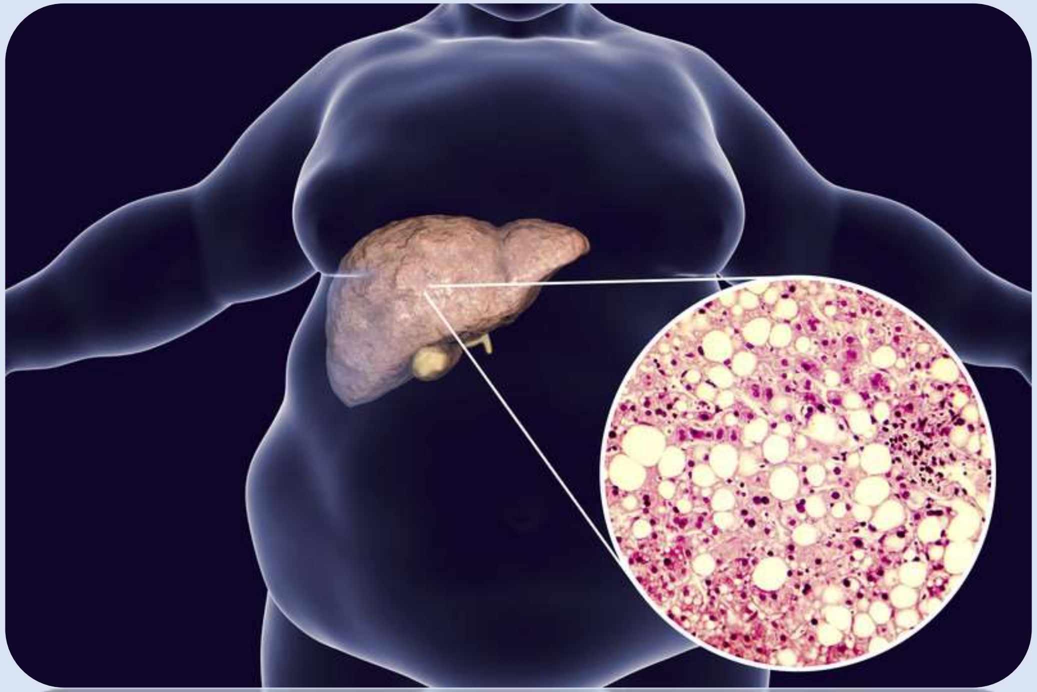


Nutritional interventions in patients with liver disease and obesity

Violeta Moizé, RDN, PhD.
Hospital Clinic Barcelona
SECO and IFSO IH-EC Representative
vmoize@clinic.cat

Clínic Barcelona | Universitat de Barcelona

I have no potential conflict of interest to report

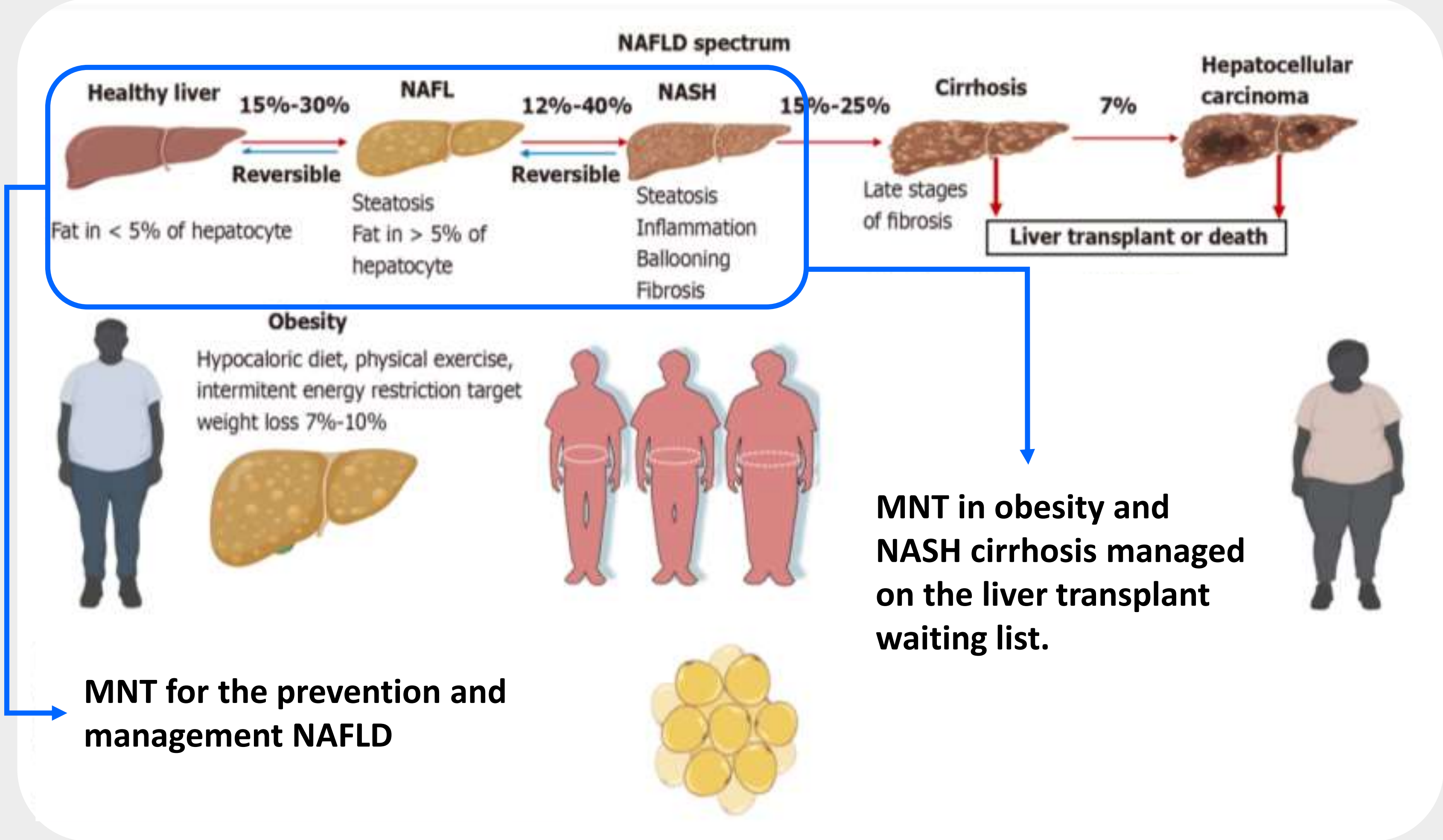
Introduction

- Nutrition and dietary interventions are a central component in the pathophysiology, but also a cornerstone in the management of patients with non-alcoholic fatty liver disease (NAFLD).

