The Role of Primary Care Providers in the Early Identification of Patients with MASLD

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Disclosure

Advisory Board: Boehringer Ingelheim; Madrigal; Novo Nordisk

Consultant: Boehringer Ingelheim; Novo Nordisk

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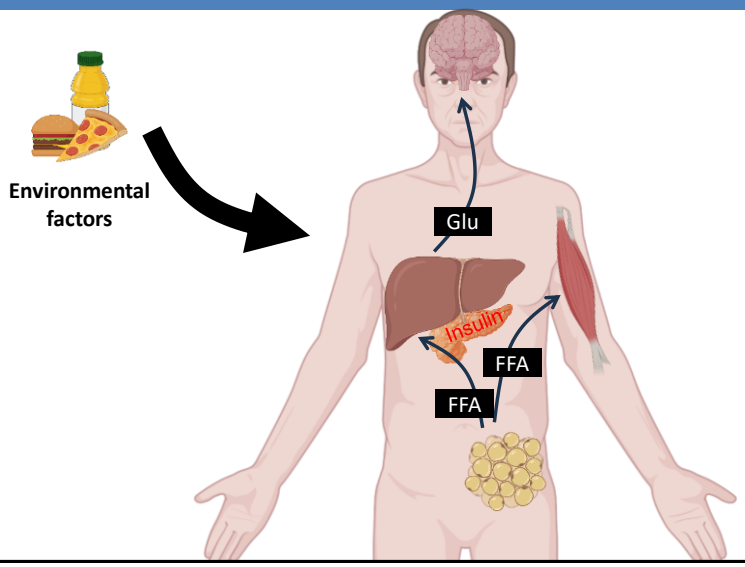
Learning Objectives

1. Discuss the pathogenesis, systemic nature, and epidemiology of MASLD.
2. Define the subpopulations of patients at high risk of progressive liver disease who would benefit from screening for liver fibrosis.
3. Describe the appropriate diagnostic approach to screen for liver disease among patients at high risk of liver disease in the primary care setting.

Outline

1. MASLD as a systemic disease
2. Definitions and magnitude of the problem.
3. The metabolic consequences of MASLD.
4. Diagnostic approach and screening.

Pathophysiology



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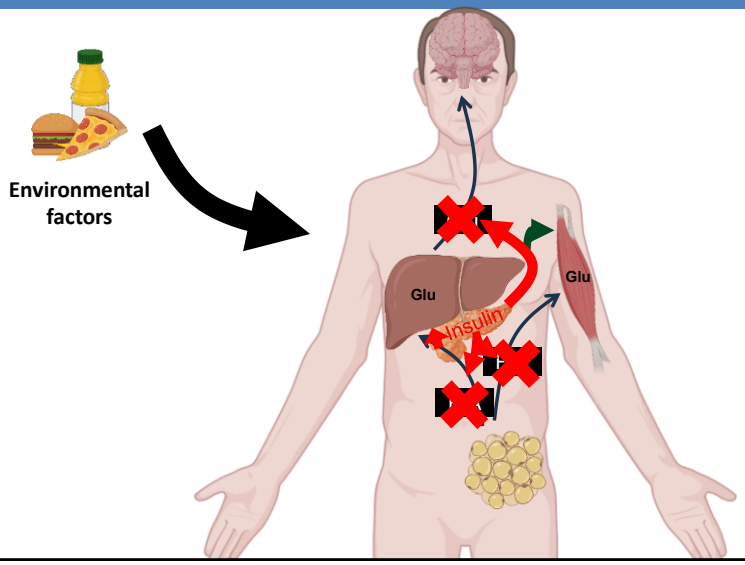
Pathophysiology



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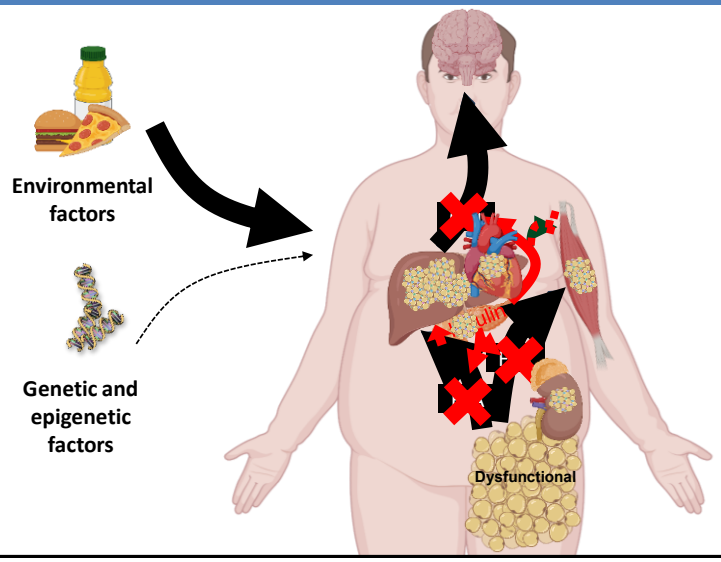
Pathophysiology



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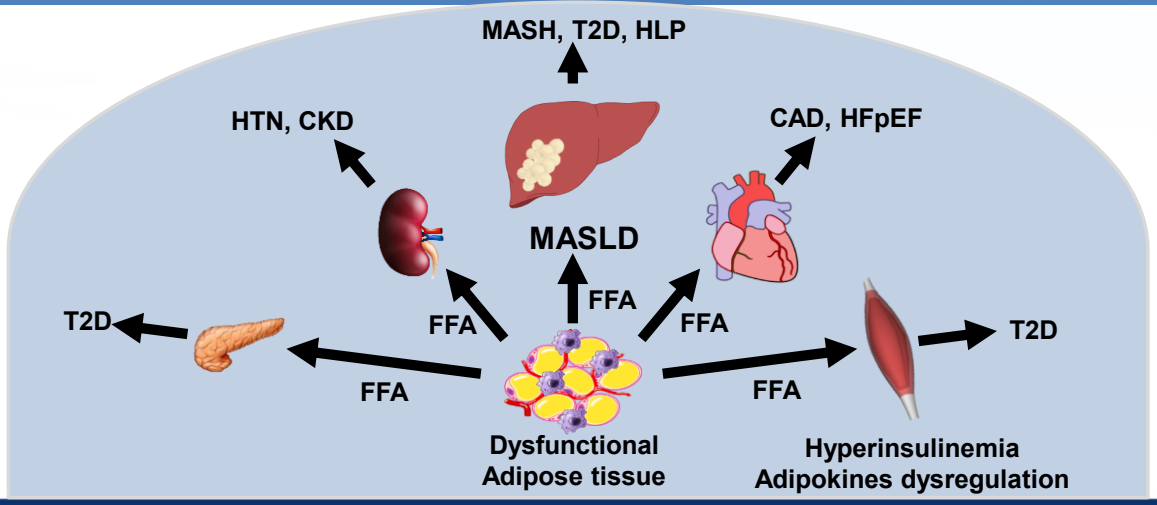
MASLD Is a Systemic Disease



Bril F. Lipotoxicity figure. Zenodo. 2025. doi:10.5281/zenodo.16294108.

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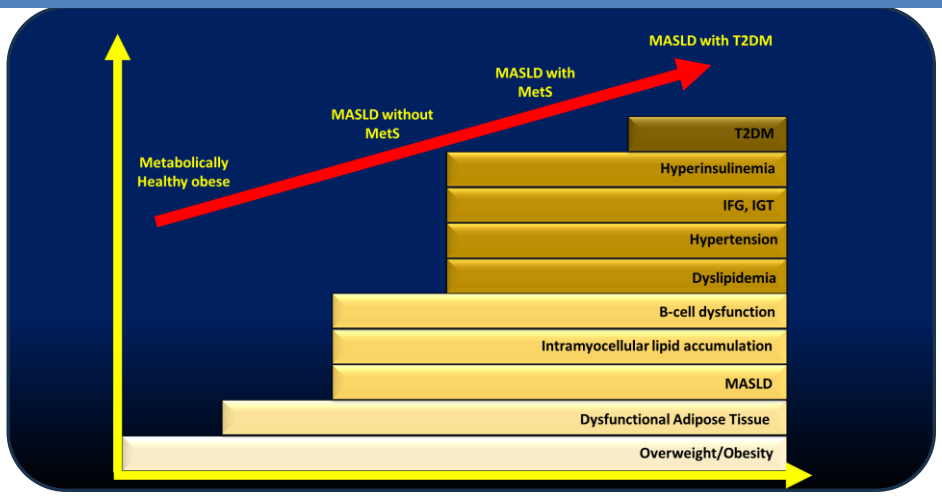
Outline



