Malaltia per fetge gras no alcohòlic: una epidèmia silenciosa

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Reus, 17 de juny 2022

ciberdem
Centro de Investigación Biomédica en Red
Diabetes y Enfermedades Metabólicas Asociadas

IGTP
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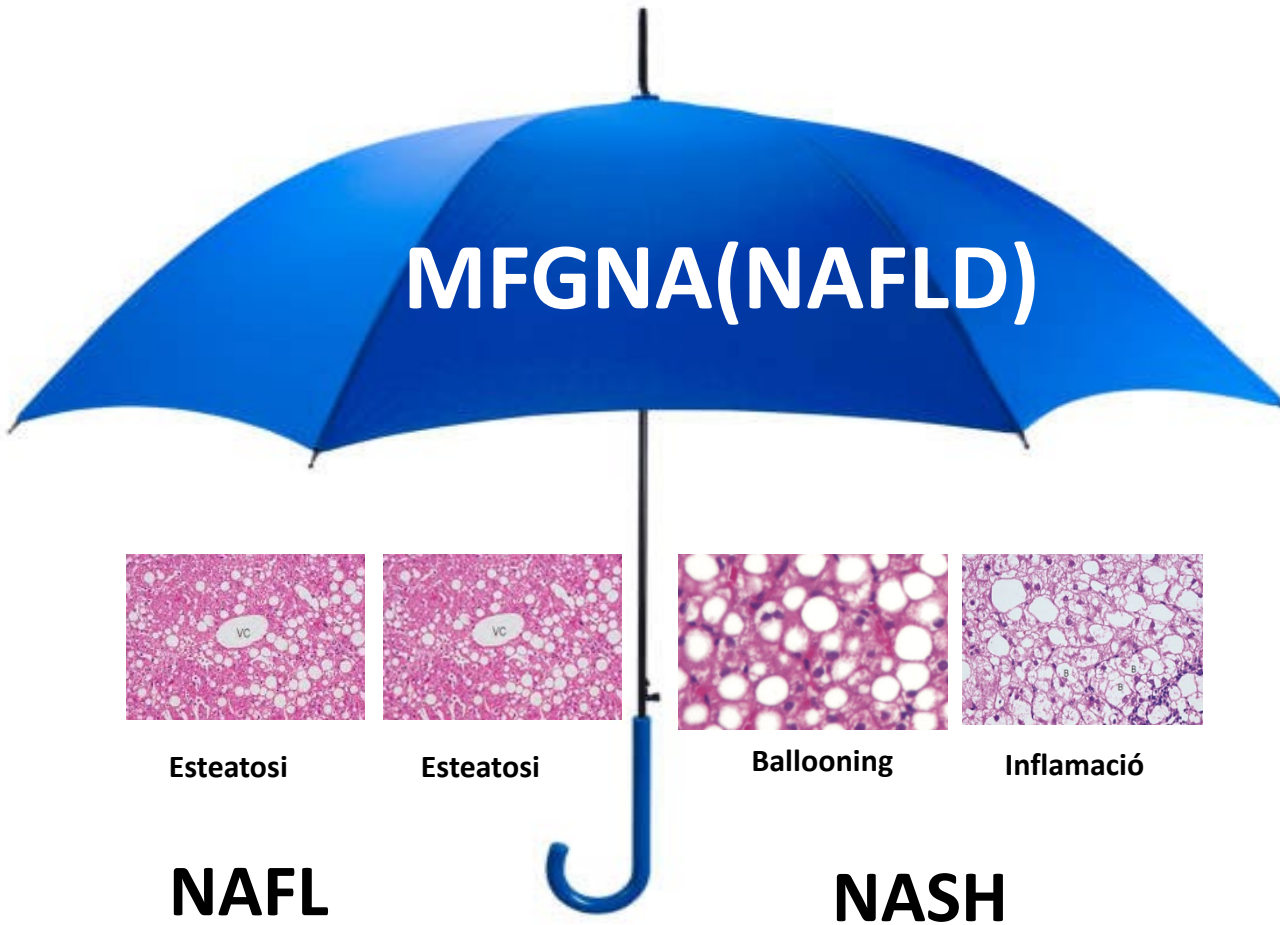
Hospital

Malaltia per fetge gras no alcohòlic (MFGNA): dipòsit d'àcids grassos lliures i triglicèrids als hepatòcits, sense consum d'alcohol ni associació a causes secundàries.

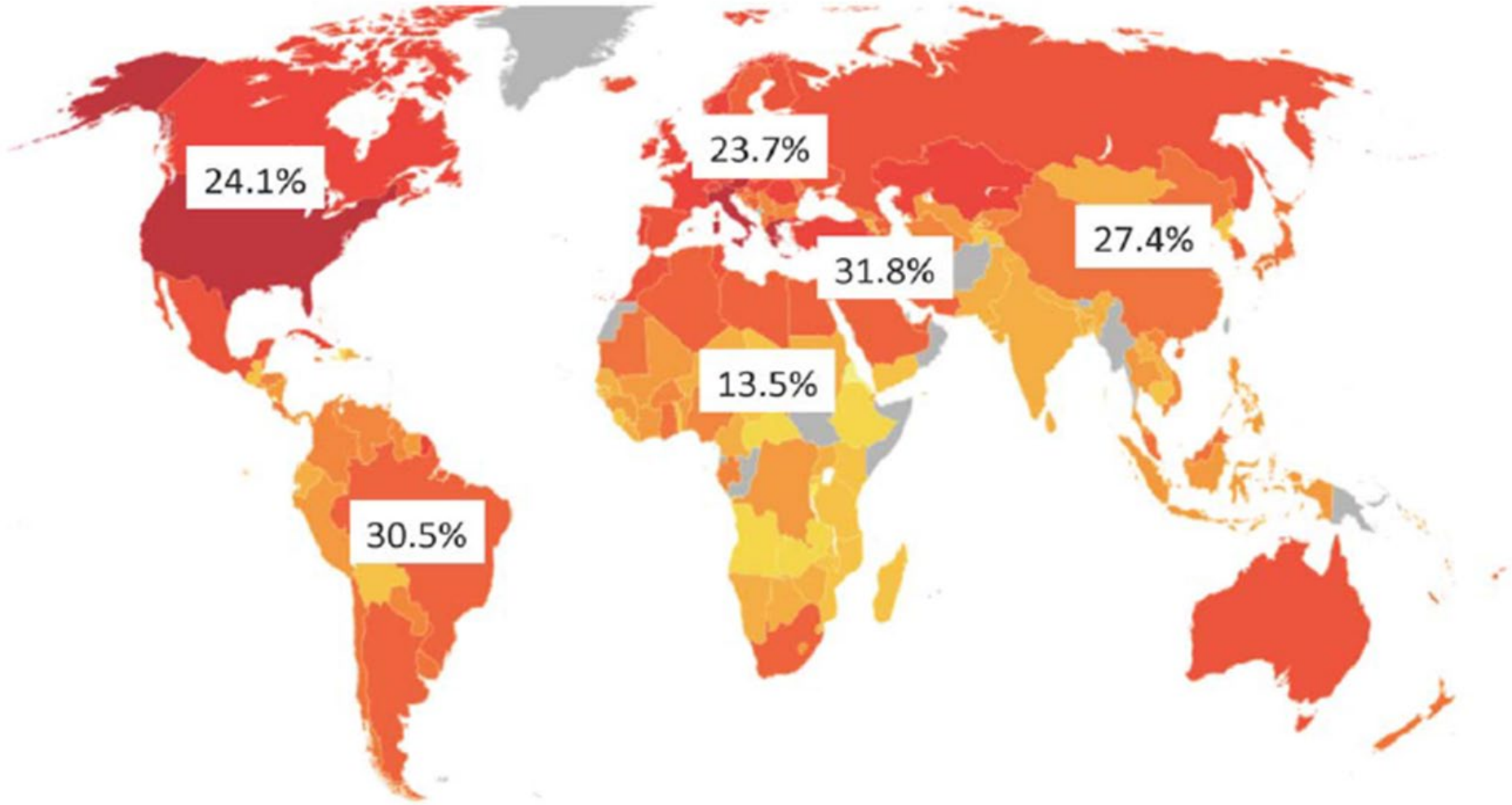


Causes

- Excessive alcohol consumption
- Hepatitis C (genotype 3)
- Lipodystrophy
- Acute weight loss (bariatric surgery and starvation)
- Malnutrition
- Parenteral nutrition
- Abetalipoproteinemia
- Reye syndrome
- Pregnancy associated
  - HELLP syndrome
  - Acute fatty liver of pregnancy
- Medications (eg, corticosteroids, mipomersen, lomitapide, amiodarone, methotrexate, tamoxifen, valproate, and antiretroviral medicines)
- Rare causes: autoimmune hepatitis, A1AT deficiency, Wilson syndrome, and other

Med Clin 2017;149:542

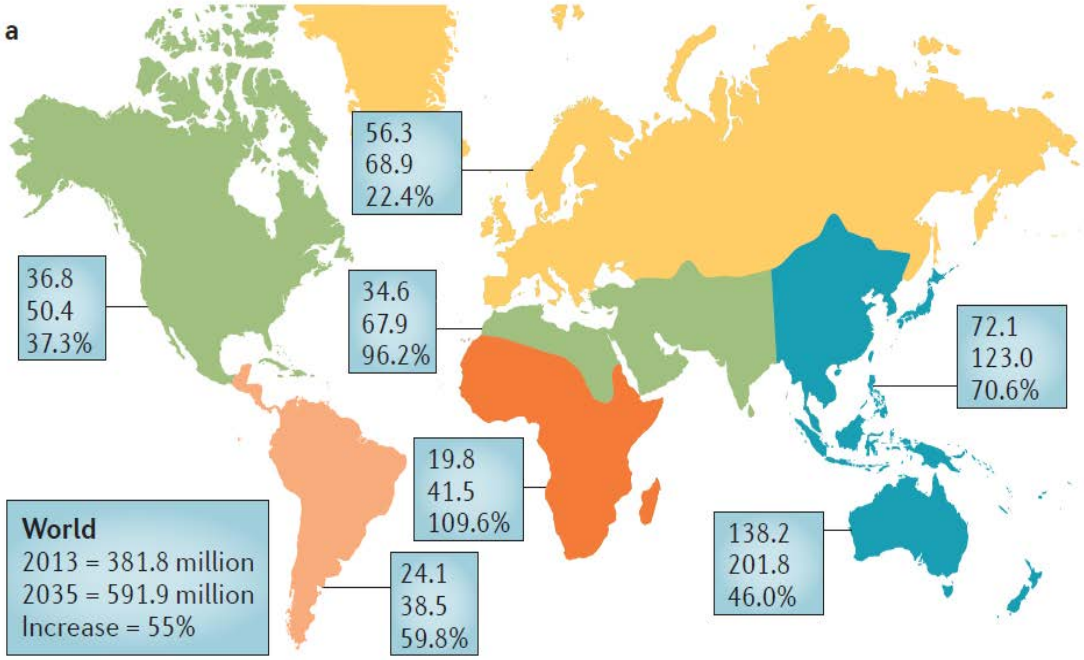
MFGNA: malaltia hepàtica crònica més prevalent



Hepatology 2016;64:19

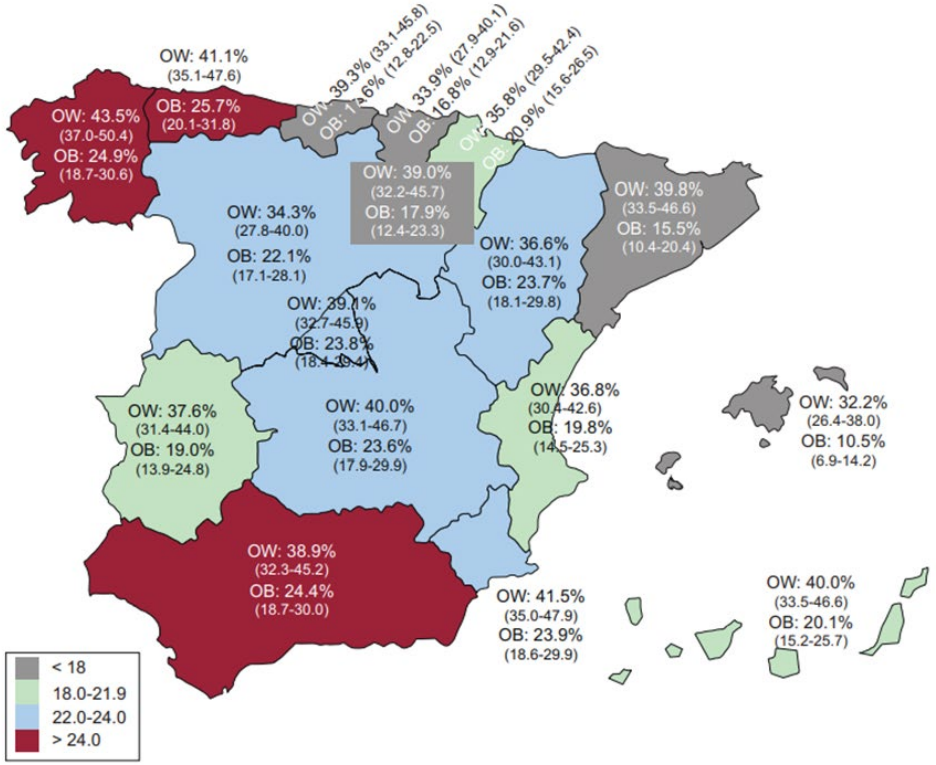
Epidèmia diabetis i obesitat

Prevalença de DM2



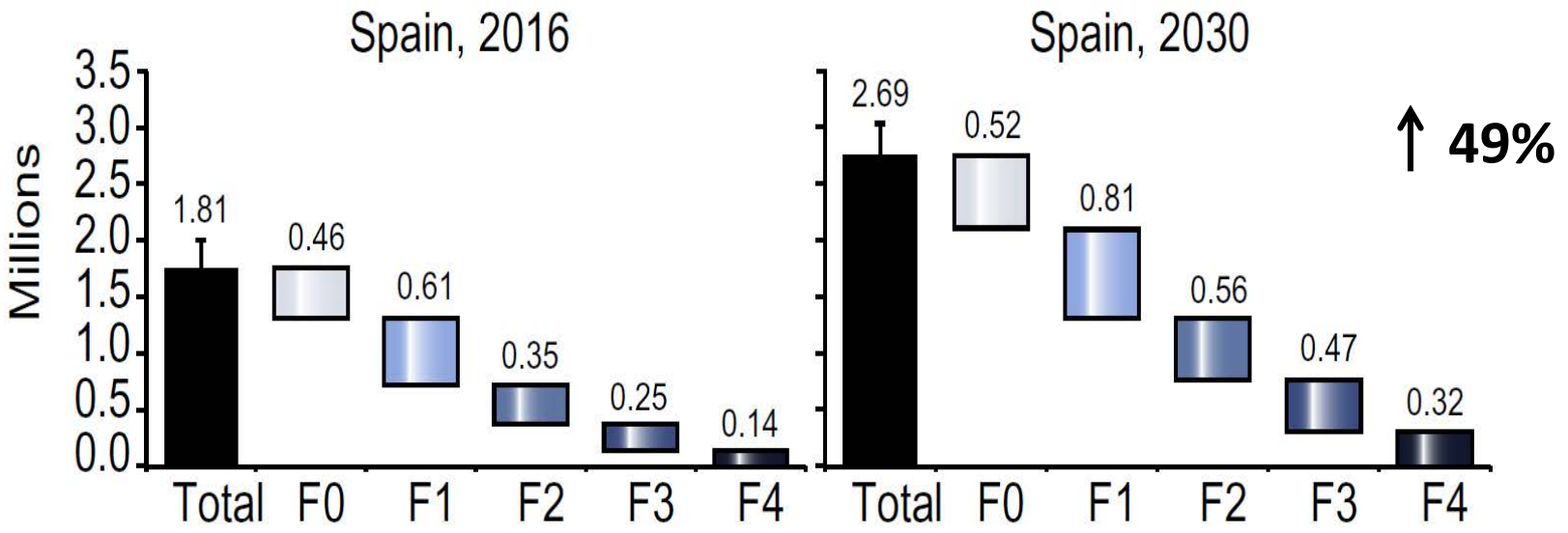
Nat Rev Dis Primers 2015;1:15019

Obesitat (IMC ≥ 30 Kg/m^2): 21,6%



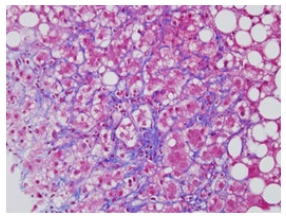
Rev Esp Cardiol. 2016;69:579

Increment prevalença EHNA



J Hepatol 2018;69:896

F1



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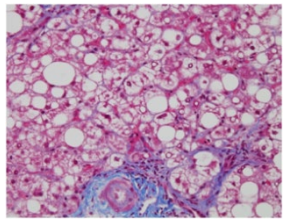

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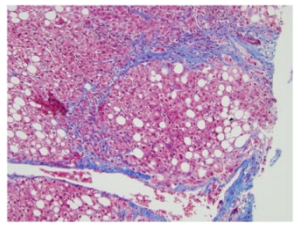