- Balanced levels of **dietary macronutrients** and **micronutrients** can act to slow or halt the progression of NAFLD.

An imbalance can contribute to the pathogenesis and progression of NAFLD.

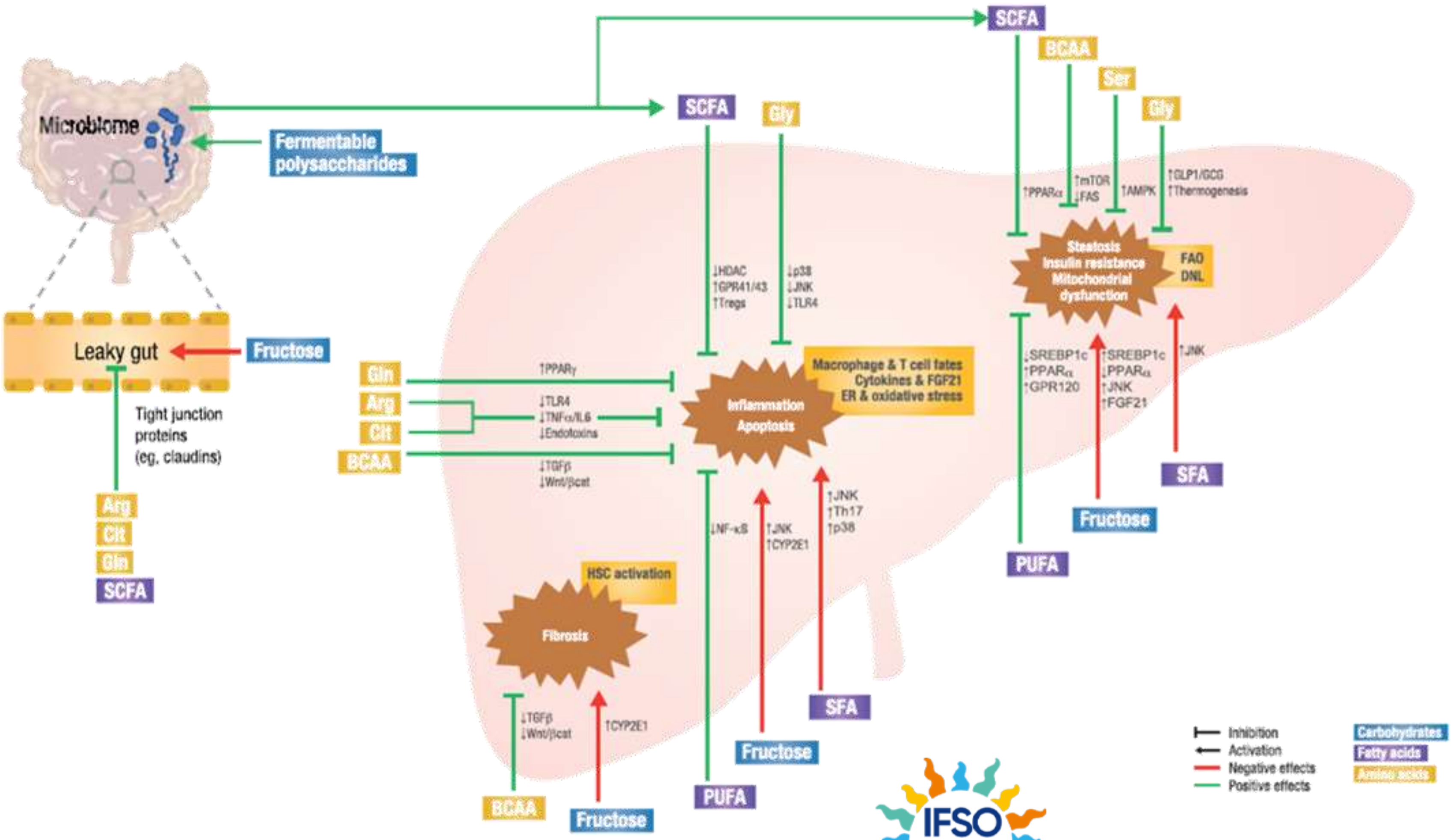
Progression of nonalcoholic fatty liver disease



Impact of key dietary nutrients on molecular mediators that orchestrate the core NAFLD pathobiological pathways.

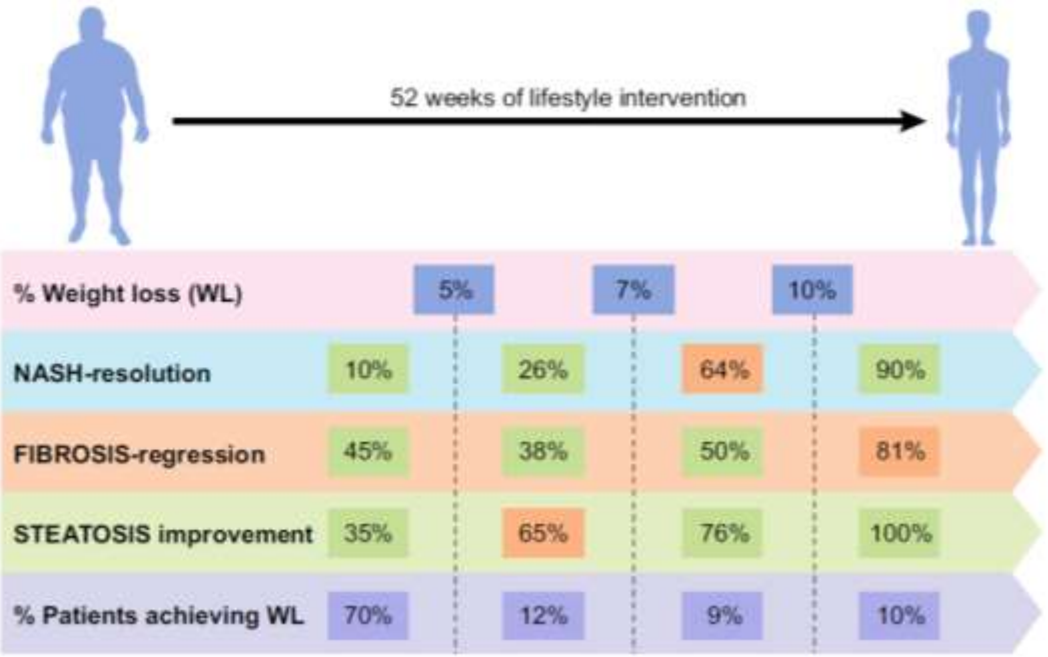
New nomenclature - will be changed soon.

