

# UPDATES IN FATTY LIVER DISEASE. MASLD (FORMALLY KNOW AS NASH)

ILLINOIS OSTEOPATHIC MEDICAL SOCIETY  
WINTER SCIENTIFIC SESSION  
DECEMBER 7-10<sup>TH</sup>  
WESTIN CHICAGO/LOMBARD

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AMERICAN LIVER FOUNDATION, BOD, NY, NY  
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## DISCLOSURE:

- ADVISORY BOARD/SPEAKER, GILEAD
- ADVISORY BOARD/SPEAKER, ABBVIE
- CLINICAL INVESTIGATOR / ADVISORY BOARD, EXACT SCIENCE

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### About American Liver Foundation (ALF)



**Mission** ALF is the nation's largest patient advocacy organization for people affected by liver disease. Their mission is to promote education, advocacy, support services and research for the prevention, treatment, and cure of liver disease.

**Programs** They offer a variety of free liver health education programs for patients, caregivers, and professionals on multiple liver diseases and complications. To view upcoming free programs and community events visit [liverfoundation.org/events](https://liverfoundation.org/events).

**Support Services** ALF also offers a free national Helpline (phone and chat), online support groups, interpretation services for non-English speakers and medically reviewed literature for patients. 1-800-GO LIVER (1-800-465-4837) or [liverfoundation.org](https://liverfoundation.org).

**Get Involved** Getting involved is easy and ALF offers many volunteer opportunities for patients, the public and healthcare professionals.

- Patients can explore volunteer opportunities at [liverfoundation.org/how-you-can-help/get-involved](https://liverfoundation.org/how-you-can-help/get-involved)
- Healthcare professionals can learn more about volunteer opportunities at [liverfoundation.org/medical-professionals/research-get-involved](https://liverfoundation.org/medical-professionals/research-get-involved)

Patients are encouraged to visit [liverfoundation.org](https://liverfoundation.org) and healthcare professionals can include the link in patient follow-up and post-appointment summaries. ALF programs, support and resources are free and available nationwide.

To learn more about ALF, scan the QR code. For a complete list of free resources, visit [liverfoundation.org/resource-center](https://liverfoundation.org/resource-center)



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**METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD), FORMERLY KNOWN AS NONALCOHOLIC FATTY LIVER DISEASE (NAFLD)**

**PROGRESSION OF MASLD**

\* OBESITY /T2DM OR RAISED LIVER ENZYMES IN PATIENTS WITH METABOLIC RISK FACTORS SHOULD PROMPT NON-INVASIVE SCREENING TO PREDICT STEATOSIS, NASH AND FIBROSIS

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**AGENDA:**

- INTRODUCTION
- DEFINITION
- UPDATES: EPIDEMIOLOGY AND NATURAL HX
- MOLECULAR & CELLULAR PATHOGENESIS
- EVALUATION OF MASLD, RISK FACTORS
- SCREENING
- LATEST UPDATES MASLD/NASH
- TREATMENT

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**METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD) FORMALLY KNOWN AS NAFLD/NASH**

MAYO ©2012

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### DEFINITION

METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD), FORMALLY KNOWN AS NAFLD, IS AN OVERARCHING TERM THAT INCLUDES ALL DISEASE GRADES AND STAGES AND REFERS TO A POPULATION IN WHICH  $\geq 5\%$  OF HEPATOCYTES DISPLAY MACROVESICULAR STEATOSIS IN THE ABSENCE OF A READILY IDENTIFIED ALTERNATIVE CAUSE OF STEATOSIS (EG, MEDICATIONS, STARVATION, GENETIC DISORDERS) IN INDIVIDUALS WHO DRINK LITTLE OR NO ALCOHOL (DEFINED AS  $< 20$  G/D FOR WOMEN AND  $< 30$  G/D FOR MEN).