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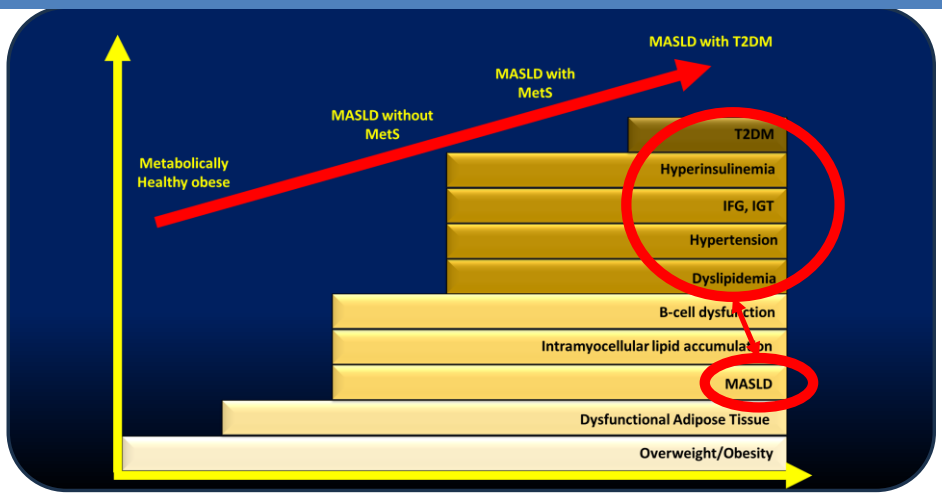
Outline



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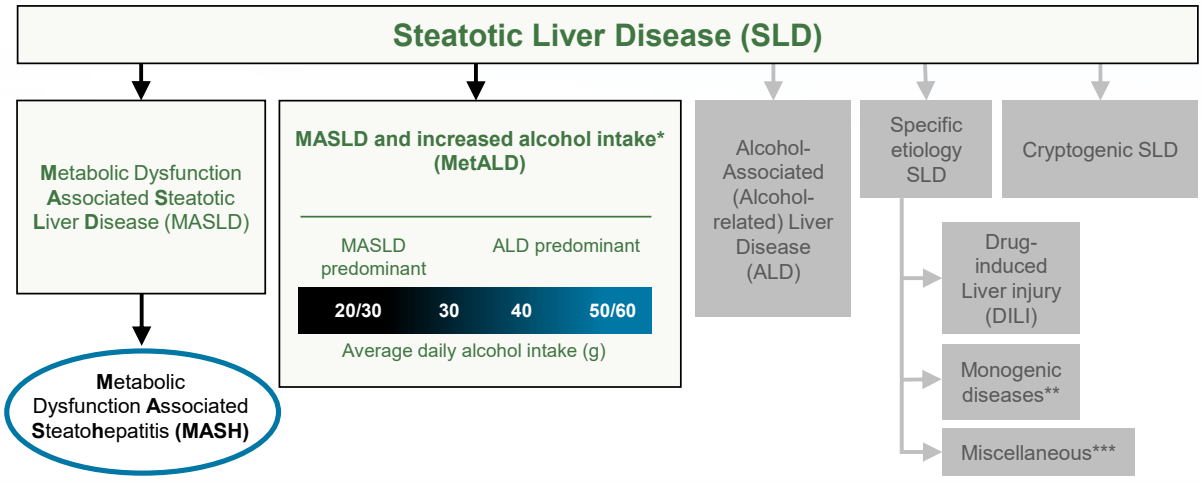
Definitions



Rinella ME, et al. Hepatology. 2023. 78:1966-1986.

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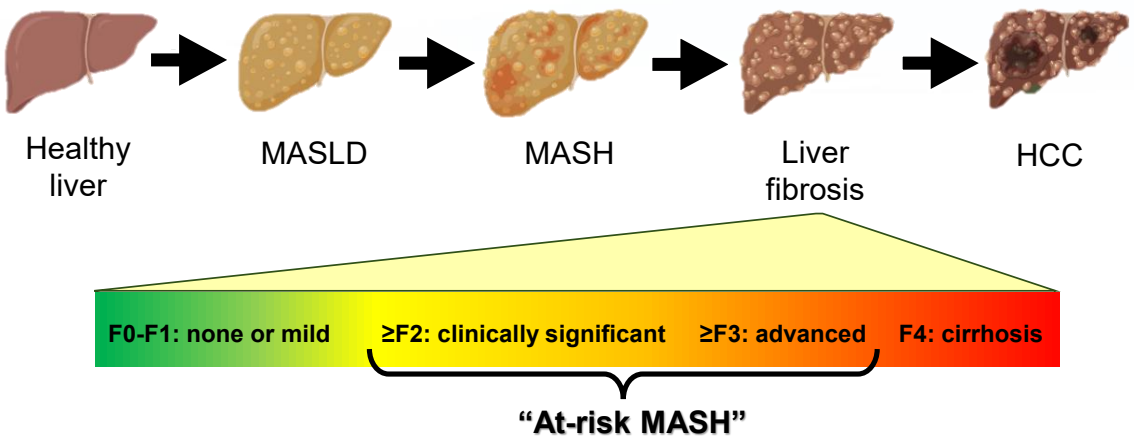
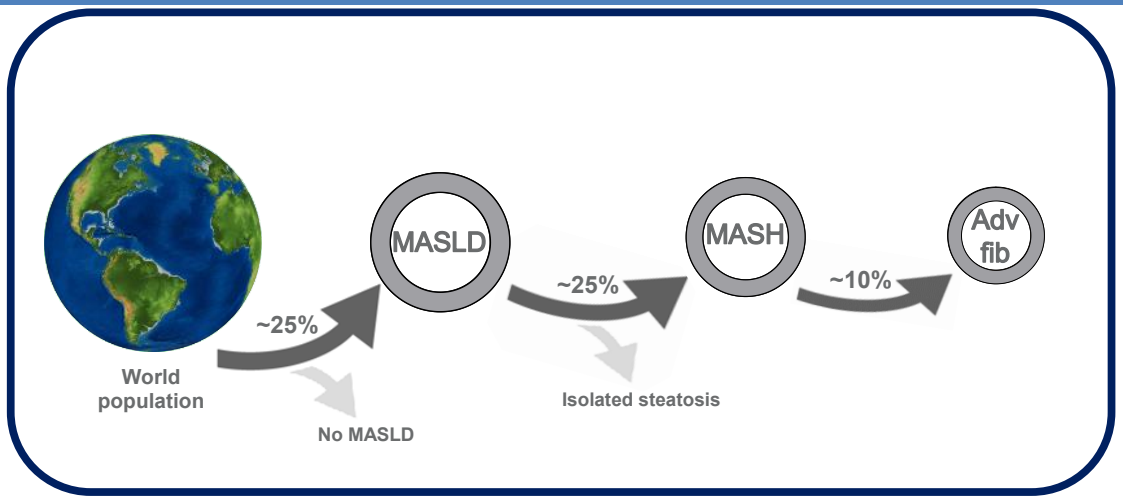
Definitions



Adapted from Godinez-Leiva E and Bril F. Curr Hypertens Rev. 2021;17(2):94-111.

12

Epidemiology



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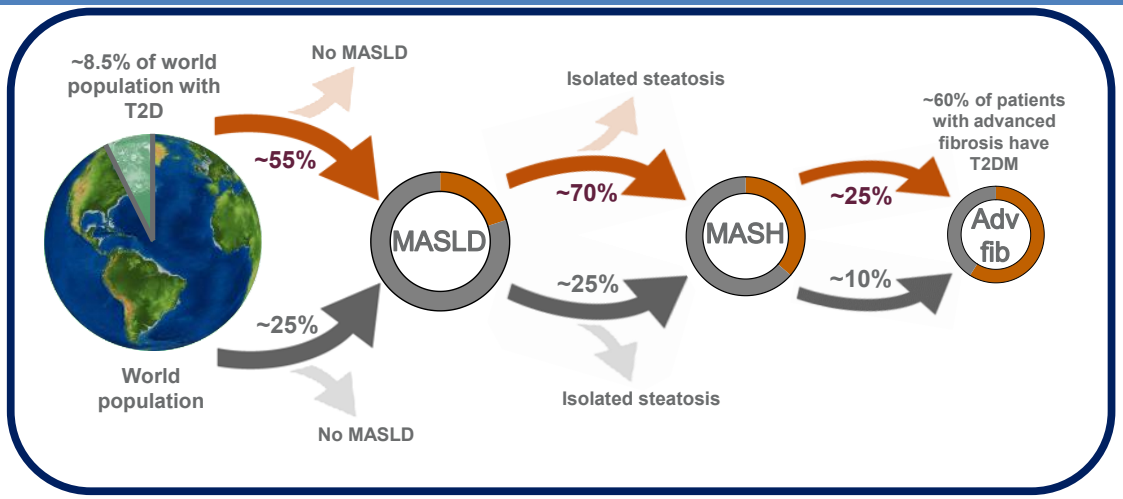
Epidemiology



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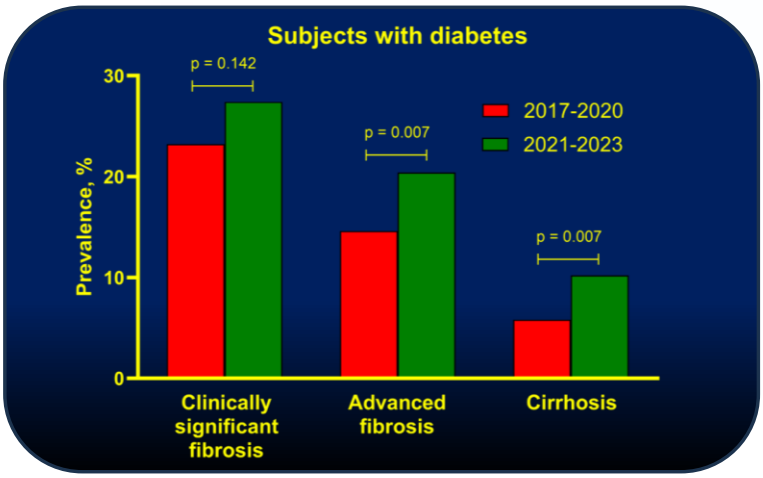
Epidemiology

If you saw ELEVEN patients with T2D last week, and you did not diagnose ONE with advanced fibrosis, you may have missed it.