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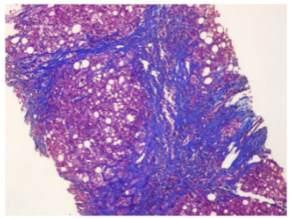
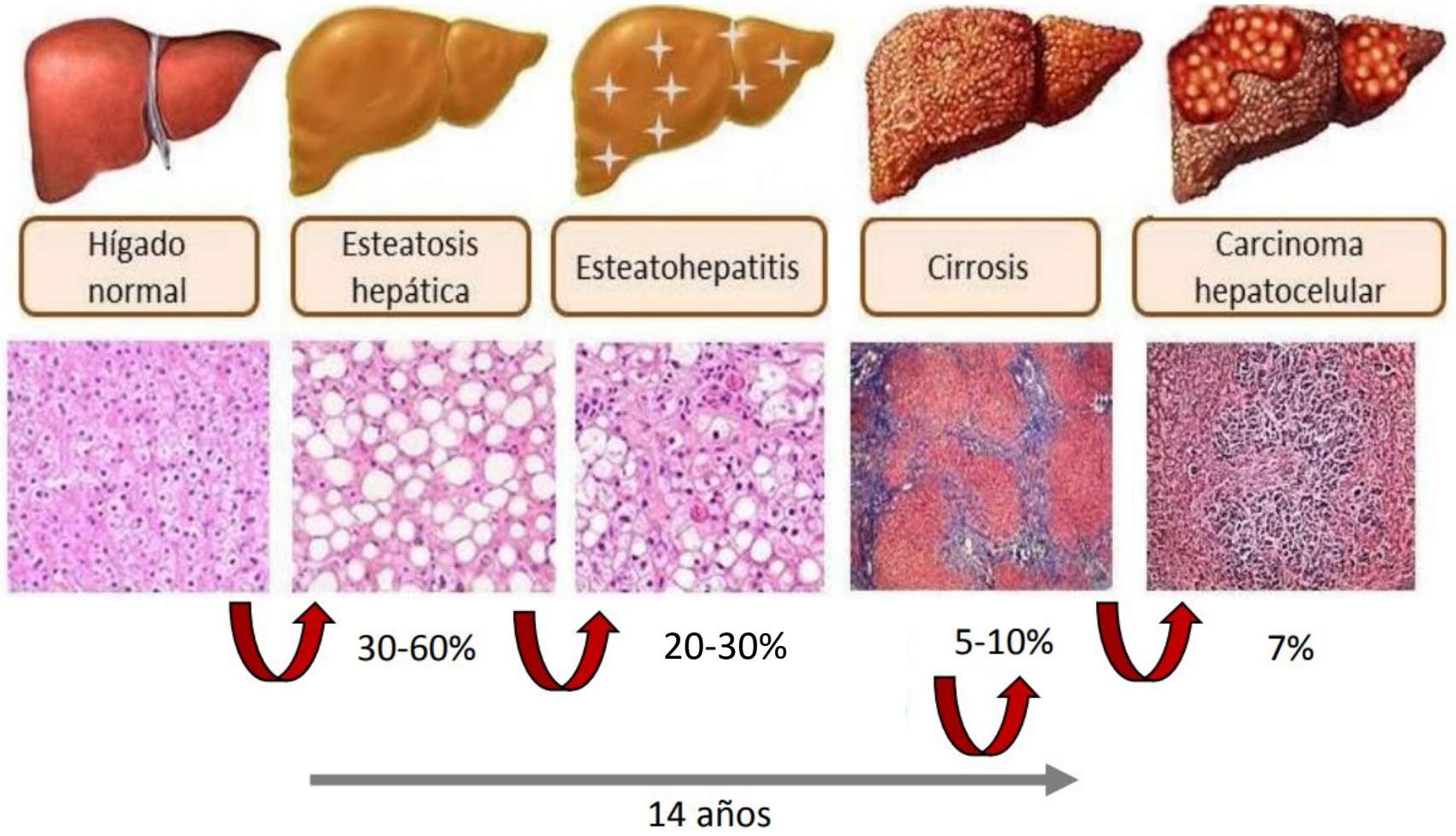
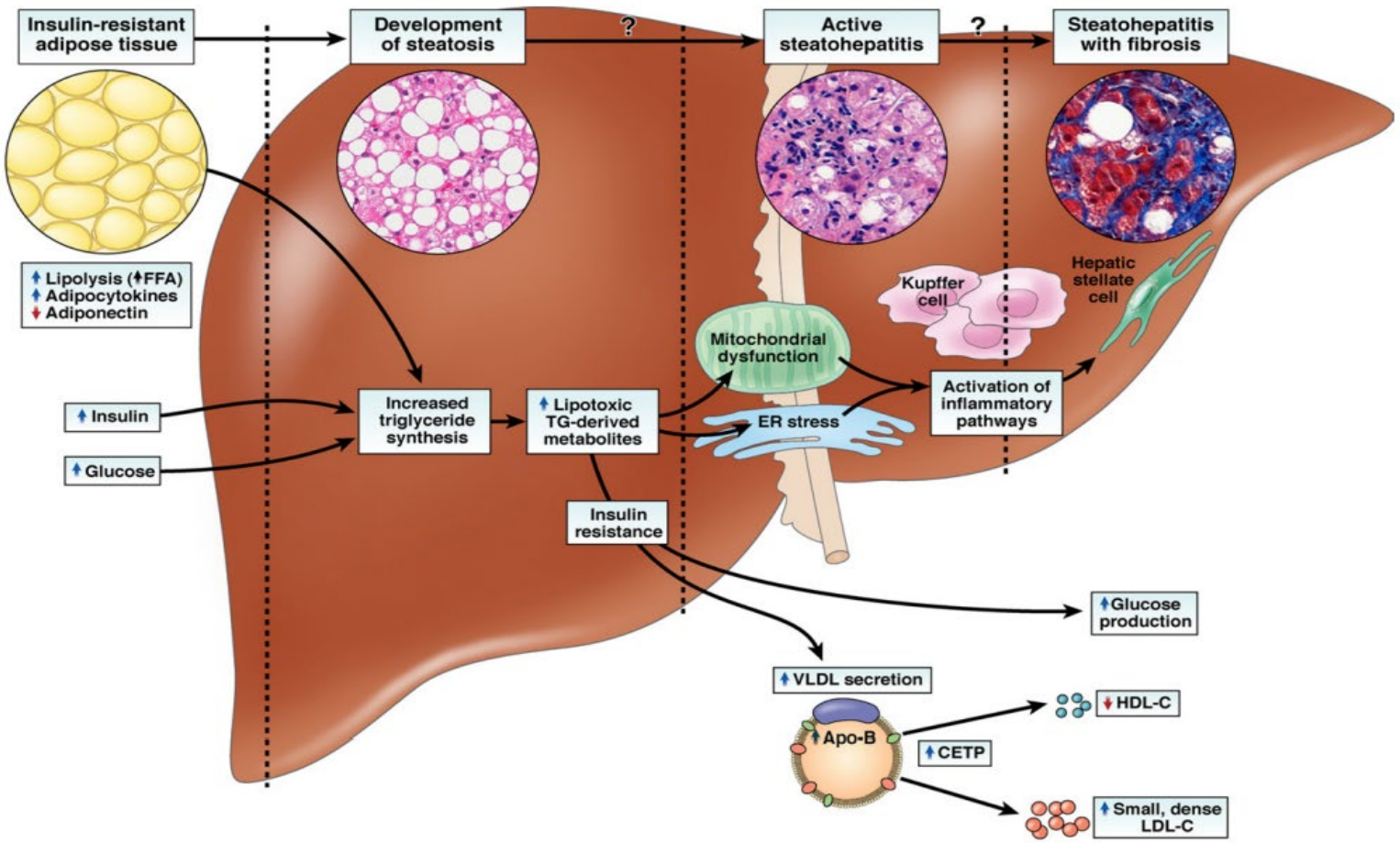


Història natural de la MFGNA



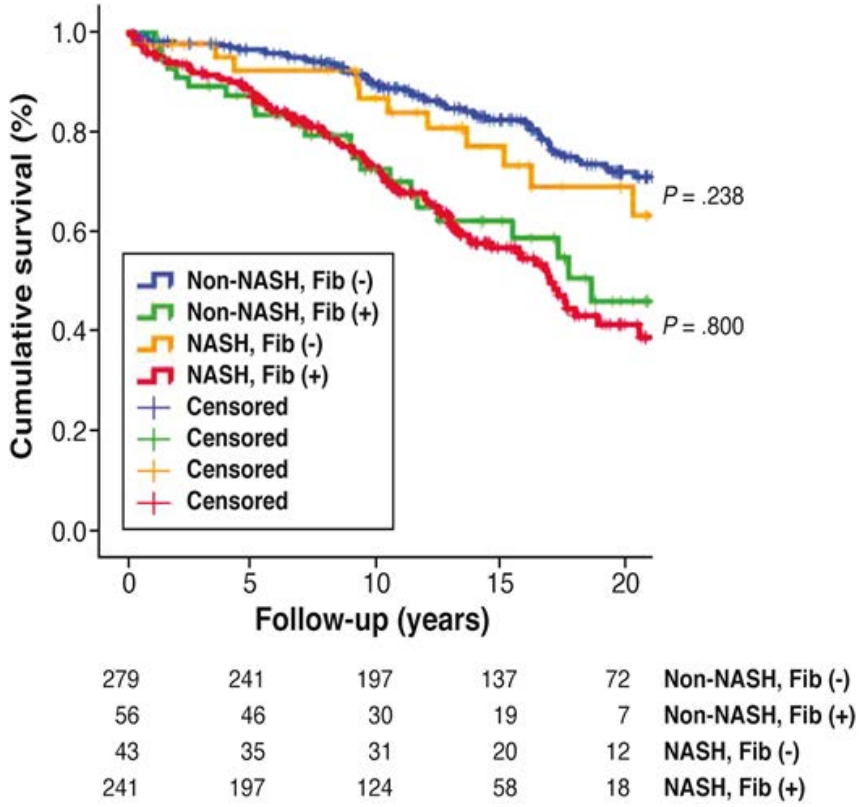
Day CP J Hepatol 2008

Fisiopatologia de la MFGNA



Gastroenterology 2012;142:711

La fibrosi hepàtica: factor predictiu de mortalitat més important en MFGNA



Gastroenterology 2015; 149:389

- El grau fibrosi (F3-F4) s'associa a mortalitat global i hepàtica

J Hepatology 2015;61:1547

- **DM:** s'associa a un major risc de progressió en el grau de fibrosi en pacients amb NASH i/o NAFLD (OR 6,28 (1,88-20)

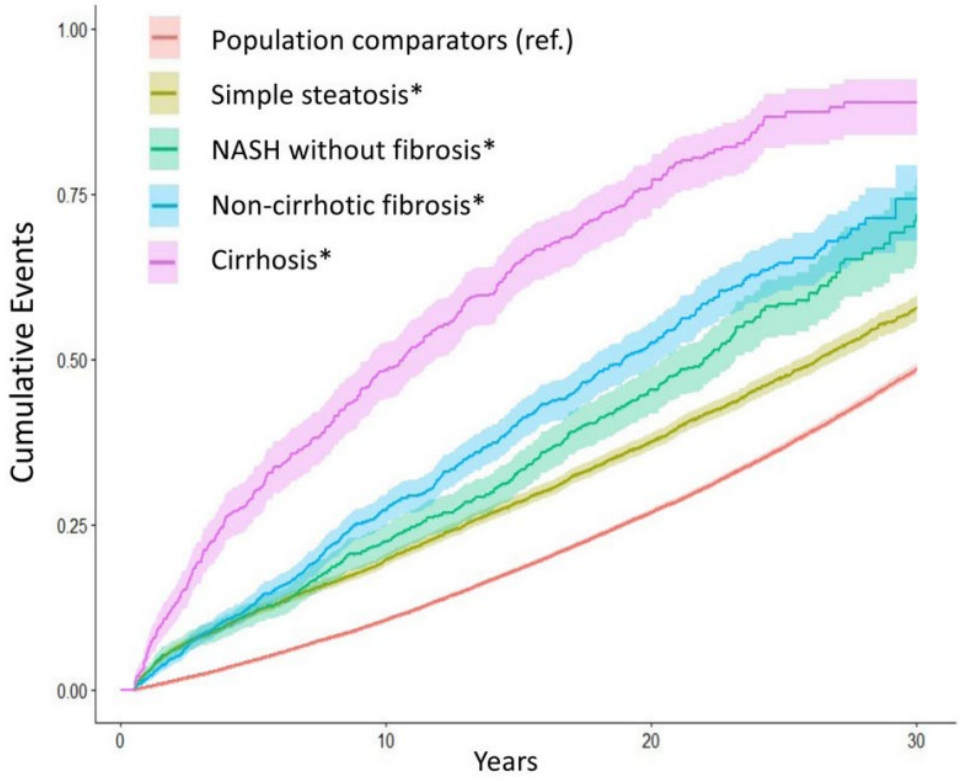
J Hepatology 2015;61:1547

- En els pacients amb CH criptogènica la prevalença de DM2 és molt més elevada que en les CH d'altres etiologies

Gastroenterology 2015;148:547

Graus histològics MFGNA i pronòstic

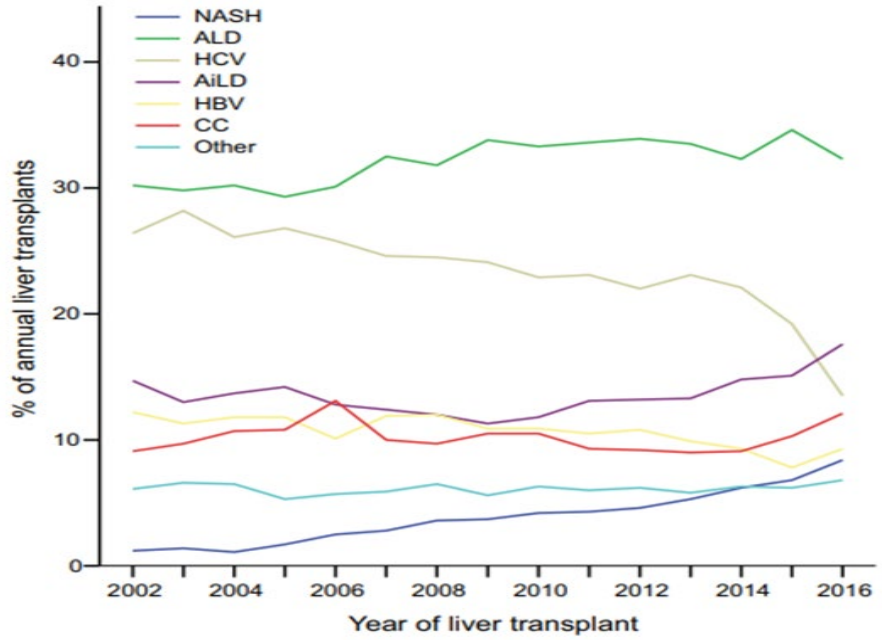
N=4338 MFGNA x biòpsia *vs* 49.925 pobl general



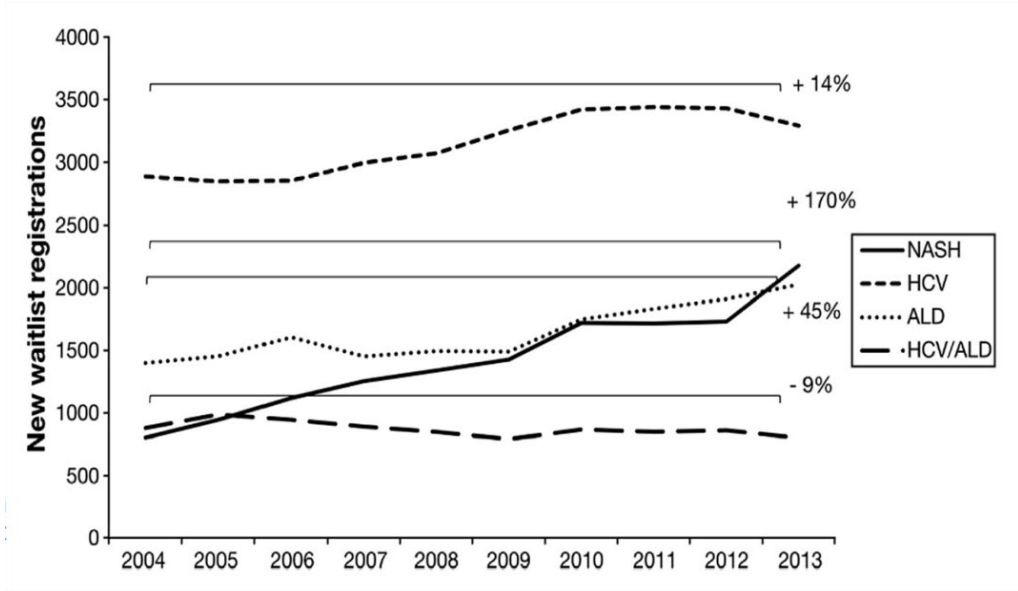
Gut 2021;70:1375

- Increment mortalitat global: OR 1,93
- **Causes mes freqüents:**
  - Càncer extrahepàtic (gi): OR 2,16
  - Cirrosi: OR 18,15
  - Malaltia CV; OR 1,35
  - Carcinoma hepatocel·lular: OR 11,12

EHNA i trasplantament hepàtic



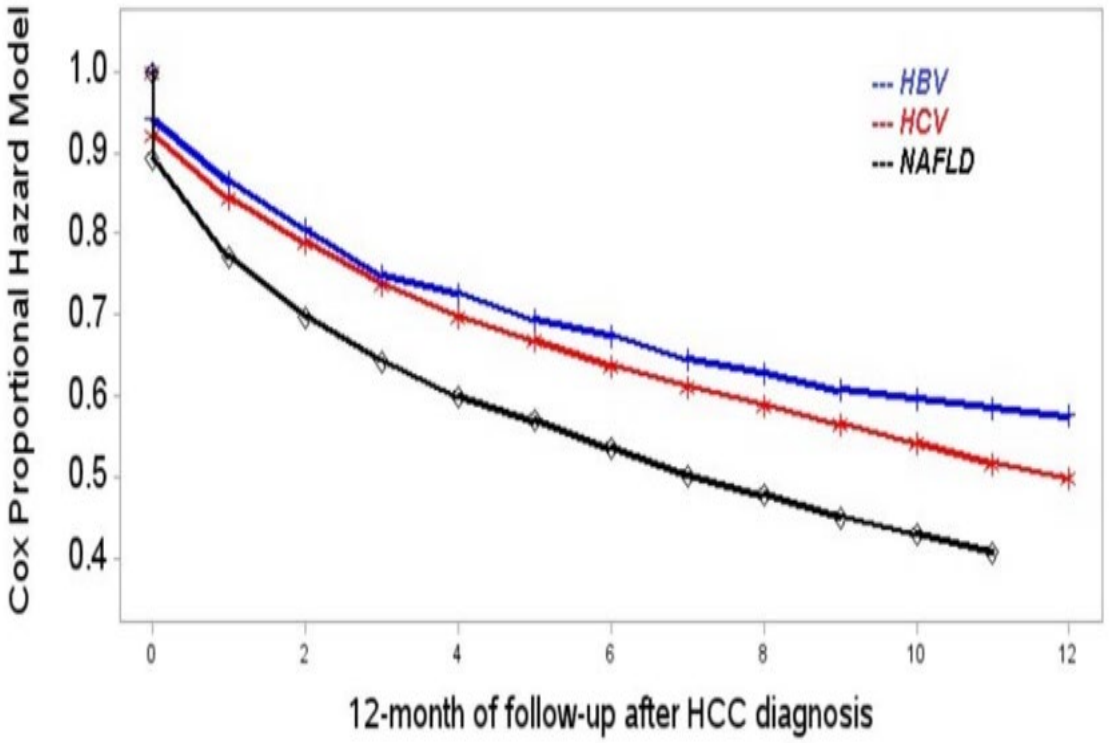
Journal of Hepatology 2019;71:313



Gastroenterology 2015;148:547

Hepatocarcinoma en els pacients amb EHNA

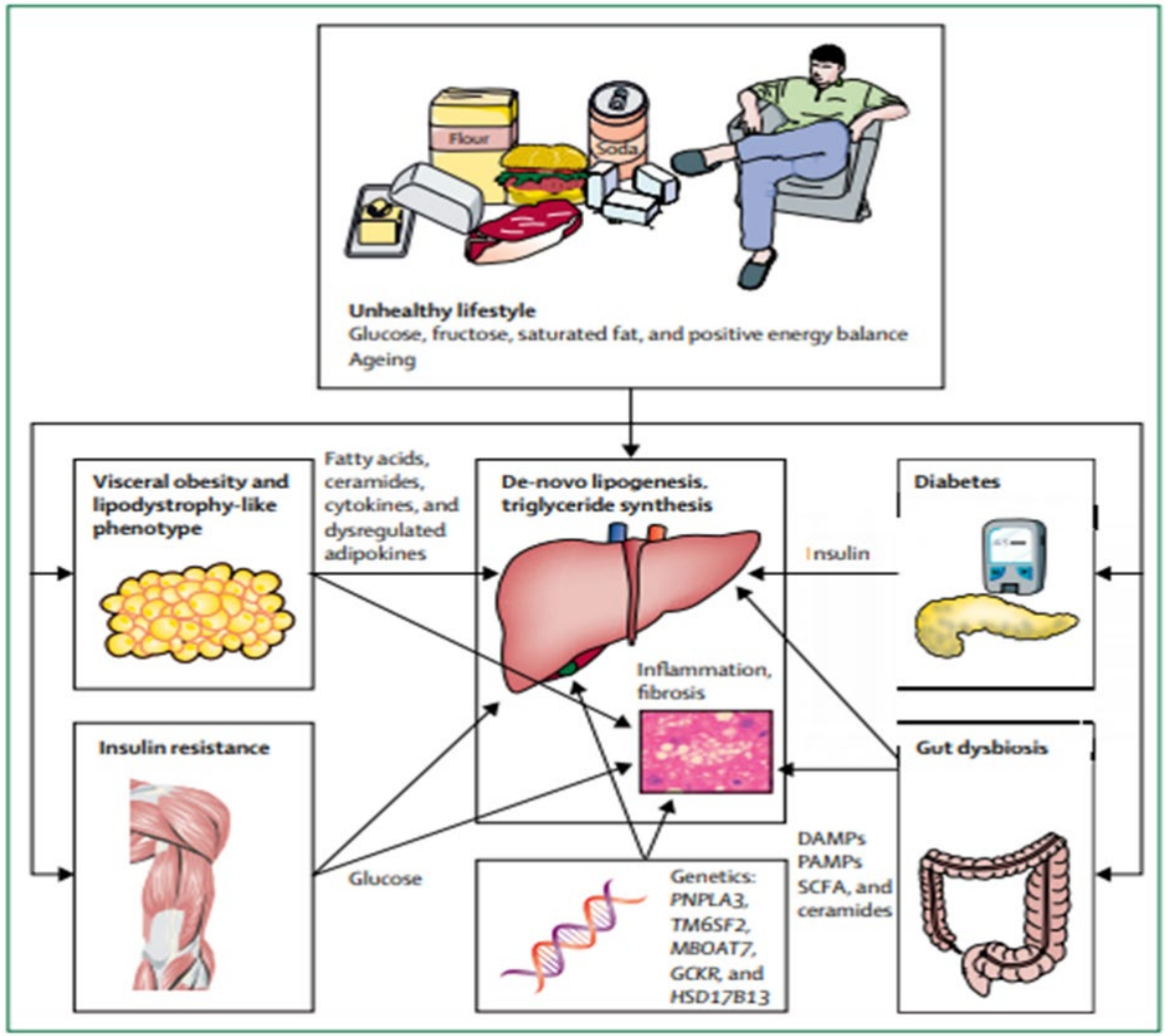
- En comparació amb HCC secundari a VHB/VHC:
  - Es diagnostica en etapes més avançades
  - Major mortalitat
  - Major prevalença de malalties cardíaques
  - Edat més avançada
  - Menor prevalença de CH
- **Diabetis mellitus:**
  - x 2 risc HCC
  - X 1,5 mort per HCC
- **Obesitat:**
  - IMC >30 Kg/m^2: risc x2
  - IMC >40 Kg/m^2: risc x 4



