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Centro de Investigación Biomédica en Red
Enfermedades Hepáticas y Digestivas

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HOSPITALES UNIVERSITARIOS
Virgen del Rocío

UNIVERSIDAD DE SEVILLA

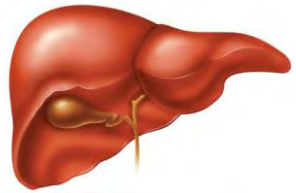
XIX JORNADAS DE AVANCES EN HEPATOLOGIA

MÁLAGA 2020
8-9 DE OCTUBRE | AULA MAGNA | FACULTAD DE MEDICINA
ASISTENCIA LIBRE

ORGANIZAN
- DPTO. DE MEDICINA Y UNIDAD DE GESTIÓN CLÍNICA DE DIGESTIVO.
- INSTITUTO DE INVESTIGACIÓN BIOMÉDICA DE MÁLAGA (IBIMA).
- HOSPITAL UNIVERSITARIO VIRGEN DE LA VICTORIA.
- FACULTAD DE MEDICINA | UNIVERSIDAD DE MÁLAGA.

DIRECTOR DE LAS JORNADAS:
RAÚL J. ANDRADE BELLIDO.

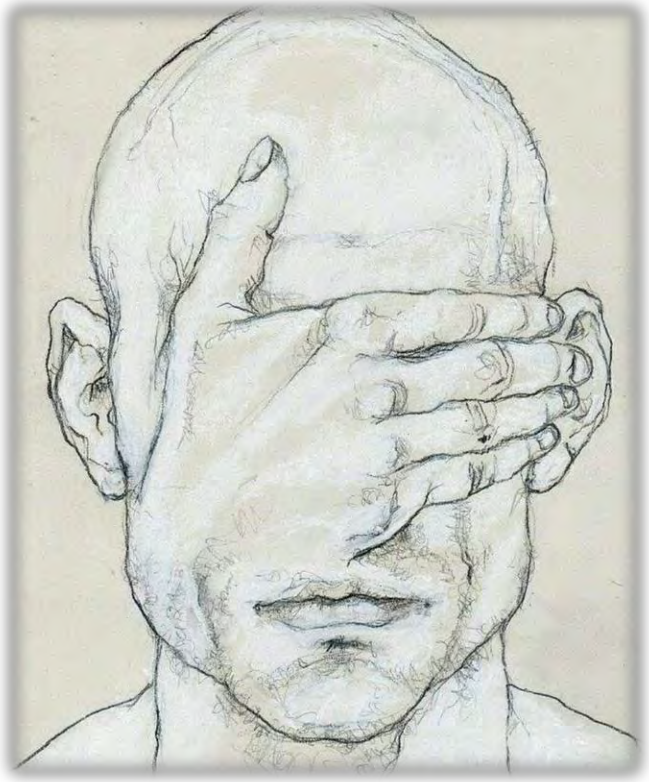
Identificación y manejo de los pacientes con NASH y alto riesgo de progresión



Dr. Javier Ampuero
UGC Enfermedades Digestivas
Hospital Universitario Virgen del Rocío
Sevilla, España

¿Estamos exagerando con la enfermedad?

Ver lo que no hay o no ver lo que hay



PREVALENCIA - INCIDENCIA

Datos

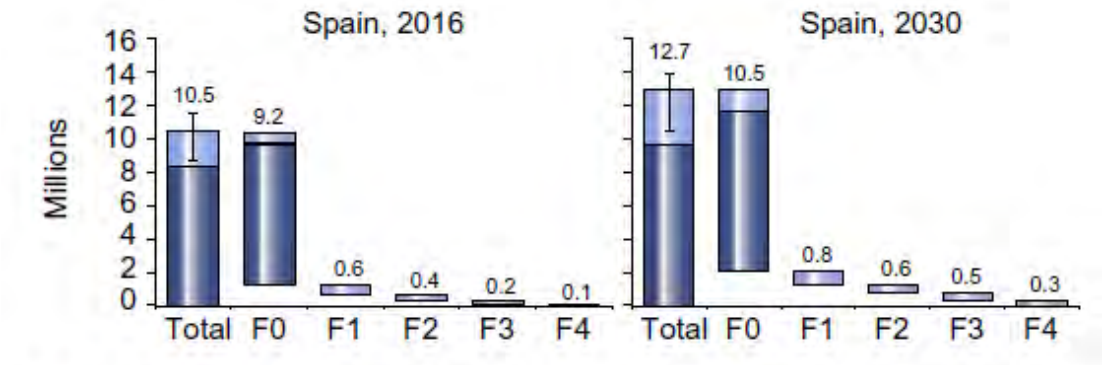


Fig. 1. Distribution of NAFLD population by fibrosis stage – 2016 & 2030.