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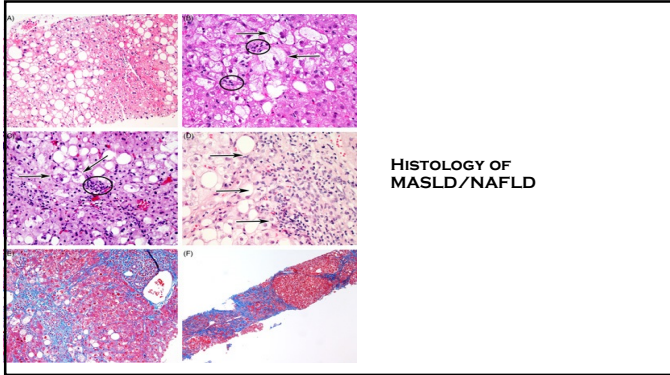
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### OBESITY, BY FAR, BIGGEST, LARGEST CAUSE OF FATTY LIVER, MASLD



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### RISK FACTORS FOR MASLD

- OBESITY, SOCIOECONOMIC CHANGES AND LIFESTYLE
- DIABETES
- AGE
- GENDER
- RACE
- THE GLOBAL BURDEN AND CHANGING TRENDS OF ALCOHOL USE
- CHRONIC VIRAL HEPATITIS
- GENETIC AND EPIGENETIC FACTORS

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### UPDATE ON EPIDEMIOLOGY AND NATURAL HISTORY

- THE PREVALENCE OF MASLD IS RISING WORLDWIDE IN PARALLEL WITH INCREASES IN THE PREVALENCE OF OBESITY AND METABOLIC COMORBID DISEASE (INSULIN RESISTANCE, DYSLIPIDEMIA, CENTRAL OBESITY, AND HYPERTENSION). THE PREVALENCE OF MASLD IN ADULTS IS ESTIMATED TO BE 25%–30% IN THE GENERAL POPULATION AND VARIES WITH THE CLINICAL SETTING, RACE/ETHNICITY, AND GEOGRAPHIC REGION STUDIED BUT OFTEN REMAINS UNDIAGNOSED.
- DATA FROM META-ANALYSES AND POOLED STUDIES DEMONSTRATE THAT FIBROSIS AND THE PRESENCE OF STEATOPHATITIS ARE THE PRIMARY PREDICTORS OF DISEASE PROGRESSION.
- THE MOST COMMON CAUSES OF DEATH IN PATIENTS WITH MASLD OVERALL ARE CARDIOVASCULAR DISEASE (CVD) AND NONHEPATIC MALIGNANCY, FOLLOWED BY LIVER DISEASE.

**KEY POINT**

*\*PATIENTS WITH MASLD AND F2–4 FIBROSIS ARE AT HIGHER RISK FOR LIVER-RELATED EVENTS AND MORTALITY AND ARE CONSIDERED TO HAVE "AT-RISK" MASLD/NASH.*

*\*THE RATES OF FIBROSIS PROGRESSION AND HEPATIC DECOMPENSATION VARY DEPENDING ON BASELINE DISEASE SEVERITY, GENETIC, INDIVIDUAL ENVIRONMENTAL, AND COMORBID DISEASE DETERMINANTS.*

*\*CVD AND NONHEPATIC MALIGNANCIES ARE THE MOST COMMON CAUSES OF MORTALITY IN PATIENTS WITH MASLD/NAFLD WITHOUT ADVANCED FIBROSIS; DEATH FROM LIVER DISEASE PREDOMINATES IN PATIENTS WITH ADVANCED FIBROSIS.*