Hepatology 2015;62:1723

JHEP 2021;3:1

Factors de risc de la MFGNA



Lancet Diabetes endocrinol 2019;7:313

- **Obesitat** (IMC ≥ 30 Kg/m^2) (abdominal)
- **Diabetis mellitus tipus 2** (DM2)
- Components sd. metabòlica: **HTA**, **dislipèmia** (>TG, c-HDL baix)
- **Sobrecàrrega fèrrica dismetabòlica** (ferritina 500-1500 mg/l)
- **Polimorfismes genètics**
- **Alteració en la composició microbiota inestinal** (disbiosi)

Med Clin 2019;153:169

Estudi poblacional: factors risc de MFGNA

- 766 individus
- Dones 58%, homes 42% → **Prevalença: 25,8%**
- NAFLD (ecografia): 198 individus

	OR	IC95%	p	OR	IC95%	p
✓ **Sexo masculino**	2,13	1,52-2,99	<0.0005	2,17	1,48-3,17	<0.0005
✓ **Edad** 40-60 años	2,49	1,47-4,23	<0.001	1,03	1,02-1,05	<0,0005
> 60 años	4,15	2,44-7,04	<0.0005			
✓ **Sobrepeso** (IMC 25-30 kg/m²)	2,43	1,45-4,10	<0.001			
✓ **Obesidad** (≥30 kg/m2)	6,80	3,96-11,7	<0.0005			
✓ **Obesidad central** (≥102cm/88cm)	2,72	1,87-2,58	<0.001			
✓ **HTA** (≥135/ ≥ 85 mmHg)	1,82	1,28-2,58	<0.001			
✓ **Diabetes** (Glicemia ≥110 mg/dl)	3,42	2,29-5,12	<0.0005			
✓ **HDL** (<40 mg/dl/ 50 mg/dl)	1,88	1,26-2,81	<0.002			
✓ **Triglicéridos** (≥150 mg/dl)	3,23	2,18-4,79	<0.0005			
✓ **ALAT** (≥ 45 U/L/ ≥ 34 U/L)	5,34	3,01-9,47	<0.0005	4,64	2,51-8,58	<0,0005
✓ **Síndrome metabólico** (NCEP)	3,78	2,38-6,01	<0.0005	2,30	1,37-3,86	0,002
✓ **Resistencia insulina** (HOMA ≥3.8)	7,47	4,55-12,1	<0.0005	5,45	3,19-9,31	<0,0005

Caballeria et al. Eur J Gastroenterol Hepatol 2010;22:24-32

Prevalença i factors de risc de fibrosi: estudi poblacional

Prevalença de fibrosi hepàtica (n=3076) (Fibroscan®; ≥ 8KPa): 5,7%

Table 2. Multivariate Analysis of Factors Associated With Increased Liver Stiffness Using 3 Different Cut-Off Values

	6.8 kPa				8.0 kPa				9.0 kPa			
	OR	95% CI		*P* value	OR	95% CI		*P* value	OR	95% CI		*P* value
Male sex	3.01	2.25	4.05	.000	2.71	1.90	3.87	.000	3.26	2.06	5.16	.000
AST and/or ALT > ULN[a]	2.15	1.48	3.12	.000	1.95	1.26	3.03	.003	2.91	1.76	4.80	.000
Abdominal obesity[b]	3.84	2.75	5.34	.000	4.28	2.78	6.59	.000	4.19	2.42	7.24	.000
Glucose level ≥100 mg/dL	1.63	1.18	2.24	.003	2.06	1.38	3.07	.000	2.20	1.29	3.73	.004
Low HDL[c]	1.51	1.10	2.07	.011	1.68	1.16	2.44	.006	1.67	1.05	2.66	.030
Triglyceride level ≥150 mg/dL	1.63	1.21	2.19	.001	1.73	1.21	2.47	.003	1.41	0.90	2.20	.137
Type 2 diabetes	2.13	1.49	3.05	.000	2.00	1.33	3.01	.001	2.28	1.40	3.74	.001

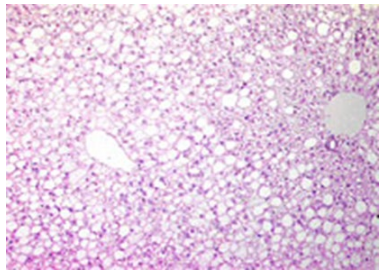
Clin Gastroenterol Hepatol 2018;16:1138

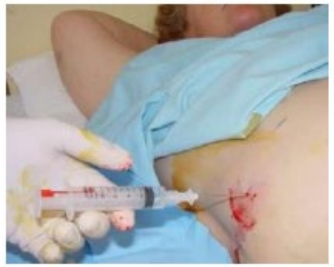
Proves diagnòstiques: esteatosi hepàtica

- *Biomarcadors:* fatty liver index (FLI)

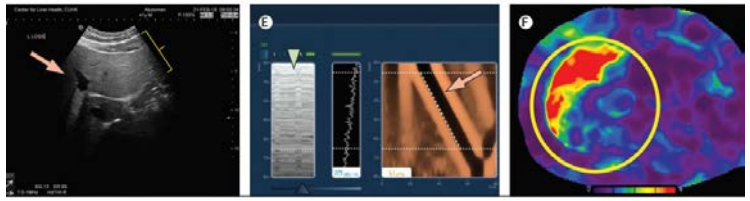
Triglicèrids, perímetre cintura, IMC, GGT

- *Biòpsia hepàtica: gold standard*





- *Proves d'imatge:*
  - **Ecografia hepàtica** (>20-30% hepatòcits)
  - **Controlled Attenuation Parameter** (CAP):
    - S1 (274-289 dB/m): esteatosi lleu
    - S2 (290-301 dB/m): esteatosi moderada
    - S3 (≥ 301 dB/m): esteatosi greu
  - **RMN amb espectroscòpia**:
    - Major sensibilitat que l'ecografía
    - Detecta ≥ 5% greix
    - Recerca i assajos clínics



Proves diagnòstiques: EHNA

- **Histològic** (biòpsia hepàtica): *Gold standard*
- Absència de biomarcador sèric

NASH clinical research network

Clasificación de la actividad de la EHGNA por el sistema NASH-CRN (NASH Activity Score, *NAS*)

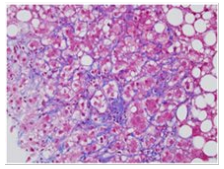
Esteatosis (%)	Inflamación lobulillar	Balonización
0: < 5	0:No	0: No
1: 5-32	1: < 2 *foci*	1: leve
2: 33-66	2: 2-4 *foci*	2: abundante
3: > 66	3: > 4 *foci*	

NAS: ≥ 5 punts: esteatohepatitis

Tabla 3b
Estadio de la fibrosis hepática según la clasificación CRN Fibrosis Stagin

Estadio	Grado de fibrosis
0	Sin fibrosis
1a	Fibrosis perisinusoidal (zona 3) leve
1b	Fibrosis perisinusoidal (zona 3) moderada
1c	Fibrosis periportal/portal exclusivamente
2	Fibrosis zona 3 + periportal /portal
3	Puentes de fibrosis
4	Cirrosis

F1



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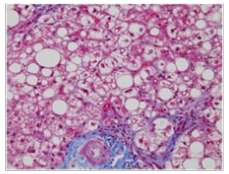
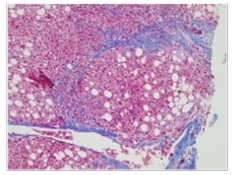


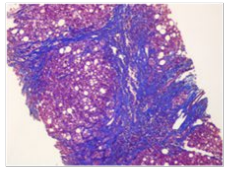
FIBROSI SIGNIFICATIVA

F3



FIBROSI AVANÇADA

F4



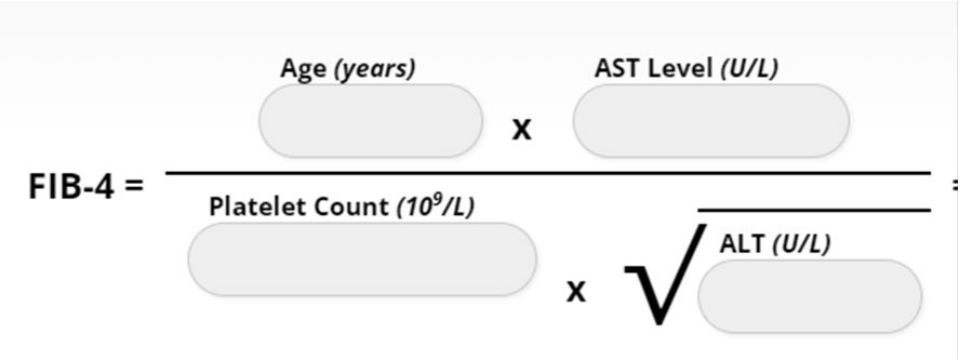
CIRROSI

Caballeria Ll. Med Clin 2019: 153:169;Stal P. WJG. 2015;21:11077

EHNA: Biomarcadors de fibrosi avançada (F3-F4)

FIB-4

Baix: <1,3 → Intermig: 1,3-2,67 → Alt: >2,67



NFS

Baix: <-1,45 → Intermig: 1,455-0,676 → Alt: >0,676

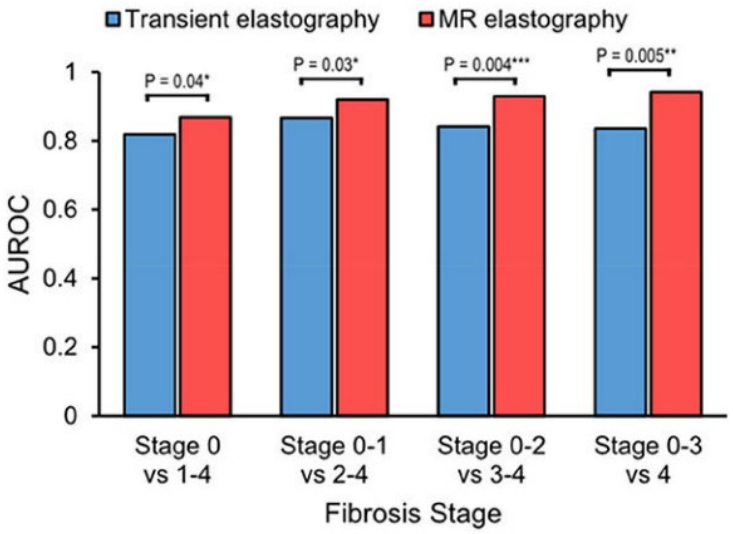
$$\begin{aligned}\text{NFS} = {} & -1.675 + 0.037 \times \text{age (years)} + 0.094 \\ & \times \text{body mass index } (\text{kg/m}^2) + 1.13 \\ & \times \text{impaired fasting glucose}^{*}/\text{diabetes (yes} = 1; \text{no} = 0) \\ & + 0.99 \times \text{aspartate aminotransferase} \\ & /\text{alanine aminotransferase ratio} - 0.013 \\ & \times \text{platelet count } (10^9/\text{L}) - 0.66 \times \text{albumin (g/dL)}.\end{aligned}$$

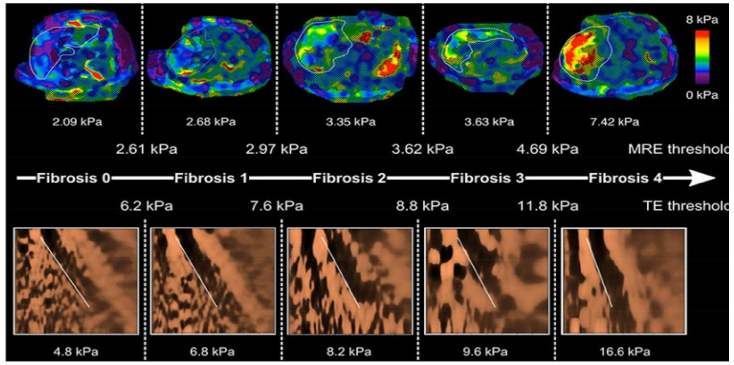
Biomarcadors de fibrosi avançada (F3-F4)

A. Blood Liver Funtion Tests	Parameter Measured	Pros	Cons	AUROC
ELF panel [39]	Hyaluronic acid (HA), Tissue inhibitor metalloproteinase 1 (TIMP1), and Aminoterminal peptide of procollagen 3 (PIIINP).	Feasible in large number of subjects Good outcome correlation	Commercial test not routinely available	0.93 in adults 0.99 in pediatric patients
Pro-C3 [42]	Pro collagen III	Able to discriminate simple fatty liver from NASH and different stages of fibrosis	Commercial test	0.86
NASH NIS4 [44]	MicroRNA 34a-5p; alpha2 macrogobulin (A2M), Haemooglobin A1c (HbA1c), and Chitinase-3-like protein 1 (CHI3L1 also known as YKL40)	This tool can enrich the selection of patients—candidate to experimental trials—with active NASH and significant fibrosis	Commercial test; performances might vary according to the baseline characteristics of the studied population	0.82
Lipidomic serum test § (OWLiver) [45]	Two subsequent analyses of 11 and 20 triglycerides panel to be used in adults with BMI > 25	Able to discriminate normal liver form NAFLD and NAFLD from NASH	Commercial test performed in a centralized laboratory	0.79 or 0.81 (according to inclusion or exclusion of patients with glucose >136 mg/dl)
B.US-Based Physical Tests	**Parameter Measured**	**Pros**	**Cons**	**AUROC**
TE [47,48]	Liver stiffness	Short processing time and outpatient clinic setting	Measurement failures reported in up to 20% and XL probe required in obese patients	0.95 for F4 0.93 for F3 0.84 for F2 fibrosis
Point shear wave elastgraphy (ARFI) [49]	Liver stiffness	Short processing and outclinic setting	Quality criteria not well defined, lack of large-scale studies	0.78–0.89 for F4 0.74–0.97 for F3 0.70–0.83 for F2 fibrosis
B. Not US-Based physical tests	**Parameter Measured**	**Pros**	**Cons**	**AUROC**
MRE [50,51]	Liver stiffness	Not influenced by BMI and inflammation	Long processing, expensive, and not largely available	0.88–0.97 for F4 0.89–0.96 for F3 0.86–0.89 for F2
LiverMultiScan (multiparametric resonance) [52]	Fibrosis and inflammation mapping	Quick and no contrast agent required	Further validation studies required	0.85 for F4

Cells 2020;9:1005

Rigidesa hepàtica: mètodes mesura





- **Elastografia hepàtica:**
  - Fibroscan® (elastografia de transició) (sonda XL obesitat)
  - ARFI
  - SWE
  - RME

Fibrosi hepàtica (LSM) (N <5kPa):

LSM 7.0-8.1: probable fibrosi lleu (F1)

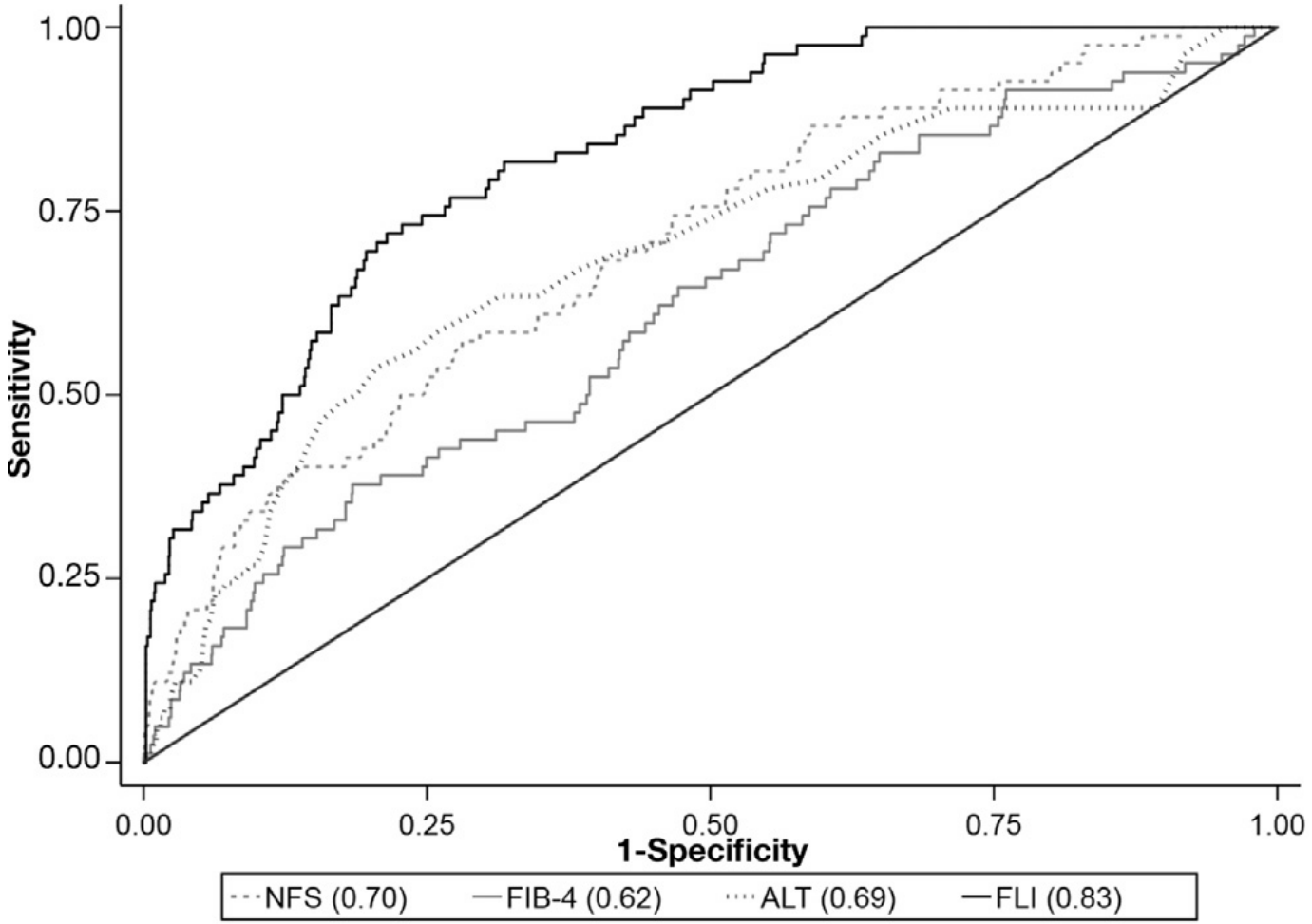
LSM 8.2-9.6: probable fibrosi moderada (F2)

