Clinical Practice Guidelines in

Non-alcoholic fatty liver disease

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General approach to the patient

- Weight loss
- Treatment of risk factors for cardiovascular disease
- Avoid alcohol consumption
- Hepatitis A and B vaccinations and pneumococcal vaccination for patients with chronic liver disease

General approach

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Weight loss

- A reasonable goal:
  - to lose 0.5 to 1 kg/week (1 to 2 lb/week).

- More rapid weight reduction may be associated with worsening of liver disease.

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Weight loss

- Options to promote weight loss:
  - lifestyle modifications
  - for patients who are candidates, bariatric surgery
  - Pharmacologic therapy ➔ can be used

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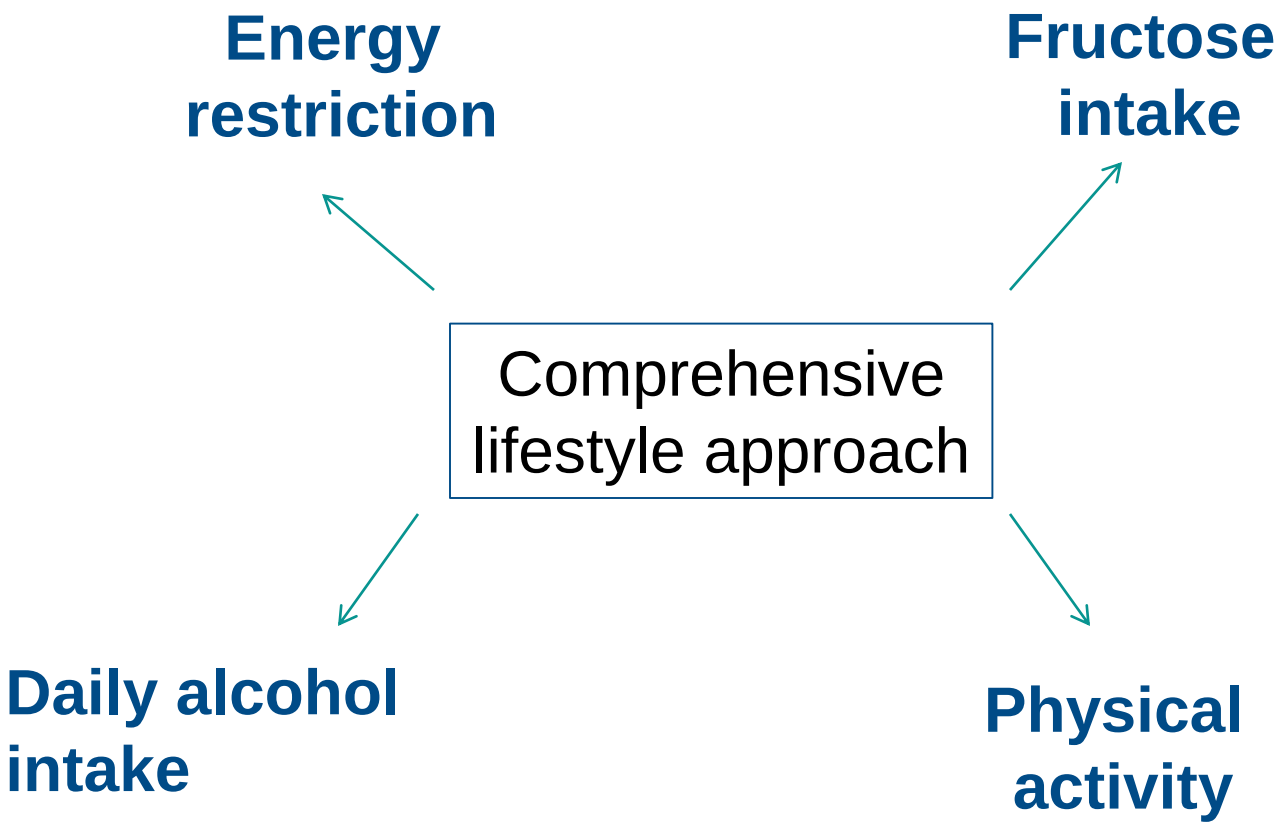
lifestyle modifications

Components of a lifestyle approach to NAFLD



lifestyle modifications

Energy restriction

- Calorie restriction
- 7–10% weight loss target
- Long-term maintenance approach

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lifestyle modifications

Fructose intake

- Avoid fructose-containing food and drink

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High fructose diet

- Soda
- Candy
- Sweetened Yogurt
- Salad Dressing
- Frozen Junk Foods
- Breads
- Canned Fruit
- Juice
- Sauces
- Breakfast cereal
- Jam and jelly
- Snack foods
- Coffee creamer
- Energy and sport drinks
- Ice cream

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lifestyle modifications

Physical activity

- 150–200 min/week moderate intensity in 3–5 sessions
- Resistance training to promote musculoskeletal fitness and improve metabolic factors

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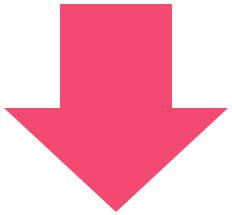
Weight loss and increased physical activity

sustained improvement in:



- liver enzymes
- Histology
- Serum insulin levels
- Quality of life in patients

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Treatment of risk factors for cardiovascular disease

- Optimization of blood glucose control in patients with diabetes
- Treatment of hyperlipidemia
- Statin therapy has been shown to be safe in patients with NAFLD

Alcohol consumption

- Heavy alcohol use is associated with disease
- Whether light to moderate alcohol consumption is harmful ➔ not clear.
- It is possible that light or moderate alcohol use may have beneficial effects ! on the liver and there are potential cardiovascular benefits as well.
- In the absence of more definitive data, we suggest that patients with NAFLD avoid all alcohol consumption.

