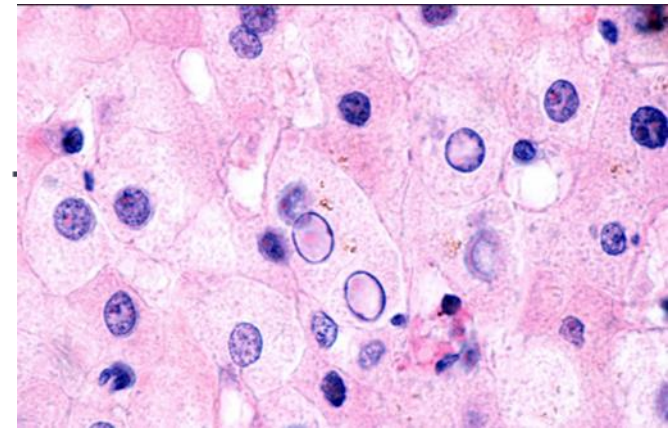




THEME II: Modern trends, new science
Hosted by Kamran Abbasi, The BMJ



Non-alcoholic fatty liver disease

Metabolic-associated steatotic liver disease



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President AEEH



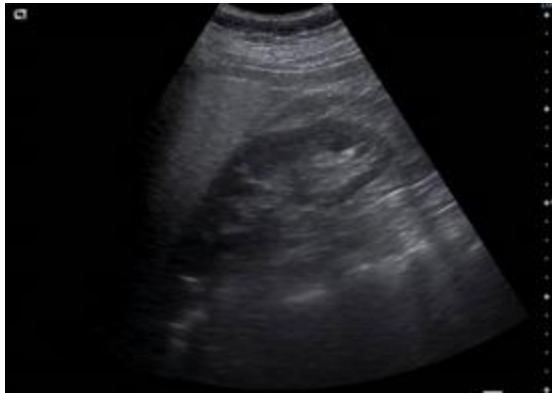
Conflict of interest

DISCLOSURES

- Consulting for: Alpha-sigma, Allergan, BMS, Boehringer-Ingelheim, Intercept, Innventia, Julius Clinical; Kaleido, MSD, Pfizer, Prosciento, Rubió, Shionogi, Siemens, Sobi, Thera, Zydus.
- Research Grants: Gilead, Intercept, Siemens, Theratechnologies, Echosens; NovoNordisk
- European funding programs: FP7 (FLIP), IMI2 (LITMUS), IHI3 (Grip-on-NASH)

Opinions expressed here are solely based on my own personal academic view and are intended to stimulate intellectual debate and not in any direct or indirect way drug prescription, clinical trial enrollment or any investment action.

- 37 years-old woman attended the first time in 2014 in our hepatology clinic due to altered liver function test
- No alcohol consumption. Smokes 6-7 cigarettes/day. Working on as office assistant.
- Blood test: normal blood count, liver biochemistry: AST 70 U/L, ALT: 112 UI/L; GGT: 26 U/L; AP: 87 U/L
- Any causes other than MASLD were ruled out.



Macro-micro steatosis in 70% of hepatocytes: **S3A0F0**
No inflammation no ballooning no fibrosis.
Bland steatosis No steatohepatitis

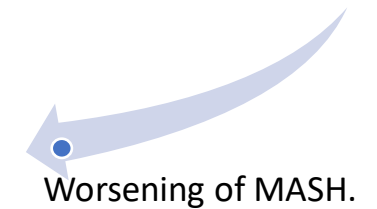
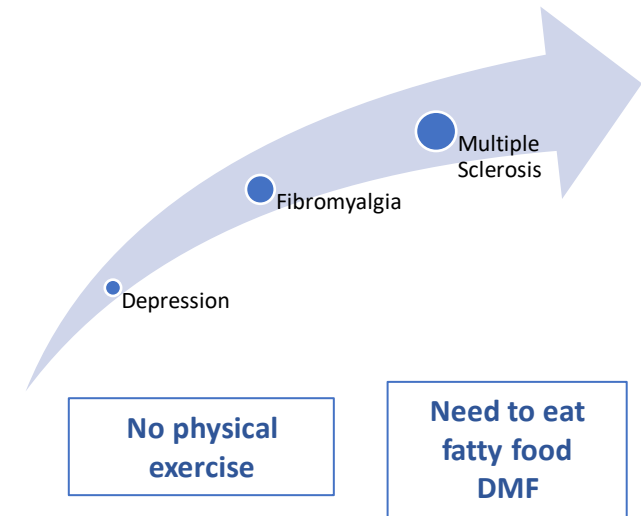
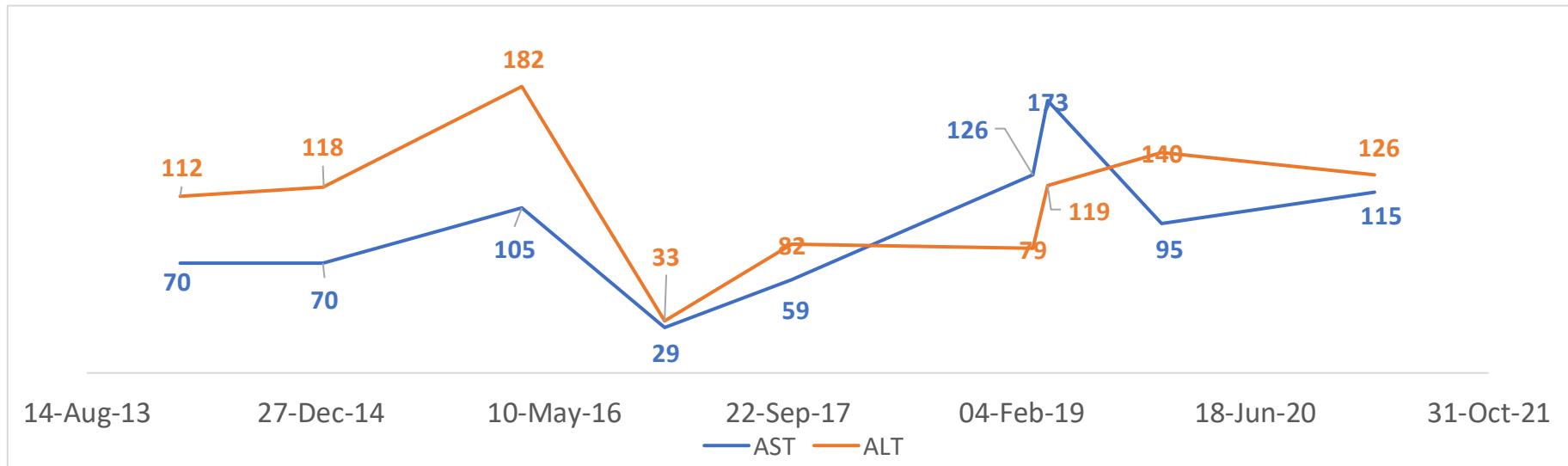
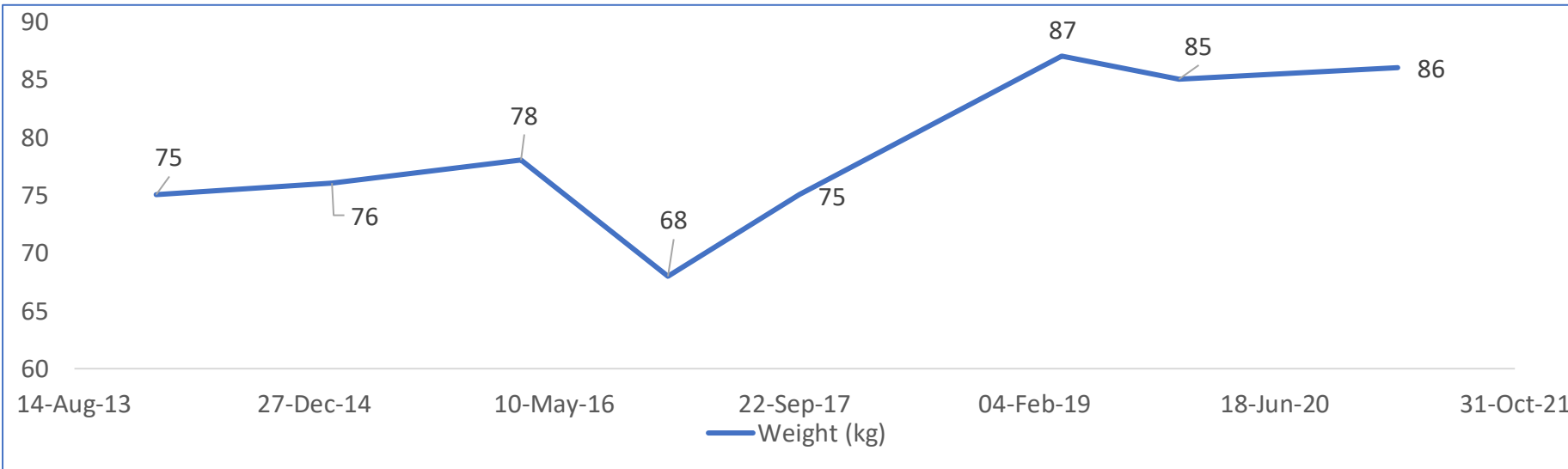
Disease progression: AST, ALT, stiffness & body weight