15

Epidemiology



Bril F, et al. J Endocr Soc 2025;9(8):bvaf110.

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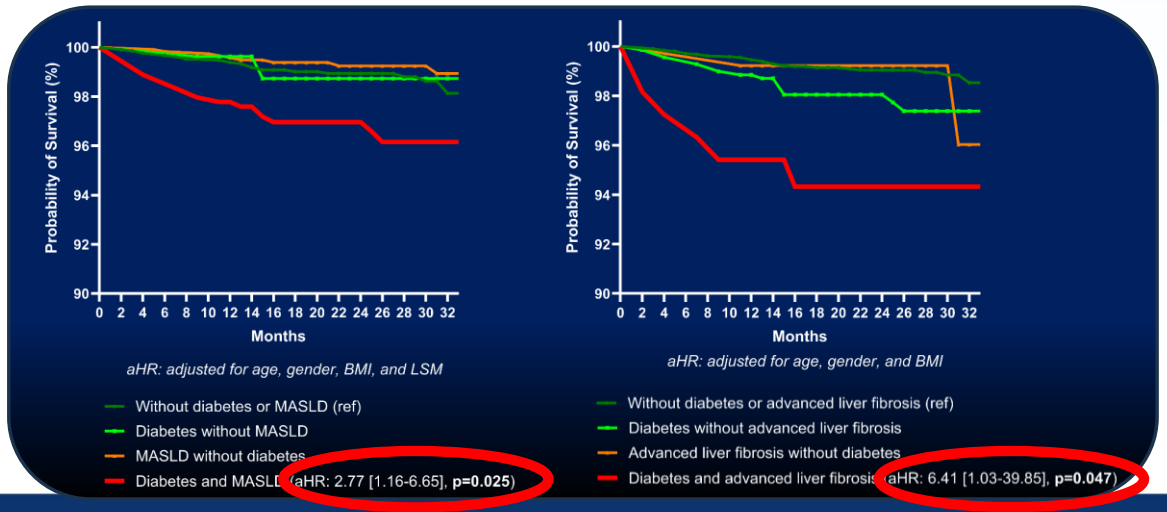
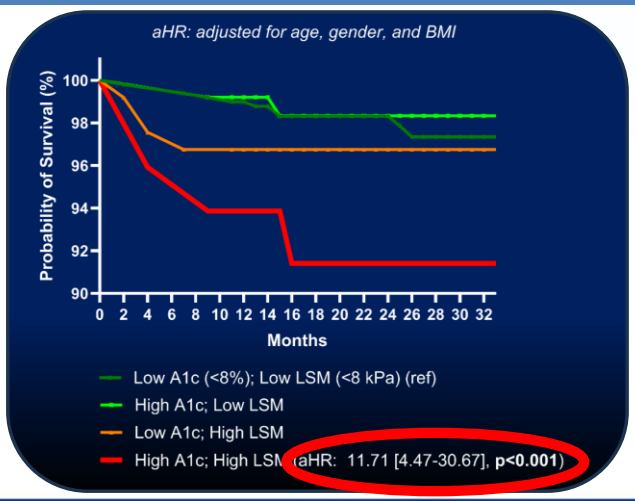
Epidemiology



Bril F, et al. JAMA Netw Open 2025 (Under review).

17

Epidemiology



Bril F, et al. JAMA Netw Open 2025 (Under review).

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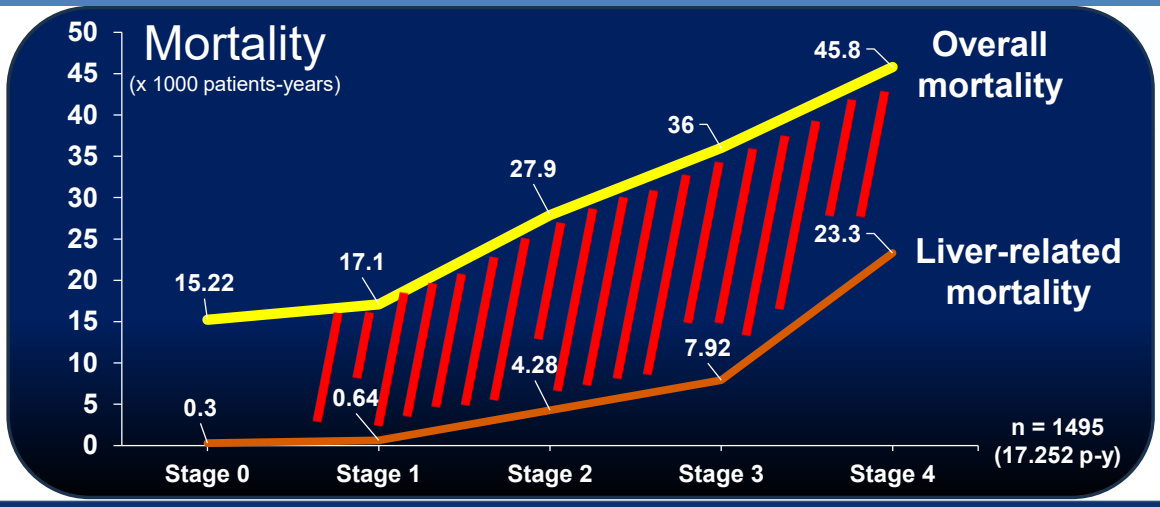
Epidemiology



Dulai PS, et al. Hepatology. 2017;65:1557–1565.

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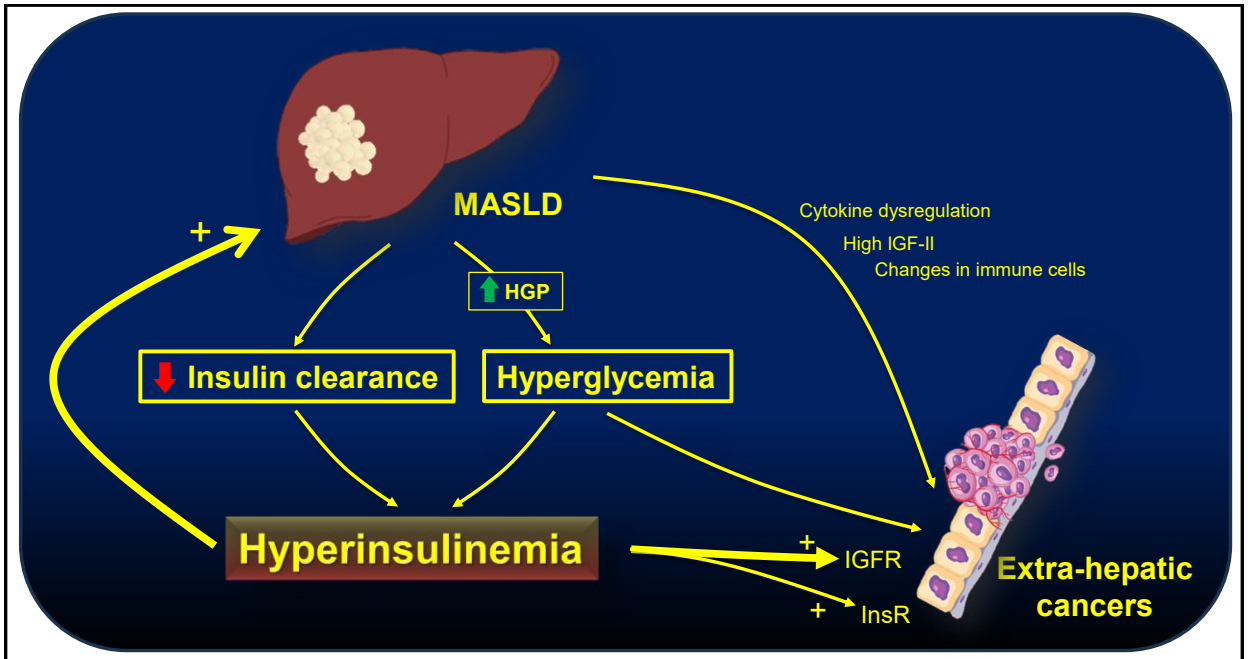

Bril F & Elbert A. Metabolism 2025;162:156066.