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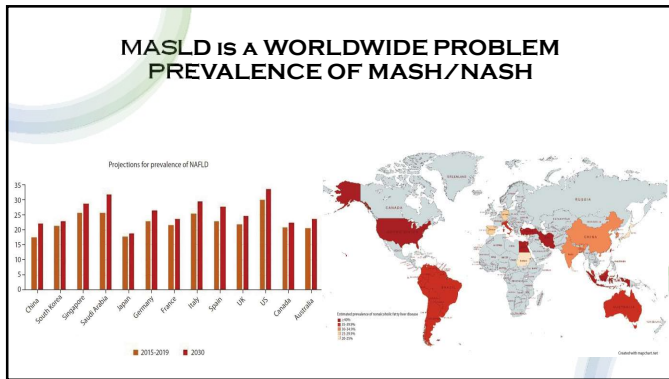
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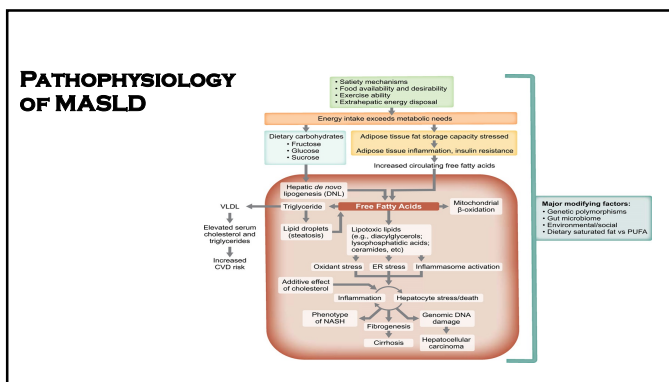
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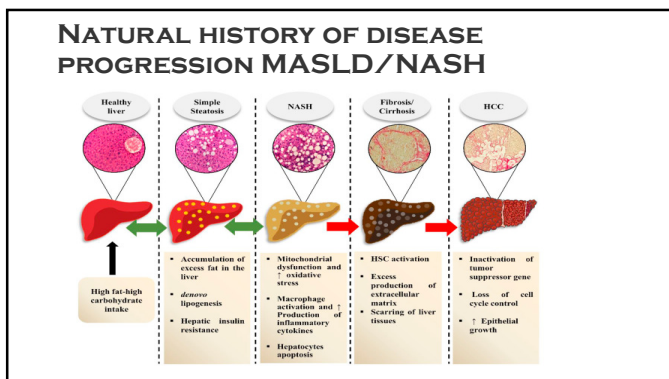
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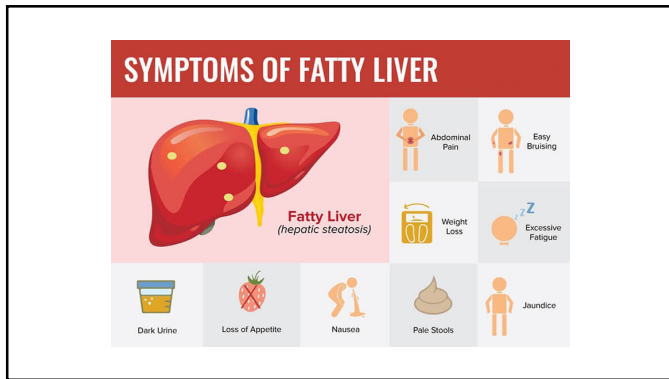
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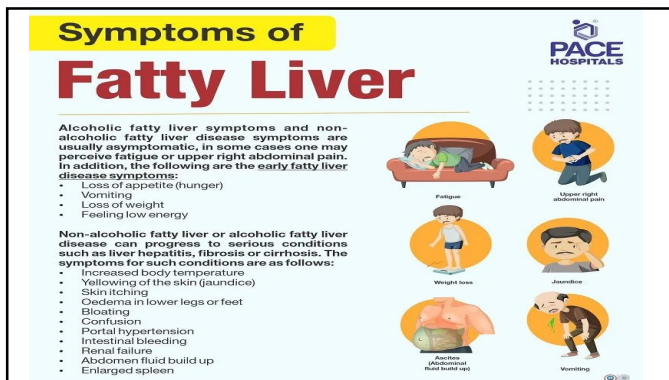
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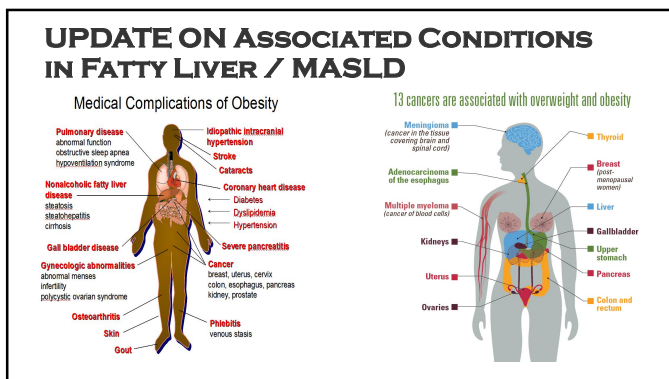
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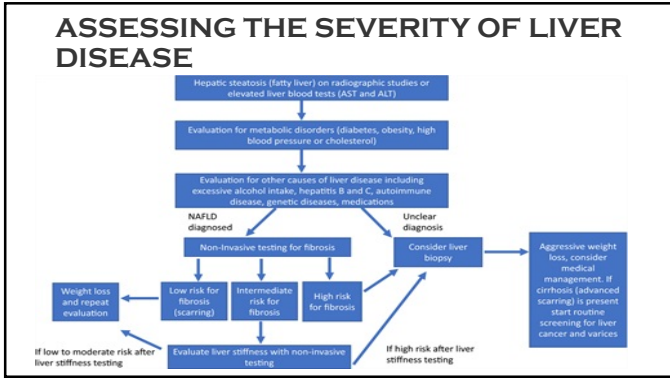
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### INITIAL EVALUATION OF A PATIENT WITH MAFLD