Transient elastography (kPa):
CAP

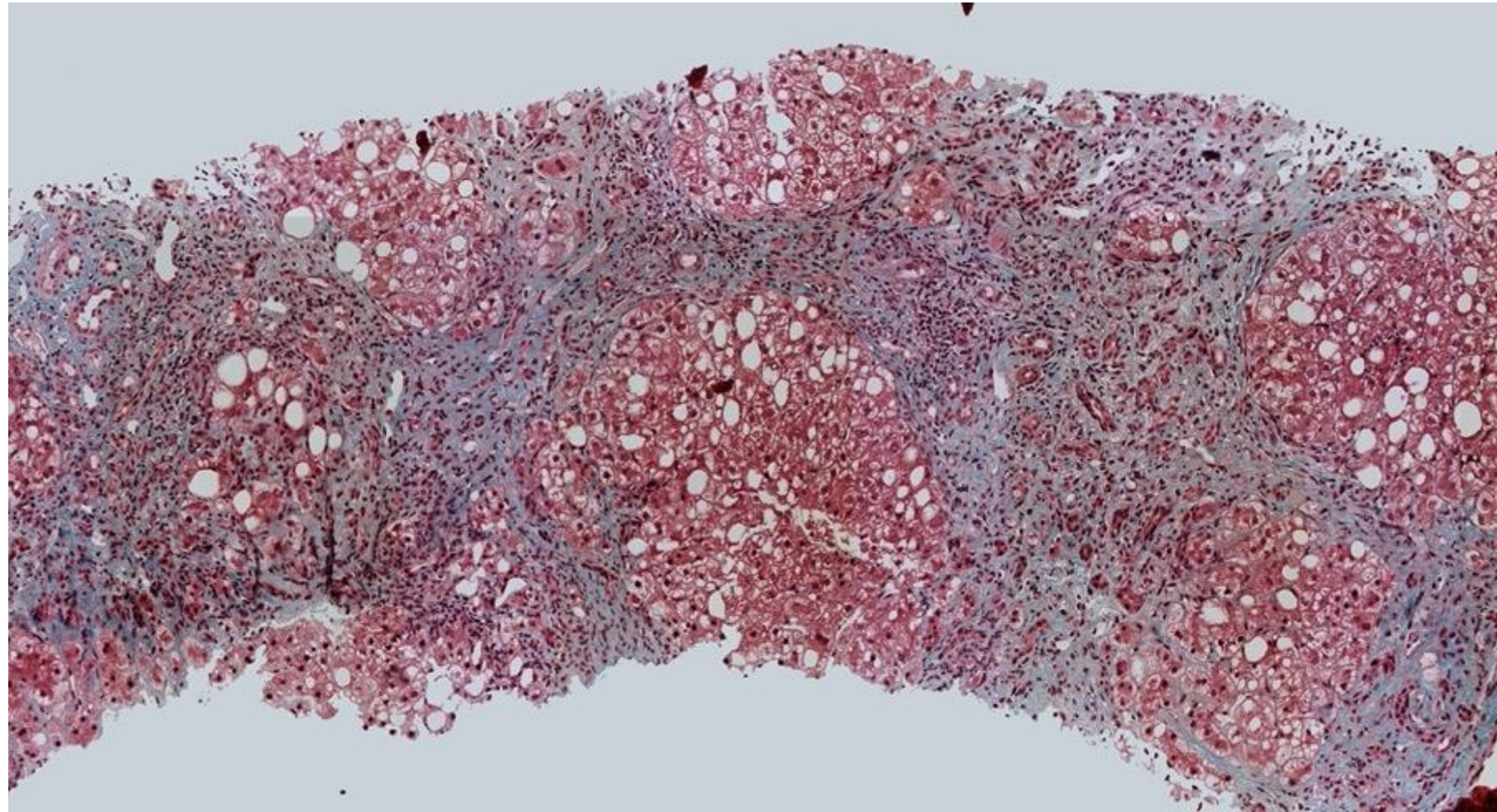
5.8 kPa
NA

9,7 kPa
363 dB7m

17.4kPa
334 dB7m



Second liver biopsy in May 2021



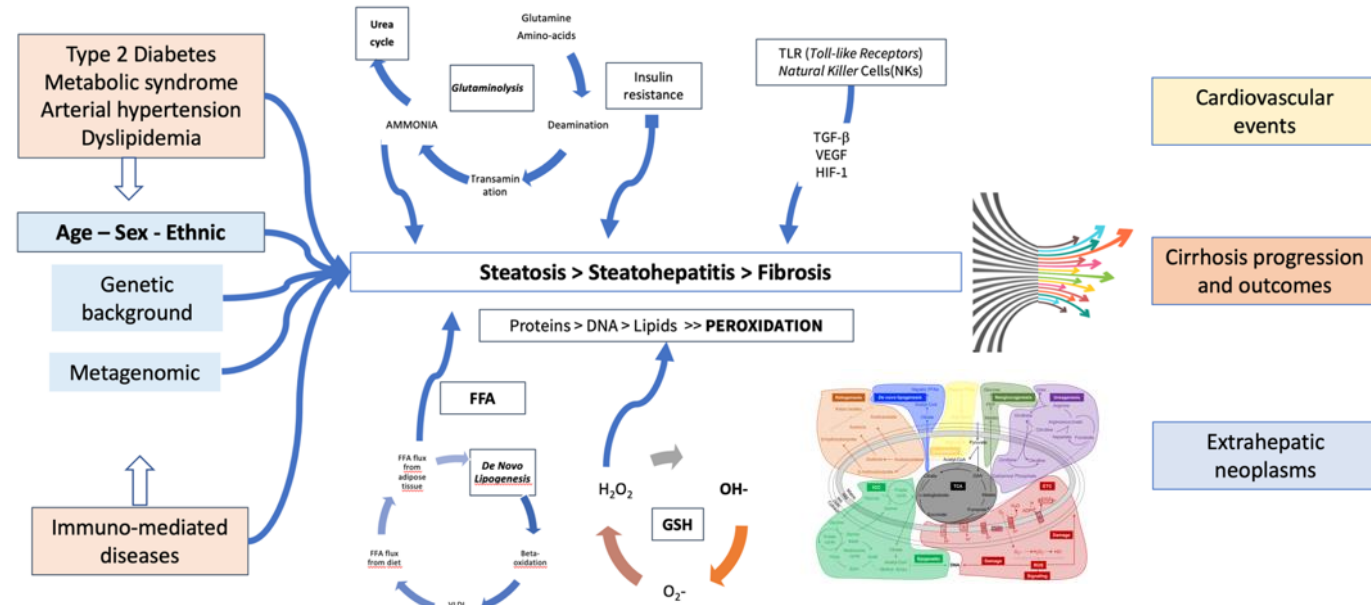
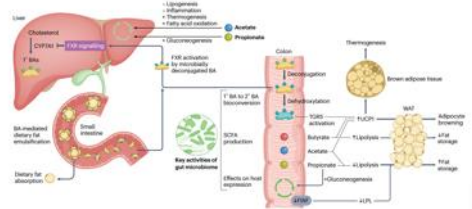
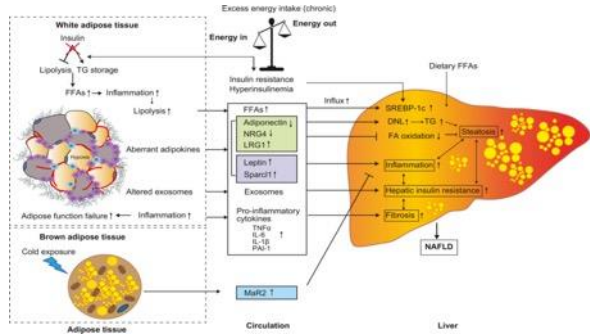
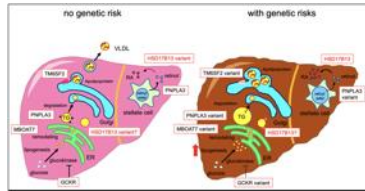
Nutrition and
diet could be
the solution and
the cause of
MASLD

Liver biopsy: Macrovesicular steatosis (75%) with ballooning and lobular inflammation with bridging portal-sinusoidal fibrosis. No iron deposits.