- Steatotic Liver Disease **(SLD),**
- Metabolic Dysfunction-associated Steatotic Liver Disease **(MASLD)**

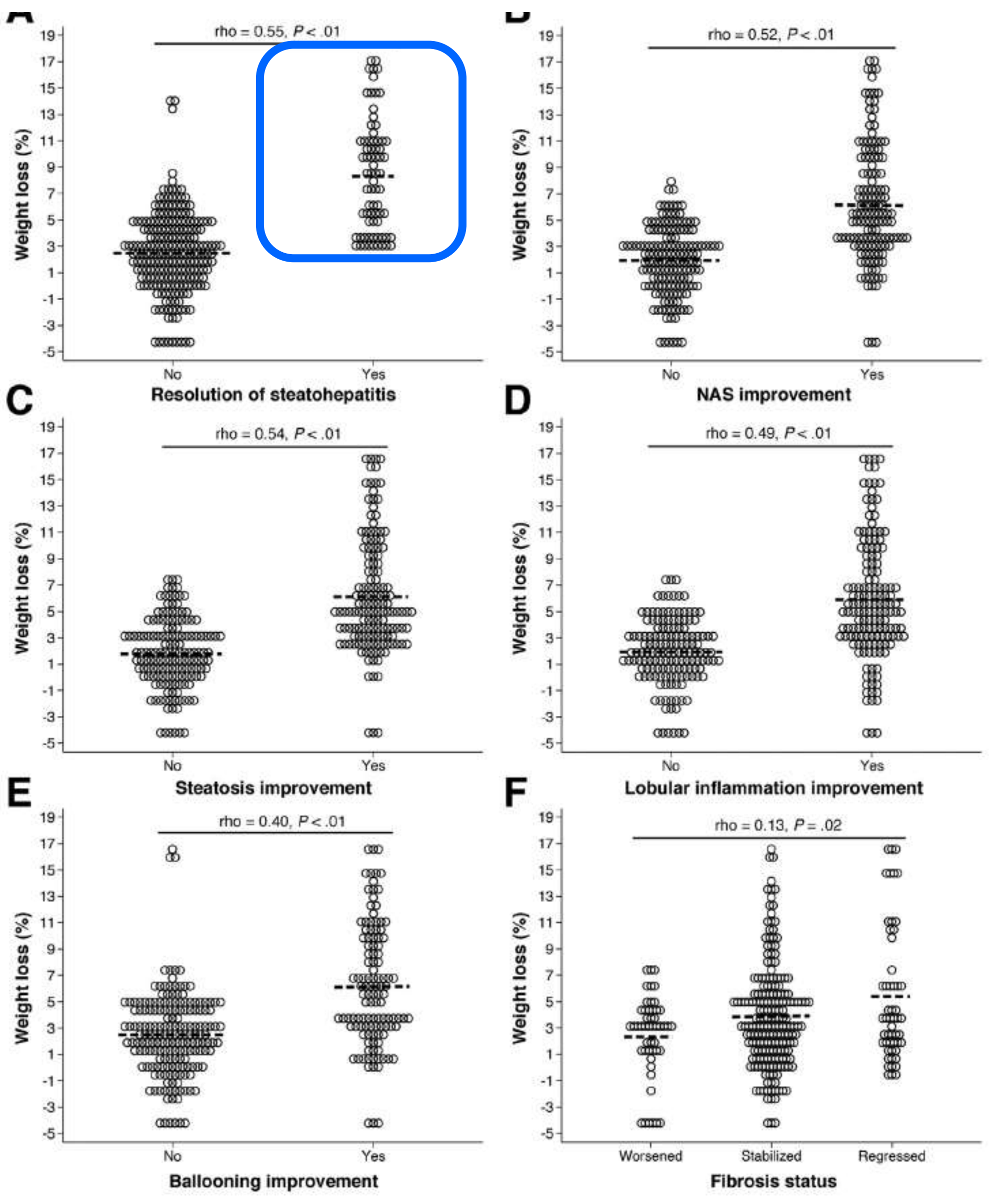


Chakravarthy MV et al. Gastroenterol Clin North Am. 2020 ;49(1):63-94. doi: 10.1016/j.gtc.2019.09.003.

Weight Loss Through Lifestyle Modification Significantly Reduces Features of Nonalcoholic Steatohepatitis



Correlation between weight-loss percentage and improvement of different histologic parameters related to NASH.



IFSO NAPOLI 2023

EASL-EASD-EASO Clinical Practice Guidelines 2016

Vilar-Gomez E et al. Gastroenterology 2015

Long-term adherence to a Mediterranean diet supplemented with EVOO is associated with a lower prevalence of NAFLD compared with a similar diet supplemented with nuts or a control diet with a lower fat content - PREDIMED steatosis substudy.

Explore the associations with liver steatosis of 3 different diets: a MedDiet + extra-virgin olive oil (EVOO), Med Diet + nuts, or a control diet.