History	Weight history, medical comorbidities; recent and current medications; family history of T2DM, NAFLD, or cirrhosis; screening for OSA; alcohol use, including amount, pattern of use, and duration
Physical examination	Body fat distribution (eg, android vs. gynoid, lipodystrophic), features of insulin resistance (eg, dorsal-cervical fat pad, acanthosis nigricans), features of advanced liver disease (eg, firm liver, splenomegaly, prominent abdominal veins, ascites, gynecomastia, spider angiomas, palmar erythema)
Laboratory tests	Hepatic panel, CBC with platelets, fasting plasma glucose and glycated hemoglobin (A1c), fasting lipid profile, creatinine and urine microalbumin or protein to creatinine ratio, hepatitis C if not previously screened. Consider as appropriate other causes of steatosis/cirrhosis/hepatitis (1). Additional evaluation if elevated liver chemistries present: autoimmune serologies, transferrin saturation, ceruloplasmin, alpha-1 antitrypsin genotype, or phenotype

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- ### TREATMENT OF MASLD
- TREATMENTS AND LIFESTYLE CHANGES MAY INCLUDE:**
1. LOSING WEIGHT.
  2. MEDICATION TO REDUCE CHOLESTEROL OR TRIGLYCERIDES.
  3. MEDICATION TO REDUCE BLOOD PRESSURE.
  4. MEDICATION TO CONTROL DIABETES/IR/REDUCE WT.
  5. LIMITING OTC DRUGS.
  6. AVOIDING ALCOHOL.
  7. SEEING A LIVER SPECIALIST.

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**COMPONENTS OF A LIFESTYLE APPROACH TO CUMULATIVE INCIDENCE OF MASLD-ASSOCIATED HCC VARIES ACCORDING TO STUDY POPULATION**

NAFLD

**Energy restriction**

- Calorie restriction (500-1,000/day)
- 7-10% weight loss target
- Long-term maintenance approach

**Fructose intake**

- Avoid fructose-containing food and drink

**Daily alcohol intake**

- Strictly below 30 g men and 20 g women

**Coffee consumption**

- No liver-related limitations

**Macronutrient composition**

- Low-to-moderate fat
- Moderate-to-high carbohydrate
- Low-carbohydrate ketogenic diets or high protein

**Physical activity**

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

**COMPREHENSIVE LIFESTYLE APPROACH**

EASL-EASD-EASO CPG NAFLD, J Hepatol 2016;64:1388-402

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**TREATMENT: DIET AND LIFESTYLE CHANGES**

- A PRAGMATIC, INDIVIDUALLY TAILORED APPROACH IS REQUIRED
  - DIETARY RESTRICTION PLUS
  - PROGRESSIVE INCREASE IN AEROBIC EXERCISE AND RESISTANCE TRAINING

**RECOMMENDATIONS**

•DIETARY RECOMMENDATIONS SHOULD CONSIDER ENERGY RESTRICTION AND EXCLUSION OF NAFLD-PROMOTING COMPONENTS (PROCESSED FOOD, AND FOOD AND BEVERAGES HIGH IN ADDED FRUCTOSE). THE MACRONUTRIENT COMPOSITION SHOULD BE ADJUSTED ACCORDING TO THE MEDITERRANEAN DIET

- BOTH AEROBIC EXERCISE AND RESISTANCE TRAINING EFFECTIVELY REDUCE LIVER FAT. THE CHOICE OF TRAINING SHOULD BE TAILORED BASED ON PATIENTS' PREFERENCES TO BE MAINTAINED IN THE LONG-TERM

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**TREATMENT: DIET AND LIFESTYLE CHANGES**

- EPIDEMIOLOGY SUGGESTS A CLOSE RELATIONSHIP BETWEEN AN UNHEALTHY LIFESTYLE AND MASLD
- DIET AND LIFESTYLE CHANGES ARE MANDATORY IN ALL PATIENTS
  - MODEST WEIGHT LOSS REDUCES LIVER FAT, IMPROVES HEPATIC IR, AND CAN RESULT IN NASH REGRESSION
  - WEIGHT LOSS OF ≥7% IS ASSOCIATED WITH HISTOLOGICAL IMPROVEMENT