Precirrhotic disease:

S3A2F3

MASLD progression



Cardiovascular events

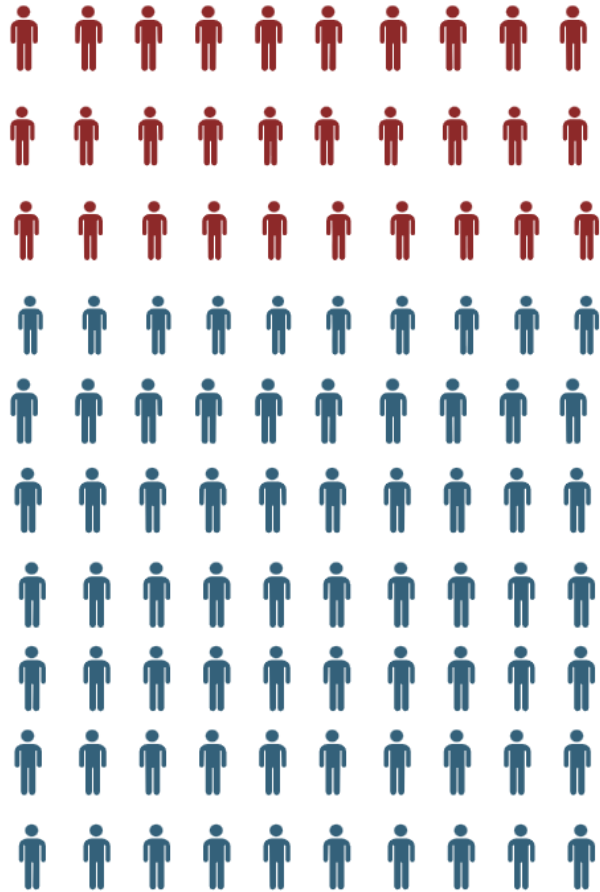
Cirrhosis progression and outcomes

Extrahepatic neoplasms

Romero-Gómez M. Med Clin 2022; Aron-Wisniewsky J et al. NRGH 2020; 17:219; Carmody RN et al. Nat Rev Microbiol 2023; Tilg et al. Nat Metab 2021; 3:1596 Lee et al. J Hepatol 2023; Morio B et al. Cell Calcium 2021;94: 102336

Prevalence of MASLD in general population, obese people and type 2 diabetes

GENERAL POPULATION



30%

OBESE PEOPLE



80%

by 3.5 times

TYPE 2 DIABETES



65%

MASLD continues to be neglected

- Lack of awareness and education about preventing the disease, among the public as well as physicians
 - Under-diagnosis and under-reporting by physicians in Europe, USA and Australia
- NAFLD is barely mentioned in international and national guidelines on obesity and type 2 diabetes and is missing from the World Health Organization webpage on obesity complications (https://www.who.int/health-topics/obesity#tab=tab_2)
- No globally accepted, evidence based practical dietary recommendations for the prevention of NAFLD.

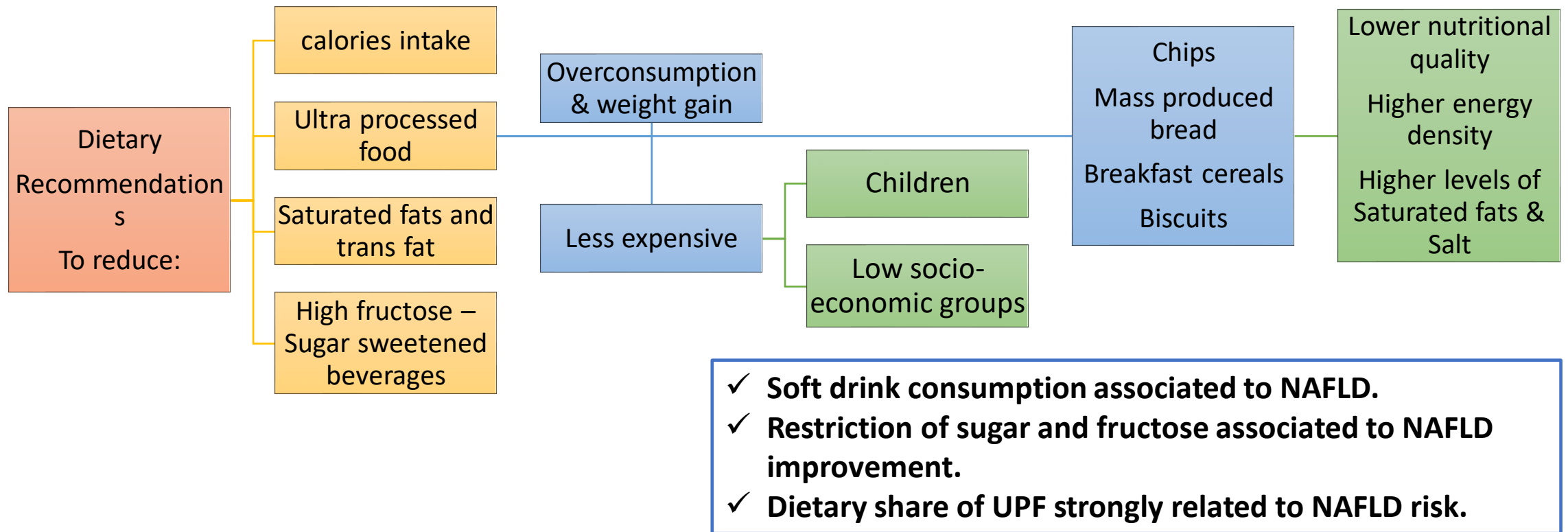
Lazarus et al. Nat Rev Gastroenterol Hepatol 2021;18:717-29

Alexander et al. BMC Med 2018;16:130

Patel et al. Intern Med J 2018;48:144-51



Modification of dietary habits



Weight Loss Through Lifestyle Modification Significantly Reduces Features of Nonalcoholic Steatohepatitis

Eduardo Vilar-Gomez,^{1,2} Yadina Martinez-Perez,¹ Luis Calzadilla-Bertot,¹ Ana Torres-Gonzalez,³ Bienvenido Gira-Oramas,³ Licet Gonzalez-Fabian,³ Scott L. Friedman,⁴ Moises Diago,³ and Manuel Romero-Gomez²

Weight loss is the ultimate and sufficient treatment for NASH (and fibrosis)

N=293

Diet Intervention

- Low-fat, average-protein diet (22% fat, 14% protein, and 64% carbohydrate).
- Saturated fat <8%, dietary fiber >20 g/d, and cholesterol <150 mg/1000 kcal.
- 3-day dietary food records completed at baseline and at 8, 16, 24, 32, 40, and 52 weeks.

Physical Activity

- ≥200 minutes per week, gradual increase from 90 minutes to 200 minutes of moderate intensity exercise per week during the first 6 months.
- Baecke physical activity questionnaire (16 items) at 8, 16, 24, 32, 40, and 52 weeks.

Behavioral Sessions

- Baseline: recommendations from research dietitians.
- Follow-up: 2 hours individual meeting every 8 weeks during the first 6 months, 2-hour group sessions every 8 weeks for 6 additional months.
- Education program emphasizing diet compliance and exercise was implemented

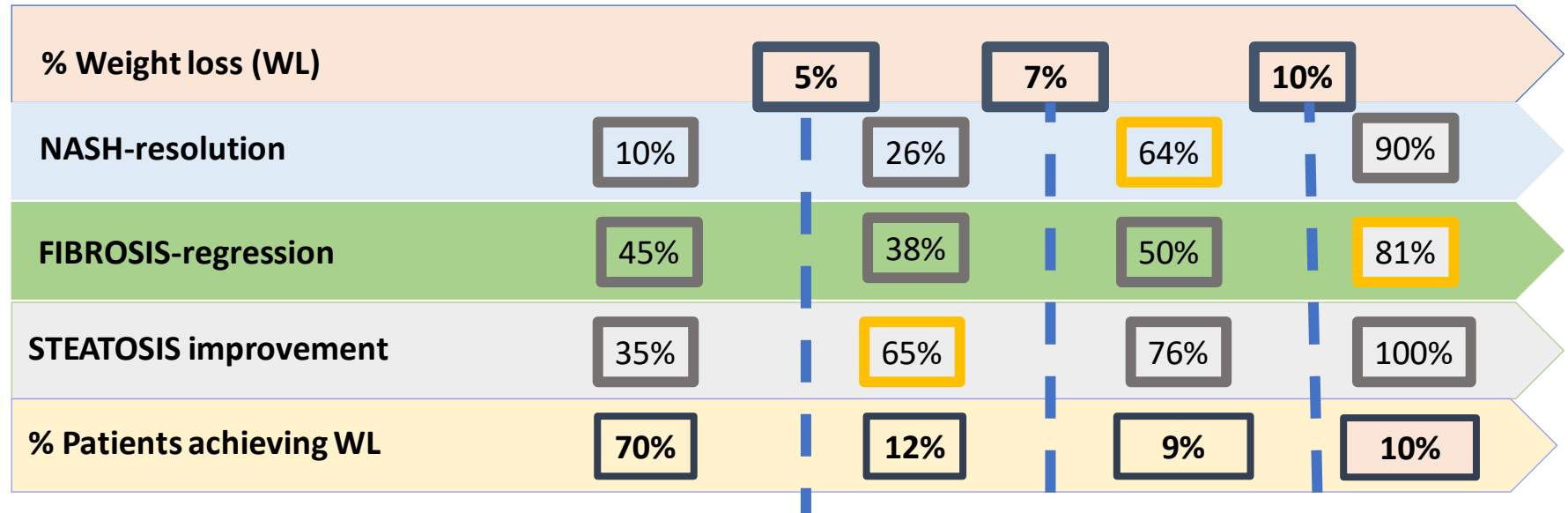


Table 2. Improvement of Histologic Outcomes Across Different Categories of Weight Loss at the End of Treatment