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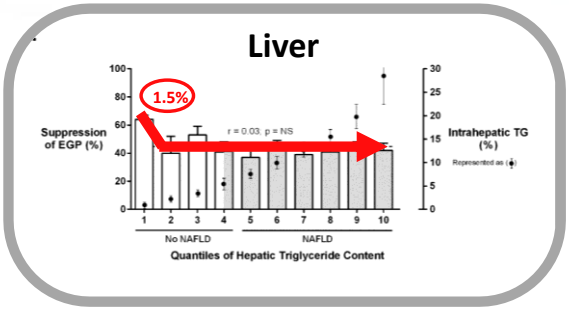
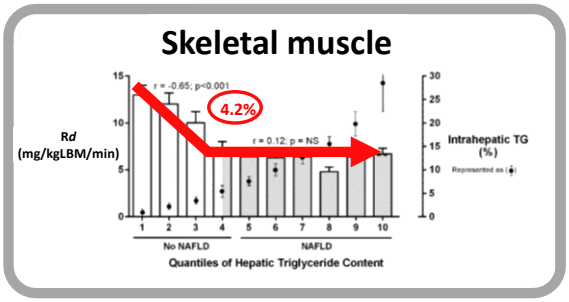
Metabolic Consequences





Bril et al. Hepatology 2017;65:1132-1144.

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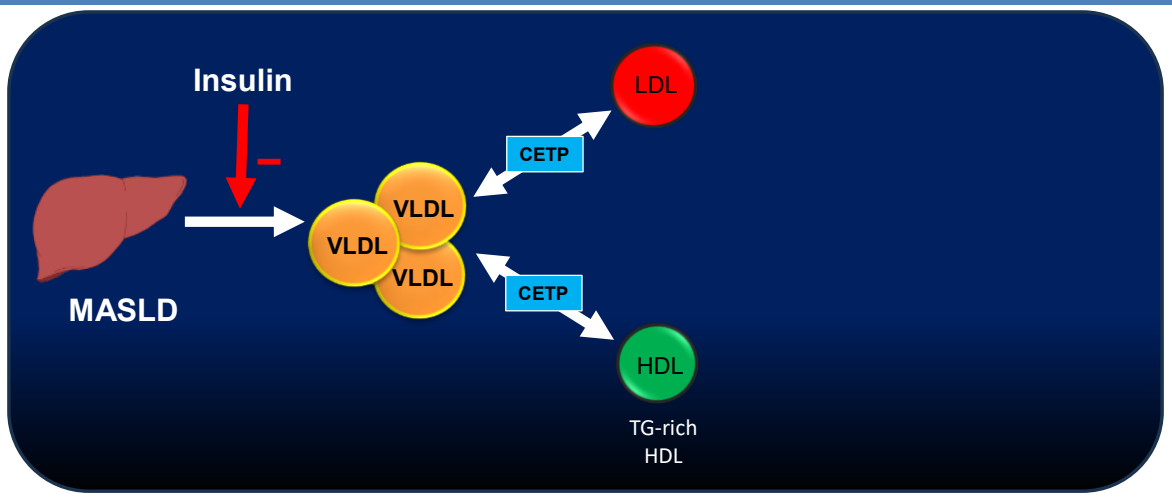
Metabolic Consequences



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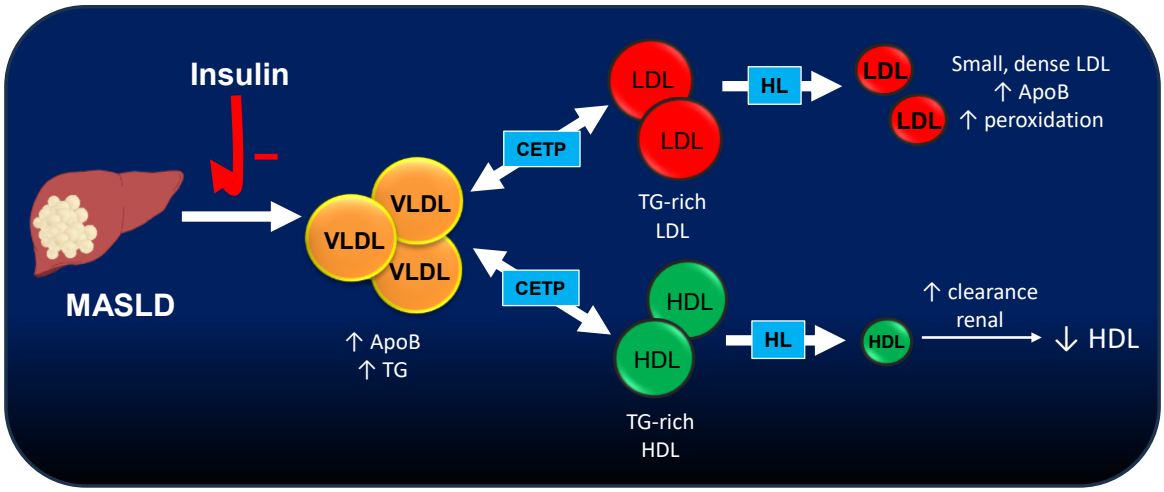
Metabolic Consequences



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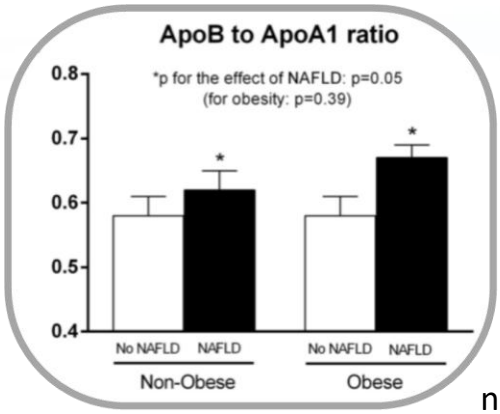
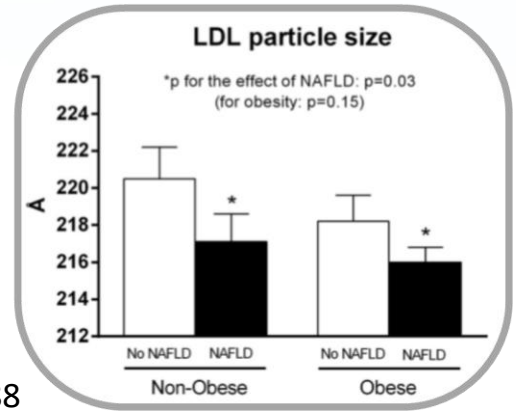
Metabolic Consequences



n = 188



Bril F, et al. J Clin Endocrinol Metab 2016; 101:644-52.

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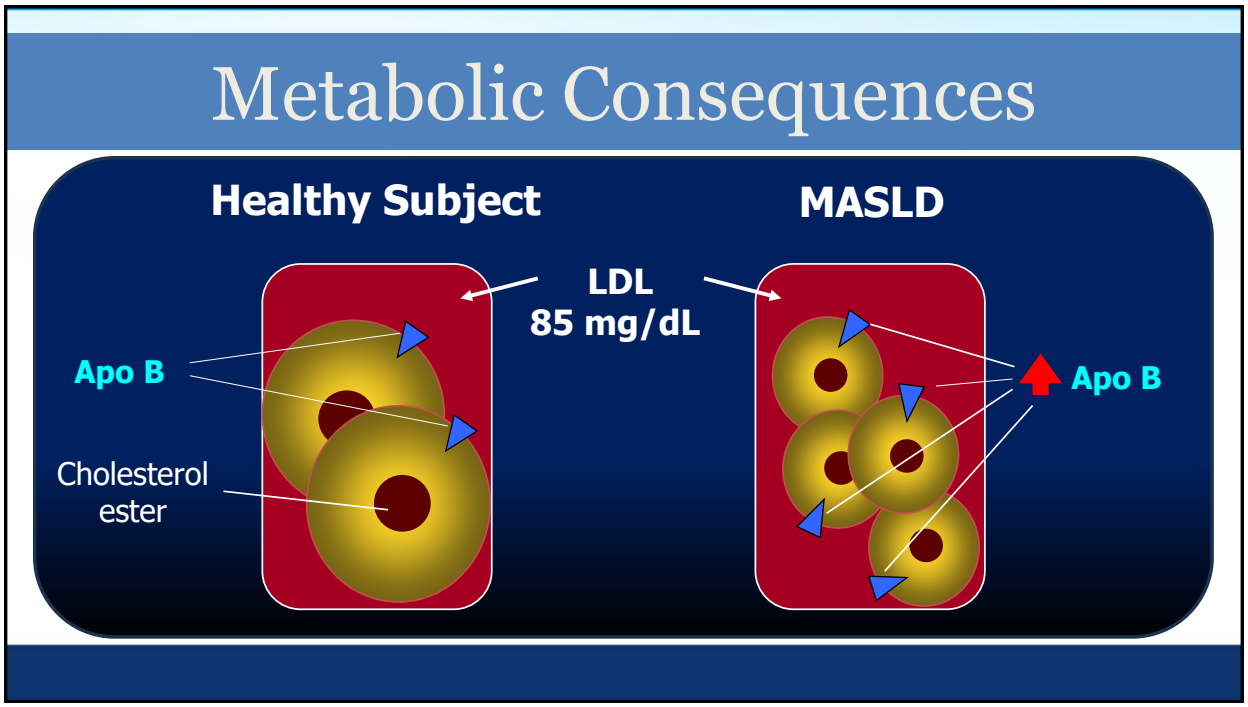