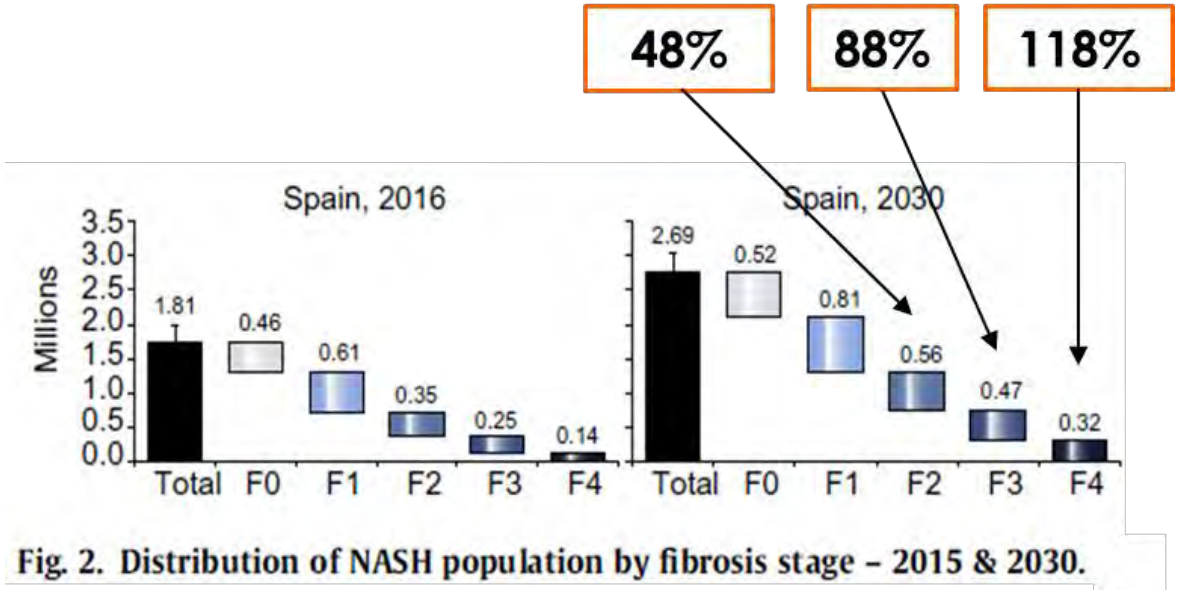


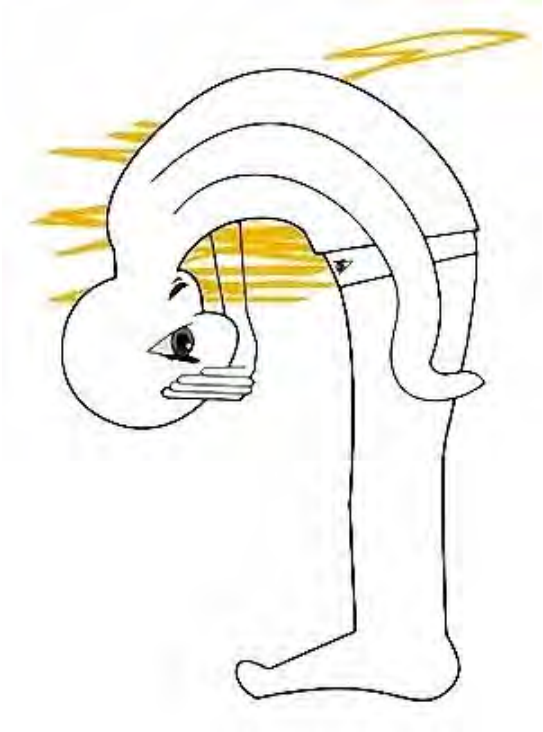
Fig. 2. Distribution of NASH population by fibrosis stage – 2015 & 2030.

	Spain
2016 Country population (000)	46,100
2030 Country population (000)	45,900
Adult obesity prevalence (BMI)	≥30 kg/m^2
2016	18.0%
2030	18.9%
NAFLD	
2016 Total cases	10,532,000
2016 Prevalence (all ages)	22.9%
2030 Total cases	12,653,000
2030 Prevalence (all ages)	27.6%
NAFL	
2016 Total cases	8,728,000
2016 Prevalence (all ages)	18.9%
2030 Total cases	9,966,000
2030 Prevalence (all ages)	21.7%
NASH	
2016 Total cases	1,803,700
2016 Prevalence (all ages)	3.9%
2030 Total cases	2,687,300
2030 Prevalence (all ages)	5.9%
Incident NAFLD	
2016 Total cases	337,000
2016 Prevalence (all ages)	7.3
2030 Total cases	330,500
2030 Prevalence (all ages)	7.2
NASH mortality	
2016 Total cases	3,260
2016 Prevalence (all ages)	4,530
2030 Total cases	7,590
2030 Prevalence (all ages)	7,850

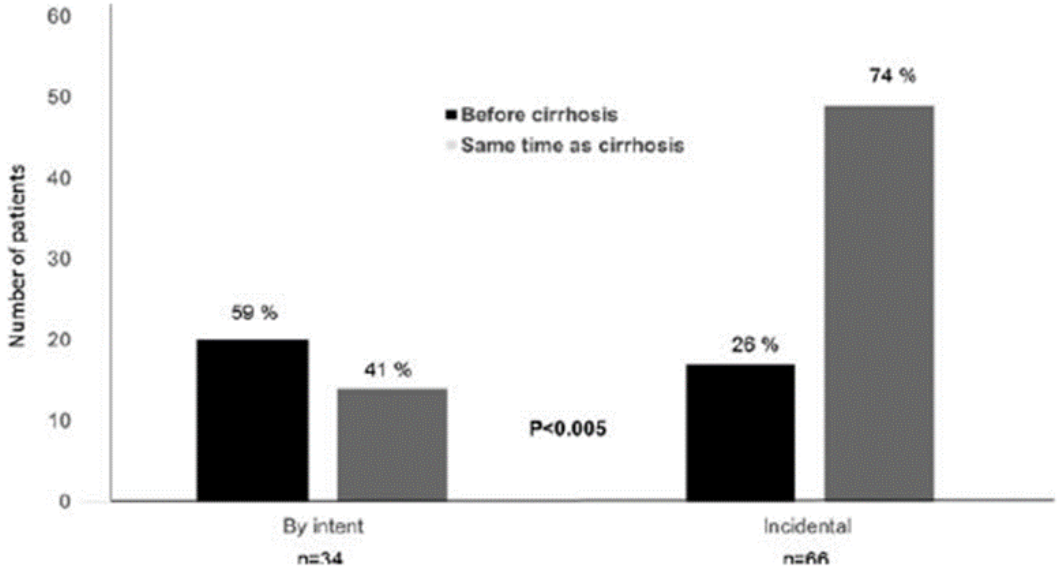
Estes et al, J Hepatol 2018

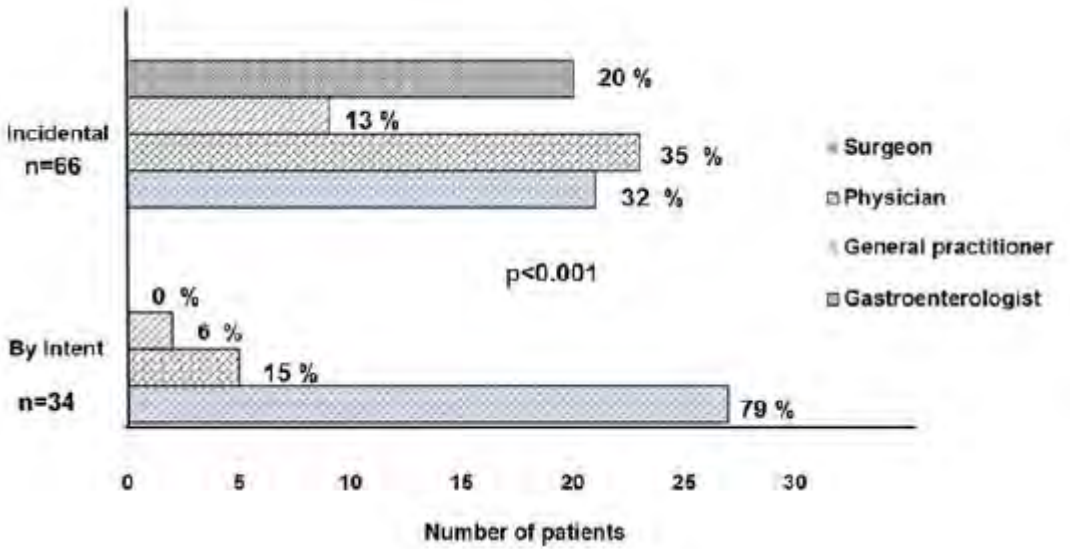
¿Estamos concienciados?