Variables	Overall (n = 293)	WL <5 (n = 205)	WL = 5–6.99 (n = 34)	WL = 7–9.99 (n = 25)	WL ≥10 (n = 29)	P value
Weight loss, %	3.8 ± 2.7	1.78 ± 0.16	5.86 ± 0.09	8.16 ± 0.22	13.04 ± 6.6	—
Resolution of steatohepatitis ^a	72 (25)	21 (10)	9 (26)	16 (64)	26 (90)	<.01

Impact of diet and nutrition on natural history of the disease

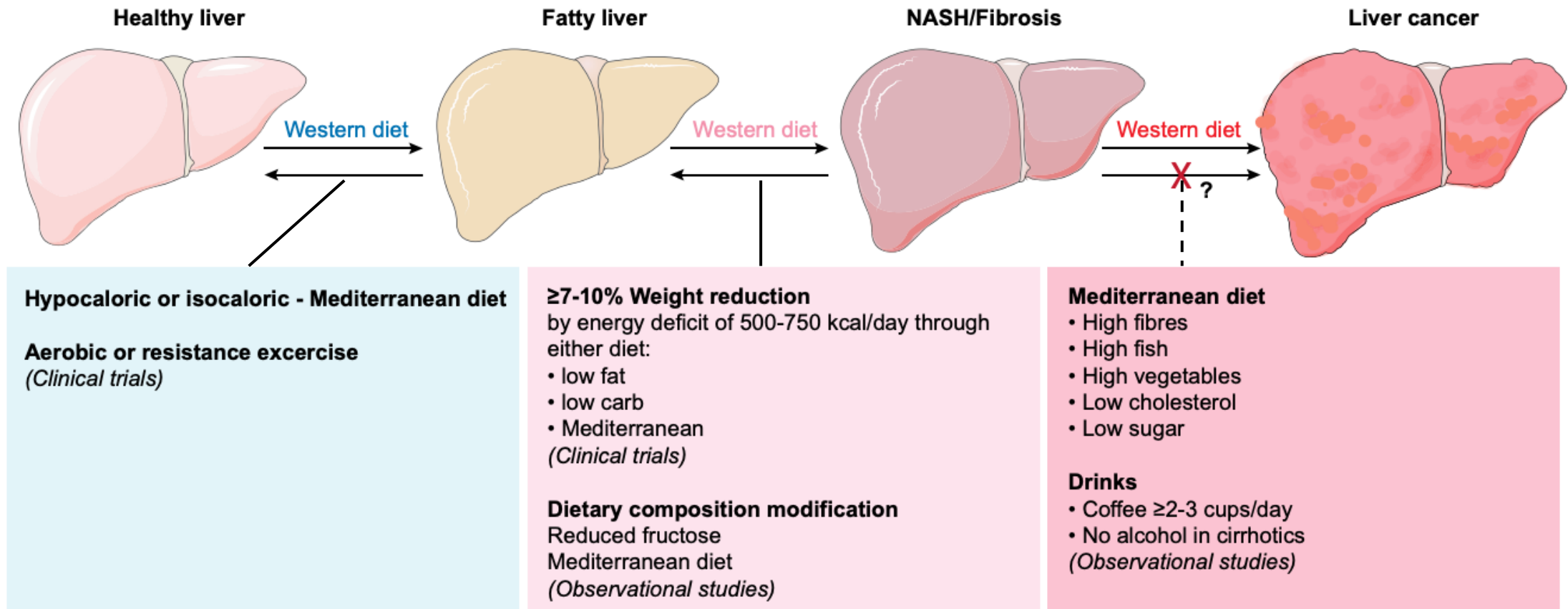


Fig. 1. A summary of the nutritional treatment options (based on clinical trials or observational studies) through the course of NAFLD. Remission of steatosis can occur with weight reduction achieved by several types of diet or with isocaloric Mediterranean diet (which induces metabolic and anti-inflammatory benefits), as indicated by clinical trials. For remission of NASH or fibrosis, there is no evidence from clinical trials for a benefit of merely improving dietary composition, while there is evidence that at least 7% weight reduction is needed. For prevention of progression to liver cancer, the evidence regarding certain foods and nutrients is derived only from large observational studies and needs further confirmation.

The role of nutrition in non-alcoholic fatty liver disease: Pathophysiology and management

Genoveva Berná¹ | Manuel Romero-Gomez²



Nutrients that promote NAFLD: UPF, SFAs: saturated fatty acids; Trans FAs: trans fatty acids.



Dietary patterns

Western dietary

Mediterranean Diet (MD)

Foods intake

- ❖ Processed foods
- ❖ Red meats
- ❖ Processed meats
- ❖ Sugary beverages
- ❖ Snacks
- ❖ cakes and biscuits
- ❖ eggs
- ❖ butter

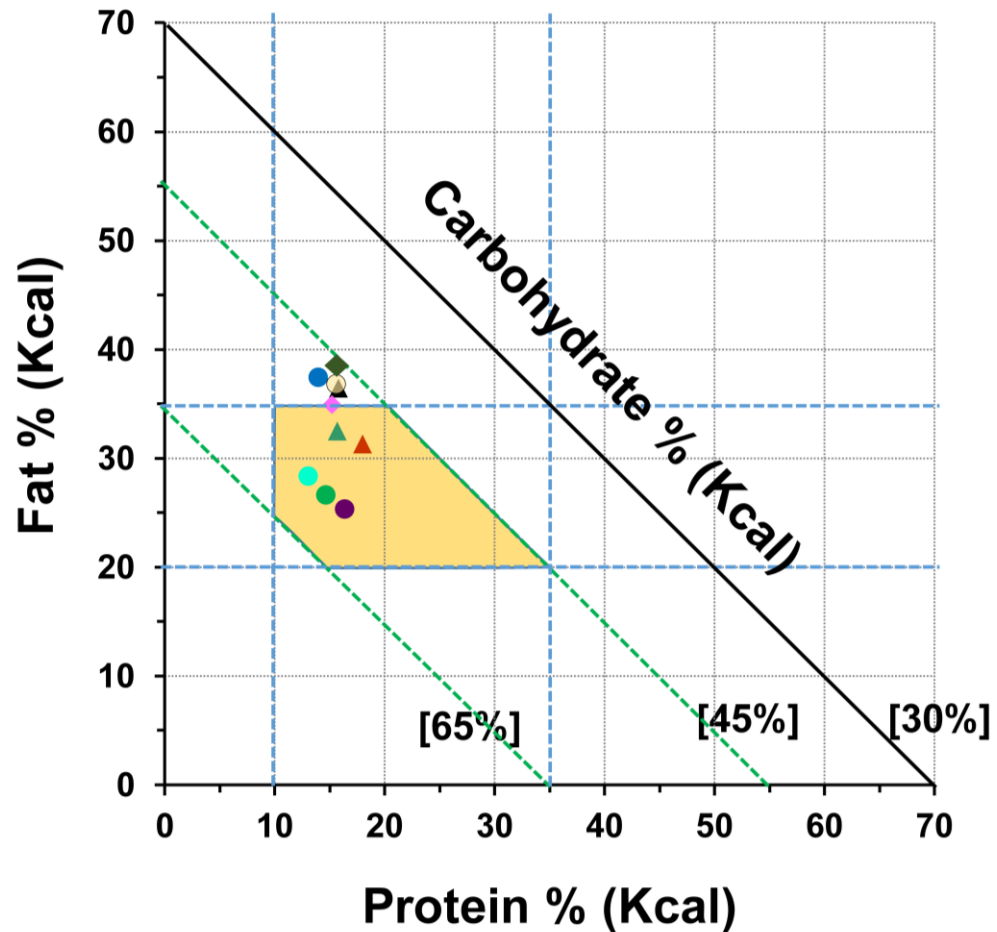
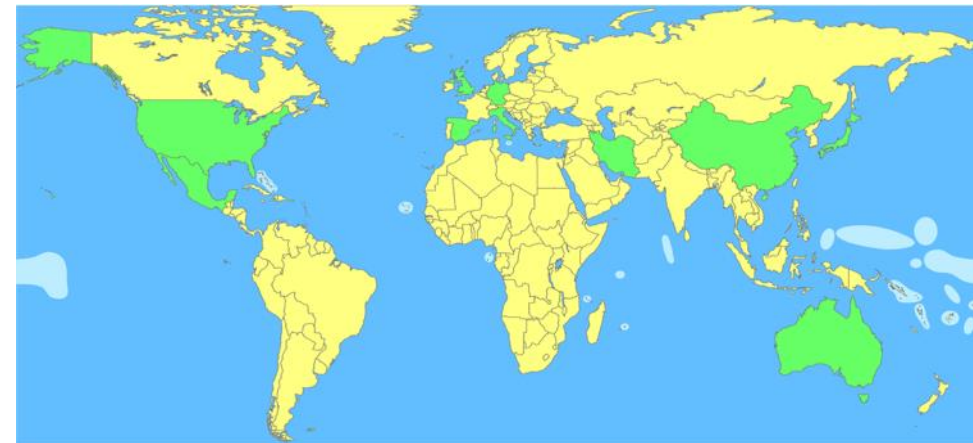
- ❖ Extra virgin olive oil
- ❖ Vegetables and Fruits
- ❖ Cereals, legumes, nuts
- ❖ Moderate intakes of fish and other meat, dairy products and red wine
- ❖ Low intakes of eggs and sweets.