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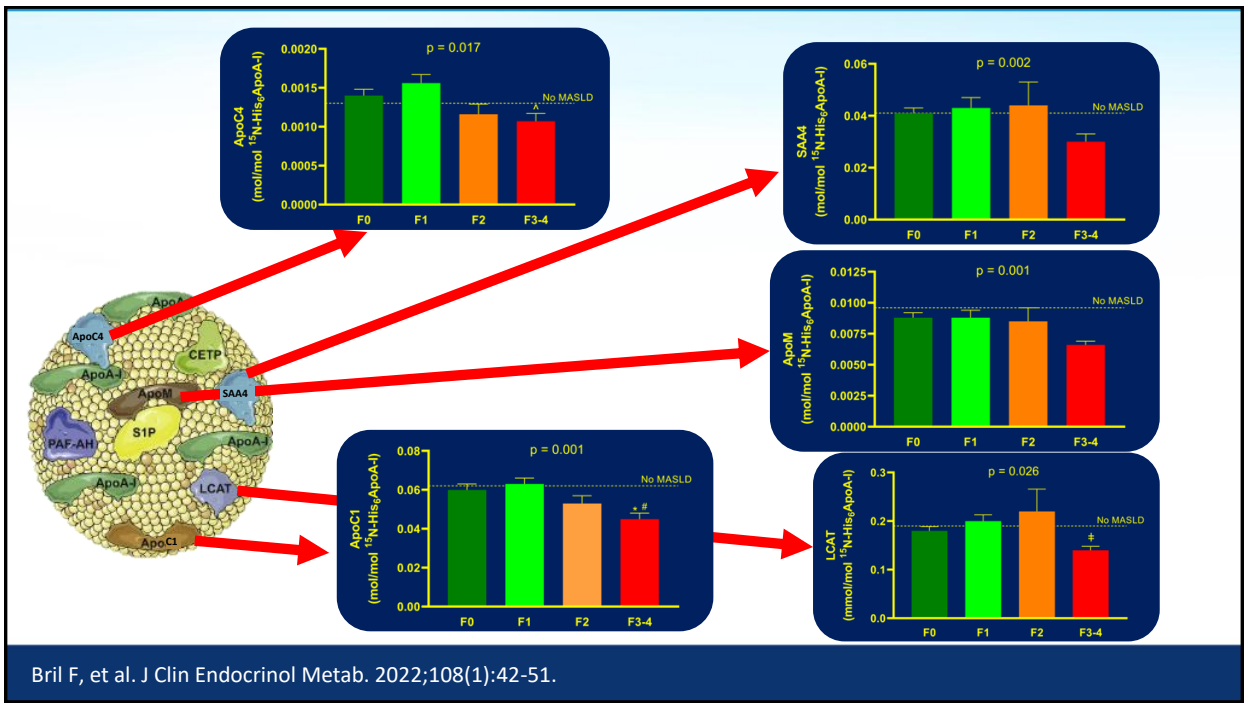
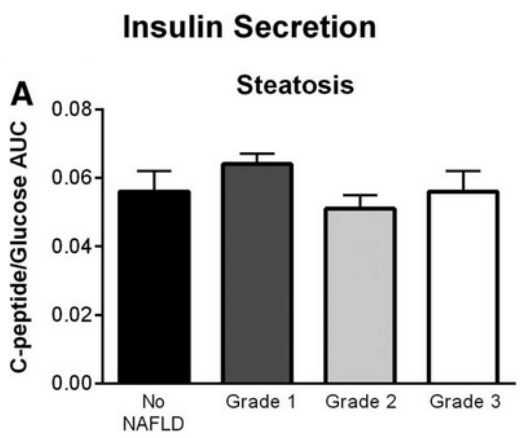
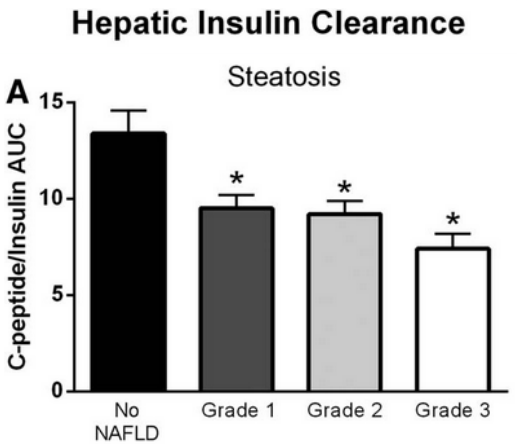


Bril F, et al. J Clin Endocrinol Metab. 2022;108(1):42-51.

26

Metabolic Consequences





Bril F, et al. Hepatology 2014;59:2178-2187.

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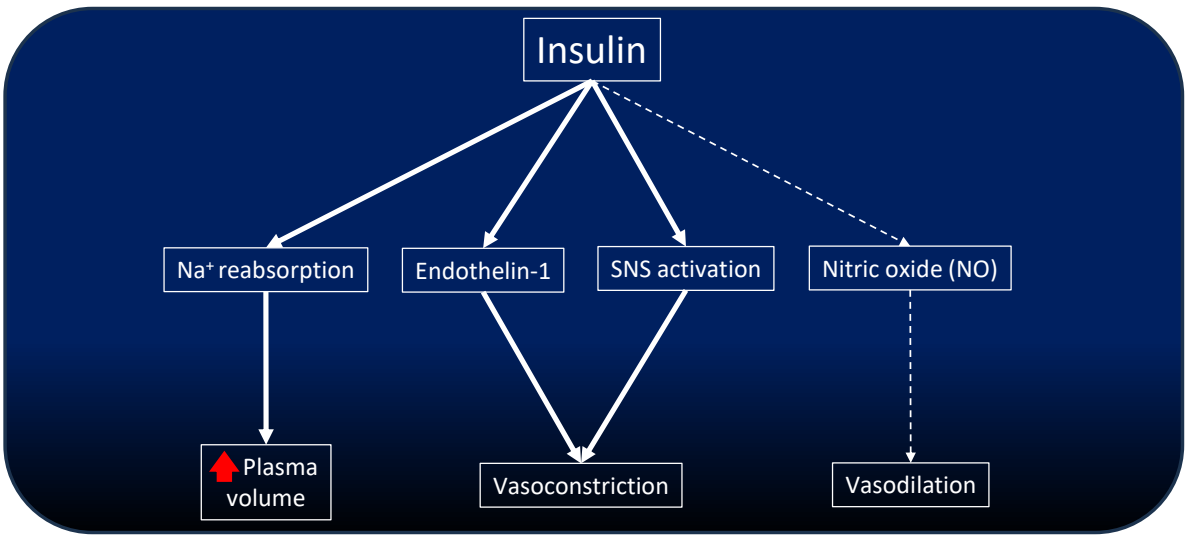
Metabolic Consequences