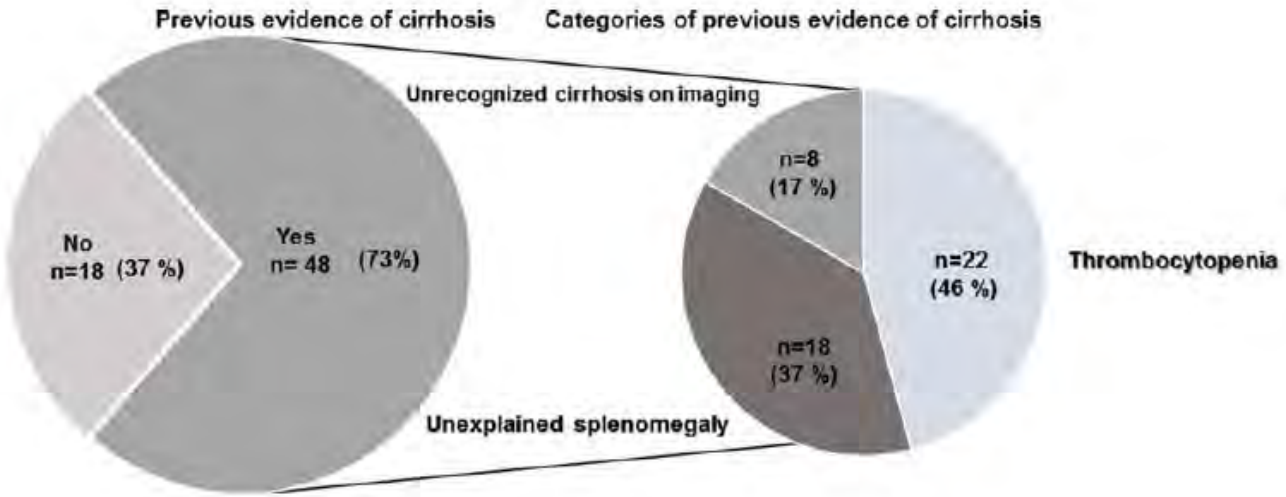
Mirándonos el ombligo

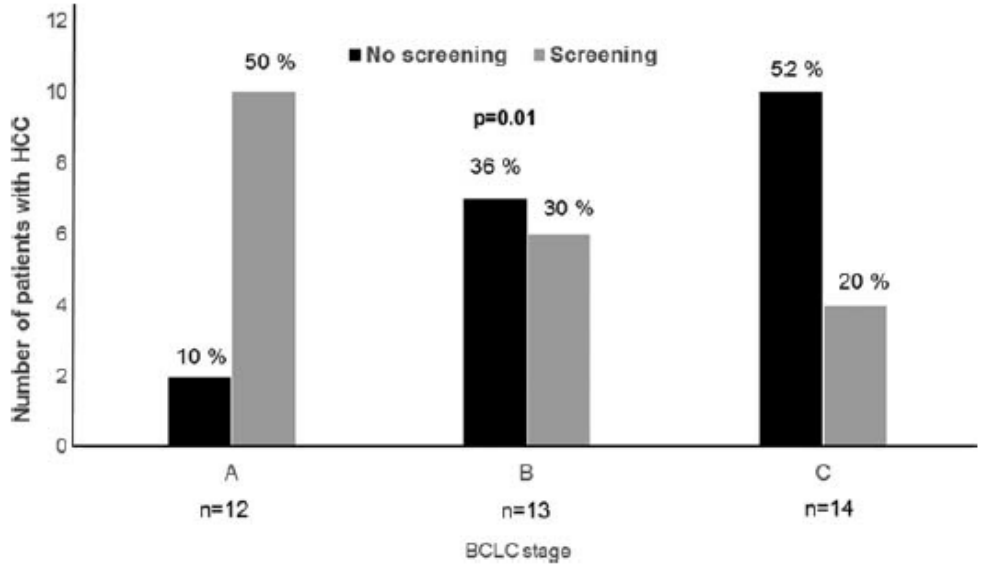


DIAGNÓSTICO POR INTENCIÓN VS. INCIDENTAL







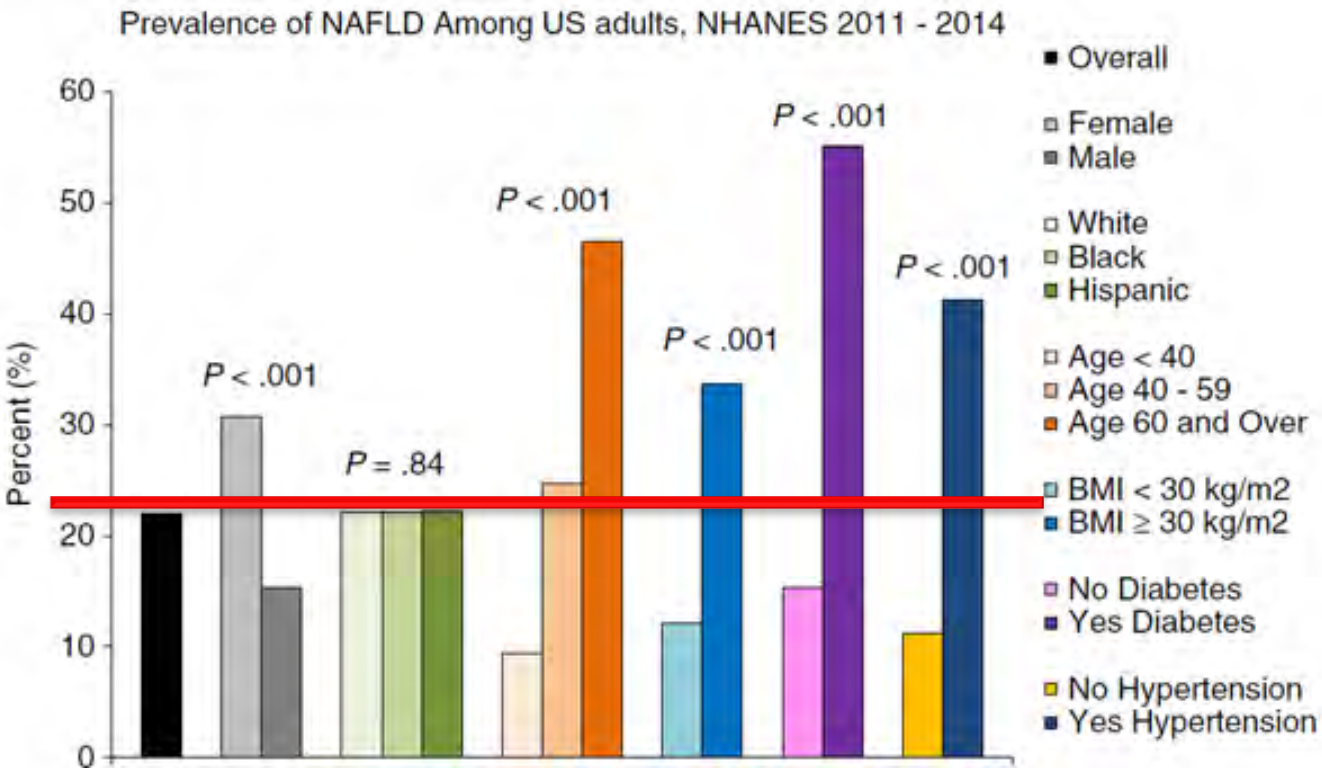


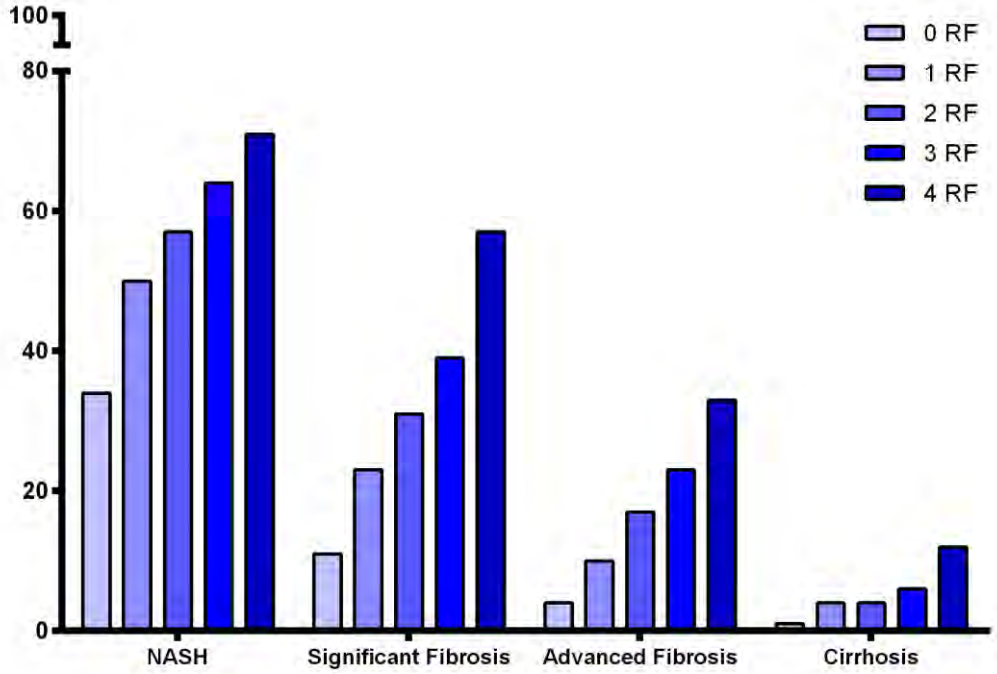
Bertot et al, Hepatol Commun 2017