LSM 9,7-13,5: probable fibrosi avancçada (F3)

LSM ≥ 13.6: probable cirrosi (F4)

Gastroenterology 2019;156:1717 *Clinical Gastroenterology and Hepatology 2019;17:630*

Fibroscan ≥ 9,2 kPa: major S i E per diagnòstic de fibrosi significativa en població general catalana



Clin Gastroenterol Hepatol 2018;16:1138

CONCISE REVIEW

Population screening for liver fibrosis: Toward early diagnosis and intervention for chronic liver diseases

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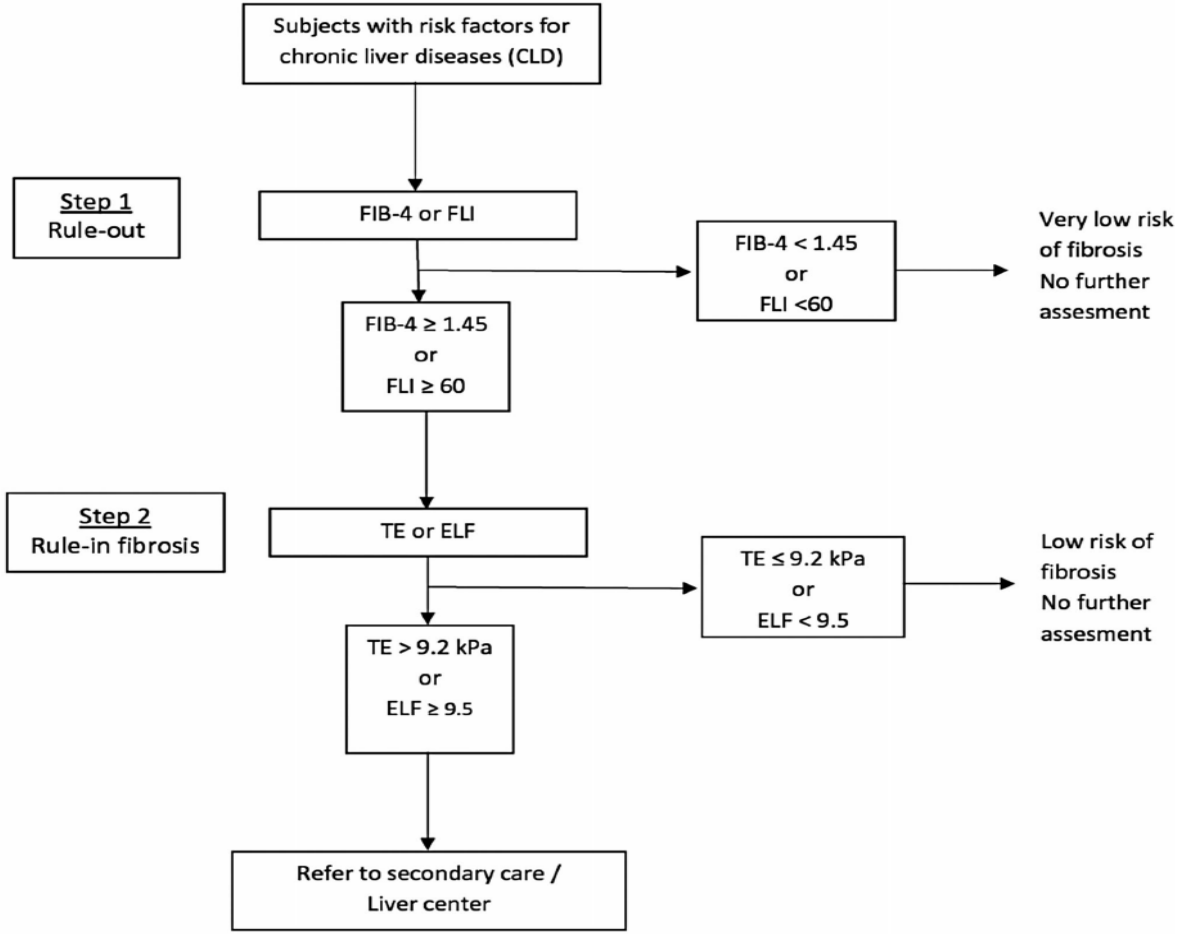


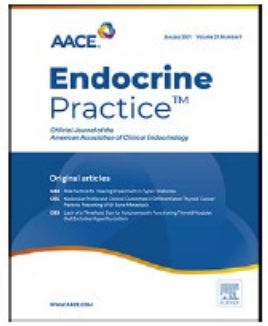
Name	Geographical area	Area and/or number of subjects	Characteristics
Renown	Nevada (United States)	30,000	Subjects with risk factors for NAFLD
Scarred Liver Project	Nottingham (UK)	GP practices in a population of 700,000	Subjects with risk factors for CLD
LiverScreen	Seven countries in Europe	30,000	Population-based
SEAL	Germany (two federal states: Rheinland-Pfalz + Saarland)	12,000 plus 22,500 controls	Detection of asymptomatic cirrhosis in primary care

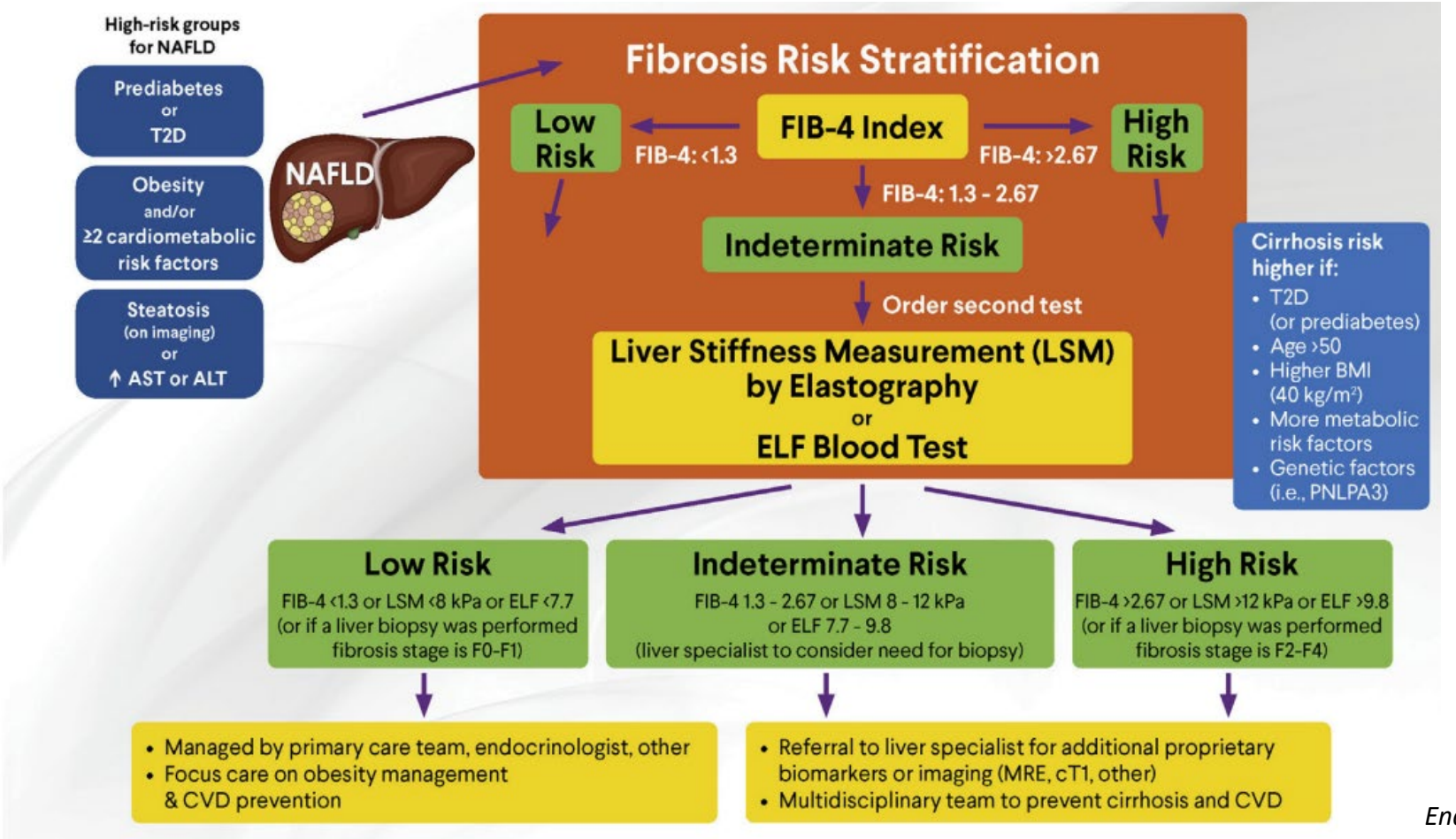
Hepatology 2022;75:219

Clinical Practice Guidelines

American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings

Co-Sponsored by the American Association for the Study of Liver Diseases (AASLD)



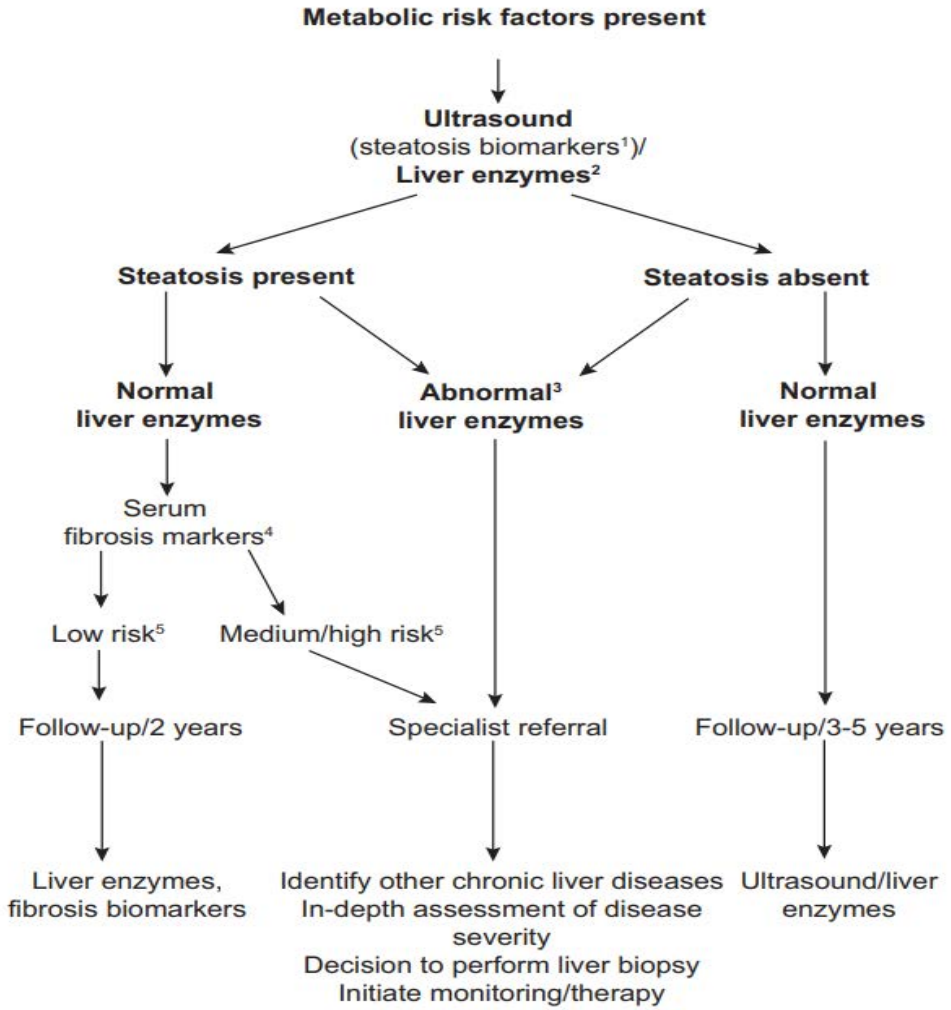


Endocrine Practice 2022;28:528

EASL | JOURNAL OF HEPATOLOGY

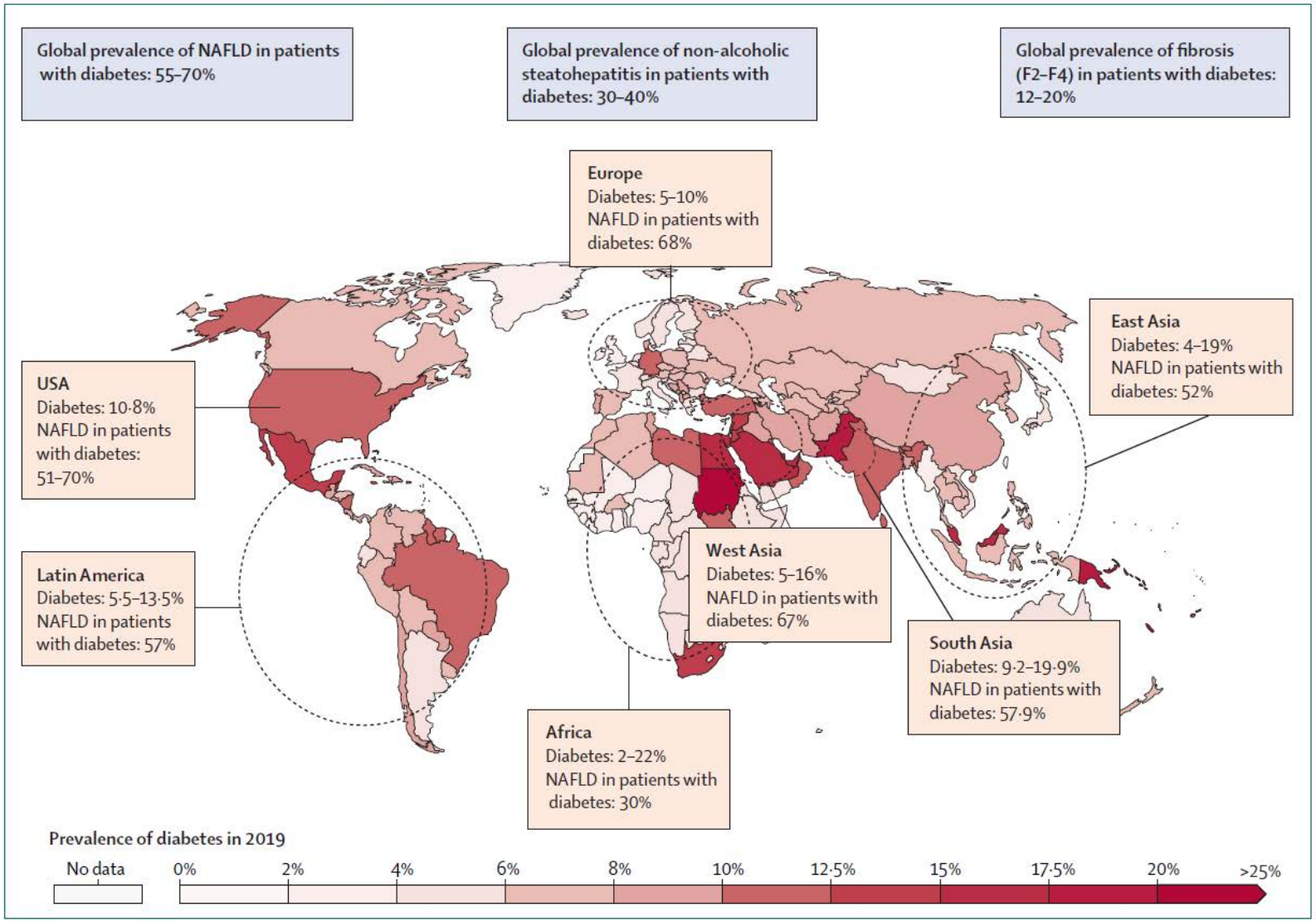
EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease☆

European Association for the Study of the Liver (EASL)*, European Association for the Study of Diabetes (EASD) and European Association for the Study of Obesity (EASO)



Diabetologia 2016;59:1121

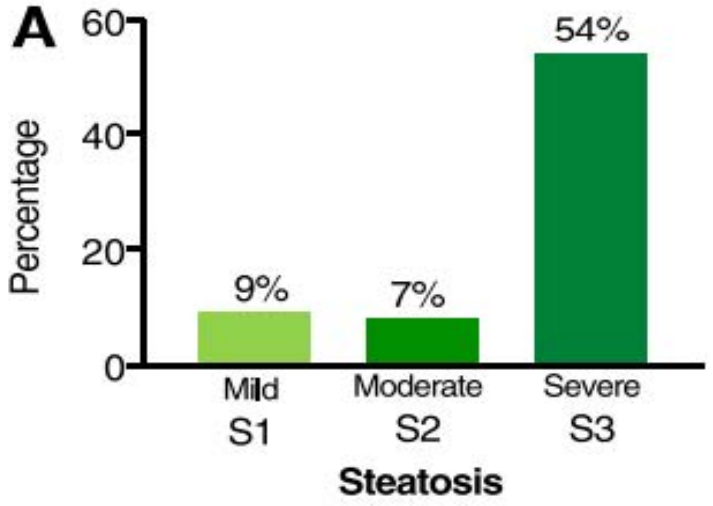
MFGNA i diabetis

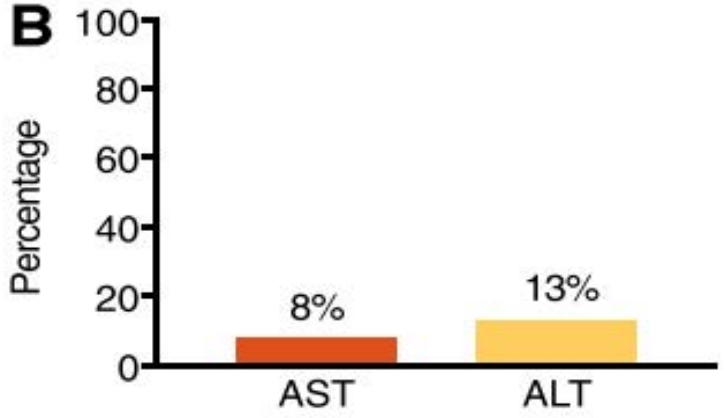


Lancet Diabetes Endocrinol 2022;10.284

DM2: alta prevalença de fibrosi hepàtica

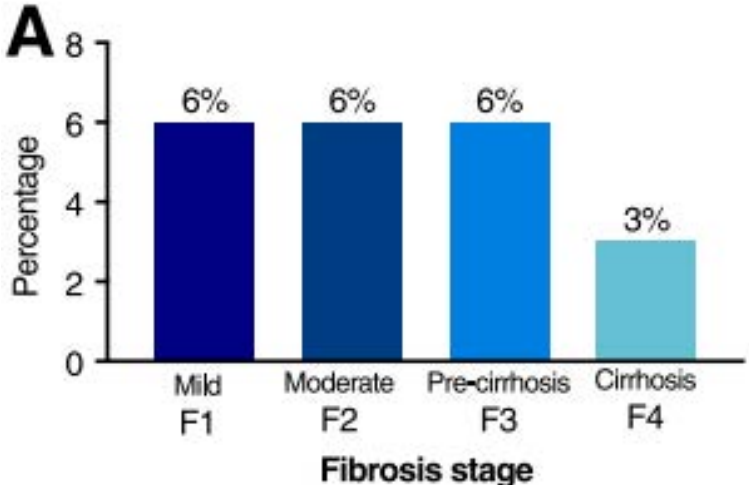
70%

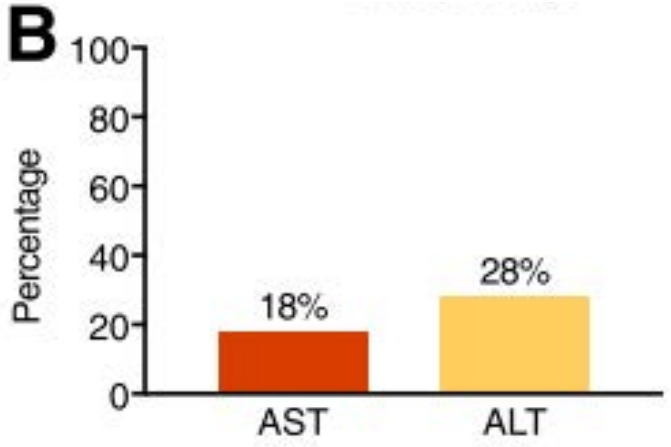




Clinical parameters (n = 561)	
Age (years)	60 ± 11
Sex (male/female)	44/56
BMI (kg/m^2)	33.4 ± 6.2
Overweight	26
Obese	66