Nutrients

- ↑Energy intake
- ↑SFA
- ↓PUFA
- ↑protein animal
- ↑sugar, fructose
- ↑cholesterol
- ↑Salt
- ↓fiber

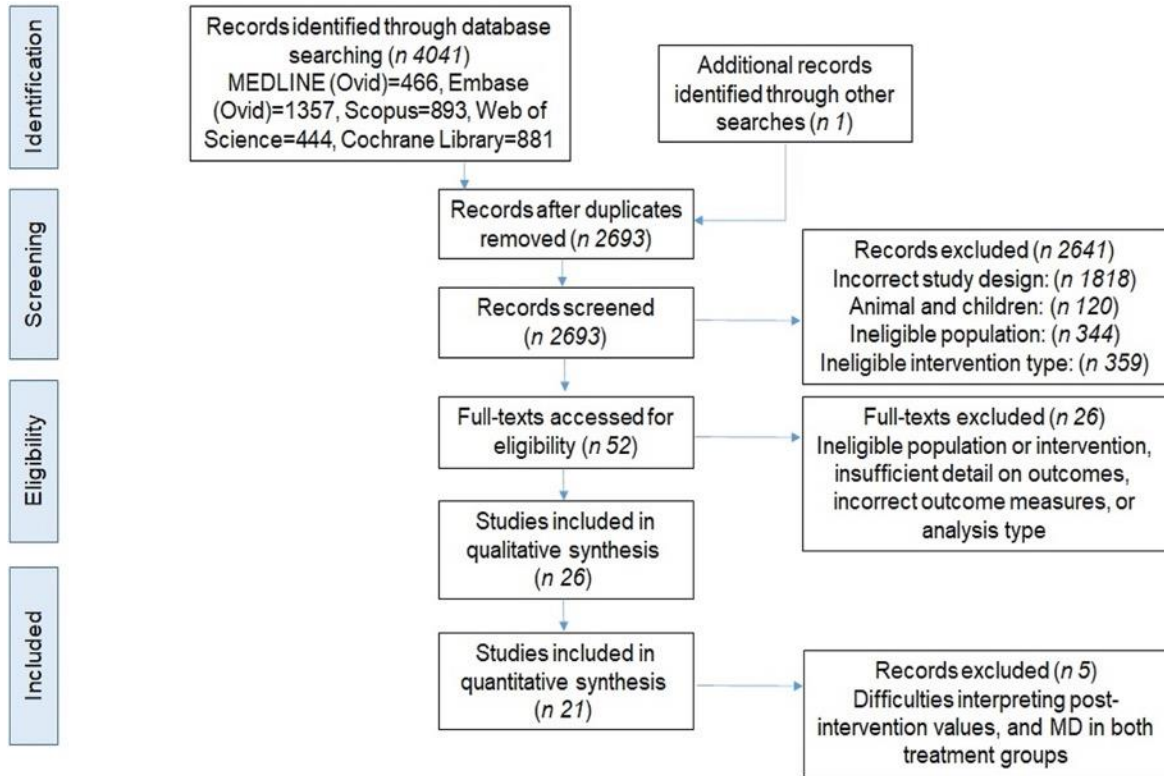
- ↓SFA
- ↑MUFA
- ↑PUFA
- ↑protein vegetables
- ↓sugar fructose
- ↓cholesterol
- ↑fiber
- ↑polyphenols,
- ↑carotenoids

**Micronutrients > macronutrients
> food > meals > patterns**



- ◆ Spain (ANIBE study)
- China (Fifth National Nutrition Survey)
- Japan (National Health and Nutrition Survey)
- ▲ Italy (Third National Food Consumption Survey)
- ▲ USA (NHANES 2017–2018)
- ▲ Australia (Australian Health Survey)
- ◆ UK (NDNS)
- German (NEMONIT)
- Mexico (Mexican National Health and Nutrition Survey)
- Iran (Isfahan Cohort Study)

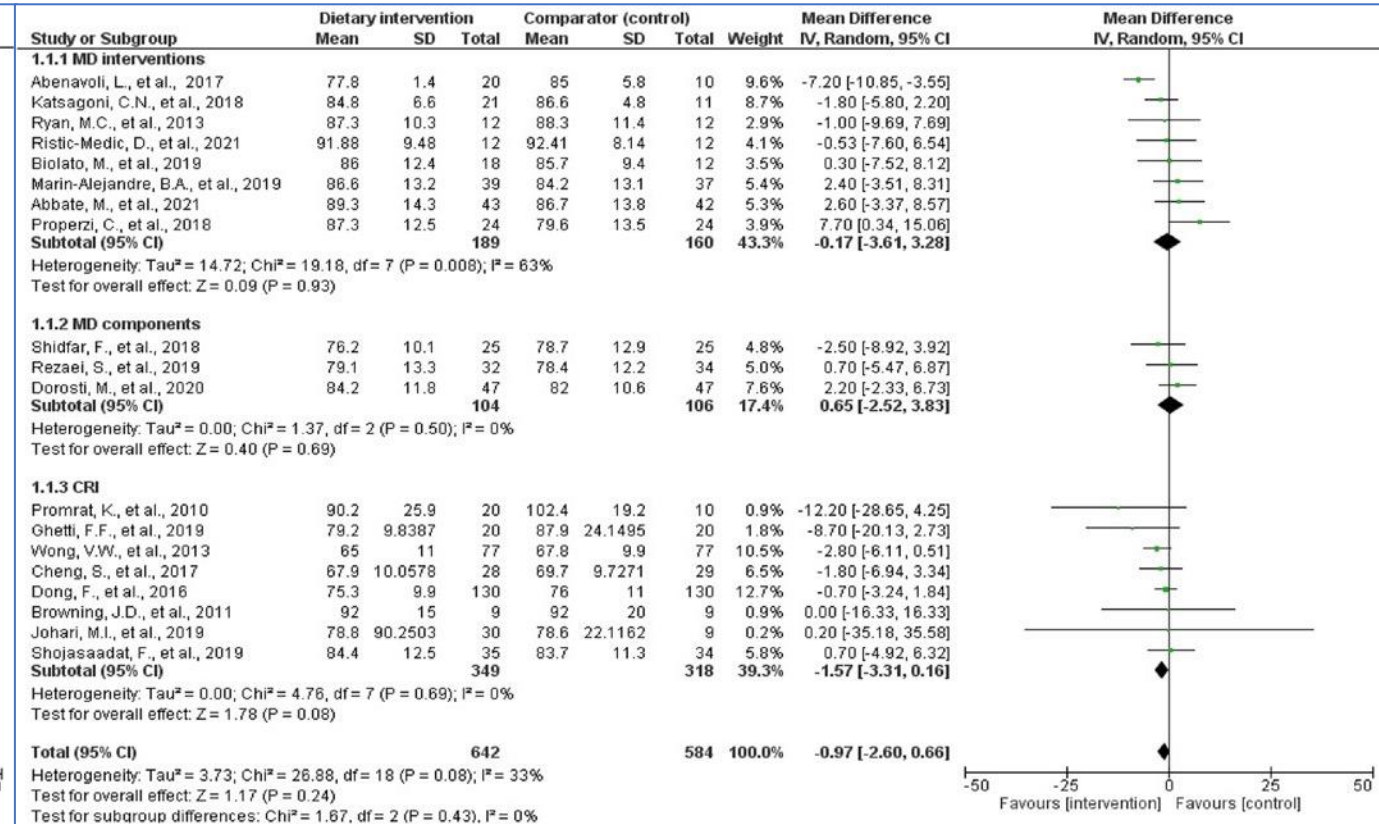
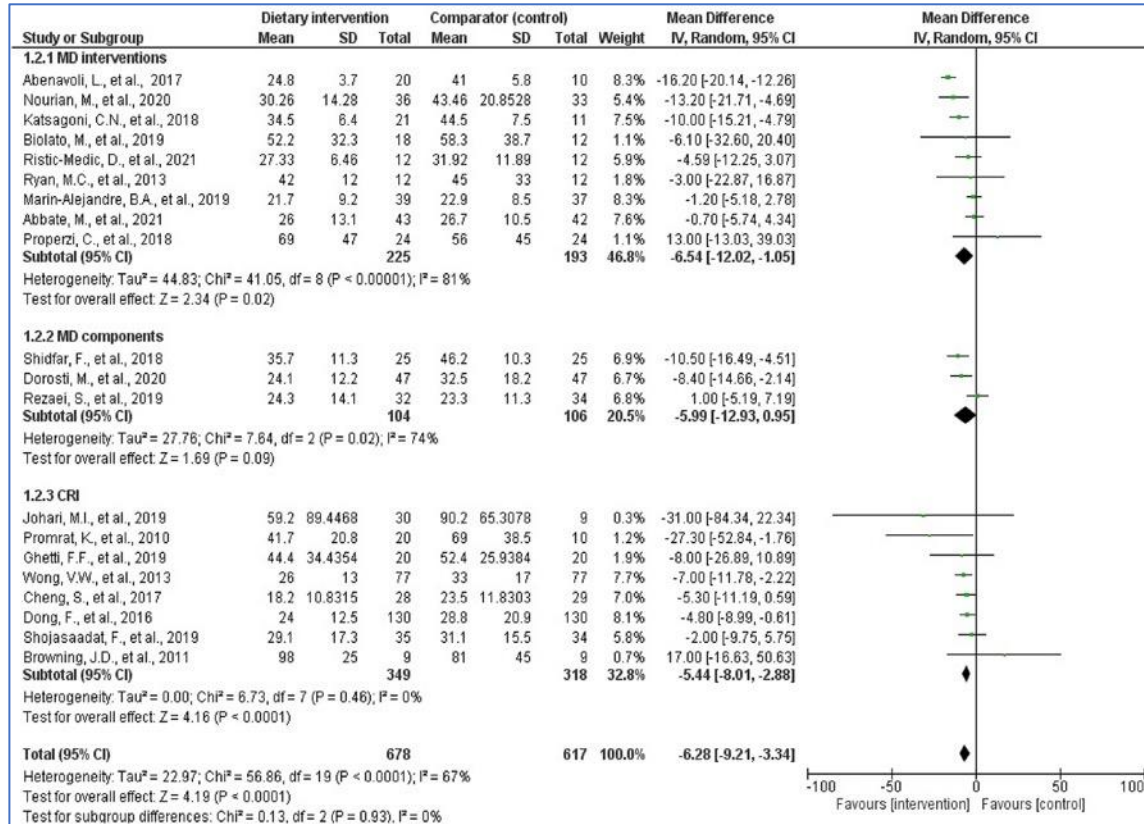
The effectiveness and acceptability of Mediterranean diet and calorie restriction in non-alcoholic fatty liver disease (NAFLD): A systematic review and meta-analysis