¿Cuáles son los factores de riesgo?

Definiendo fenotipos clínicos

Fenotipo Metabólico



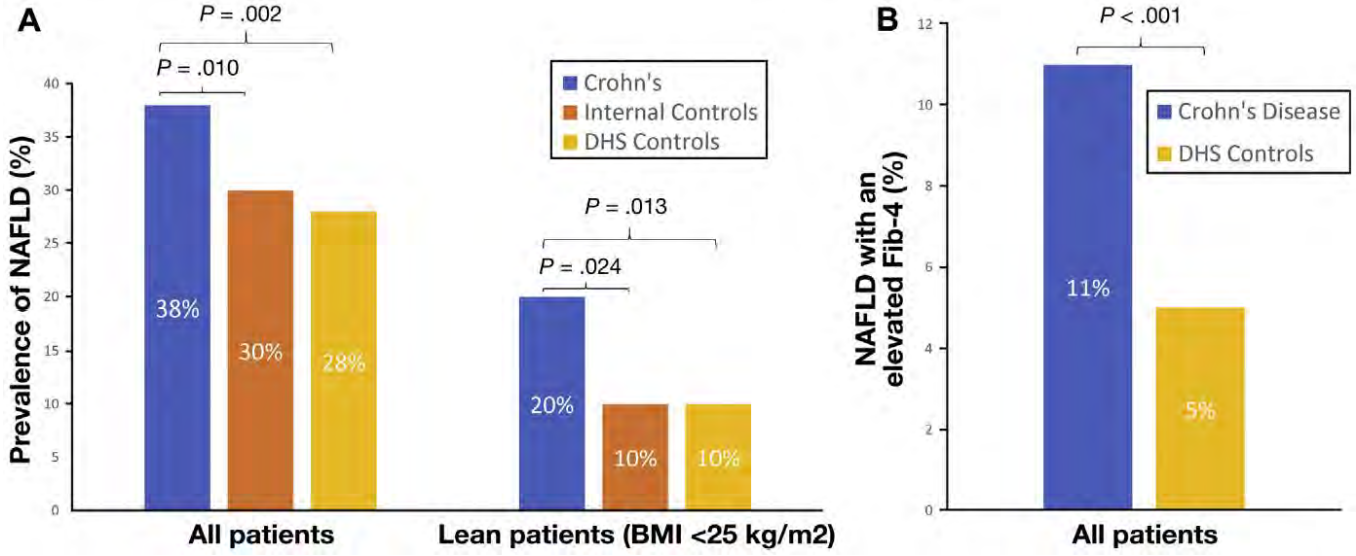


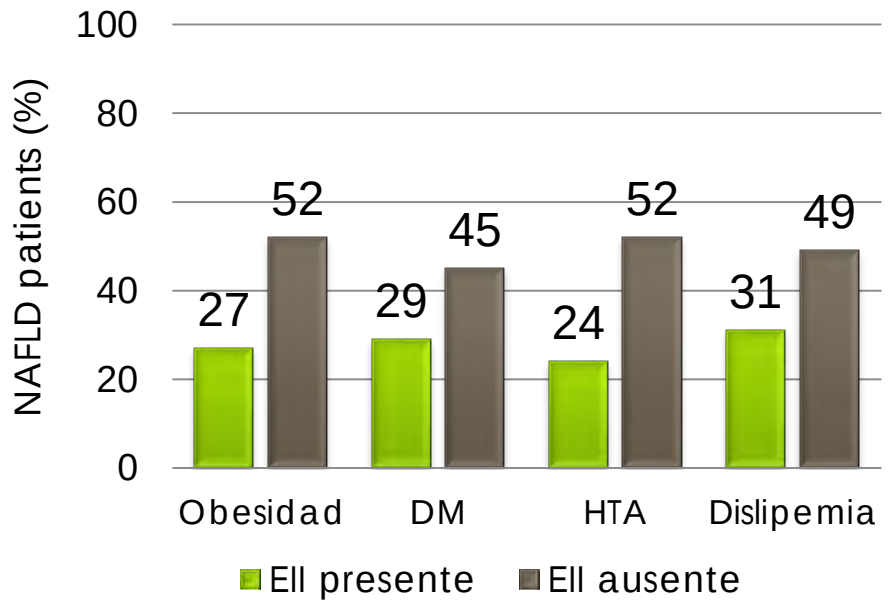
Wong et al, Aliment Pharmacol Ther 2017

Ampuero et al, Aliment Pharmacol Ther 2018

¿HEMOS CAMBIADO EN LOS ÚLTIMOS AÑOS?