21%

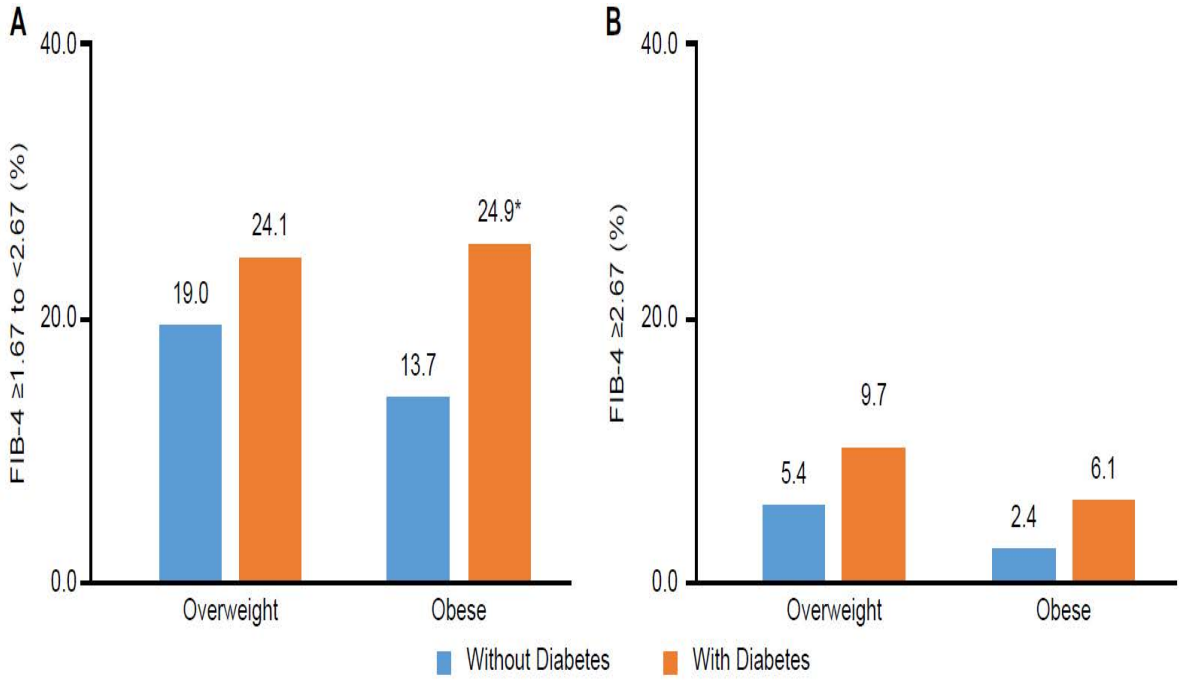




Diabetes care 2021; 44:399

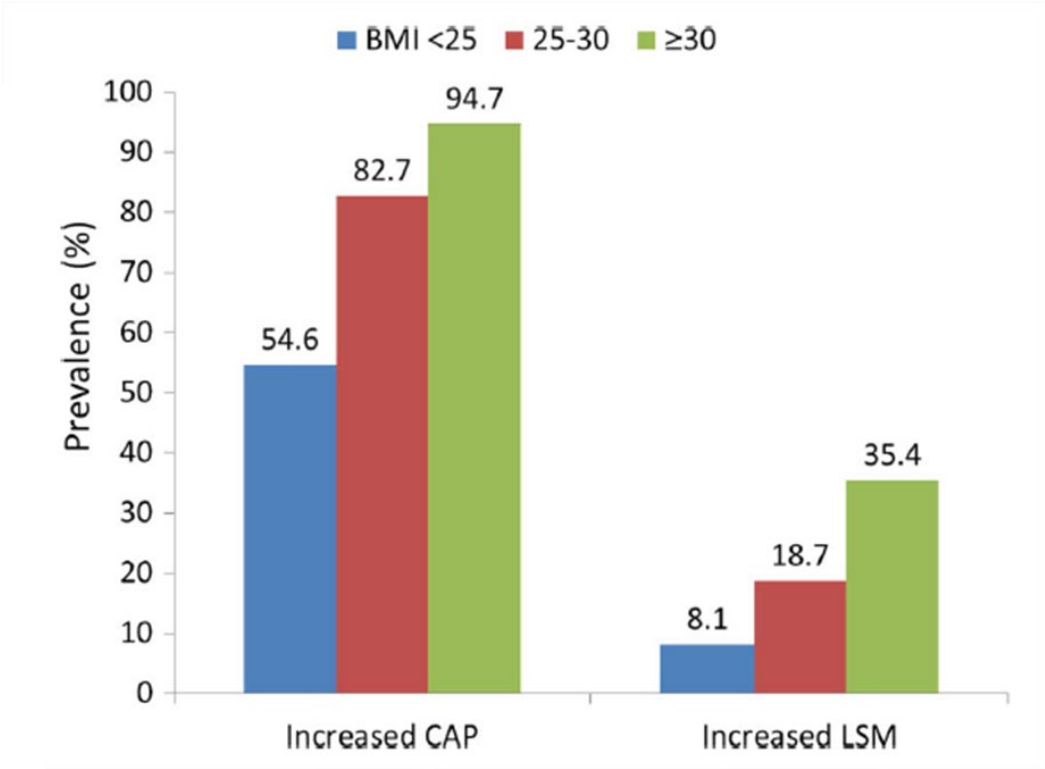
Fibrosi hepàtica i DM2: efecte de l'obesitat

n=834 individus (21,7% DM; 56% obesitat (FLI, Fibroscan)



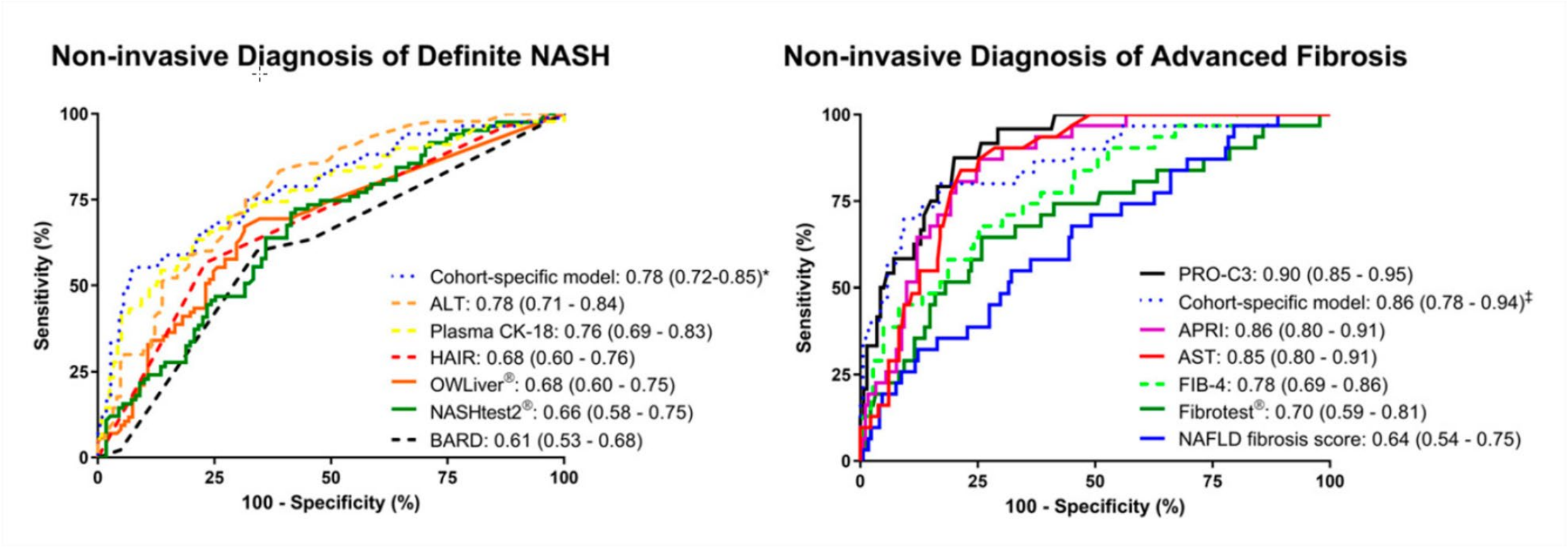
Cusi K, Obesity 2021; 29:1950

n=1918 DM2 (CAP, Fibroscan)



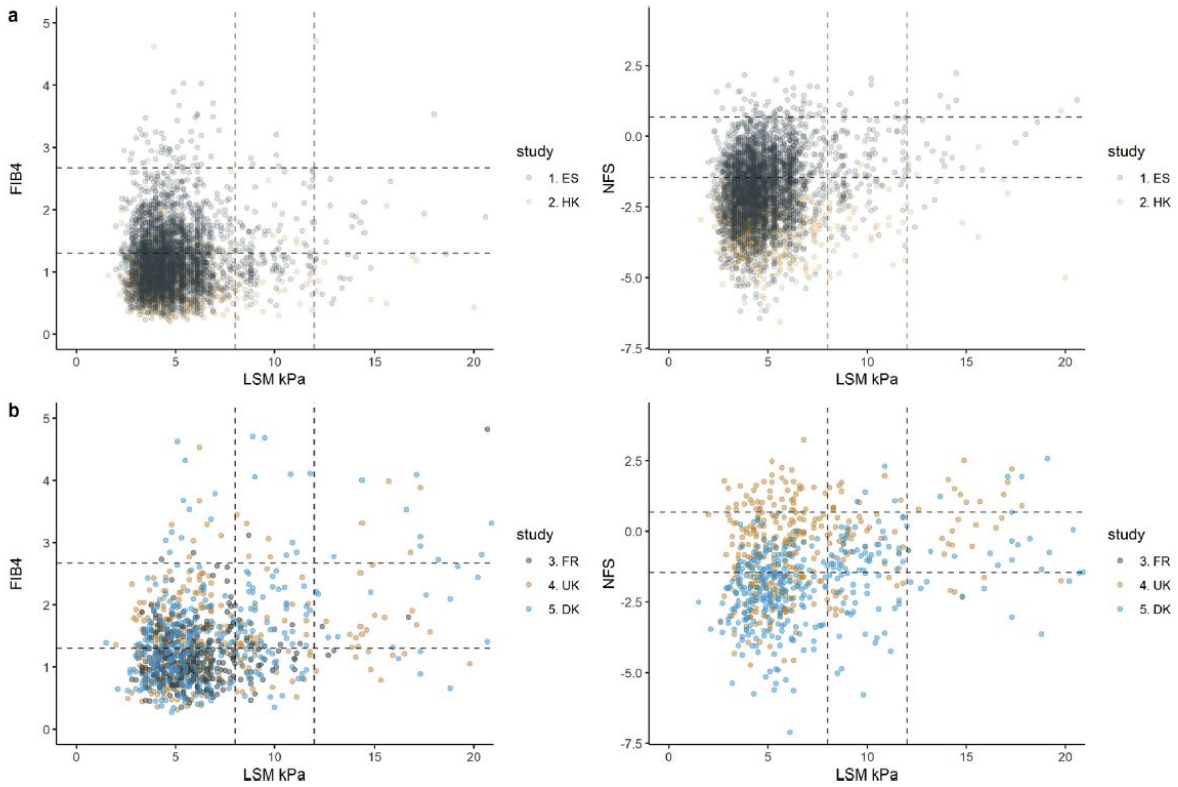
Gut 2016;65:1359

DM2: Biomarcadors fibrosi avançada



Cusi K, Diabetes Care 2019

FIB-4 i NFS: baixa precisió diagnòstica fibrosi hepàtica



Diabetis

LSM	FIB-4 ≥1.3 Negative n = 337	FIB-4 ≥1.3 Positive n = 305	FIB-4 ≥2.7 Negative n = 600	FIB-4 ≥2.7 Positive n = 42
8 kPa				
Positive	72 (21.4)	99 (32.5)	141 (23.5)	30 (71.4)
Negative	265 (78.6)	206 (67.5)	459 (76.5)	12 (28.6)
12 kPa				
Positive	28 (8.31)	53 (17.4)	58 (9.67)	23 (54.8)
Negative	309 (91.7)	252 (82.6)	542 (90.3)	19 (45.2)

LSM	NFS ≥−1.45 Negative n = 98	NFS ≥−1.45 Positive n = 536	NFS ≥−0.67 Negative n = 490	NFS ≥−0.67 Positive n = 144
8 kPa				
Positive	16 (16.3)	153 (28.5)	108 (22.0)	61 (42.4)
Negative	82 (83.7)	383 (71.5)	382 (78.0)	83 (57.6)
12 kPa				
Positive	3 (3.06)	78 (14.6)	39 (7.96)	42 (29.2)
Negative	95 (96.9)	458 (85.4)	451 (92.0)	102 (70.8)

Clin Gastroenterol Hepatol 2022; Graupera I

DM2: dislipèmia aterogènica i fibrosi hepàtica

	OR	95% CI		*P*- value
(A) Subjects with T2D (*n* = 198)				
Atherogenic dyslipidemia†	2.86	1.43	5.72	0.003
ALT and/or AST > 40 U/L	2.79	1.21	6.43	0.016
BMI	1.17	1.09	1.26	<0.001
Age	1.07	1.01	1.13	0.020
Female	0.49	0.23	1.03	0.059
(B) Subjects without T2D (*n* = 732)				
BMI	1.13	1.07	1.20	<0.001
Glucose	1.03	1.01	1.05	0.007
Female	0.41	0.23	0.73	0.002

Fibrosi moderada-significativa: Fibroscan® ≥8 kPa

	Non-fibrosis (*n* = 137)	Fibrosis (*n* = 61)	*P*-value
Age, years	62 ± 7	63 ± 7	NS
Female	58 (42)	24 (39)	NS
BMI, kg/m^2	32 ± 4	35 ± 5	< 0.001
Ab. obesity	118 (86)	53 (88)	NS
Glucose, mg/dL	148 ± 45	151 ± 50	NS
HbA1c, %	7.0 ± 1.2	7.1 ± 1.3	NS
TG, mg/dL	191 ± 118	235 ± 142	0.022
TC, mg/dL	202 ± 39	193 ± 37	NS
LDL-C, mg/dL	121 ± 38	110 ± 38	NS
HDL-C, mg/dL	47 ± 10	43 ± 10	0.014
Chol. remnants†, mg/dL	33 ± 18	39 ± 24	0.035
Non HDL-C‡, mg/dL	155 ± 38	150 ± 35	NS
Ath. dyslipemia§	35 (26)	29 (48)	0.002
ALT and/or AST > 40 U/L	22 (16)	16 (26)	NS
FLI¶	81 ± 13	90 ± 11	<0.001
FLI ≥ 60	135 (99)	59 (98)	NS
NFS‖,*	−0.49 ± 1.10	−0.22 ± 1.22	NS
Low	25 (19)	9 (17)	NS
Indeterminate	91 (68)	33 (61)	
High	18 (13)	12 (22)	
FIB-4¥,*	1.3 ± 0.6	1.5 ± 1.2	0.049
Low	79 (59)	31 (53)	NS
Indeterminate	51 (38)	24 (41)	
High	5 (4)	3 (5)	
Liver fibrosis by LSM (kPa)	5.6 ± 1.1	12.1 ± 5.9	0.001

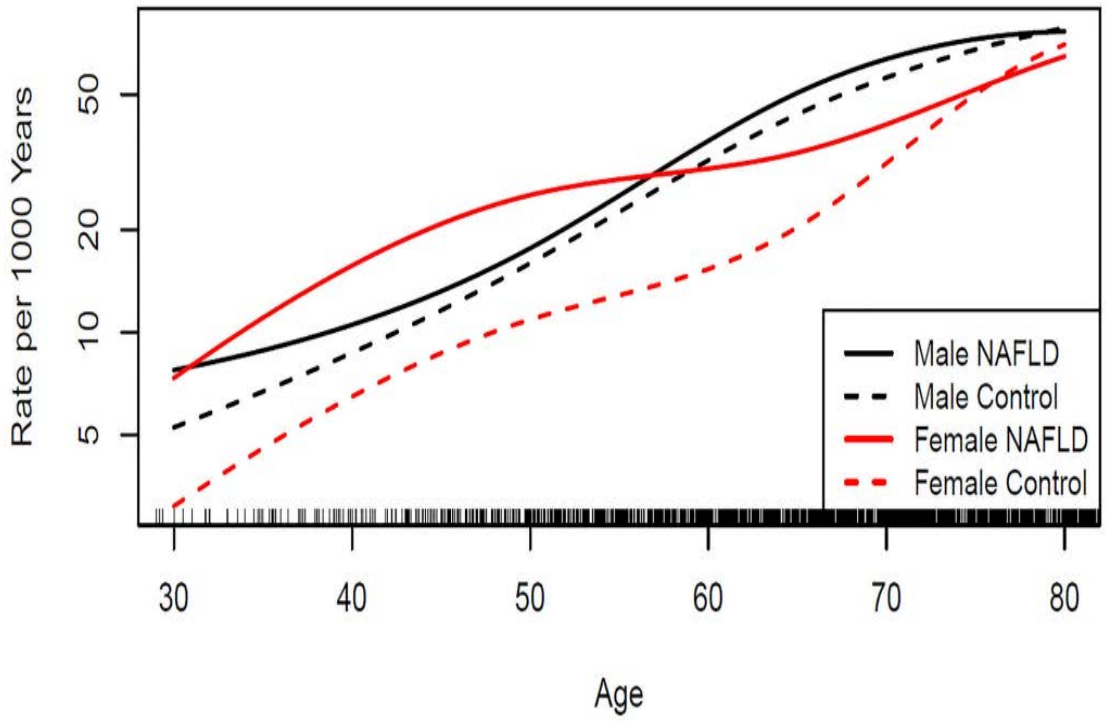
Julián MT, Alonso N et al. EJE 2021;184:587

Gènere i MFGNA

N= 2790

Global			<50 years old			≥50 years old		
	Prevalence (%)	p		Prevalence (%)	p		Prevalence (%)	p
Global								
Men (n=1115)	50	<0.001	Men (n=364)	38	<0.001	Men (n=751)	56	<0.001
Women (n=1675)	34		Women (n=509)	19		Women (n=1166)	41	
Dysglycemia								
Men (n=432)	68	0.021	Men (n=75)	68	0.635	Men (n=357)	68	0.024
Women (n=457)	61		Women (n=47)	64		Women (n=410)	60	
Non-dysglycemia								
Men (n=683)	39	<0.001	Men (n=289)	30	<0.001	Men (n=394)	46	<0.001
Women (n=1218)	24		Women (n=462)	14		Women (n=756)	30	