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Pharmacotherapy

Pharmacotherapy

No drugs are approved for NASH

No specific therapy can be recommended

Any drug treatment is off label

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Pharmacotherapy

- Do not suggested using pharmacologic agents solely for the treatment of NASH.

- It could be reasonable for those with:
  - Significant fibrosis (stage F2 and higher)
  - Active NASH with high necroinflammatory activity

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Pharmacotherapy

- Lipid-lowering agents
  - Statins
- Insulin sensitizers
  - Metformin
  - Pioglitazone
  - Liraglutide (glucagon-like peptide-1).
- Antioxidants
  - Vitamin E
- UDCA
- Orlistat
- Losartan
- Omega -3

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Vitamin E

- For:
  - Patients with advanced fibrosis on biopsy who do not have diabetes or coronary artery disease (**Grade 2C**).
- Suggested dose:
  - 400 international units/day
- 800 international units/day of vitamin E:
  - Some data ➔ beneficial effect on liver
  - Observational studies ➔ possible increase in all-cause mortality

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Thiazolidinediones

- Pioglitazone and rosiglitazone
- We suggest **not using** thiazolidinediones primarily for the treatment of NASH (**Grade 2B**).
- Is reasonable in patients who are candidates for thiazolidinedione treatment for **type 2 diabetes**
- Effects of drug:
  - improve histologic parameters in patients with NASH
  - need to be used long-term ➔ serious adverse events, including heart failure.

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Metformin

- Lowers blood glucose by:
  - decreasing hepatic gluconeogenesis
  - stimulating glucose uptake by muscle
  - and increasing fatty acid oxidation in adipose tissue.

- However, it does not appear to be effective for the treatment of NASH.

Metformin

- In a meta-analysis ➔ no difference between the patients who received metformin and the control patients:
  - histologic response (steatosis, ballooning, inflammation, or fibrosis),
  - changes in alanine aminotransferase levels
  - or changes in BMI.

Liraglutide

- Liraglutide may be an option for treating patients with NASH, but additional studies are needed.

- It is a glucagon-like peptide-1 (GLP-1)-based therapy that affects glucose control through several mechanisms:
  - including enhancement of glucose-dependent insulin secretion
  - slowed gastric emptying
  - reduction of postprandial glucagon
  - Reduction of food intake.

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Orlistat

- Orlistat is a gastrointestinal lipase inhibitor
- used in the treatment of obesity and type 2 diabetes mellitus.

- We suggest using orlistat when needed as an adjunct for weight loss, but not as a primary treatment for NASH.

- No benefit on:
  - liver histology
  - insulin resistance
  - liver biochemical tests

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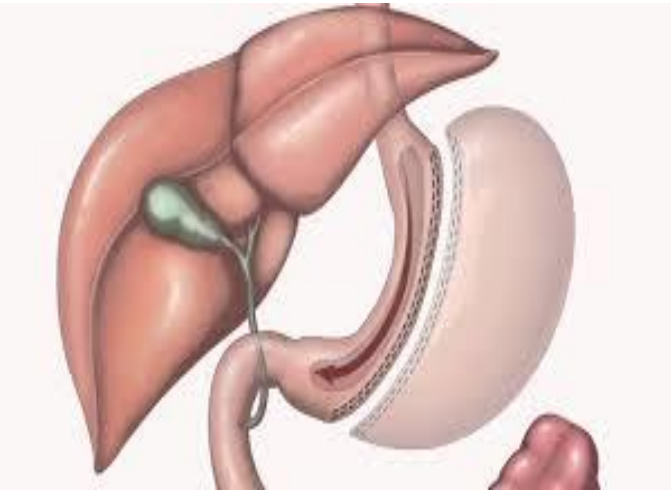
Other drugs

- Ursodeoxycholic acid
  - antiapoptotic and anti-inflammatory effects in the liver
  - no significant difference in overall liver

- Obeticholic acid
  - Synthetic variant of the bile acid chenodeoxycholic acid and is
  - a potent activate of the farnesoid X nuclear receptor
  - When the farnesoid X nuclear receptor is activated, it promotes insulin sensitivity and decreases hepatic gluconeogenesis and circulating triglycerides

Treatment: surgery

- Bariatric surgery
  - unresponsive to lifestyle changes and pharmacotherapy



- Liver transplantation
  - one of the top three indications

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Thank you!