Fenotipo IMID



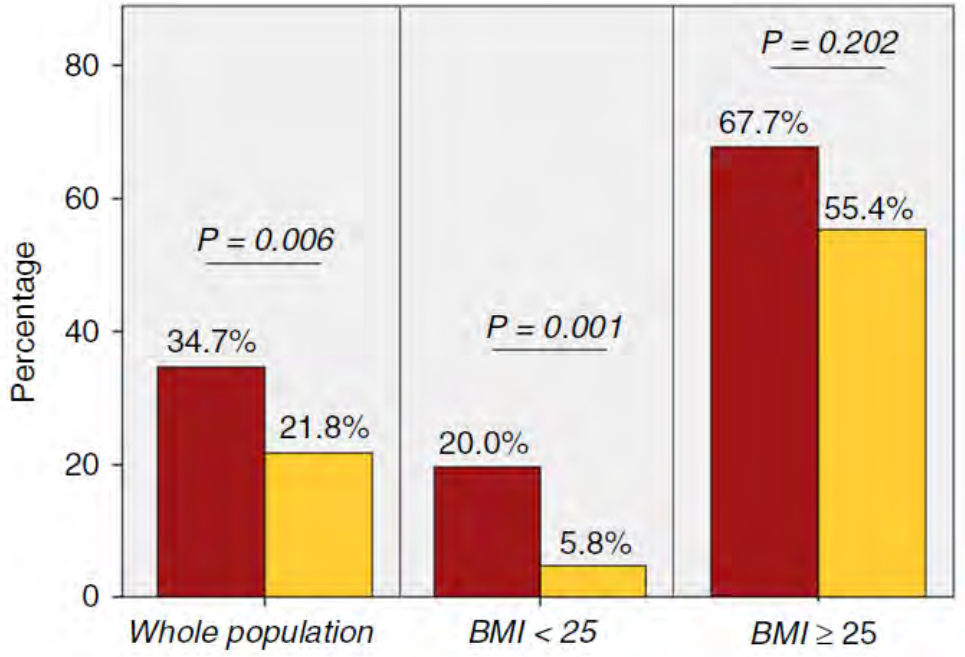


Clinical Gastroenterology and Hepatology 2019

Crohn's Disease Is Associated With an Increased Prevalence of Nonalcoholic Fatty Liver Disease: A Cross-Sectional Study Using Magnetic Resonance Proton Density Fat Fraction Mapping

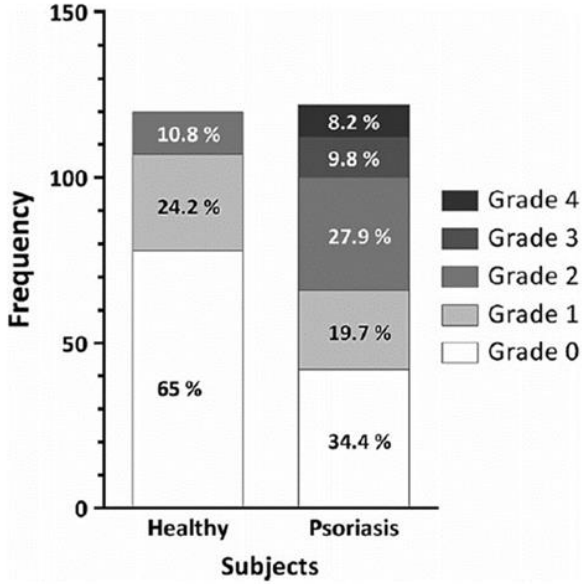
WILEY APT Alimentary Pharmacology & Therapeutics

Increased risk of nonalcoholic fatty liver disease in patients with coeliac disease on a gluten-free diet: beyond traditional metabolic factors



McHenry et al, Clin Gastroenterol Hepatol 2019

Tovoli et al, Alimentary, Pharmacol, Ther 2018



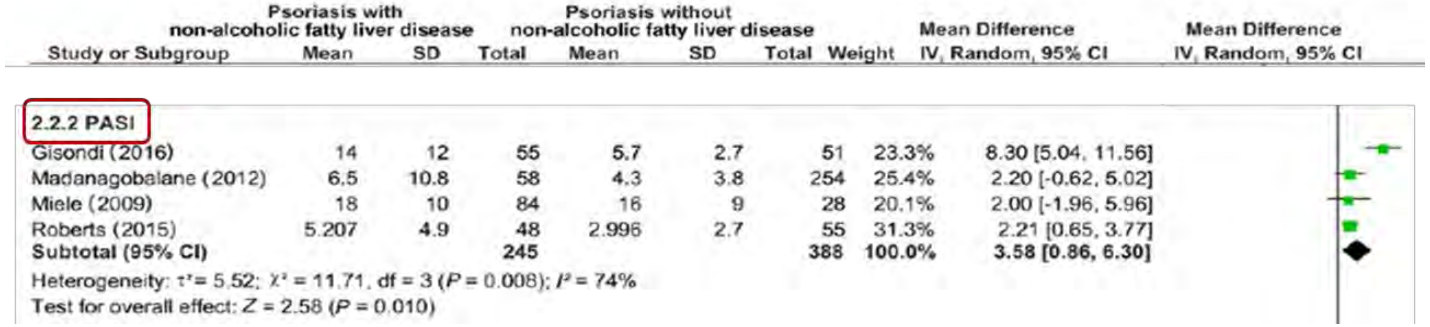


Table 2. Event Rate per 1000 Person-years and Hazard Ratios (HRs)

	Psoriasis			No Psoriasis				
Outcome	No.	Person-years	Event Rate per 1000	No.	Person-years	Event Rate per 1000	HR (95% CI)	*P* Value
Elevated lipid levels	699	101 070.6	6.9	412	90 300.4	4.6	1.40 (1.24-1.58)	<.001
Hypertension	499	101 729.8	4.9	261	90 733.7	2.9	1.57 (1.35-1.82)	<.001
Diabetes	269	102 284.4	2.6	138	91 023.2	1.5	1.63 (1.32-2.00)	<.001
Metabolic syndrome	115	102 705.3	1.1	57	91 236.5	0.6	1.52 (1.10-2.10)	.01
Polycystic ovarian syndrome	228	54 436.4	4.2	123	48 402.1	2.5	1.52 (1.22-1.89)	.002
Nonalcoholic liver disease	97	102 762.9	0.9	43	91 272.6	0.5	1.64 (1.14-2.36)	.008
Elevated liver enzyme levels	604	101 454.1	6.0	342	90 572.7	3.7	1.49 (1.30-1.70)	<.001

Table 3. Effects of Psoriasis in Obese vs Nonobese Children: Hazard Ratios (95% CIs)[a]

Outcome	With Psoriasis	Without Psoriasis
Nonalcoholic liver disease		
Nonobese	1.76 (1.16-2.65)	1 [Reference]
Obese	22.54 (13.62-37.30)	18.11 (8.63-38.03)
Elevated liver enzyme levels		
Nonobese	1.46 (1.27-1.67)	1 [Reference]
Obese	4.76 (3.59-6.33)	2.26 (1.24-4.13)