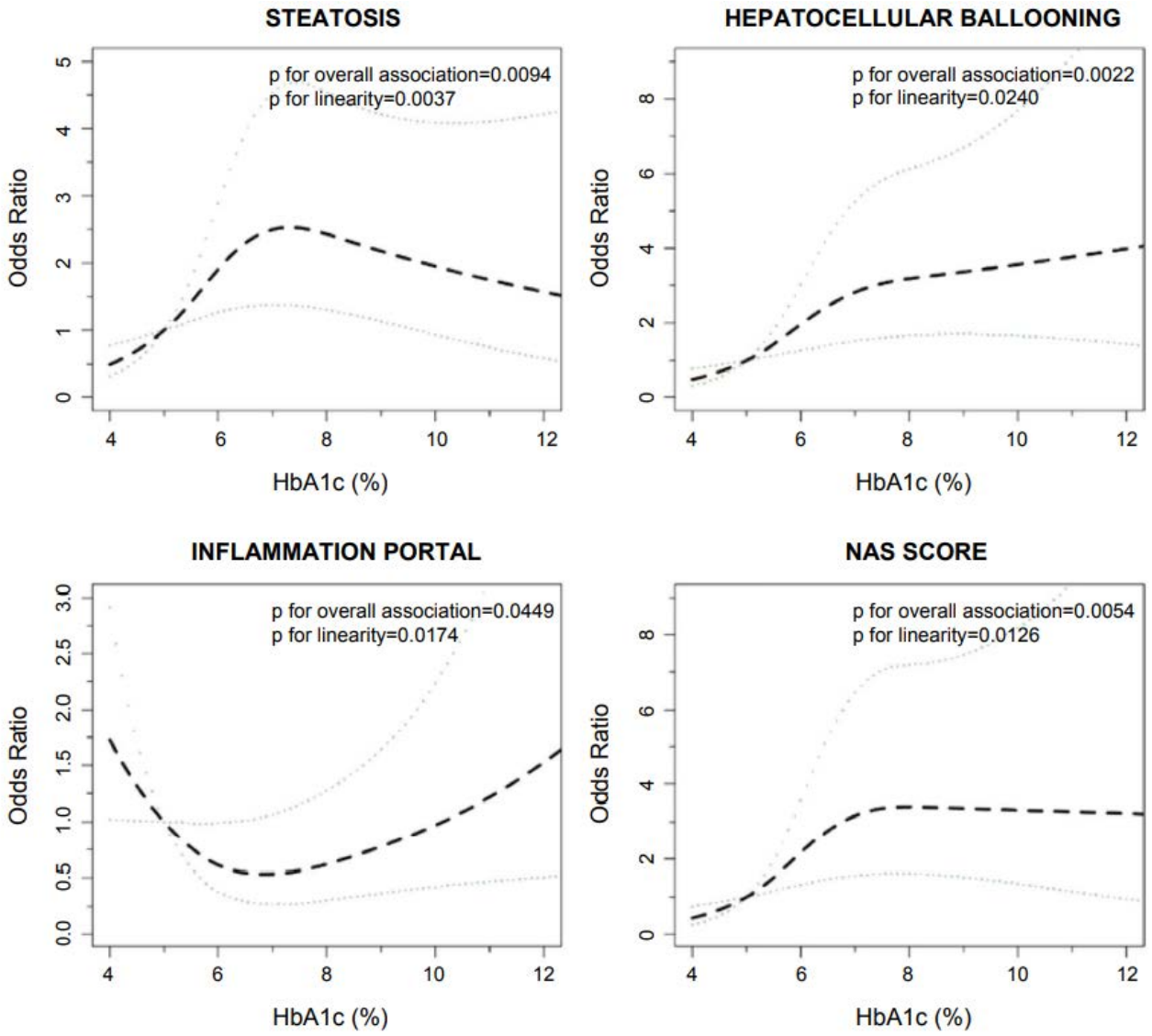
Incidència events cardiovasculars



Pérez Montes de la Osa. A, Alonso et al. Dades no publicades

Am J Gastroenterol 2019;114:1764

Grau control glucèmic i histologia hepàtica



- n=348 DM2 i biòpsia hepàtica
- Increment 1% de la HbA1c s'associa a un increment de risc del 15% del grau de fibrosi

Hepatology 2021;74:1220

ADA: recomanacions cribratge EHNA

4. Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Medical Care in Diabetes—2019*

Diabetes Care 2019;42(Suppl. 1):S34–S45 | https://doi.org/10.2337/dc19-S004

4. Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Medical Care in Diabetes—2022*

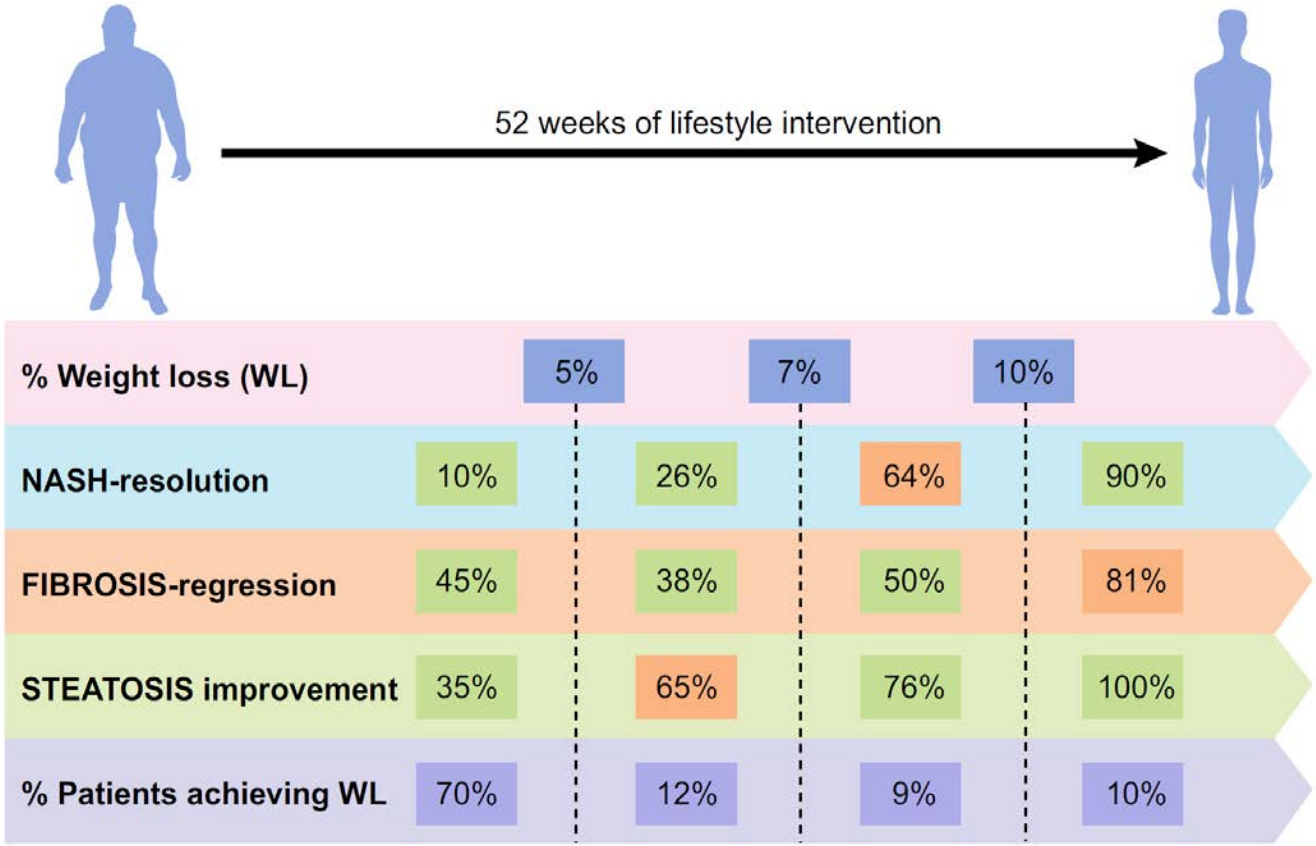
Diabetes Care 2022;45(Suppl. 1):S46–S59 | https://doi.org/10.2337/dc22-S004

Nonalcoholic Fatty Liver Disease

Recommendation

4.10 Patients with type 2 diabetes or prediabetes and elevated liver enzymes (ALT) or fatty liver on ultrasound should be evaluated for presence of nonalcoholic steatohepatitis and liver fibrosis. **C**

Pèrdua pes: milloria paràmetres histològics



Journal of Hepatology 2017;67:829

Guia EASL-EASD-EASO de FGNA

En la EHGNA con sobrepeso/obesidad, el objetivo de la mayor parte de intervenciones en el estilo de vida es una reducción de peso del 7-10%, y ello da lugar a una mejoría de las enzimas hepáticas y la histología (**B1**)

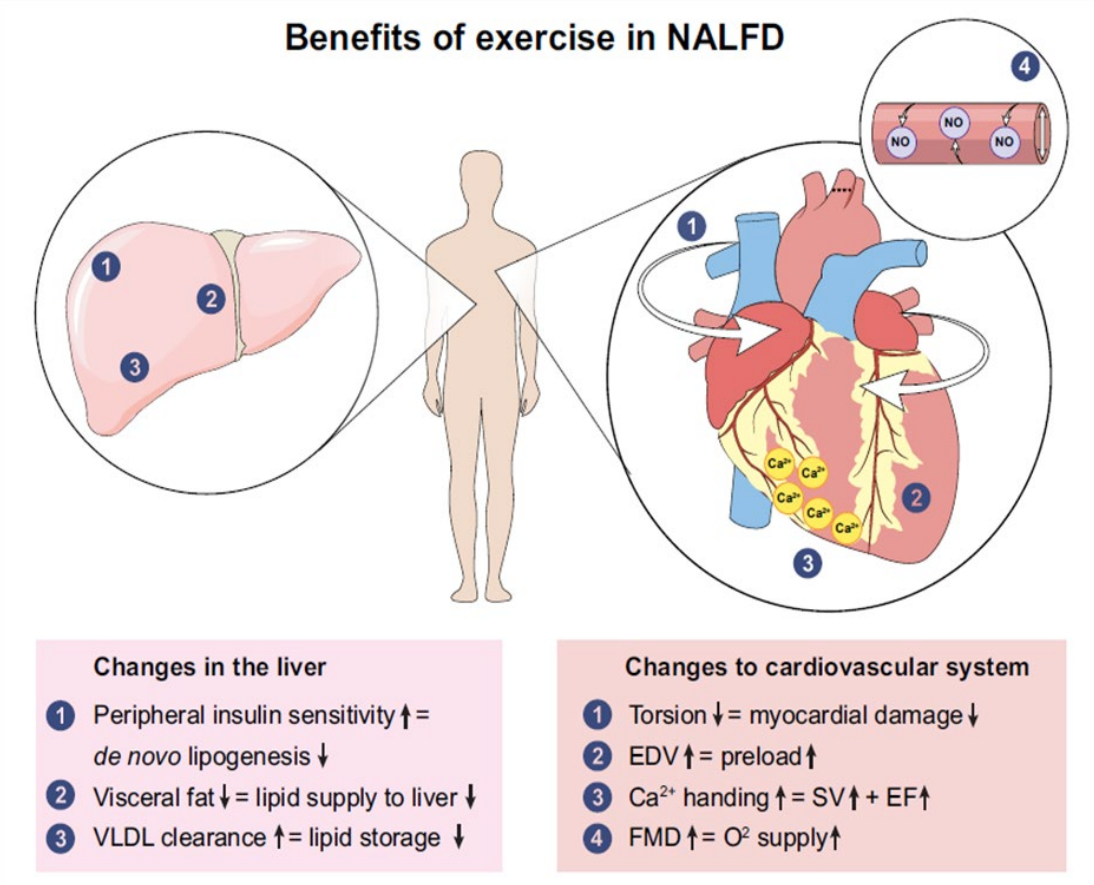
J Hepatol 2016;64:1388

EHNA: recomanacions dietètiques

- Dieta hipocalòrica (sobrepès-obesitat) (reduïr 500-100Kcal/dia)
- Preferentment tipus **mediterrània** (oli oliva, fruits secs, llegum, vegetals, peix blau)
- Evitar hidrats de carboni d'absorció ràpida (begudes ensucrades)
- Evitar ingesta excessiva de fructosa (altera flora intestinal, incrementa síntesi de TGs)

Seminars in liver disease 2021;41:248

MFGNA: beneficis exercici físic



J Hepatol 2017;68:829

- L'exercici, sense pèrdua de pes associat, produeix una disminució del 20-30% del greix intrahepàtic
- Escasses dades amb EHNA
- El benefici és independent del tipus d'exercici (aeròbic o de resistència)

  J Hepatol 2017;68:829
- El benefici només es manté si la pràctica d'exerici físic és mantinguda en el temps

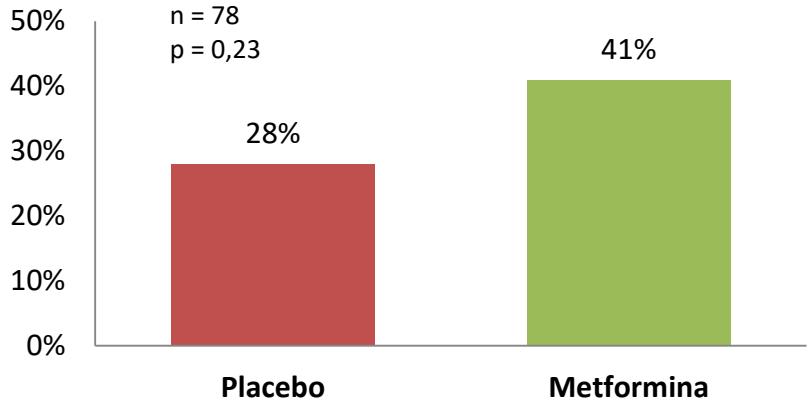
  Int J Obes 2016;40:1927
- Té un benefici CV

Tractament hipoglucemiant i MFGNA

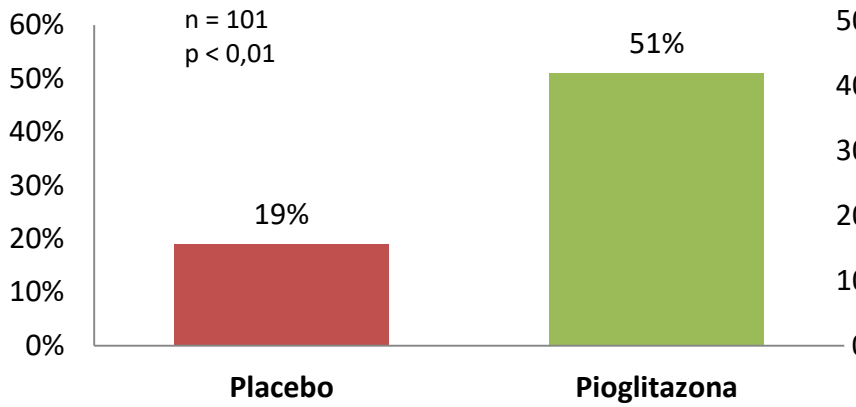
	Liver enzymes	Liver fat*	Liver inflammation†	Liver fibrosis†	NASH resolution†	Major adverse effects
Metformin	Improved	Improved	No effect	No effect	No effect	Gastrointestinal
Glitazones (pioglitazone, rosiglitazone)	Improved	Improved	Improved	Improved	Improved	Weight gain (mild), oedema, heart failure, bone fractures
GLP-1 receptor agonists (liraglutide, exenatide)	Improved	Improved	Improved	No effect	Improved	Gastrointestinal
DPP-4 inhibitors (sitagliptin, vildagliptin)	Improved	No effect	Unknown	Unknown	Unknown	Pancreatic, joint pain
SGLT-2 inhibitors (dapaglifozin, empagliflozin, canaglifozin)	Improved	Improved	Unknown	Unknown	Unknown	Genitourinary infections, dehydration