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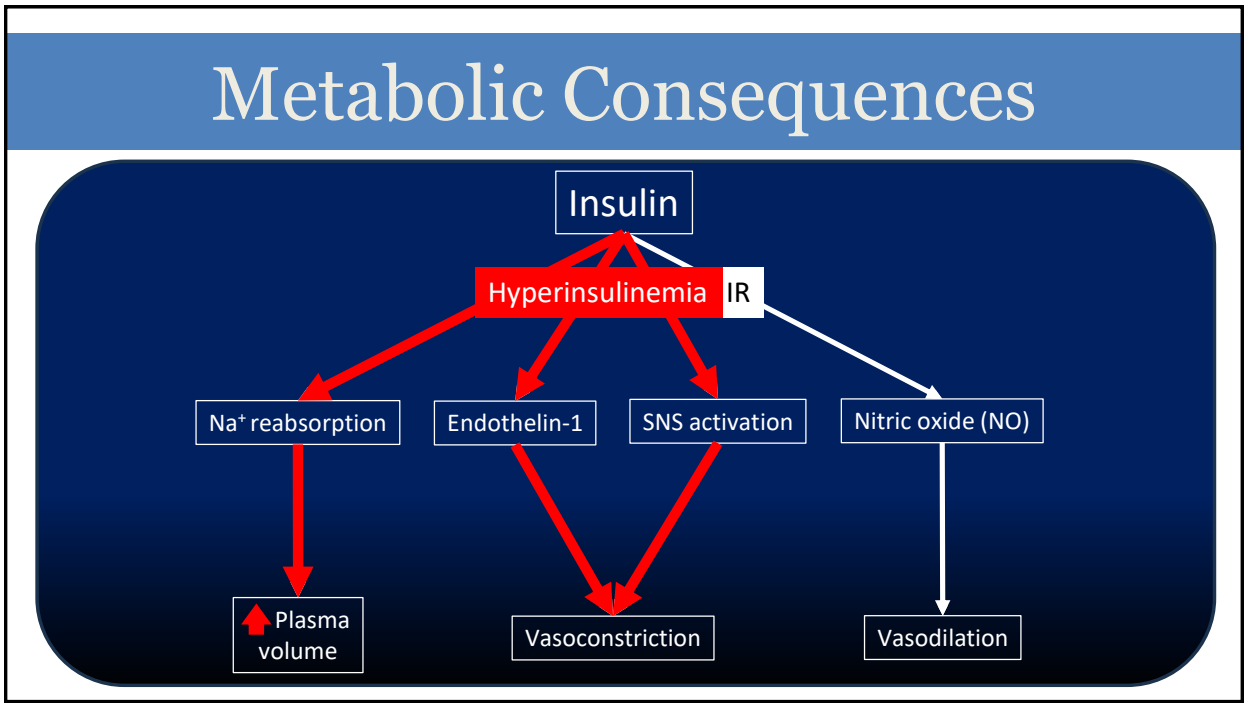
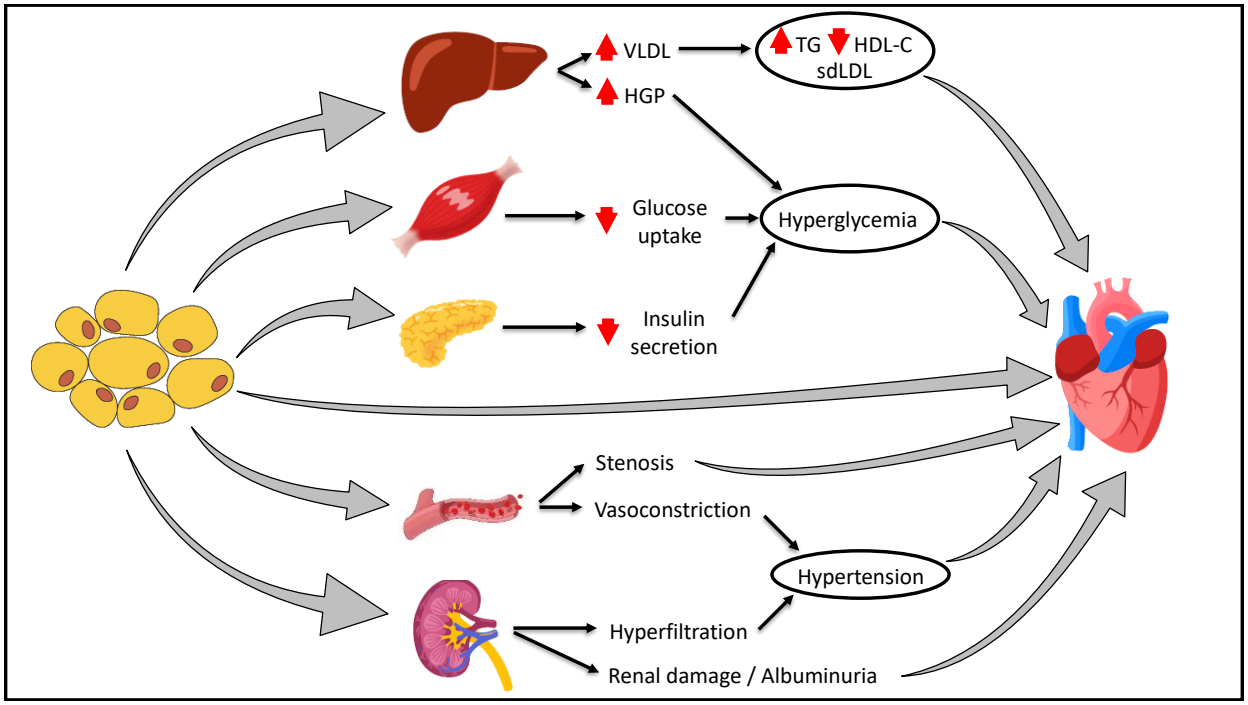
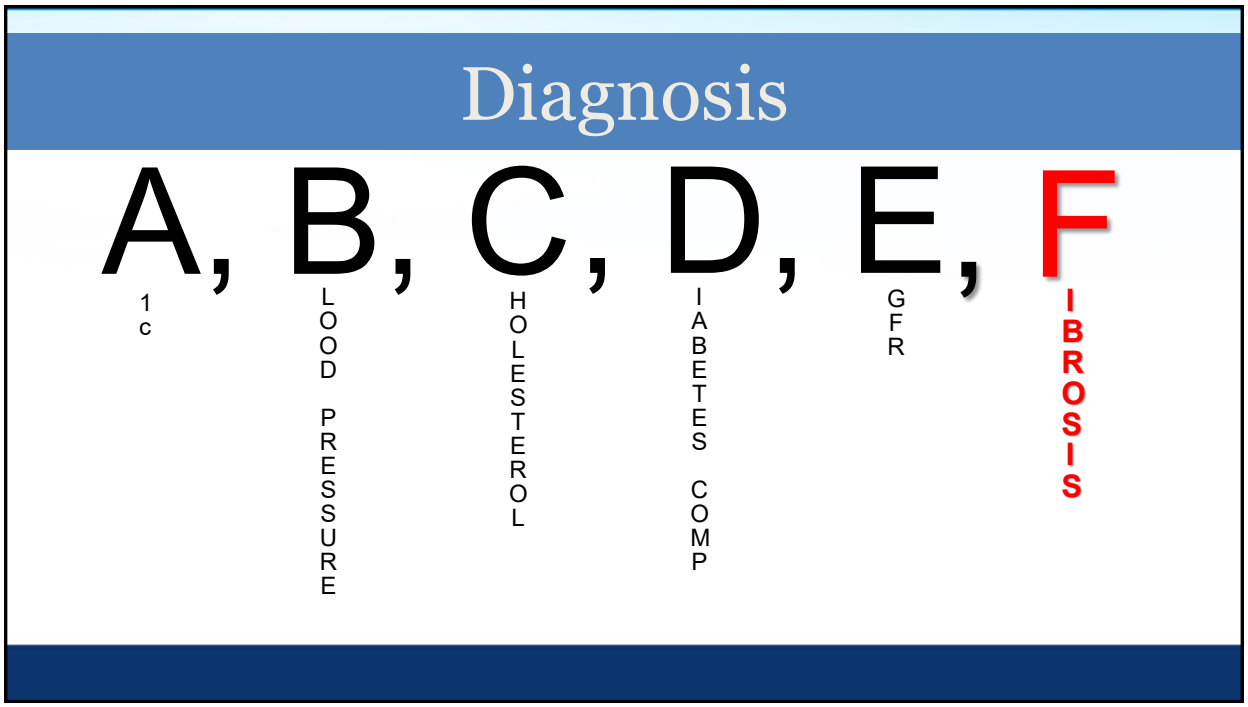

Metabolic Consequences
Insulin
Hyperinsulinemia
IR
Na+ reabsorption
Endothelin-1
SNS activation
Nitric oxide (NO)
Plasma volume
Vasoconstriction
Vasodilation

29


VLDL
HGP
TG HDL-C sdLDL
Glucose uptake
Hyperglycemia
Insulin secretion
Stenosis
Vasoconstriction
Hypertension
Hyperfiltration
Renal damage / Albuminuria

30


Diagnosis
A, B, C, D, E, F
1c
LOOD PRESSURE
HOLESTEROL
IABETES COMP
GFR
IBROSIS

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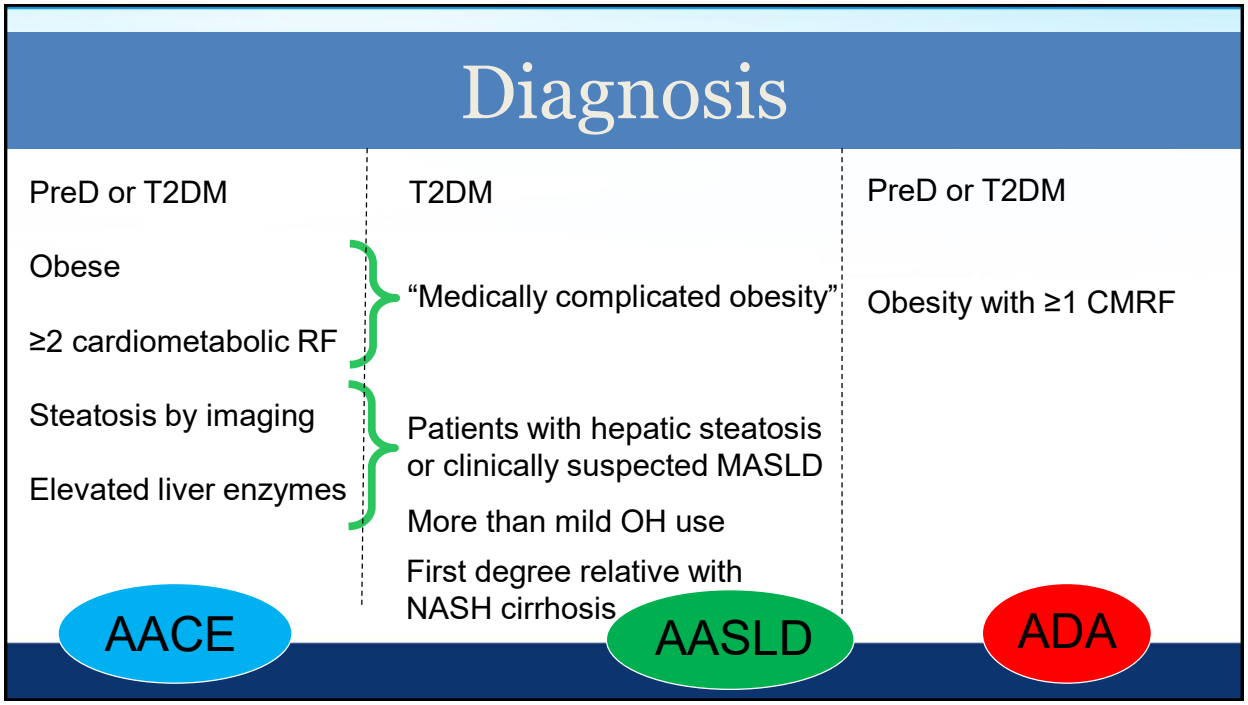
Diagnosis
PreD or T2DM
Obese
≥2 cardiometabolic RF
Steatosis by imaging
Elevated liver enzymes
T2DM
"Medically complicated obesity"
Patients with hepatic steatosis or clinically suspected MASLD
More than mild OH use
First degree relative with NASH cirrhosis
PreD or T2DM
Obesity with ≥1 CMRF
AACE
AASLD
ADA