Study ID	D1	D2	D3	D4	D5	Overall	
Properzi 2018, Australia	+	-	+	+	+	-	+
Katsagoni 2018, Greece	!	!	+	+	+	!	!
Misciagna 2017, Italy	!	!	+	+	+	!	
Abenavoli 2017, Italy	!	+	+	+	+	!	
Marin-Alejandro 2019, Spain	!	+	-	+	!	-	D1 Randomisation process
Ristic-Medic 2021, Serbia	!	+	-	+	+	-	D2 Deviations from the intended interventions
Nourian 2020, Iran	!	+	-	+	+	-	D3 Missing outcome data
Abbate 2021, Spain	!	!	+	+	!	!	D4 Measurement of the outcome
Yaskolka Meir 2021, Israel*	!	!	+	+	+	!	D5 Selection of the reported result
Willmann 2019, Germany*	!	+	-	+	+	-	
Dorosti 2020, Iran	!	+	-	+	+	-	
Shidfar 2018, Iran	!	+	-	+	+	-	
Rezaei 2019, Iran	!	+	+	+	!	!	
Wong 2013, Hong Kong	+	+	+	+	+	+	
Dong 2016, China	!	+	+	+	+	!	
Promrat 2010, USA	!	-	+	+	+	-	
Cheng 2017, China	!	+	+	+	!	!	
Johari 2019, Malaysia	!	+	+	+	+	!	
Shojasaadat 2019, Iran	!	-	+	+	+	-	
Ghetti 2019, Brazil	!	-	+	+	+	-	
Holmer 2021, Sweden*	+	+	+	+	+	+	

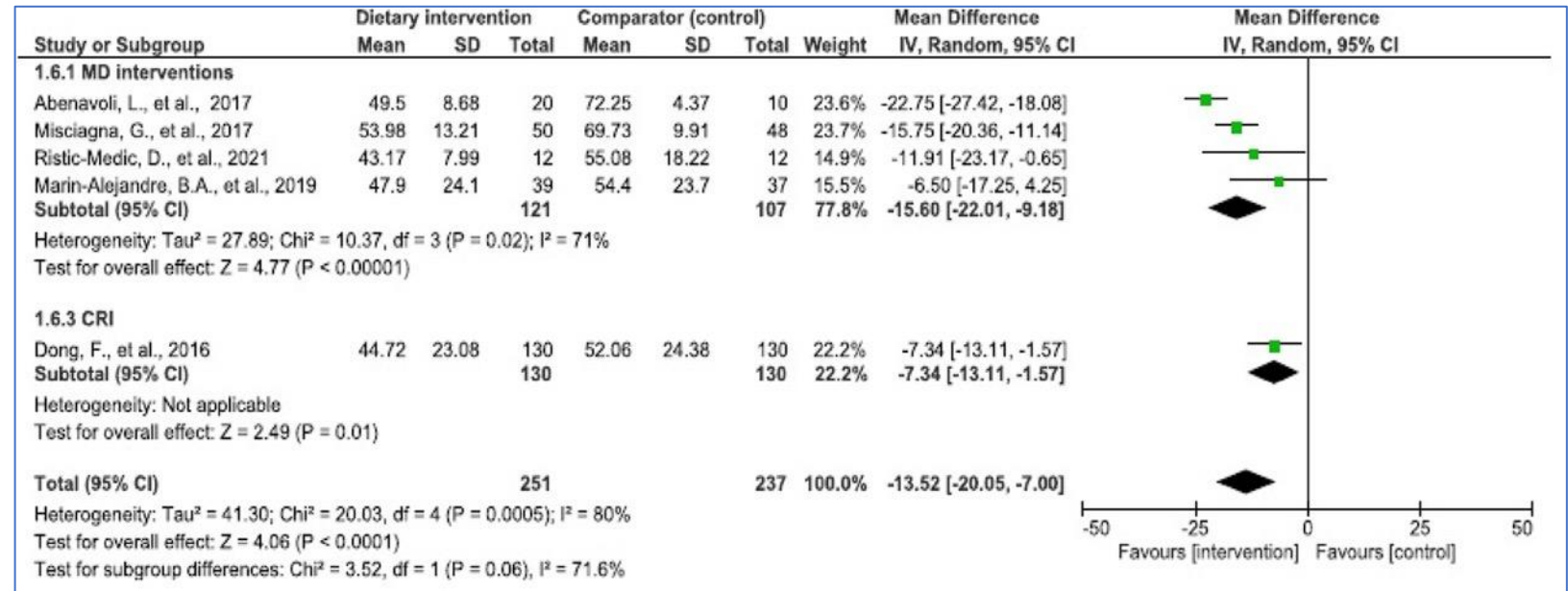
Effects of dietary interventions on ALT (n=1295)

Effects of dietary interventions on body weight (n=1226)

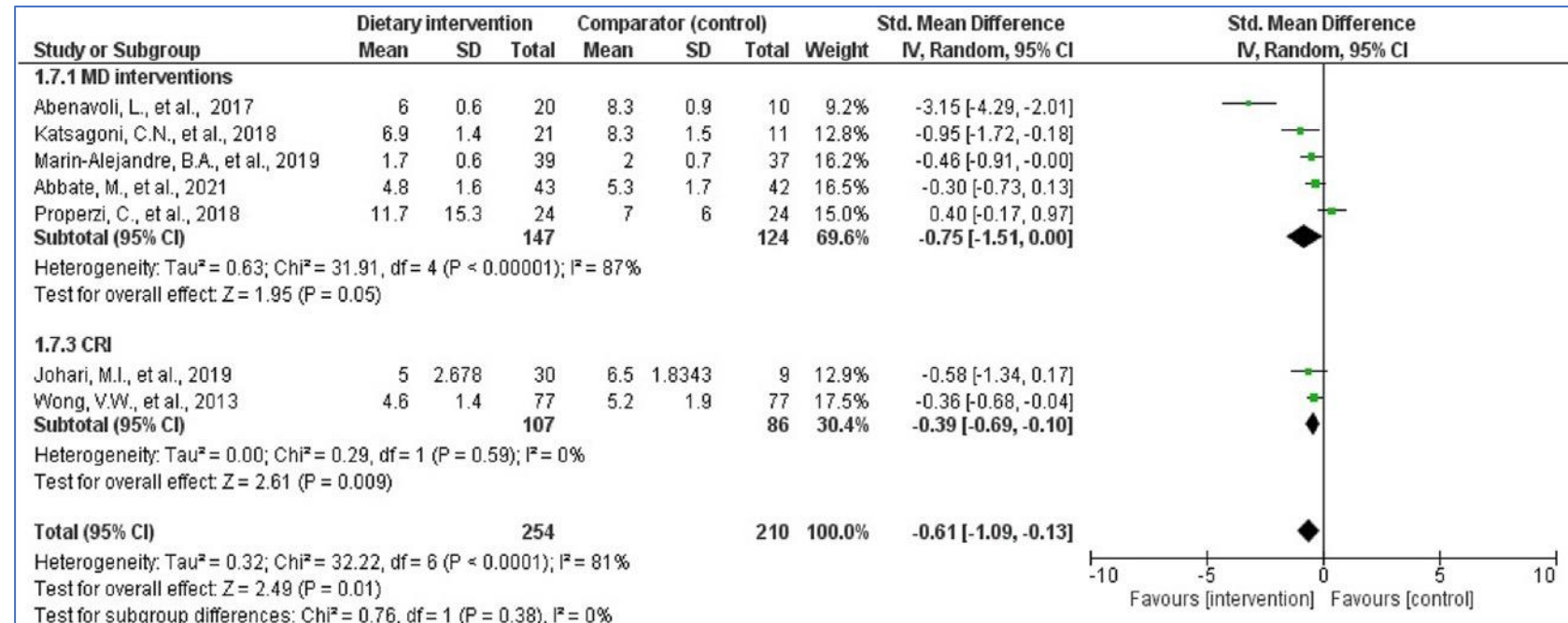


SD, standard deviation; IV, inverse variance; CI, confidence interval; MD, Mediterranean diet; CRI, calorie restricted interventions.