**RECOMMENDATIONS:**

- PATIENTS WITHOUT MASH OR FIBROSIS SHOULD RECEIVE COUNSELLING FOR HEALTHY DIET AND PHYSICAL ACTIVITY BUT NO PHARMACOTHERAPY
- IN OVERWEIGHT/OBESE MASLD, A 7-10% WEIGHT LOSS IS THE TARGET OF MOST LIFESTYLE INTERVENTIONS, AND RESULTS IN IMPROVEMENT OF LIVER ENZYMES AND HISTOLOGY

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## TREATMENT OF MASLD

**• WEIGHT LOSS THROUGH LIFESTYLE MODIFICATION SIGNIFICANTLY REDUCES FEATURES OF NONALCOHOLIC STEATOHEPATITIS**

Eduardo Vilari-Gomez<sup>1</sup>, Yadhira Martinez-Perez<sup>1</sup>, Luis Caballero-Bertrán<sup>1</sup>, Ana Torres-Gonzalez<sup>2</sup>, Bienvenido Gra-Coronas<sup>1</sup>, Licet Gonzalez-Fabian<sup>1</sup>, Scott L. Friedman<sup>1</sup>, Moises Diego<sup>1</sup>, Manuel Romero-Gomez<sup>2\*</sup> *Frontiers in Hepatology*, 2023, Aug 14(2023):1-12. doi: 10.3389/fhep.2023.1010101. https://doi.org/10.3389/fhep.2023.1010101

**• CONCLUSIONS: A GREATER EXTENT OF WEIGHT LOSS, INDUCED BY LIFESTYLE CHANGES, IS ASSOCIATED WITH THE LEVEL OF IMPROVEMENT IN HISTOLOGIC FEATURES OF NASH. THE HIGHEST RATES OF NAS REDUCTION, NASH RESOLUTION, AND FIBROSIS REGRESSION OCCURRED IN PATIENTS WITH WEIGHT LOSSES ≥ 10%.**

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## TREATMENT OF MASLD

GREATER THAN 10% WEIGHT LOSS LED TO REGRESSION IN LIVER FIBROSIS WITH GREATER THAN 5% WEIGHT LOSS REDUCING HEPATIC STEATOSIS. THE DEGREE OF WEIGHT LOSS WAS INDEPENDENTLY ASSOCIATED WITH STATISTICALLY SIGNIFICANT IMPROVEMENTS IN ALL NASH-RELATED HISTOLOGIC PARAMETERS AND PROVIDES STRONG EVIDENCE THAT WEIGHT LOSS IS AN EFFECTIVE TREATMENT FOR NAFLD.

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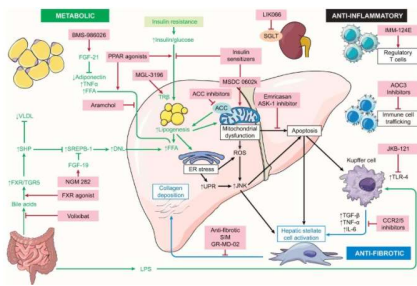
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## MOA OF PHARMACOLOGICAL TREATMENTS FOR MAFLD



Rosenbaum MA, et al. J Hepatol 2018;69:362-75. Copyright © 2018. Published by Elsevier B.V. This is an open access article under the CC BY license.

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# THANK YOU!!!

NOW IS THE TIME TO ASK GREAT QUESTIONS,  
THAT I WILL PRETEND TO KNOW THE  
ANSWERS

ROCKFORD G YAPP, MD, MPH, AGAF  
FELLOW LIVER LOVER

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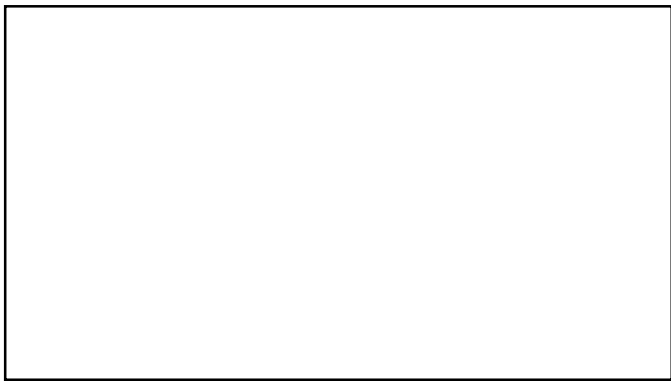
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