	MedDiet + EVOO ($n = 34$)	MedDiet + nuts ($n = 36$)	Control diet ($n = 30$)	P
Liver fat, %	1.2 [0–4.4]	2.7 [0.2–11.0]	4.1 [0.6–10.4]	0.068
Steatosis,[2] n (%)	3 (8.8)[a]	12 (33.3)[b]	10 (33.3)[b]	0.027
Serum hs-CRP, mg/dL	0.22 [0.13–0.43]	0.18 [0.12–0.31]	0.19 [0.14–0.35]	0.646
Plasma HbA1c, %	6.1 [5.7–6.6][a]	6.4 [5.9–7.2][b]	5.8 [5.4–6.5][a]	0.015
Serum fasting insulin, mU/L	12.8 [8.7–18.6]	12.7 [9.0–26.8]	12.3 [7.3–21.1]	0.794
HOMA-IR	3.8 [2.6–5.1]	3.7 [2.4–7.3]	3.5 [1.8–7.2]	0.636
Serum nitrites + nitrates, μM	25.1 [19.4–32.0]	28.1 [20.3–39.2]	21.5 [16.1–32.4]	0.223
Serum 3-nitrotyrosine, nM	15.3 [13.0–20.0]	15.2 [12.2–22.0]	14.9 [11.7–16.8]	0.694
FRAP, mEq quercetin	60.9 [55.7–72.4]	57.9 [53.6–80.9]	57.5 [52.0–62.2]	0.266
Urine 12-HETE/creatinine, ng/mg	2.3 [1.4–3.8][a]	5.0 [3.3–11.6][b]	3.9 [1.6–7.2][b]	0.001
Plasma ALT, U/L	19.2 [16.6–28.4]	26.0 [19.8–36.5]	22.8 [17.1–38.1]	0.271

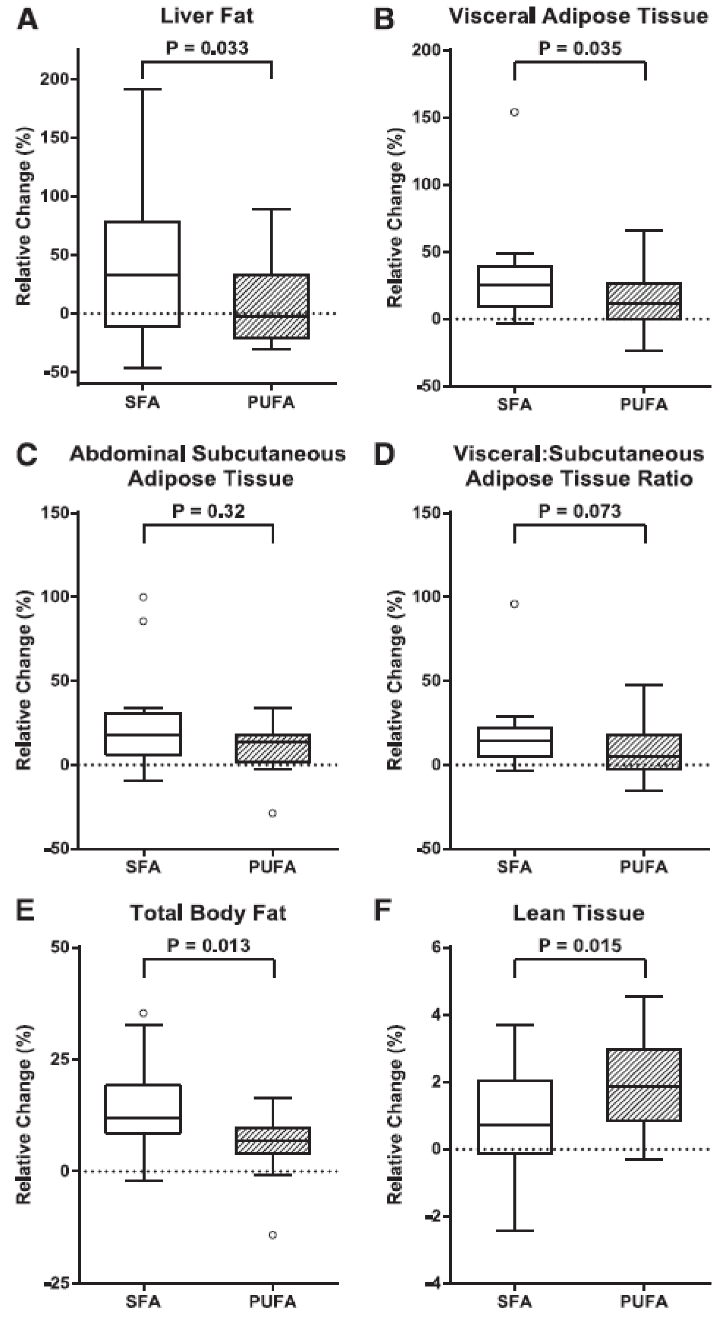
Pintó Xavier et al. PREDIMED Jnutr 2019;149:1920–1929.

Overfeeding Polyunsaturated and Saturated Fat Causes Distinct Effects on Liver and Visceral Fat Accumulation in Humans

Table 2—Liver fat and body composition before and after 7 weeks of PUFA or SFA overeating

	PUFA (n = 18) baseline	Mean absolute change	SFA (n = 19) baseline	Mean absolute change	Mean difference in change (95% CI)	P value
Body weight, kg	67.4 ± 8.2	1.6 ± 0.85	63.3 ± 6.8	1.6 ± 0.96	−0.02 (−0.63 to 0.58)	0.94
BMI, kg/m^2	20.8 (19.5–23.1)	0.5 ± 0.3	19.9 (18.9–20.7)	0.5 ± 0.3	0.01 (−0.18 to 0.20)	0.98
Waist girth, cm	79.4 ± 5.6	0.97 ± 2.2	76.1 ± 5.1	1.0 ± 2.3	−0.03 (−1.53 to 1.47)	0.97

- **The SFAs markedly increased liver fat compared with PUFAs and caused a twofold increase in visceral fat compared to PUFAs.**