Table 4 Best set of predictors of NAFLD risk in the multivariable analysis

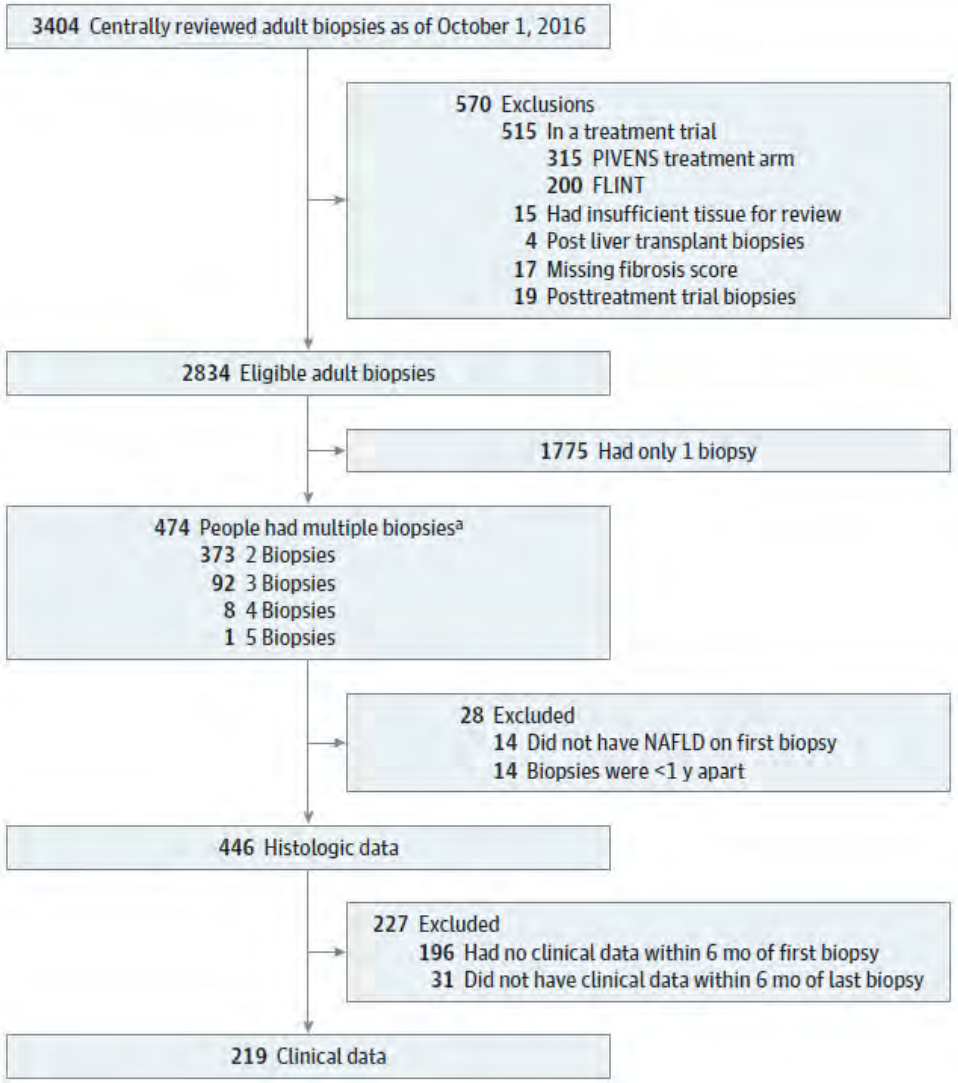
	OR (95% CI)†	*P*
Male gender	0.25 (0.09–0.69)	0.007
Abdominal perimeter, cm	1.15 (1.08–1.21)	<0.001
Hidradenitis suppurativa	7.75 (2.54–23.64)	<0.001
ALT, U/L	1.03 (1.003–1.07)	0.03

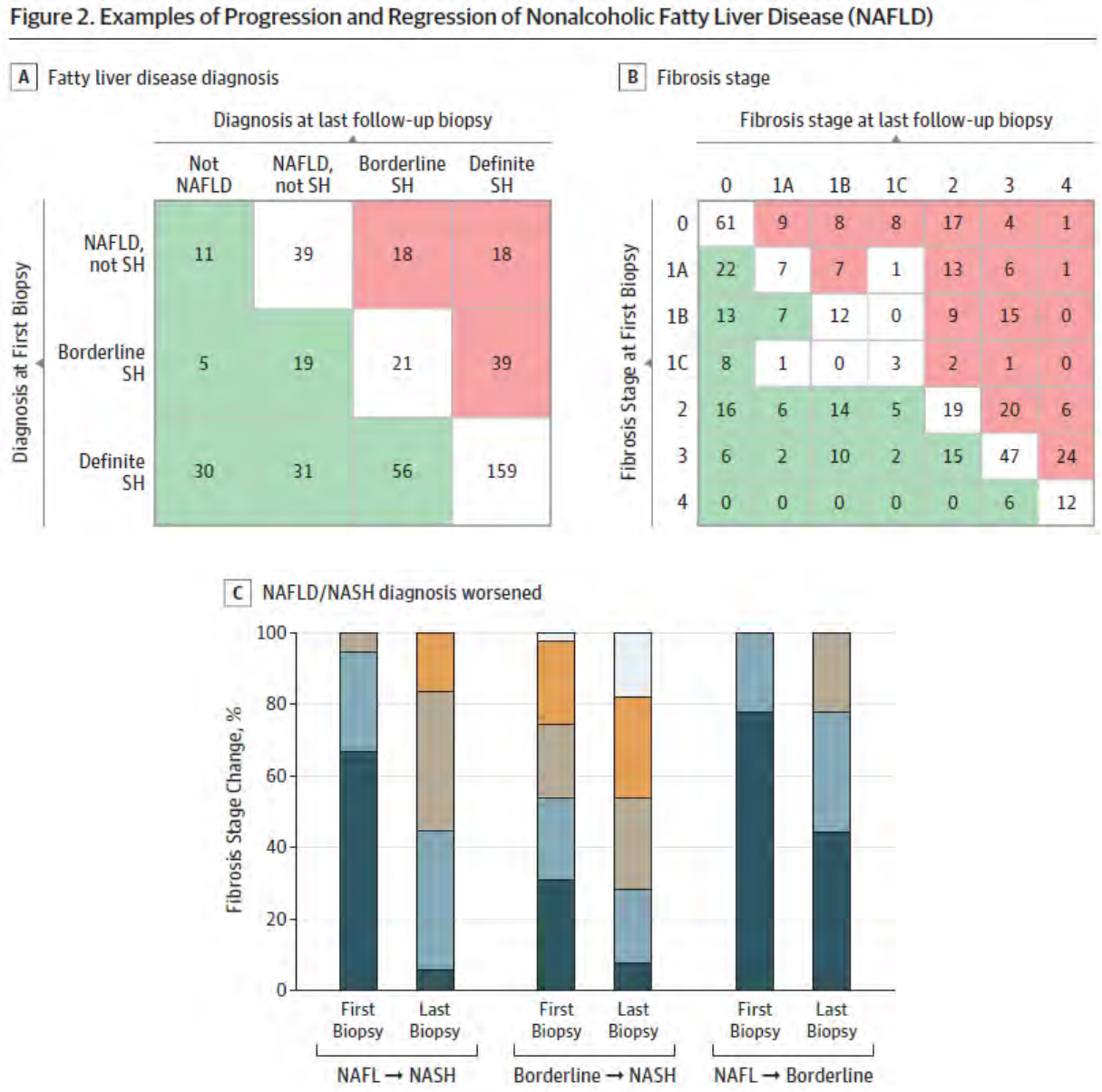
Tollefson et al, JAMA Dermatol 2018 Phan et al, Australas J Dermatol 2019 Duran-Vian et al, J Eur Acad Dermatol Venereol 2019

¿Qué tipo de pacientes progresan?