Gut 2020; Targher G

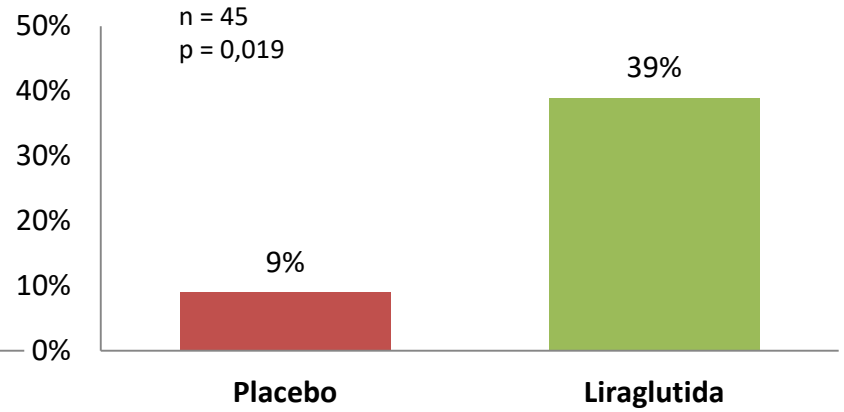
NASH: tractament hipoglucemiant



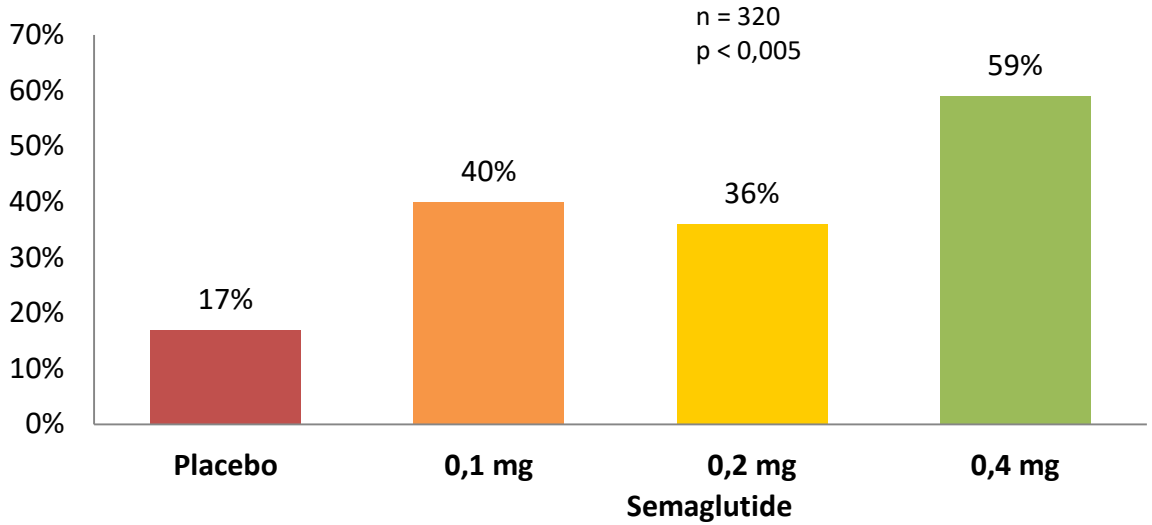
Lavine et al. JAMA 2011



Cusi et al. Ann Int Med 2016

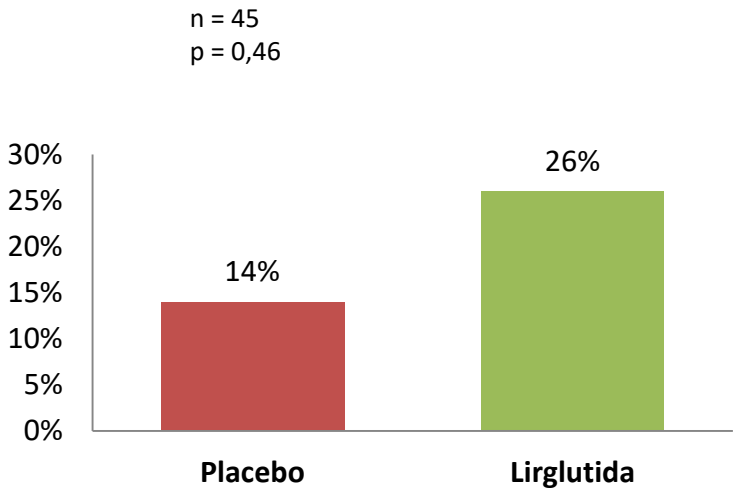


Amstrong et al. Lancet 2016

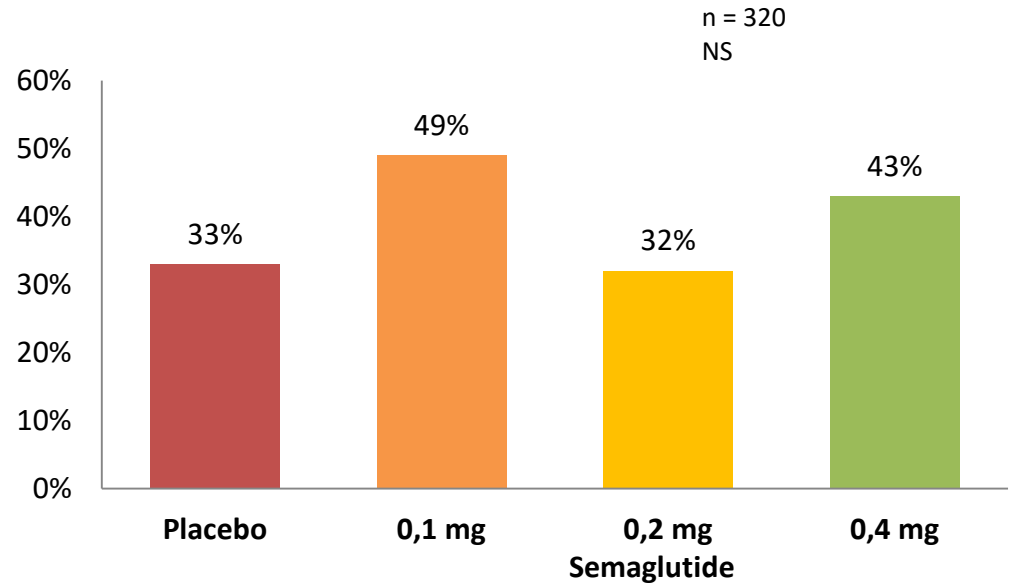


Newsome et al. NEJM 2021

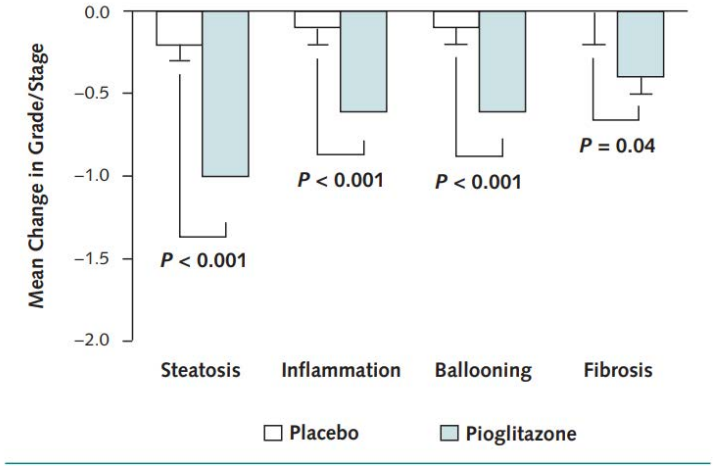
Tractament hipoglucemiant: fibrosi hepàtica



Amstrong et al. Lancet 2016

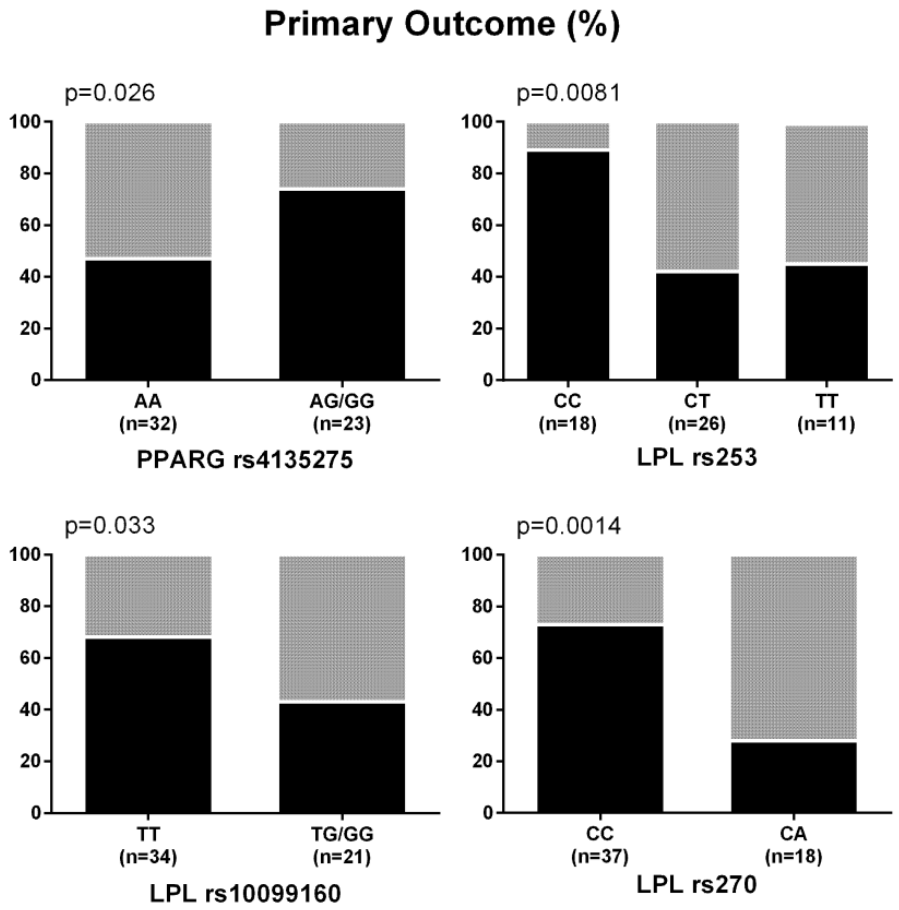


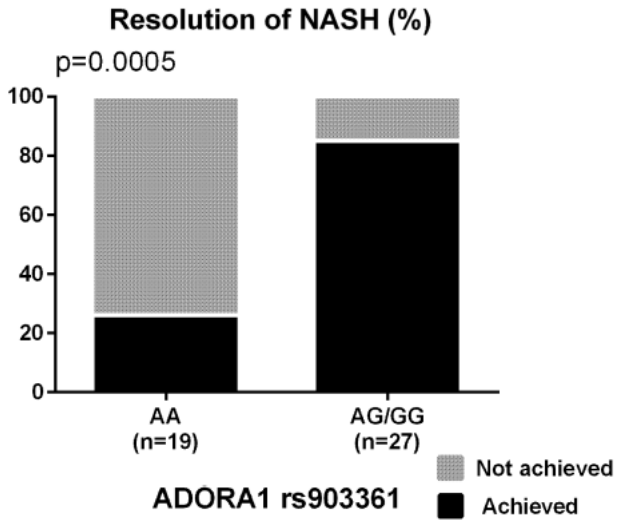
Newsome et al. NEJM 2021



Ann Intern Med 2016;165:365

Resposta a pioglitazona: fàrmacogenètica



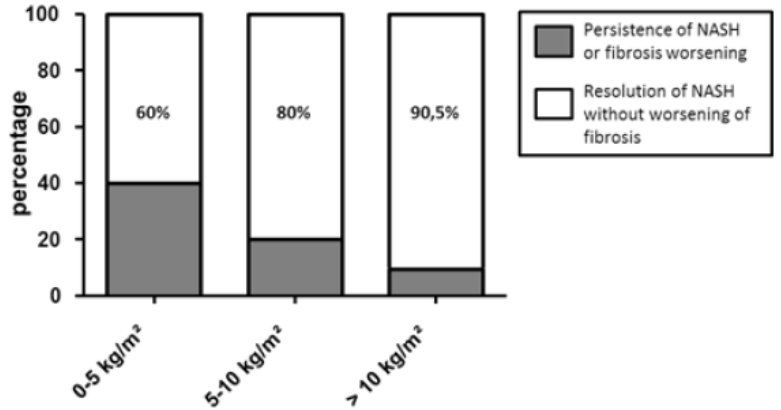


Variabilitat resposta inter-pacients: relacionada amb polimorfismes de gens implicats en la fàrmacocinètica i fàrmacodinàmica de la pioglitazona

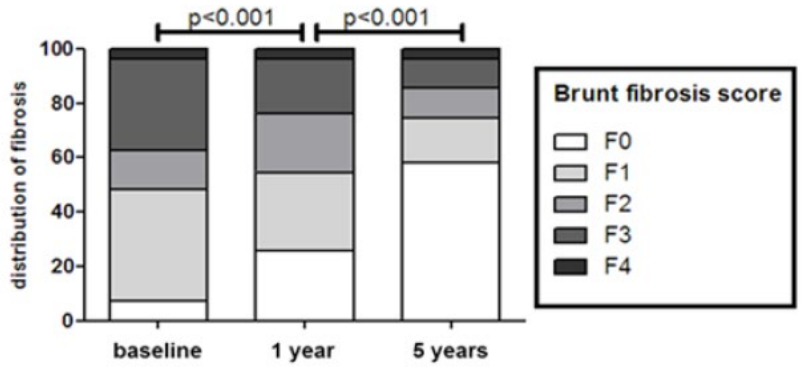
Frontiers in pharmacology 2018;9:752

Cirurgia bariàtrica: milloria NASH i fibrosi hepàtica

NASH resolution according to weight loss



Fibrosis evolution after surgery



Gastroenterol 2020;159:1290

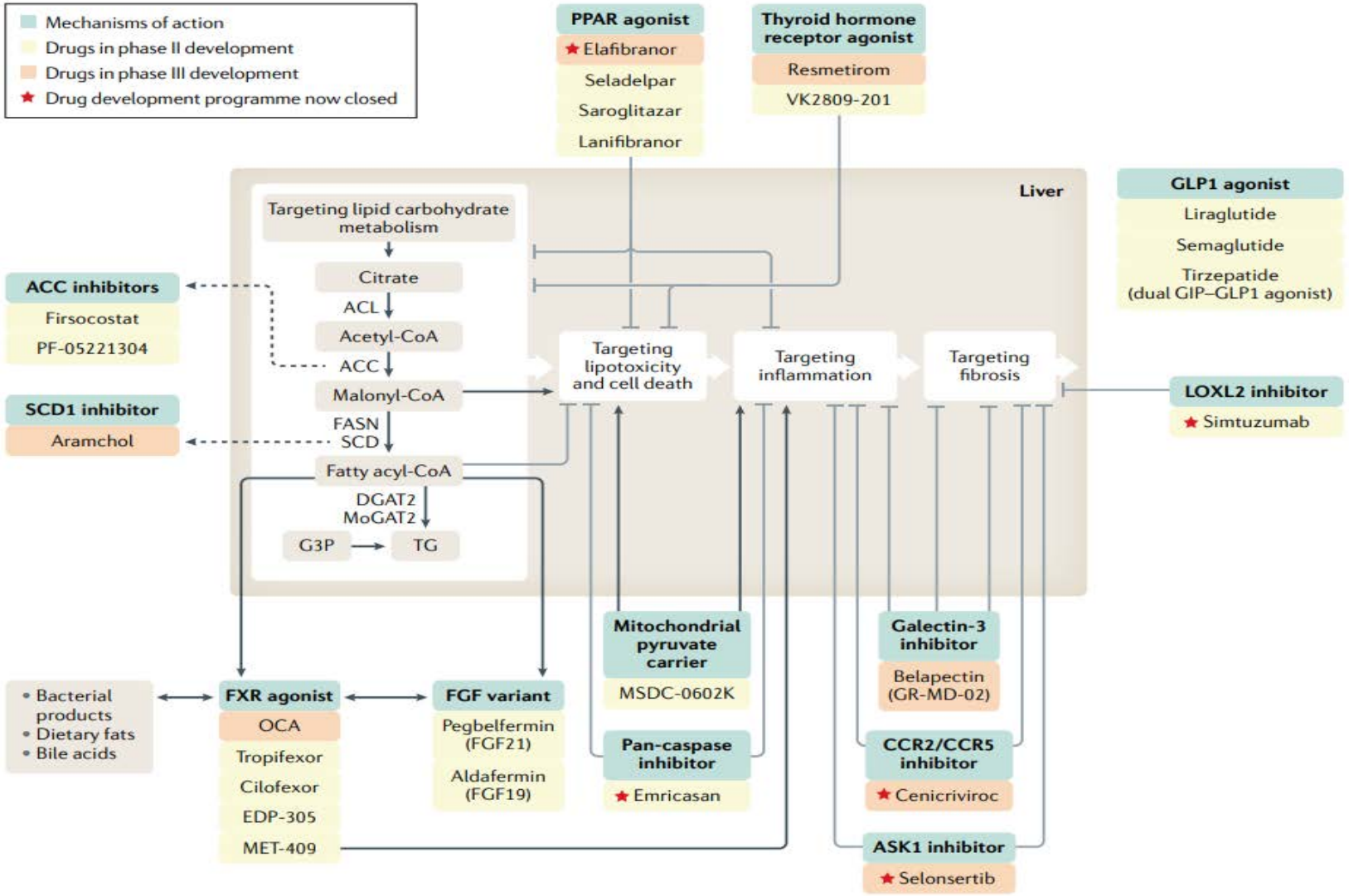
Characteristics of patients at 5 years	Resolution of NASH Without worsening of fibrosis	Persistence of NASH And/or worsening of fibrosis	P value
Baseline BMI kg/m², mean ± SD	49.3 ± 7.0	47.7± 7.9	.86
BMI at 5 years, kg/m², mean ± SD	35.3 ± 7.1	40.9 ± 10.7	.028 [a]
Evolution of BMI, mean ± SD	-13.4 ± 7.4	- 6.3 ± 4.1	.017 [a]
Histological characteristics			
Brunt Fibrosis score, median [IQR]	0 [0-1]	2 [2-3]	<.001 [b]
Brunt fibrosis evolution, median [IQR]	-1 [0; -2]	1 [0-1.3]	.003 [b]
NAS, median [IQR]	1 [0-2]	4 [3.5-5.5]	<.001 [b]
NAS evolution, median [IQR]	-4 [-5; -2]	0 [-2; 0]	.005 [b]
steatosis, %, median [IQR]	5 [1-10]	60 [30-75]	<.001 [b]

Recommendations

- By improving obesity and diabetes, bariatric (metabolic) surgery reduces liver fat and is likely to reduce NASH progression; prospective data have shown an improvement in all histological lesions of NASH, including fibrosis (**B1**)

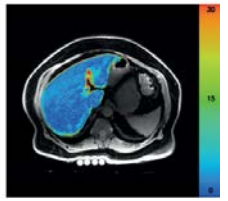
J Hepatol 2016;64:1388

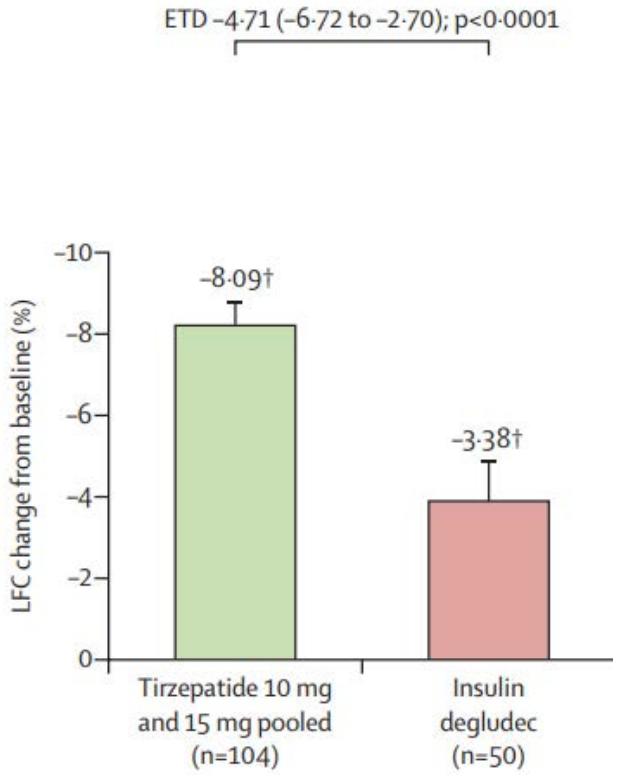
Futurs tractaments per la MFGNA

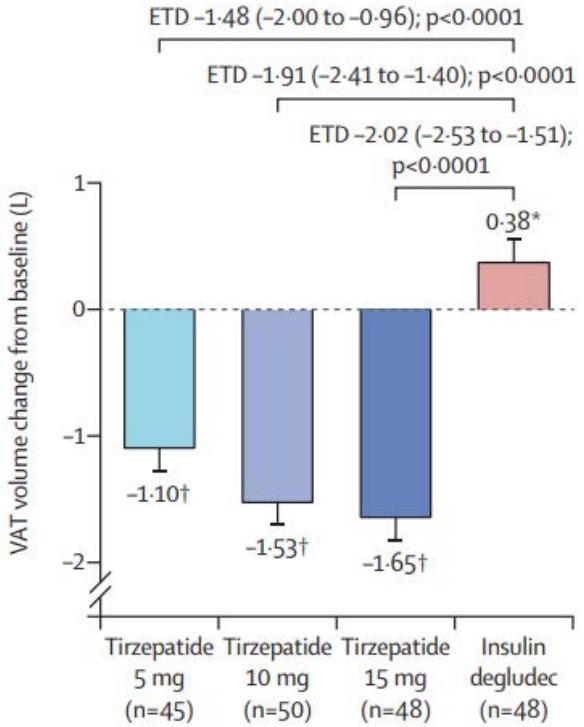


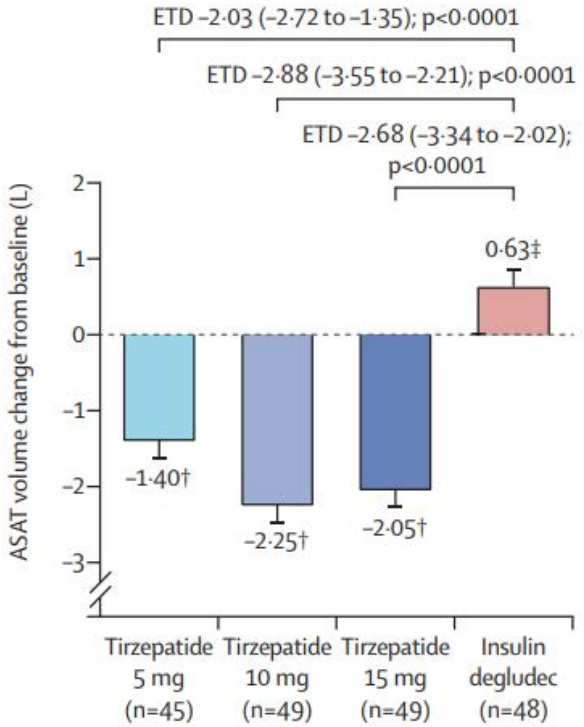
Nat Rev Gastroenterol Hepatol 2021;18:373