IFSO NAPOLI 2023

Fredrik Rosqvist et al. Diabetes 2014;63:2356–2368 | DOI: 10.2337/db13-1622

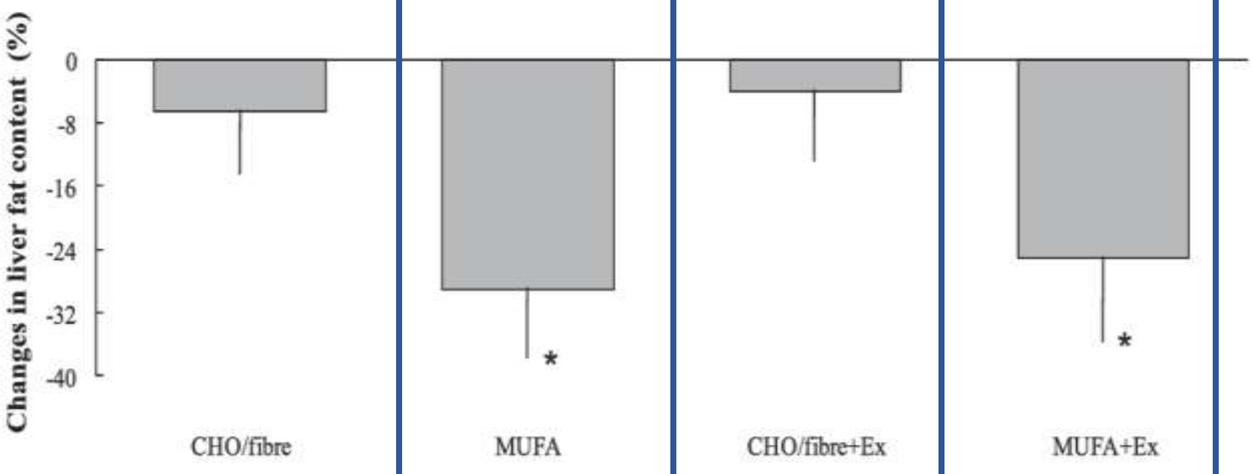
Liver Fat Is Reduced by an Isoenergetic MUFA Diet in a RCT (8w intervention) in patients with Type 2 Diabetes

@37 ♂ and 8 ♀
Aged 35 –70 years

The benefits of MD are independent of WL.

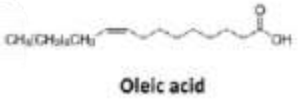
	CHO/fiber		MUFA		CHO/fiber+Ex		MUFA+Ex	
	Baseline	End	Baseline	End	Baseline	End	Baseline	End
Body weight (kg)	85 ± 13	85 ± 13	79 ± 13	79 ± 13	83 ± 13	83 ± 13	87 ± 13	87 ± 13
Waist circumference (cm)	103 ± 6	104 ± 6	100 ± 8	99 ± 8	101 ± 8	101 ± 8	104 ± 11	103 ± 10
Plasma total cholesterol (mg/dL)	157 ± 38	164 ± 46	167 ± 25	166 ± 23	175 ± 39	176 ± 36	171 ± 37	168 ± 39
HDL cholesterol (mg/dL)	37 ± 8	37 ± 7	35 ± 6	36 ± 4	44 ± 11	49 ± 21	40 ± 7	39 ± 6
LDL cholesterol (mg/dL)	98 ± 29	107 ± 40	110 ± 20	109 ± 21	116 ± 36	121 ± 35	110 ± 29	111 ± 30
Plasma triglycerides (mg/dL)	110 ± 68	131 ± 106	122 ± 37	114 ± 33	90 ± 26	100 ± 30	126 ± 104	102 ± 70
Plasma glucose (mg/dL)	137 ± 15	138 ± 25	145 ± 37	141 ± 21	133 ± 27	142 ± 32	136 ± 15	143 ± 31
Plasma AST (UI)	18 ± 5	20 ± 5	21 ± 13	21 ± 8	20 ± 11	18 ± 5	19 ± 3	17 ± 3*
Plasma ALT (UI)	22 ± 8	23 ± 6	34 ± 34	30 ± 17	26 ± 22	24 ± 13	28 ± 8	25 ± 6
HbA_{1c} (%)†	6.3 ± 0.3	6.3 ± 0.4	6.6 ± 0.8	6.2 ± 0.7*	6.5 ± 0.7	6.5 ± 0.8	6.9 ± 0.6	6.8 ± 0.5
Plasma insulin (μU/mL)	17 ± 8	16 ± 5	11 ± 6	11 ± 5	16 ± 6	16 ± 8	12 ± 3	11 ± 3
HOMA-IR	4.8 ± 1.8	5.2 ± 1.2	3.6 ± 1.5	3.9 ± 2.0	5.1 ± 1.6	5.4 ± 2.9	4.2 ± 1.2	4.0 ± 1.6
Peak V_{O_2} (mL/kg/min)	16 ± 4	16 ± 4	15 ± 3	15 ± 4	14 ± 4	14 ± 4	17 ± 2	18 ± 2*
Liver fat (%)†	17.7 ± 9.7‡	16.1 ± 6.8	7.4 ± 2.8	5.2 ± 2.7*	8.8 ± 4.9	8.9 ± 5.7	11.6 ± 8.0	9.1 ± 7.4*

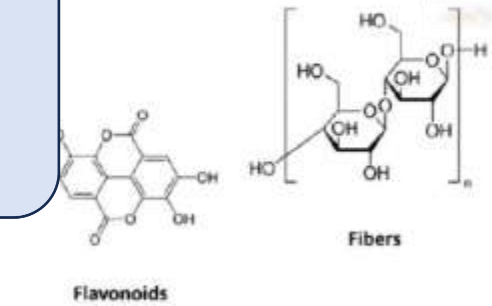
Data are means ± SD. †$P < 0.05$ for diet × time effect by repeated-measures ANOVA; *$P < 0.05$ vs. baseline; ‡$P < 0.05$ vs. MUFA baseline values.