Esa es la cuestión

Mean Interval 4.9 (±2.8) years between biopsies





Kleiner et al, JAMA Network Open 2019

CARACTERÍSTICAS BASALES

Variable	cOR (95% CI)[a] Fibrosis Regression vs No Change	*P* Value	Fibrosis Progression vs No Change	*P* Value
First Model: Clinical and Histologic (n = 216)[b]				
Baseline clinical and histologic features				
Age at biopsy (per 10 y)	0.7 (0.5-1.0)	.05	1.3 (0.9-1.8)	.10
Current smoker	0.1 (0.0-0.5)	.009	2.4 (0.8-7.2)	.12
AST (per 10 U/L)	0.6 (0.4-0.7)	<.001	1.3 (1.1-1.5)	.002
HOMA-IR (per 5 U)	0.5 (0.4-0.8)	.003	1.1 (0.9-1.3)	.25
Portal inflammation	0.4 (0.2-0.9)	.02	1.4 (0.7-2.7)	.36
Fibrosis stage	3.0 (1.8-4.8)	<.001	0.6 (0.4-0.8)	.007
Change[c]				
ΔALT (per 10 U/L)	0.7 (0.5-0.9)	.002	1.0 (0.9-1.2)	.93
ΔAST (per 10 U/L)	0.9 (0.6-1.2)	.47	1.3 (1.0-1.6)	.02
Years between biopsies	1.1 (0.9-1.3)	.56	1.2 (1.0-1.4)	.04
Second Model: Histologic (n = 445)[d]				
Baseline				
Ballooning	0.6 (0.3-0.9)	.02	3.7 (2.2-6.0)	<.001
Portal inflammation	0.4 (0.2-0.8)	.007	4.0 (2.1-7.7)	<.001
Fibrosis stage	2.0 (1.5-2.8)	<.001	0.4 (0.3-0.5)	<.001
Change (last biopsy vs first)				
ΔSteatosis grade	0.6 (0.4-0.8)	<.001	0.8 (0.6-1.1)	.24
ΔBallooning	0.6 (0.4-0.8)	.002	3.0 (2.0-4.4)	<.001
ΔLobular inflammation	0.8 (0.6-1.2)	.33	1.3 (0.9-1.8)	.14
ΔPortal inflammation	0.5 (0.3-0.9)	002	4.1 (2.3-7.3)	<.001
Years between biopsies	0.9 (0.9-1.0)	.24	1.1 (1.0-1.2)	.07

Factors associated with progression to advanced fibrosis	Progression to advanced fibrosis (stage 3 or 4) Yes	No	Mean difference (95% CI)	P*
Baseline clinical factors				
N	**21**	**152**		
ALT (U/L)	91 ± 45	70 ± 46	21 (0, 42)	0.05
AST (U/L)	75 ± 57	48 ± 39	26 (8, 45)	0.05
Alkaline Phosphatase (U/L)	88 ± 20	83 ± 23	5 (-5, 15)	0.35
Insulin (μU/mL)†	23.9 ± 15.0	23.1 ± 25.7	0.8 (-10.9, 12.4)	0.85
Weight (kg)	91 ± 15	99 ± 21	-8 (-17, 2)	0.11
BMI (kg/m^2)	34.5 ± 6.1	35.1 ± 6.7	-0.5 (-3.6, 2.5)	0.73
Metabolic syndrome†	20 (95%)	108 (72%)	--	0.03
Diabetes	7 (33%)	35 (23%)	--	0.29
Baseline histology				
N	**54**	**268**		
Steatosis	1.9 ± 0.9	2.0 ± 0.8	0.0 (-0.3, 0.2)	0.81
Lobular inflammation	1.7 ± 0.6	1.5 ± 0.7	0.2 (0.0, 0.4)	0.07
Ballooning	1.4 ± 0.8	0.8 ± 0.8	0.5 (0.3, 0.8)	<0.001
Mallory-Denk bodies	24 (44%)	36 (13%)	--	<0.001
Portal inflammation	1.1 ± 0.5	0.9 ± 0.6	0.3 (0.1, 0.4)	0.001
Fibrosis stage	1.4 ± 0.7	0.8 ± 0.8	0.5 (0.3, 0.8)	<0.001
NAS	5.0 ± 1.4	4.3 ± 1.6	0.7 (0.2, 1.1)	0.005
Interval between biopsies (years)	5.7 ± 2.7	4.9 ± 2.8	0.8 (0.0, 1.7)	0.04

Kleiner et al, JAMA Network Open 2019

Mean Interval 13.7 (±1.3) years

	Progressive Fibrosis (n = 29)	Nonprogressive Fibrosis (n = 41)	P
Age (years)	61.1 ± 11.0	60.1 ± 11.1	NS
Follow-up time (years)	14.0 ± 1.0	13.7 ± 1.3	NS
Sex (male)	21 (72%)	29 (71%)	NS
BMI (kg/m^2)	29.6 ± 3.3	28.3 ± 5.3	NS
BMI > 25	28 (97%)	34 (83%)	NS
Weight gain > 5 kg	16 (55%)	10 (24%)	.02
IGT	7 (24%)	7 (17%)	NS
Diabetes	15 (52%)	24 (58%)	NS
Hypertension	28 (97%)	38 (93%)	NS
Metabolic syndrome	18 (62%)	21 (51%)	NS
Alcohol consumption (g/week)	46 ± 44	28 ± 36	NS
ALT (U/L)	75 ± 44	51 ± 25	.005
AST (U/L)	42 ± 17	31 ± 13	.003
AST/ALT ratio	0.6 ± 0.2	0.7 ± 0.4	NS
ALP (U/L)	61 ± 21	67 ± 51	NS
Bilirubin (mg/dL)	0.8 ± 0.4	0.7 ± 0.2	NS
Albumin (g/dL)	4.2 ± 0.4	4.1 ± 0.4	NS
Platelet count (× 10^9/L)	205 ± 59	252 ± 62	.003
Prothrombin (INR)	1.0 ± 0.1	1.0 ± 0.09	NS
Ferritin (μg/L)	207 ± 193	174 ± 125	NS
Glucose (mg/dL)	124 ± 32	127 ± 44	NS
IR_{HOMA}	5.2 ± 5.3	2.9 ± 1.5	.04
Triglycerides (mg/dL)	167 ± 96	144 ± 84	NS
Cholesterol (mg/dL)	201 ± 44	205 ± 43	NS
HDL (mg/dL)	48 ± 11	55 ± 25	NS
LDL (mg/dL)	123 ± 38	127 ± 35	NS

Ekstedt et al, Hepatol 2006

Median Interval 6.6 years (range 1.3–22.6)