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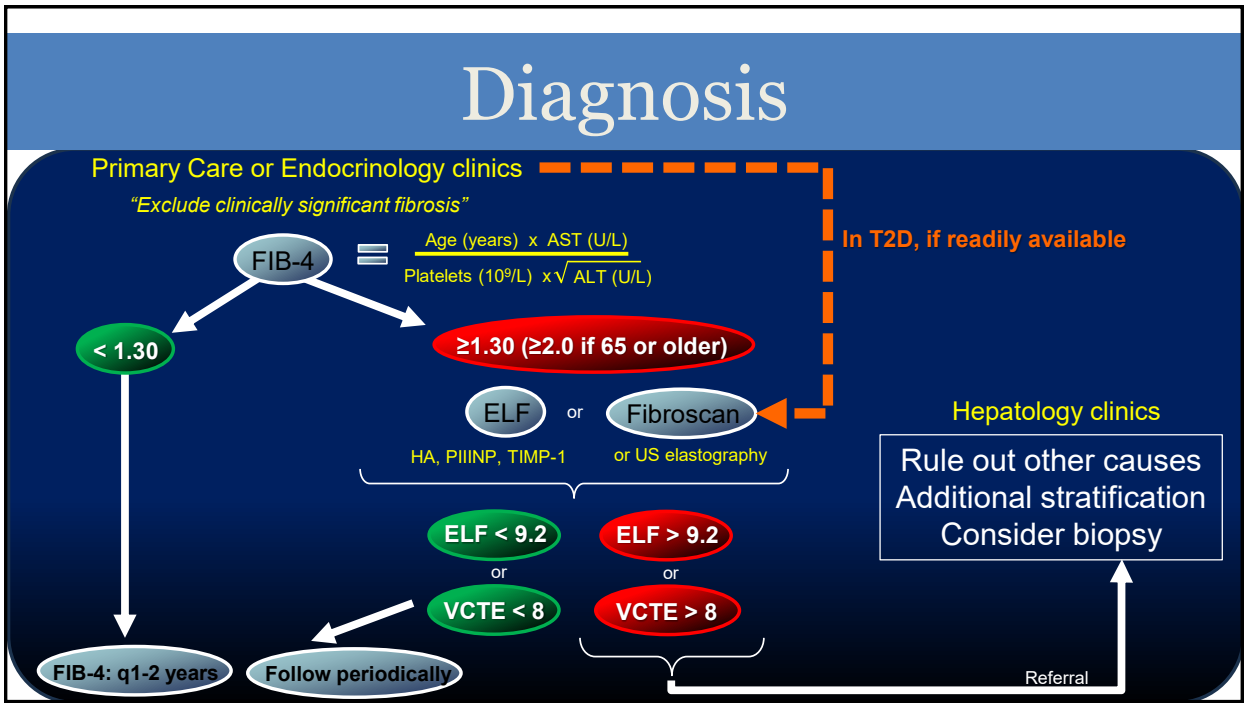
Diagnosis
Primary Care or Endocrinology clinics
"Exclude clinically significant fibrosis"
FIB-4
Age (years) x AST (U/L)
Platelets (10^9/L) x √ ALT (U/L)
In T2D, if readily available
< 1.30
≥1.30 (≥2.0 if 65 or older)
ELF
or
Fibroscan
HA, PIIINP, TIMP-1
or US elastography
Hepatology clinics
Rule out other causes
Additional stratification
Consider biopsy
ELF < 9.2
or
VCTE < 8
ELF > 9.2
or
VCTE > 8
FIB-4: q1-2 years
Follow periodically
Referral

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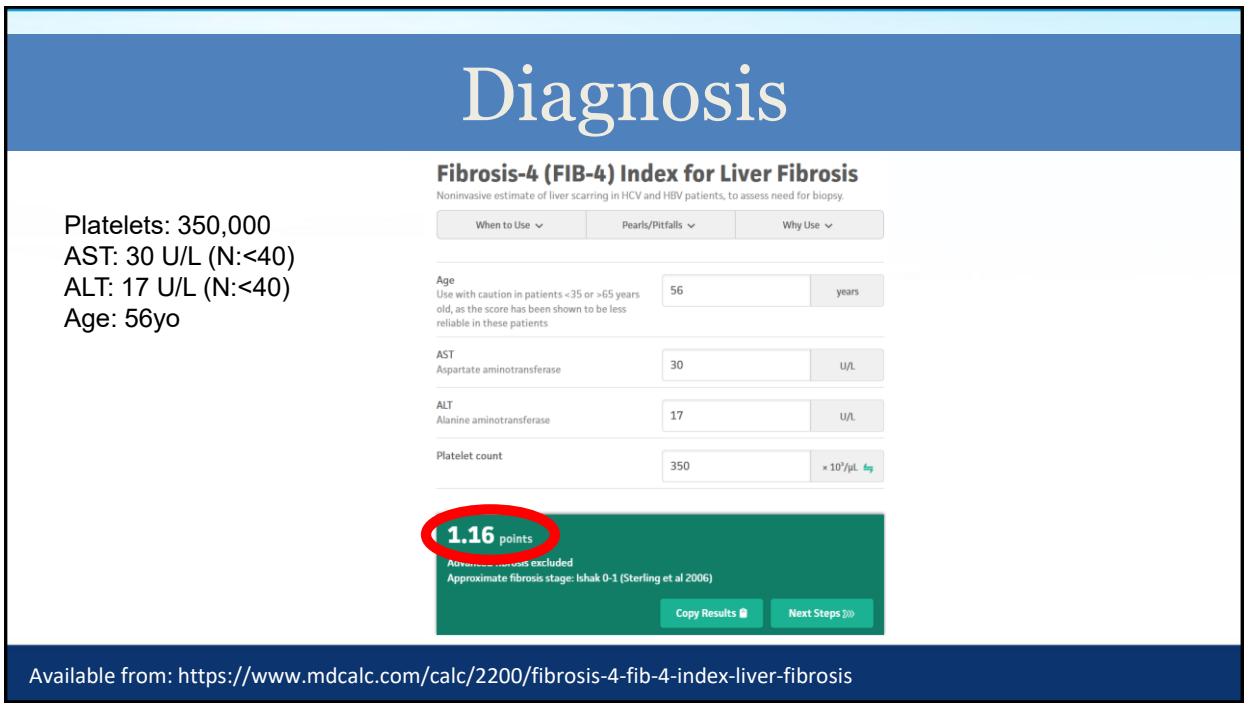
Diagnosis
Platelets: 350,000
AST: 30 U/L (N:<40)
ALT: 17 U/L (N:<40)
Age: 56yo
Fibrosis-4 (FIB-4) Index for Liver Fibrosis
Noninvasive estimate of liver scarring in HCV and HBV patients, to assess need for biopsy.
When to Use
Pearls/Pitfalls
Why Use
Age
Use with caution in patients <35 or >65 years old, as the score has been shown to be less reliable in these patients
56
years
AST
Aspartate aminotransferase
30
U/L
ALT
Alanine aminotransferase
17
U/L
Platelet count
350
1.16 points
Approximate fibrosis stage: Ishak 0-1 (Sterling et al 2006)
Copy Results
Next Steps
Available from: https://www.mdcalc.com/calc/2200/fibrosis-4-fib-4-index-liver-fibrosis

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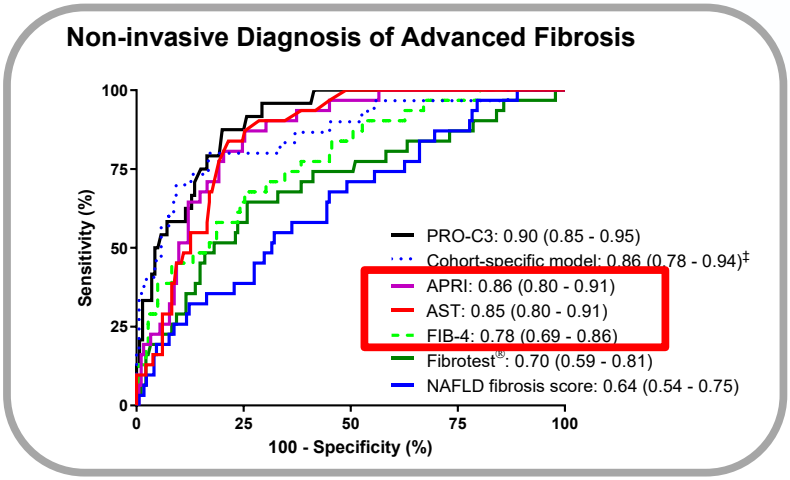
Diagnosis



Bril F, et al. Diabetes Care. 2020;43:290-297.