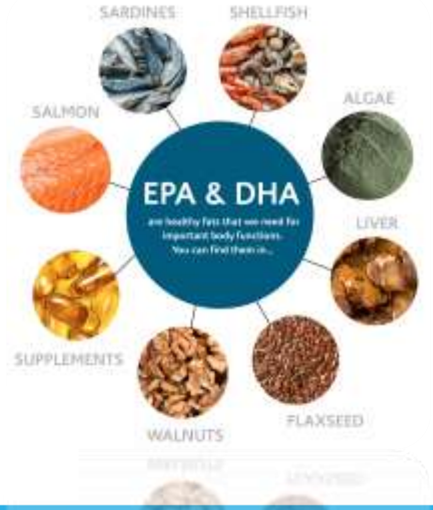


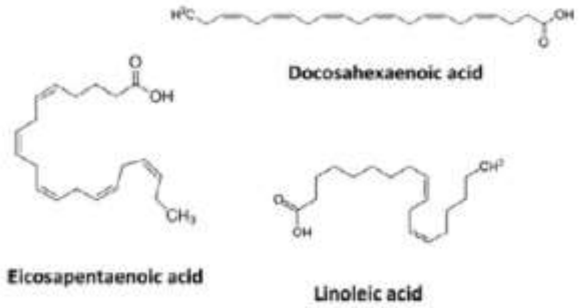
Plausible molecular determinants of the beneficial effect of the Mediterranean diet on NAFLD

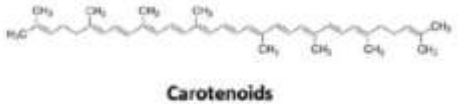
- ↓ de *novo* lipogénesis
- ↑ fatty acids β-oxidation
- ↓ Insulin resistance
- ↓ Oxidative stress
- ↓ Inflamation
- ↓ fibrogenesis

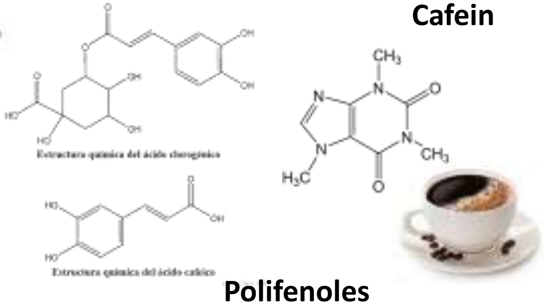




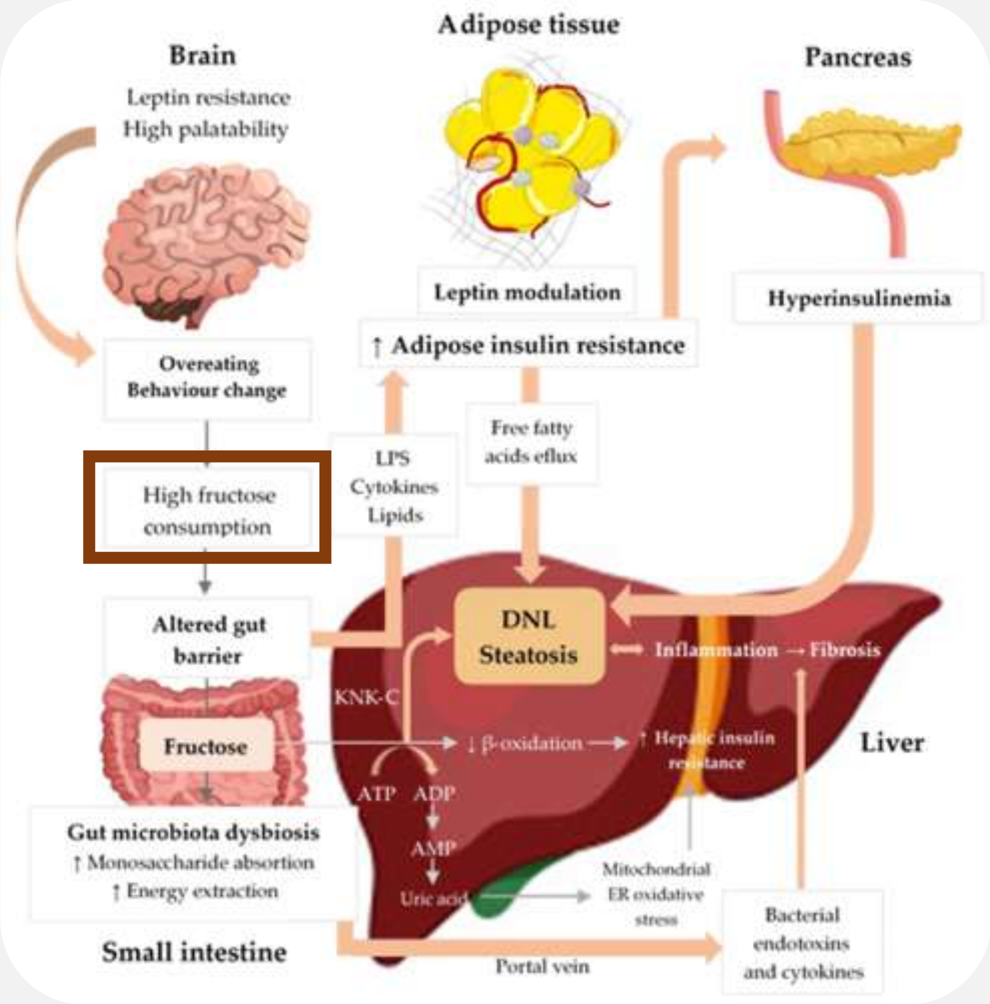






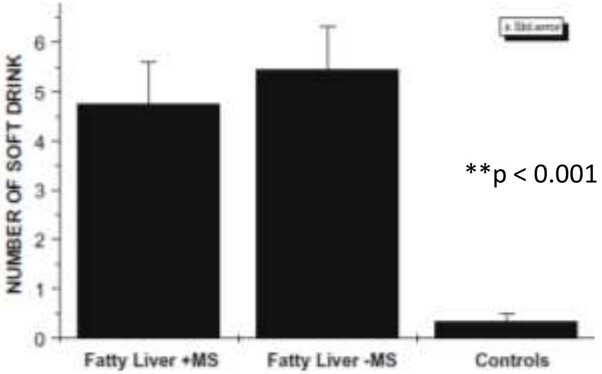


Fructose consumption promotes hepatic steatosis and NAFLD.