Tirzepatide (SURPASS-3MRI): disminució greix hepàtic i visceral



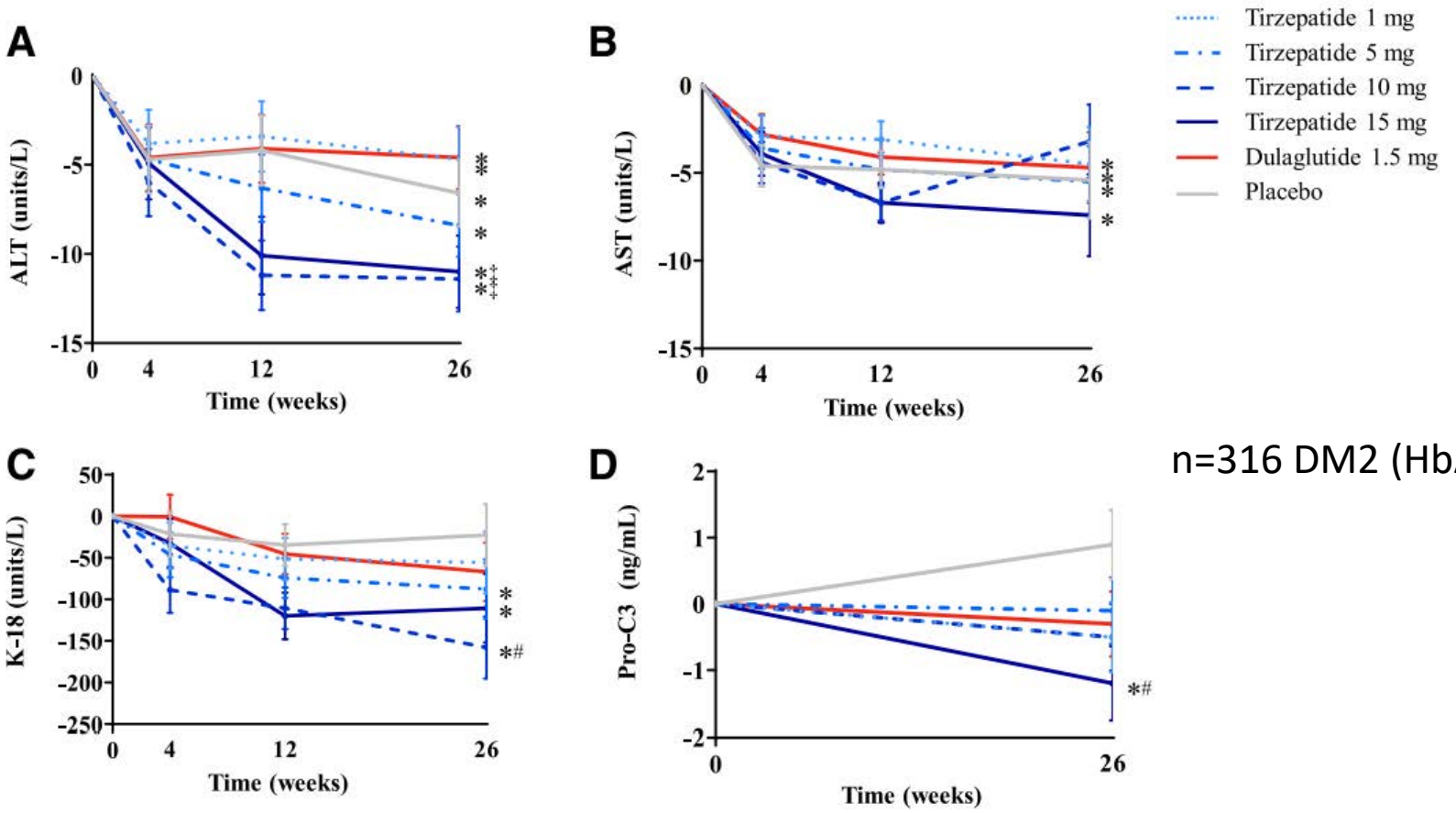






Lancet Diabetes Endocrinol 2022; 10: 393

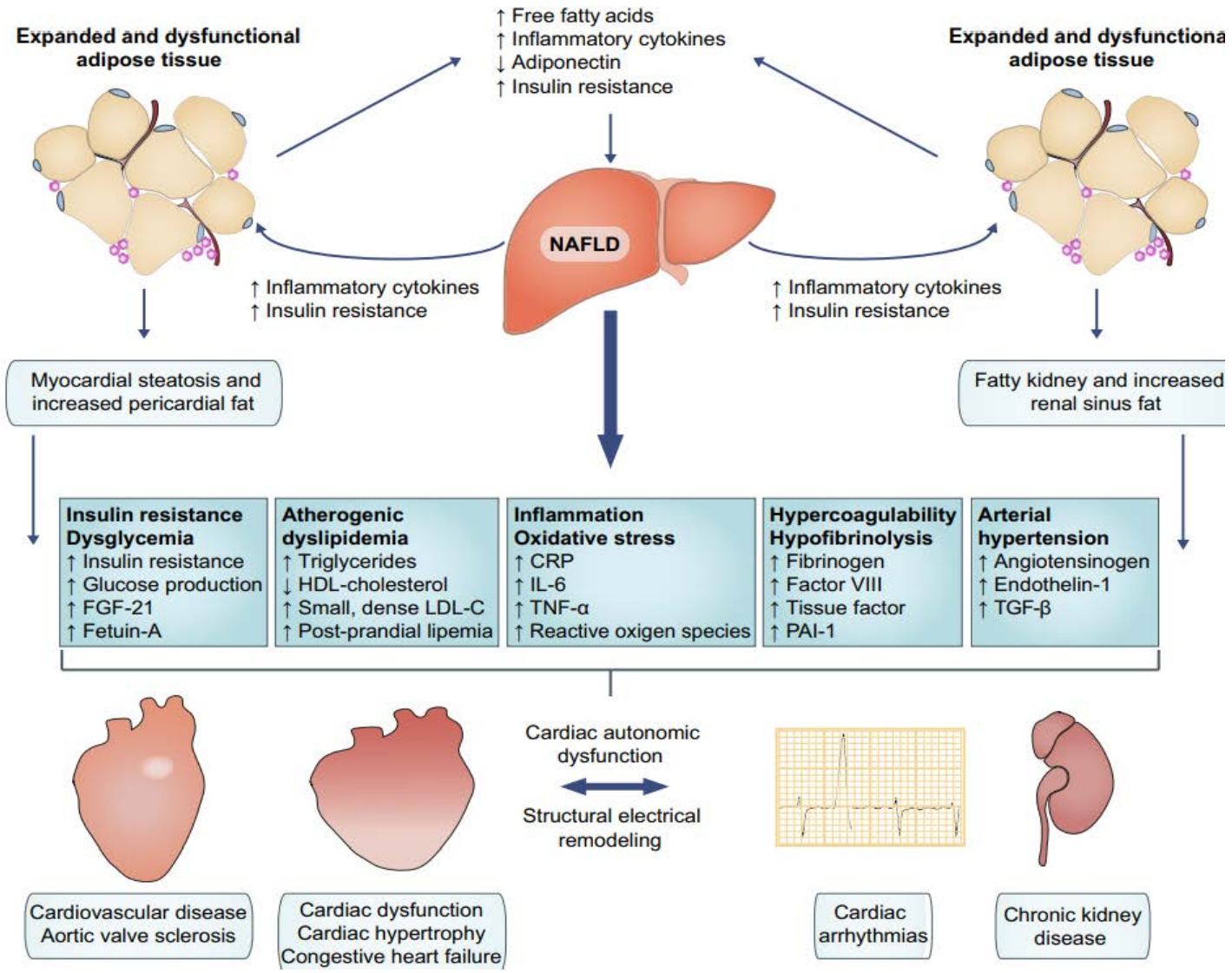
Tirzepatide disminueix biomarcadors de NASH/fibrosi hepàtica



n=316 DM2 (HbA1c 7-10,5%)

Diabetes Care 2020; 43:1352

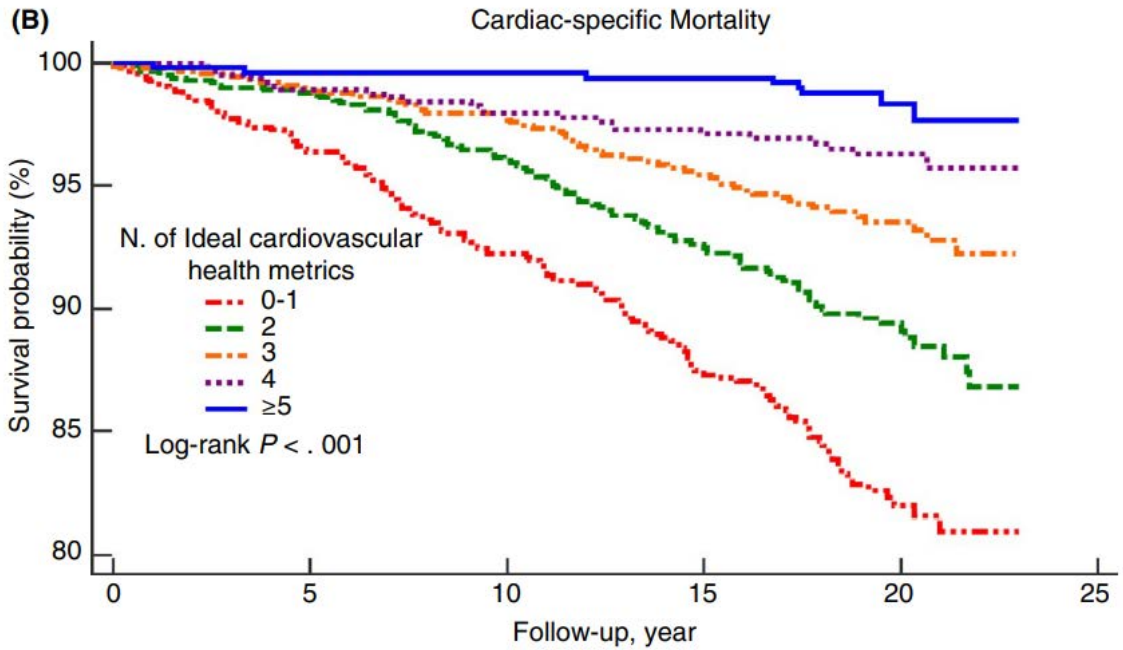
MFGNA: malaltia multisistèmica

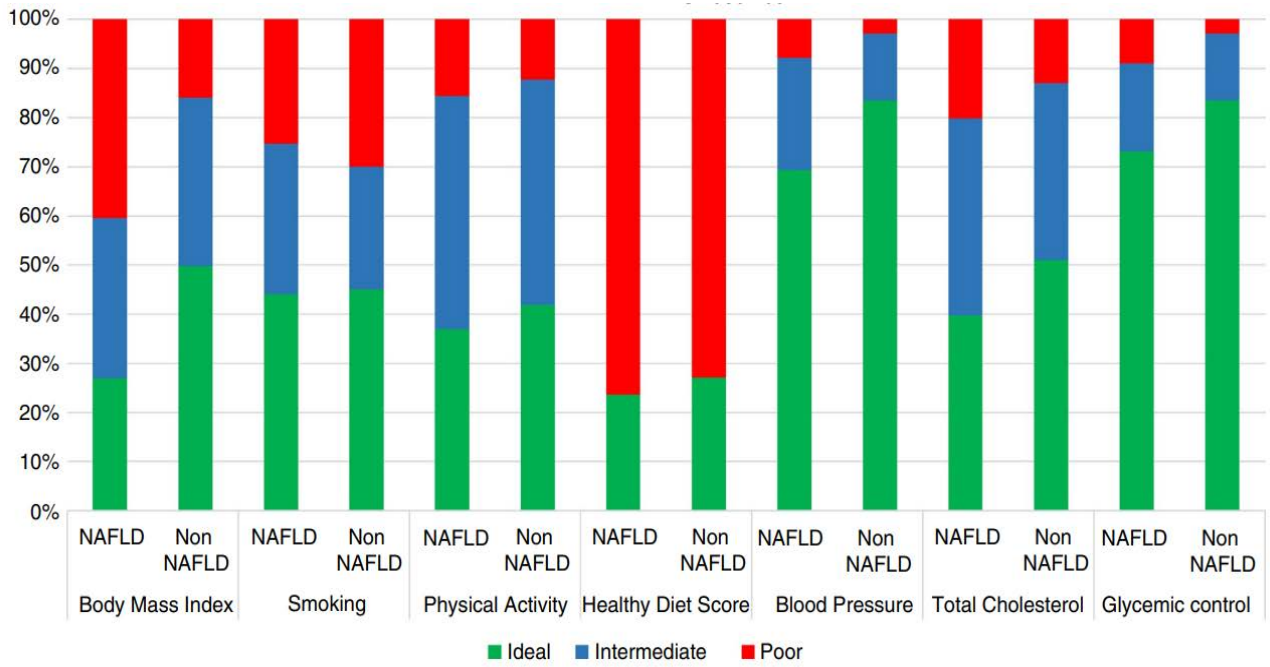


Journal of Hepatology 2015;62:S47

MFGNA: mortalitat CV

n=4040 NAFLD x eco; seguiment 19 anys (17,5-21)

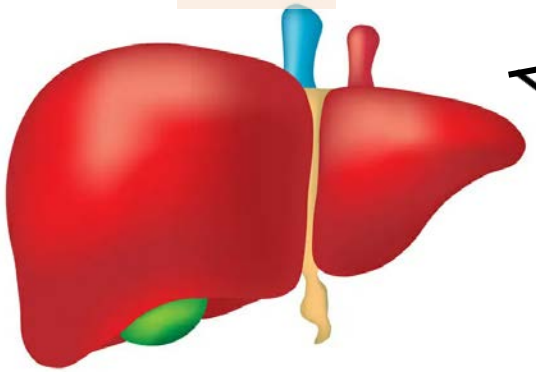




Aliment Pharmacol 2020;51:291

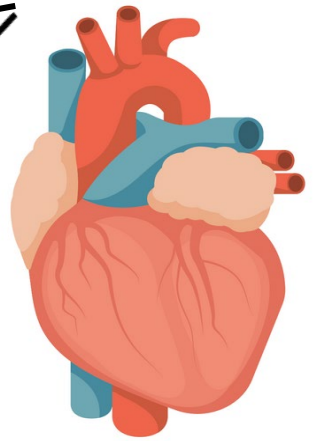
Disminució del risc cardiometabòlic: a “triangle of care”

NASH



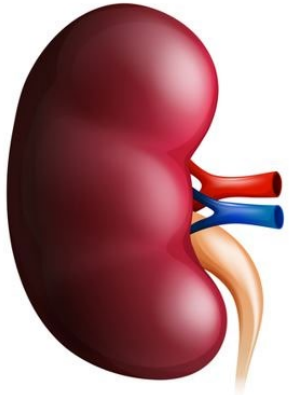
- ✓ Pioglitazona
- ✓ GLP-1aR
- ✓ SGLT2i (?)

CVD



- ✓ GLP-1 aR
- ✓ SGLT2i
- ✓ Pioglitazona

Nefropatia



- ✓ SGLT2i
- ✓ GLP-1 aR

MFGNA: enfoc multidisciplinar

Atenció Primària

Hepatòleg

Endocrinòleg

Medicina Interna

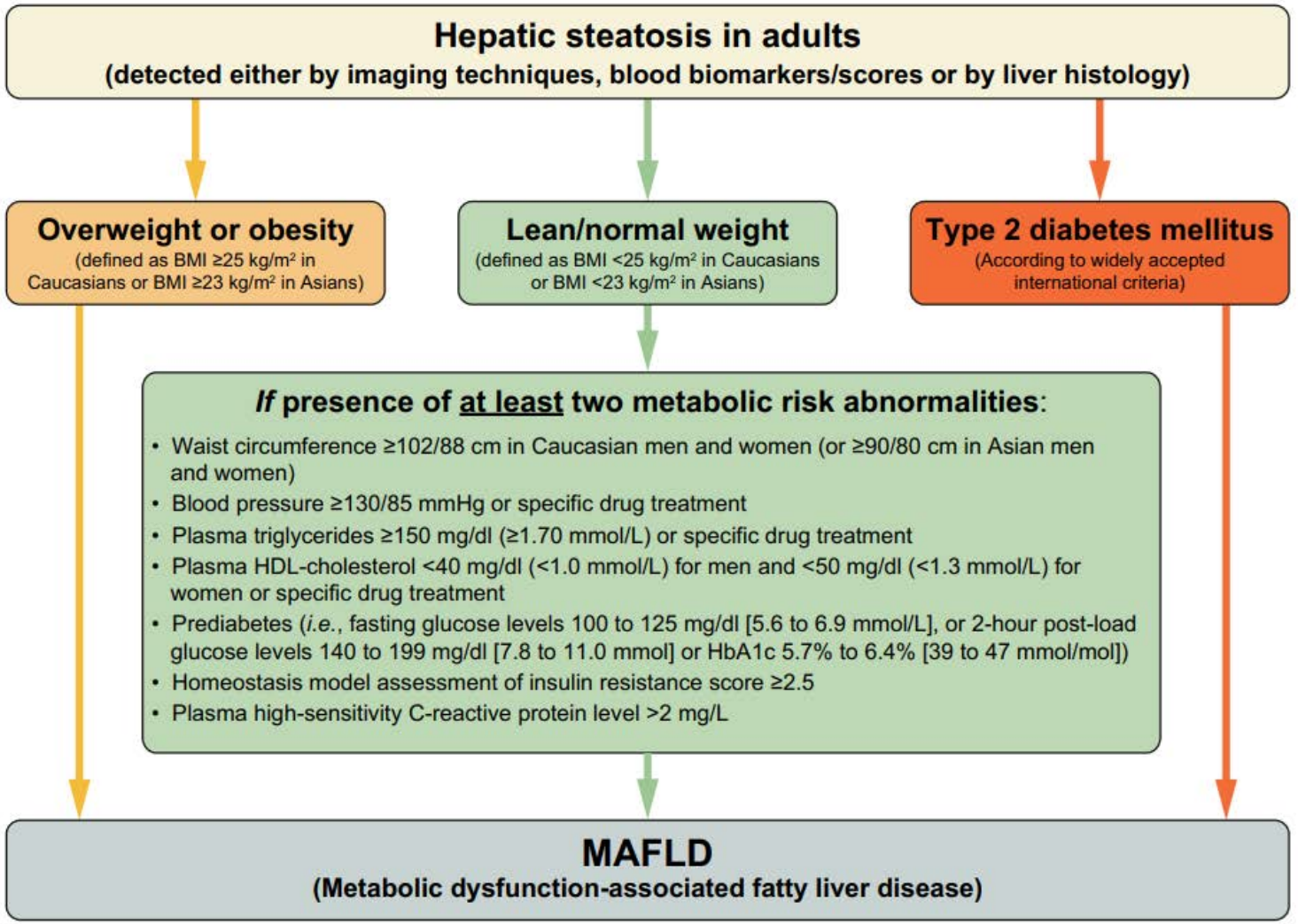
Infectòleg (VIH)

Dietista/Nutricionista

Psicòleg

Pediatria

MAFLD: metabolic associated fatty liver disease



J Hepatol 2020;73:202

Conclusions

- La majoria d'individus que presenten MFGNA estan assimptomàtics.
- El cribratge de la MFGNA permet aplicar intervencions en etapes poc evolucionades de la EHNA (+/-fibrosi) i enlentir/regressar la progressió de la malaltia.
- Cal realitzar el cribratge en població amb alt risc d' EHNA i fibrosi associada (DM2, obesitat,≥ 2 factors de risc cardiometabòlics)
- La patogènesi de la MFGNA i EHNA és complexa.
- És probable que es necessiti més d'un fàrmac per disminuir la inflamació i la fibrosi hepàtiques.

Conclusions

- Cal aplicar les mesures que han demostrat ser efectives per a milllorar la histologia hepàtica (hàbits vida cardiosaludables:pèrdua pes, dieta mediterrània, pràctica exercici físic)

- Cal tractar tots els factors de risc cardiovascular per disminuir el risc d'events CV

- En pacients amb DM2: prioritzar fàrmacs que hagin demostrat una milloria en els paràmetres histològics hepàtics, perfil CV favorable i bon control glucèmic (pioglitazona, agonistes receptor de GLP-1)

- El tractament de la MFGNA ha de ser multidisciplinar

Moltes gràcies per la vostra atenció