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Diagnosis

	Hispanic	Non-Hispanic White	Non-Hispanic Black	Non-Hispanic Asian	p value	Entire cohort
Advanced Fibrosis (F3-4 vs. F0-2; VCTE ≥9.7 kPa)						
FIB-4	0.61 (0.51-0.70)	0.51 (0.43-0.60)	0.48 (0.38-0.58)	0.72 (0.57-0.86)	**0.029**	0.55 (0.49-0.60)

	Hispanic	Non-Hispanic White	Non-Hispanic Black	Non-Hispanic Asian	p value	Entire cohort
Cirrhosis (F4 vs. F0-3; VCTE ≥13.6 kPa)						
FIB-4	0.70 (0.57-0.84)	0.57 (0.43-0.71)	0.44 (0.26-0.63)	0.88 (0.80-0.96)	**<0.001**	0.60 (0.51-0.69)

n = 6,359

Bril F, Gray M. Obesity (Silver Spring). 2024;32(3):612-622.

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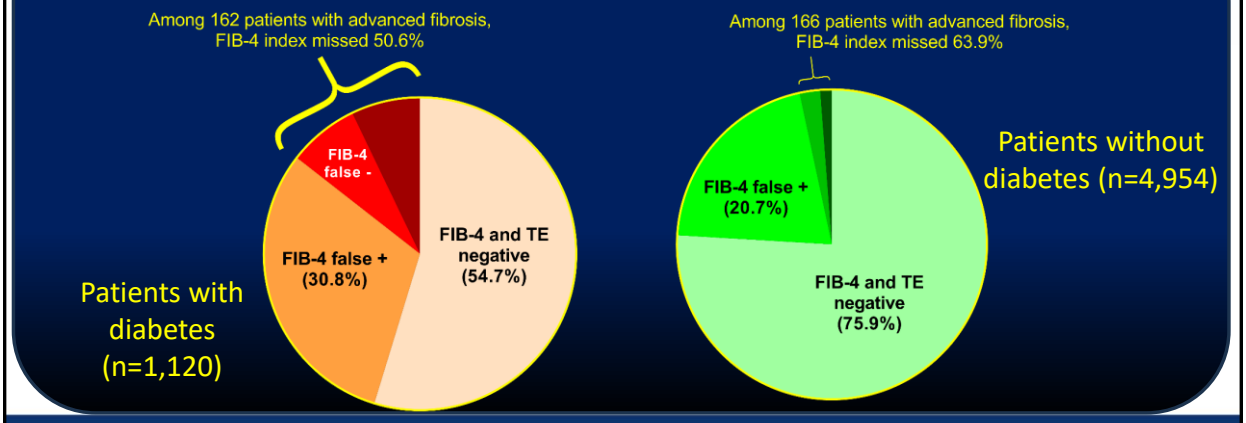
Diagnosis

High degree of incongruence between FIB-4 index and transient elastography (VCTE or Fibroscan®).



Bril F, et al. Presented at ADA 2024.

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Diagnosis

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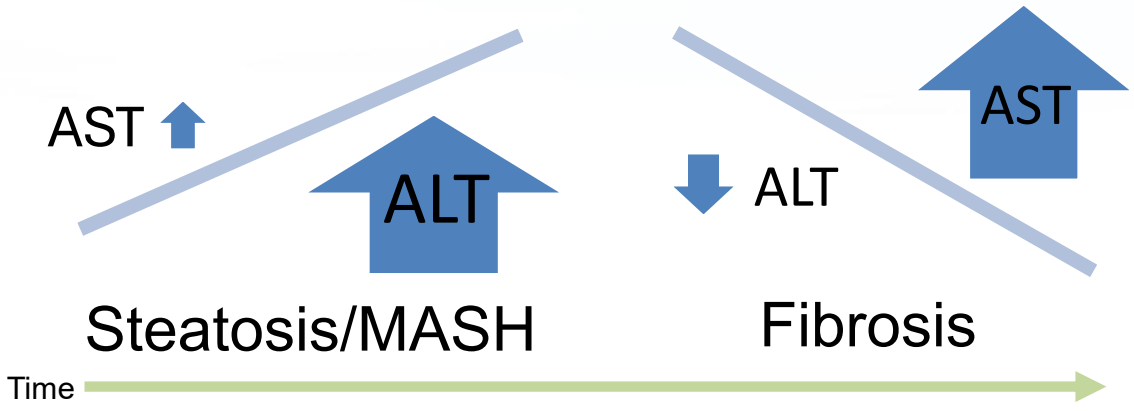
Diagnosis



Current cut-offs are too high: 30 U/L for men, 19 U/L for female (ALT); 20U/L for AST?

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Diagnosis

- Assess for excessive alcohol use (e.g., AUDIT-C & follow up questions[1])
- Consider medications (e.g., estrogen, steroids, amiodarone, methotrexate, etc.)
- HCV antibody with reflex testing of HCV RNA
- Consider HBsAg, HBsAb, HBcAb[2]
- Consider ANA, AMA, ASMA, immunoglobulins
- Ferritin and transferrin saturation
- Ceruloplasmin
- A1AT

40

Diagnosis

	Number of participants with biomarker data	NASH and clinically significant fibrosis*			Advanced fibrosis†		
		Number of participants with target condition	AUC for marker	AUC for FIB-4	Number of participants with target condition	AUC for marker	AUC for FIB-4
CK-18 M30	795	280 (35%)	0·69 (0·65–0·73)	0·70 (0·66–0·73)	224 (28%)	0·70 (0·66–0·74)	0·79 (0·75–0·82)
CK-18 M65	817	281 (34%)	0·70 (0·66–0·74)	0·69 (0·65–0·73)	228 (28%)	0·70 (0·66–0·74)	0·79 (0·75–0·82)
PRO-C3	444	160 (36%)	0·68 (0·63–0·74)	0·73 (0·68–0·78)	126 (28%)	0·75 (0·70–0·80)	0·76 (0·71–0·81)
PRO-C6	229	95 (41%)	0·68 (0·61–0·75)	0·70 (0·63–0·77)	82 (36%)	0·71 (0·63–0·78)	0·73 (0·66–0·80)
PRO-C4	391	155 (40%)	0·63 (0·57–0·68)	0·72 (0·67–0·77)	123 (31%)	0·66 (0·60–0·71)	0·75 (0·70–0·81)
NFS	933	327 (35%)	0·66 (0·62–0·69)	0·69 (0·66–0·73)	265 (28%)	0·75 (0·72–0·79)	0·77 (0·74–0·81)
APRI	966	335 (35%)	0·68 (0·64–0·71)	0·69 (0·66–0·73)	273 (28%)	0·72 (0·68–0·75)	0·77 (0·74–0·81)
ELF	919	306 (33%)	0·67 (0·63–0·71)	0·68 (0·65–0·72)	249 (27%)	0·80 (0·76–0·83)	0·77 (0·74–0·81)
SomaSignal	264	122 (46%)	0·81 (0·75–0·86)	0·66 (0·60–0·73)	95 (36%)	0·90 (0·86–0·94)	0·72 (0·66–0·79)
MACK-3	538	185 (34%)	0·76 (0·71–0·80)	0·69 (0·64–0·73)	131 (24%)	0·74 (0·69–0·79)	0·76 (0·71–0·80)
Cao 2013	635	236 (37%)	0·67 (0·63–0·72)	0·69 (0·65–0·73)	189 (30%)	0·68 (0·64–0·73)	0·79 (0·75–0·83)
ADAPT	444	160 (36%)	0·77 (0·73–0·81)	0·73 (0·68–0·78)	126 (28%)	0·85 (0·81–0·89)	0·76 (0·71–0·81)
FIBC3	440	159 (36%)	0·74 (0·69–0·79)	0·73 (0·68–0·78)	124 (28%)	0·82 (0·78–0·87)	0·76 (0·71–0·81)
ABC3D	440	159 (36%)	0·74 (0·69–0·79)	0·73 (0·68–0·78)	124 (28%)	0·81 (0·76–0·85)	0·76 (0·71–0·81)
LSM-VCTE	632	249 (40%)	0·74 (0·70–0·78)	0·66 (0·62–0·71)	190 (30%)	0·83 (0·80–0·86)	0·73 (0·70–0·78)

Vali Y, et al. Lancet Gastroenterol Hepatol. 2023;8(8):714-725.

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Diagnosis

Fibroscan GO

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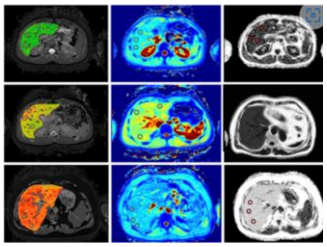
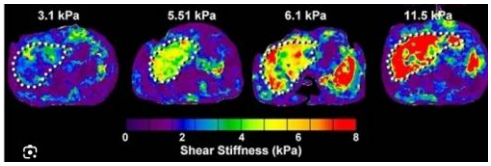
Diagnosis



Multiparametric resonance
(cT1 mapping)



MRE

±

New Scores / biomarkers

Agile3+
Agile4
FAST
NIS2+
PRO-C3

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Conclusions

1. MASLD is a systemic disease; mostly a metabolic condition.
2. Highly prevalent; progressive.
3. Early diagnosis is key.
4. Primary care providers are at center stage in diagnosing (and treating) these patients.