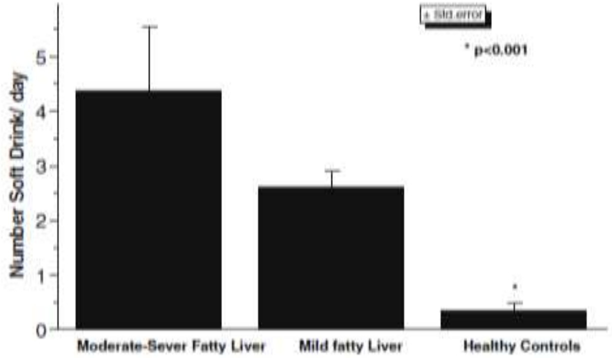


Soft drink consumption is associated with fatty liver disease independent of metabolic síndrome (MS).

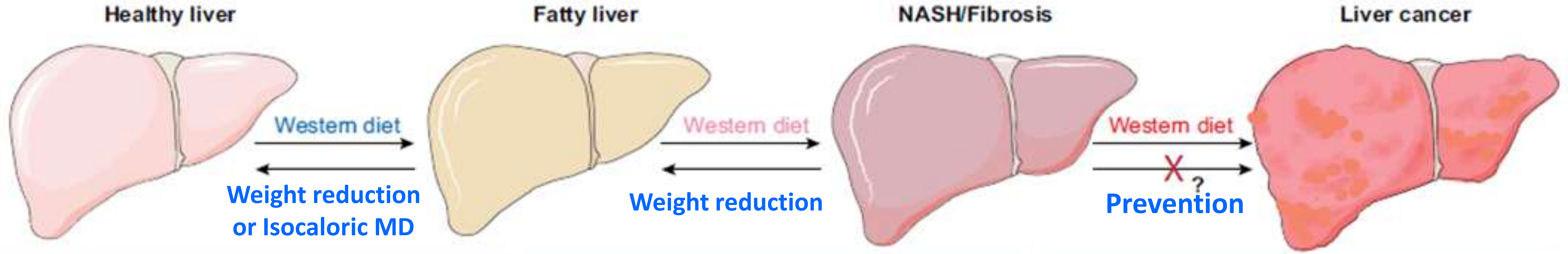
Number of daily soft drinks in patients with NAFLD with or without MS



Association of soft drink consumption and severity of fatty liver disease.



A summary of the nutritional treatment options through the course of NAFLD



Hypocaloric or isocaloric - Mediterranean diet **Aerobic or resistance excercise** *(Clinical trials)*	**≥7-10% Weight reduction** by energy deficit of 500-750 kcal/day through either diet: • low fat • low carb • Mediterranean *(Clinical trials)* **Dietary composition modification** Reduced fructose Mediterranean diet *(Observational studies)*	**Mediterranean diet** • High fibres • High fish • High vegetables • Low cholesterol • Low sugar **Drinks** • Coffee ≥2-3 cups/day • No alcohol in cirrhotics *(Observational studies)*	Nutritional Intervention + moderate physical exercise → offered to patients with obesity and NASH cirrhosis managed on the liver transplant waiting list to support weight loss and improve muscle mass*.

*Grade B - strong consensus 100% agreement

IFSO NAPOLI 2023

Adapted from: Romero-Gomez Manuel et al. Journal of Hepatology 2017

Clinical Nutrition 41 (2022) 2364–2405

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

ESPEN Guideline

European guideline on obesity care in patients with gastrointestinal and liver diseases – Joint ESPEN/UEG guideline*

Pre-hab structured and multidisciplinary program – specialized center*

The risk of sarcopenia is high in patients with NAFLD/NASH

Given the very high prevalence of overweight and obesity among NAFLD patients, sarcopenic obesity is also common in this setting

The risk of further increases during weight loss.

Sarcopenia is related to poor outcome in cirrhotic patients

Results

Most promising effects with:

- At least 8 weeks
- High protein diet
- \+ Supervised exercise 3 days/week (cycling or weightlifting)
- \+ Potential added benefit of BCAAs

Johnston H et al. Nutrients 2022

NAFLD/NASH patients with overweight or obesity not undergoing WL treatment → at least 1 g Pro/kg ABW*/ d.

Undergoing a hpocaloric diet (7-10%) weight loss → 1.2 g Pro/kg ABW/d. to prevent loss of muscle mass.

NAFLD/NASH patients with overweight or obesity and **malnutrition or sarcopenia** → at least 1.2 and up to 1.5 g Pro /kg ABW/d.

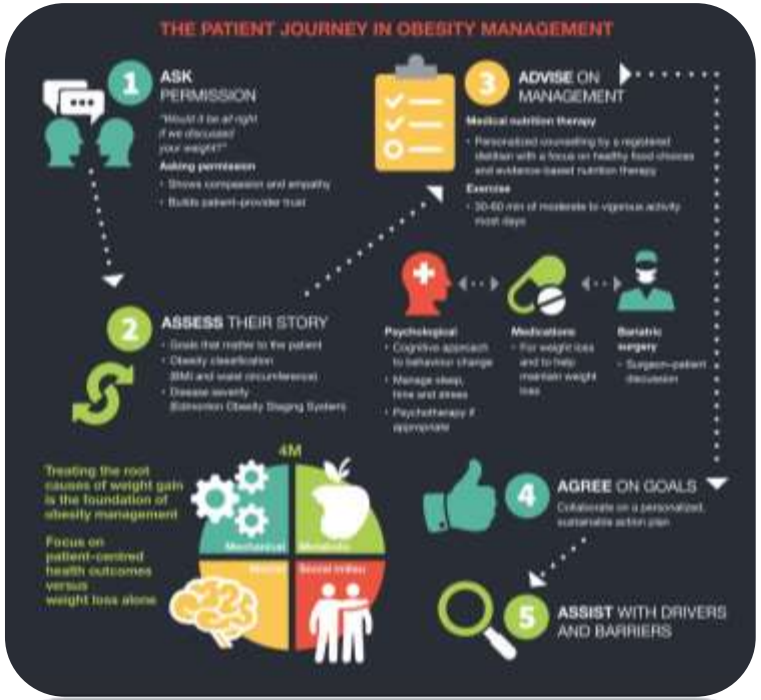
Patients with overweight or obesity and **compensated liver cirrhosis and malnutrition or sarcopenia** → 1.5 g Pro /kg ABW/d protein.