Effects of dietary interventions on Fatty Liver Index (n=488)

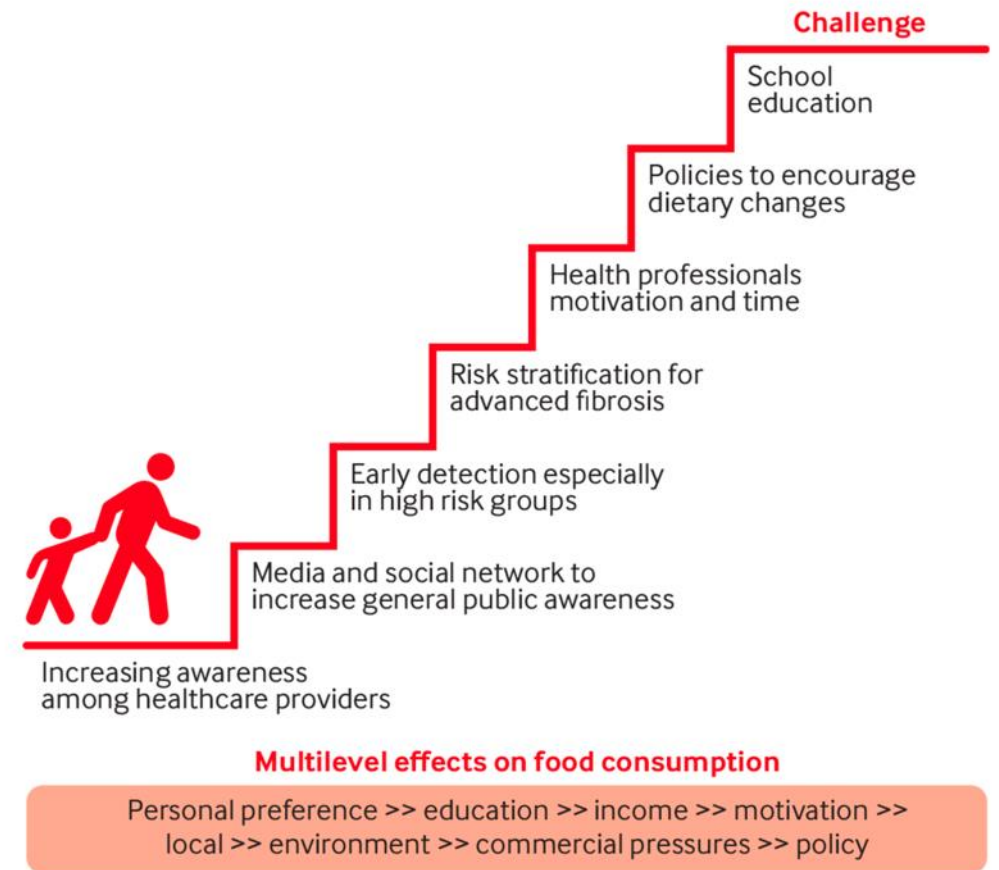
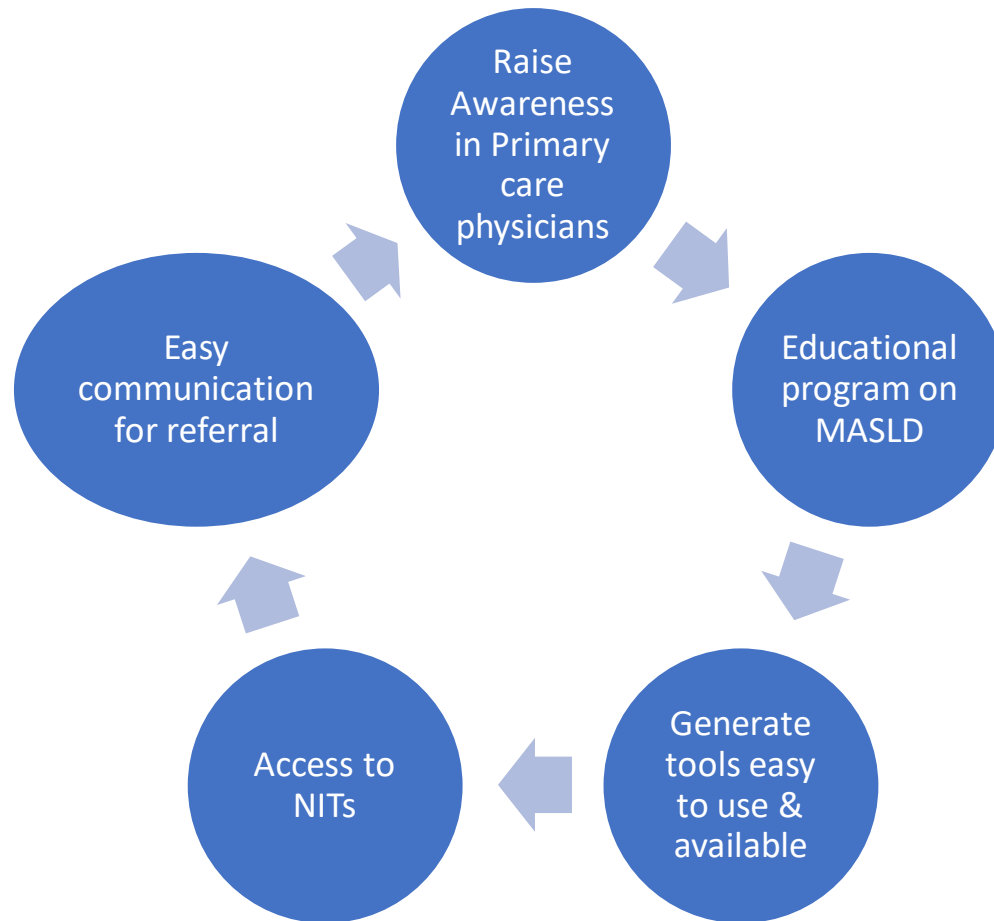


Effects of dietary interventions on Transient Elastography (LSM) (n=464)



A societal approach to preventing NAFLD

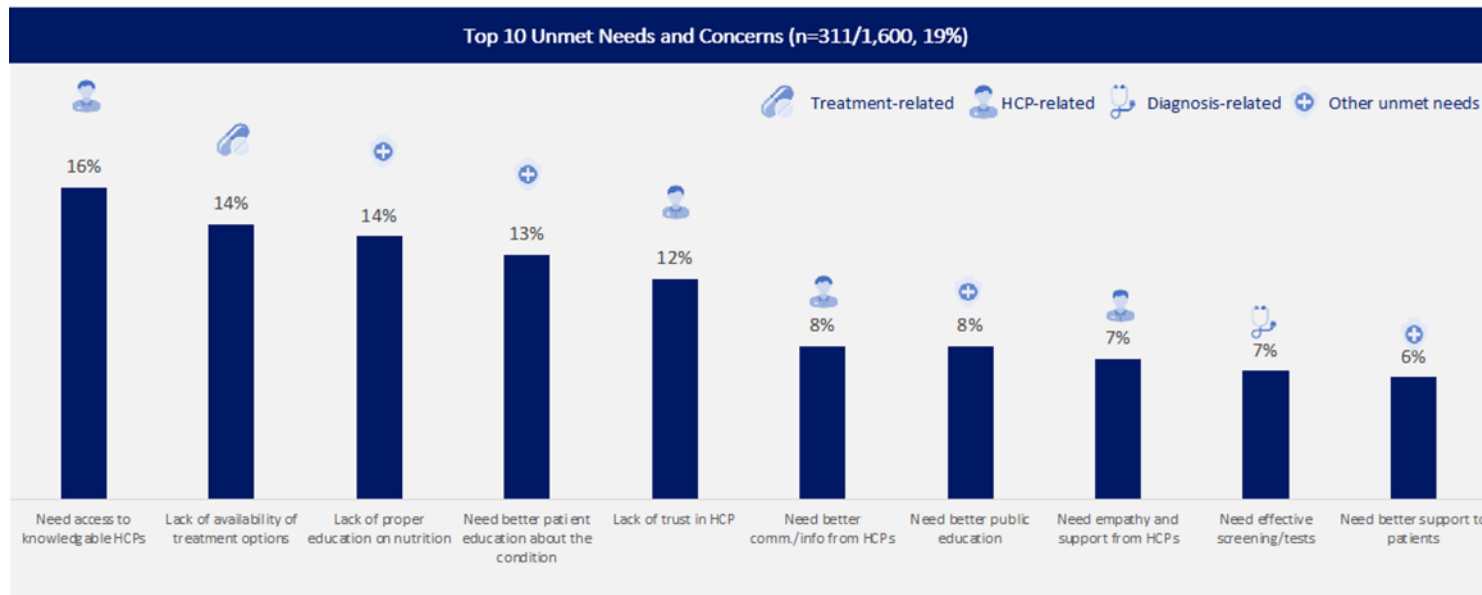
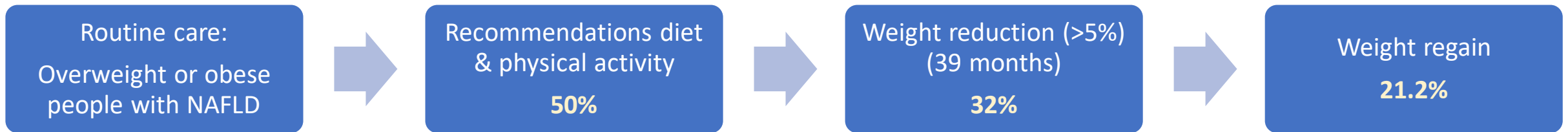
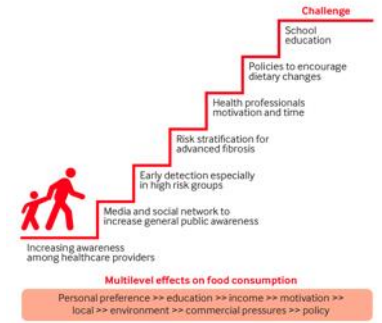
i. Prevention, early detection and referral



A societal approach to preventing NAFLD

ii. Patient centered multidisciplinary care for NAFLD:

- a. Educational programs
- b. Public health campaigns:
 - i. Interventions in families and primary schools
 - ii. Social media & internet



By listening to the voices of people living with NAFLD, the community of practice can grow and develop more effective ways to help them manage their condition

Lazarus et al. AASL2023

Malespin et al. Clin Gastroenterol Hepatol 2021;

A societal approach to preventing NAFLD: Reformulation of unhealthy foods

ii. Patient centered multidisciplinary care for NAFLD:

i. Regulate advertising and marketing:

- i. Front of package labelling system
- ii. Limiting promotion of sugar and fat.
- iii. To reduce children exposure
- iv. Taxation on unhealthy foods

Most policy evaluations are observational in nature

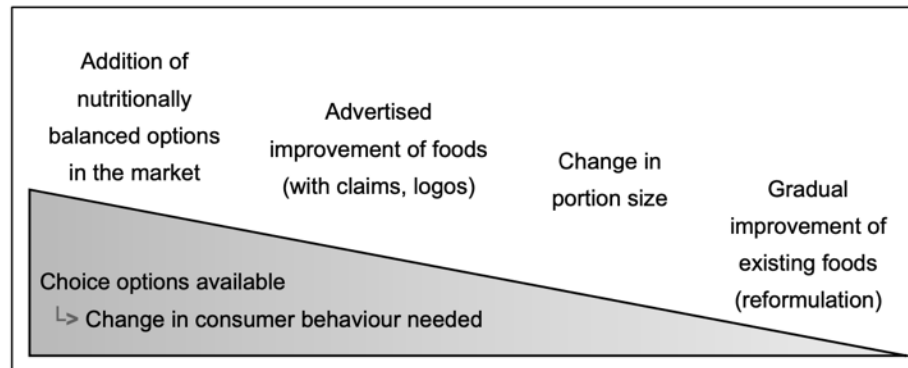


Figure 1. Classifications of strategies changing the characteristics of food available for a population along a gradient of change in consumer behaviour needed to get a benefit from the new food products.

UK parliament
British liver Trust
Liver Cancer UK

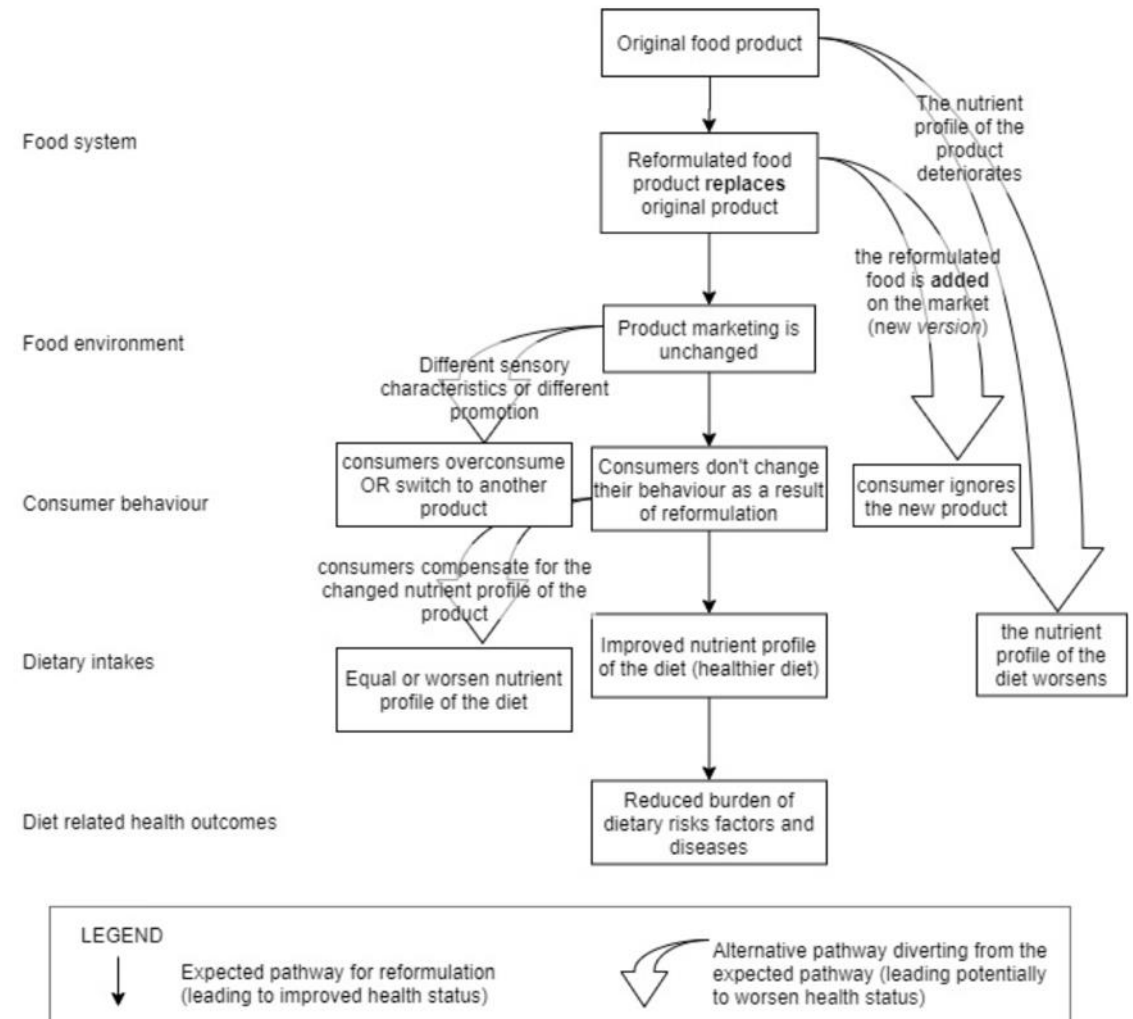


Figure 2. Logic model of the effect of reformulating existing food products, and sources of diversion from the expected health benefits.

A societal approach to preventing NAFLD

iii. Nutrition and dietary guidelines for NAFLD prevention

- a. To reach general population
- b. To reach health professionals
- c. To promote multidisciplinary teams
- d. Integration of NAFLD management in Diabetes and obesity guidelines.



No direct evidence linking food taxation to NAFLD risk

Taxation of sugar added foods & sugar sweetened drinks reduced SSB consumption but increased unhealthy food untaxed.

Specific taxes alone did not work and should be added to other taxes and subsidy for fruits and vegetables.

Tackling NAFLD necessitates a multifaceted approach requiring collaboration across governments, healthcare institutions, communities, families, and individuals.

Policy interventions when paired with individual efforts to adopt a healthy lifestyle, can help to prevent and control NAFLD.



Shira Zelber-Sagi



Elisabetta Bugianessi



Franz Martin



Bernat Soria

Post:

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