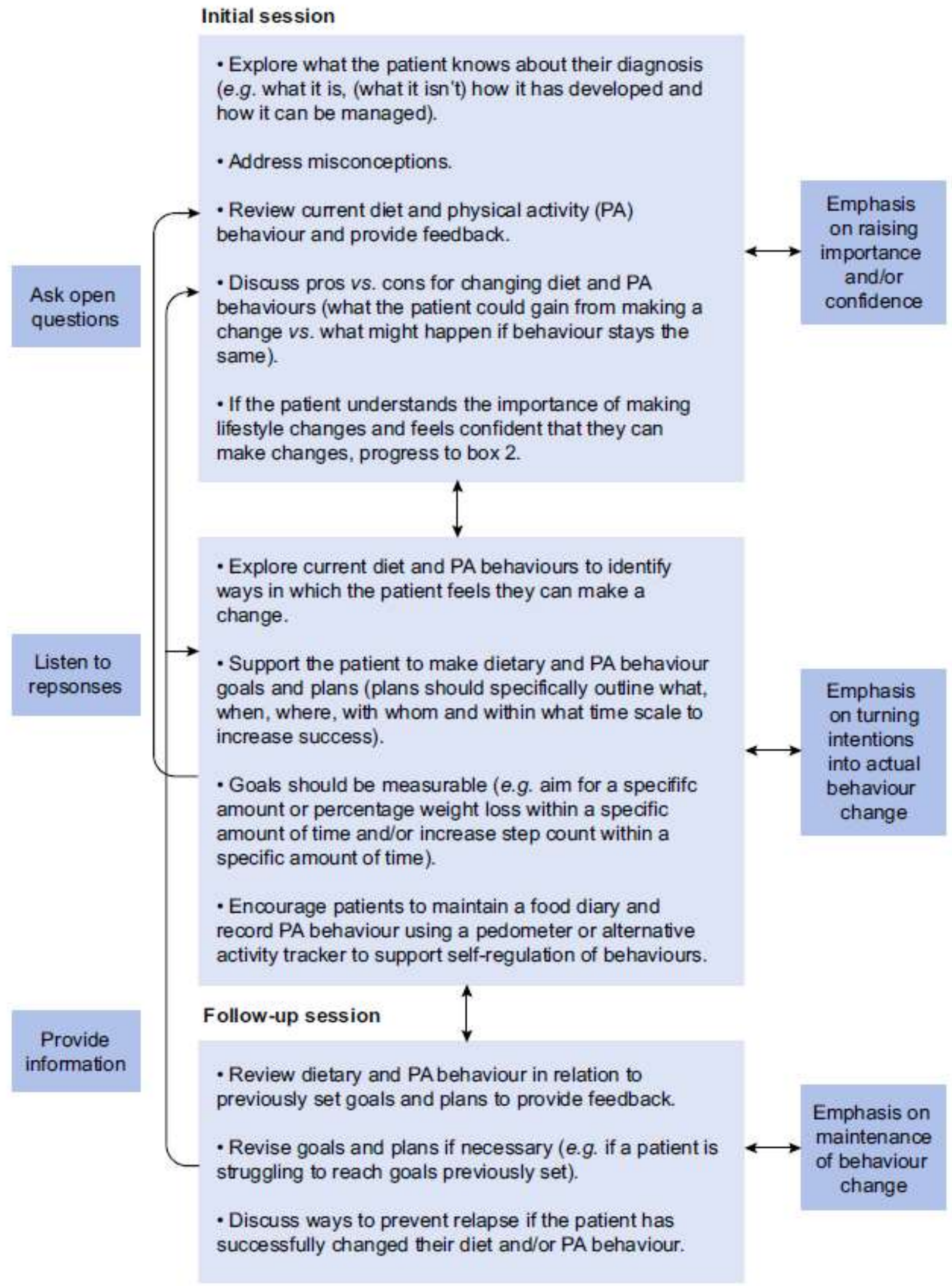
***Grade B strong consensus 100% agreement**

Bischoff SC et al. Clinical Nutrition 2022

Behavioral aspects of lifestyle modification

A practical guide for behavioral therapy in the lifestyle treatment of NASH.





Wharton S et al. CMAJ 2020

Hallsworth K et al. Curr Gastroenterol Rep 2016

IFSO NAPOLI 2023

CULINARY MEDICINE
FOR HEALTHCARE PROVIDERS & PATIENTS

https://diabetesalacarta.org/recetas/hamburguesa-de-sardina/

IFSO

Clínic Barcelona | UNIVERSITAT DE BARCELONA

Conclusions

- Potential therapeutic role of a "high quality healthy diet" to improve hepatic steatosis and metabolic dysfunction in patients with NAFLD, independent of caloric restriction and weight loss.
- The limited data suggest that MD may be an effective dietary approach.
- Prevention and management of sarcopenia are essential.
- Further studies, which robustly evaluate the effects of interventions on dietary intake, acceptability and sustainability of the interventions, and QoL and other patient-related outcomes are needed to support effective care delivery (personalized nutrition intervention).
- Motivation to change → Shared decision making → Adherence
- Develop innovative strategies to implement lifestyle as a therapy in everyday clinical care – sustainability (Culinary Medicine)

Thank you for your attention!

Clínic Barcelona | Universitat de Barcelona

IFSO NAPOLI 2023

SEDYN Sociedad Científica Española de Dietética y Nutrición

seco sociedad española de cirugía de la obesidad

@Violetamoize

@HospitalClinic

vmoize@clinic.cat

@violetaMoize