Characteristic	All patients (n = 108)	No progression of fibrosis (n = 63)	Progression of fibrosis (n = 45)	p value
Results at baseline biopsy				
Age (years)	48 ± 12	47 ± 12	49 ± 13	0.39*
Gender (% male)	66%	67%	64%	0.81#
BMI (kg/m^2)	33.9 ± 5.0	33.4 ± 4.1	34.5 ± 5.8	0.28*
Change in BMI (kg/m^2)	1.0 ± 3.4	0.92 ± 2.6	1.1 ± 4.2	0.77*
T2DM	48%	43%	53%	0.30
ALT (IU/L)	112 ± 80	113 ± 82	110 ± 77	0.89*
AST (IU/L)	73 ± 48	65 ± 40	84 ± 57	0.06*
GGT (IU/L)	117 ± 105	112 ± 91	124 ± 122	0.55*
Platelets (x10^9/L)	244 ± 67	255 ± 69	229 ± 60	0.04*
IgA (g/L)	2.88 ± 1.36	2.87 ± 1.48	2.88 ± 1.19	0.96*
IgG (g/L)	12.7 ± 12.9	11.7 ± 2.6	14.2 ± 20	0.36*
Ferritin	281 ± 536	322 ± 700	230 ± 187	0.40*
AST/ALT ratio	0.7 ± 0.27	0.65 ± 0.22	0.78 ± 0.32	0.04*
FIB-4 score	1.5 ± 1.0	1.26 ± 0.57	1.85 ± 1.31	0.02*
NAFLD score	-1.49 ± 1.42	-1.71 ± 1.23	-1.18 ± 1.62	0.11*
NAS	4 (1-8)	4 (1-8)	4 (2-7)	0.19^
Steatosis	2 (1-3)	2 (1-3)	2 (1-3)	0.08^
Inflammation	1 (0-3)	1 (0-3)	1 (0-3)	0.89^
Ballooning	1 (0-2)	1 (0-2)	1 (0-2)	0.08^
Fibrosis stage	2 (0-3)	2 (0-3)	1 (0-3)	0.90^
0	23 (21%)	16 (25%)	7 (16%)	
1	29 (27%)	13 (21%)	16 (36%)	
2	33 (31%)	19 (30%)	14 (31%)	
3	23 (21%)	25 (24%)	8 (18%)	
4	0 (0%)	0 (0%)	0 (0%)	
Steatosis/NASH	27 (25%)/81 (75%)	17 (27%)/46 (73%)	10 (22%)/35 (78%)	0.65#

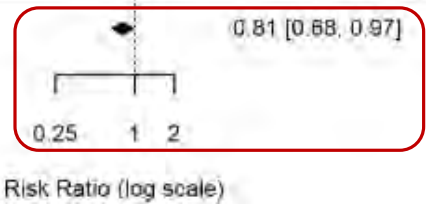
McPherson et al, J Hepatol 2015

¿MÁS RIESGO EN HOMBRES O EN MUJERES?

Riesgo de NAFLD

Author(s) and Year	Female NAFLD	Female None-NAFLD	Male NAFLD	Male None-NAFLD	Relative Risk [95% CI]
Chen, 2006	148	1230	224	918	0.55 [0.45, 0.66]
Zelber-Sagi, 2007	39	126	69	115	0.63 [0.45, 0.88]
Riquelme, 2009	126	428	69	209	0.92 [0.71, 1.18]
Das, 2010	76	817	88	930	0.98 [0.73, 1.32]
Zhang, 2011	403	1665	223	1292	1.32 [1.14, 1.54]
Huang, 2012	1778	4176	812	1866	0.98 [0.92, 1.06]
Amirkalali, 2014	996	1179	1203	1645	1.08 [1.02, 1.15]
Bai, 2014	179	1036	134	837	1.07 [0.87, 1.31]
Chan, 2015	102	361	118	212	0.62 [0.49, 0.77]
Ostovaneh, 2015	1454	2040	1623	2606	1.08 [1.03, 1.15]
Pan, 2015	156	134	74	78	1.10 [0.91, 1.34]
Fattahi, 2016	579	1537	285	579	0.83 [0.74, 0.93]
Li, 2016	101	436	247	222	0.36 [0.29, 0.43]
Majumdar, 2016	43	100	11	22	0.90 [0.52, 1.55]
Jinjuvadia, 2017	1010	5461	1103	4100	0.74 [0.68, 0.80]
Zhai, 2017	610	876	214	311	1.01 [0.89, 1.14]
Shen, 2016	696	5021	1362	3319	0.42 [0.39, 0.45]
RE Model					0.81 [0.68, 0.97]

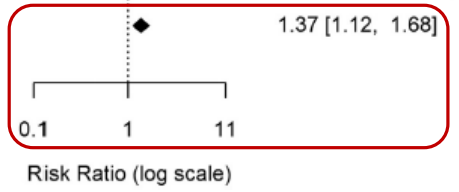
All Studies (Q = 601.41, df = 16, P = .00; I^2 = 97.5%)



Riesgo de F3-F4

Author(s),Year	Female Advanced Fibrosis Present	Female Advanced Fibrosis Absent	Male Advanced Fibrosis Present	Male Advanced Fibrosis Absent	Relative Risk [95% CI]
Jun, 2017	20	76	40	192	1.21 [0.75, 1.96]
Petta, 2017	41	43	30	111	2.29 [1.56, 3.37]
Atay, 2017	10	1	7	5	1.56 [0.93, 2.60]
Bambha, 2014	137	350	62	233	1.34 [1.03, 1.74]
McPherson, 2014	34	77	21	153	2.54 [1.56, 4.14]
Nakahara, 2014	185	471	118	591	1.69 [1.38, 2.08]
Subramanian, 2013	33	20	41	47	1.34 [0.98, 1.82]
Xun, 2012	9	22	15	106	2.34 [1.13, 4.84]
Cichoz-Lach, 2012	11	42	16	57	0.95 [0.48, 1.87]
Francanzani, 2011	32	39	98	262	1.66 [1.22, 2.25]
Hossain, 2009	50	283	25	74	0.59 [0.39, 0.91]
Harrison, 2008	123	302	59	343	1.97 [1.49, 2.61]
Wong, 2008	6	60	12	84	0.73 [0.29, 1.84]
Miyaaki, 2008	27	81	5	69	3.70 [1.49, 9.17]
Malik, 2007	5	28	13	24	0.43 [0.17, 1.08]
Arun, 2006	22	205	6	47	0.86 [0.37, 2.01]
Ong , 2005	11	146	6	34	0.47 [0.18, 1.19]
Suzuki , 2005	13	36	7	23	1.14 [0.51, 2.53]
Hashimoto , 2005	50	67	39	91	1.42 [1.02, 1.99]
Park, 2004	3	6	4	30	2.83 [0.77, 10.44]
de Ledinghen, 2004	7	15	13	32	1.10 [0.51, 2.37]
RE Model					1.37 [1.12, 1.68]

All Studies (Q = 61.04, df = 20, P = .00; I^2 = 74.0%)



Balakrishnan et al, Clin Gastroenterol Hepatol 2020

Characteristic	All patients (n = 108)	No progression of fibrosis (n = 63)	Progression of fibrosis (n = 45)	*p* value
Results at follow up biopsy				
BMI (kg/m²)	34.9 ± 5.2	34.4 ± 4.7	35.6 ± 5.9	0.27*
T2DM	65%	51%	84%	<0.001
ALT (IU/L)	79 ± 66	82 ± 77	76 ± 48	0.63*
AST (IU/L)	57 ± 35	52 ± 34	63 ± 36	0.13*
GGT (IU/L)	148 ± 195	109 ± 143	202 ± 239	0.03*
Platelets (x10⁹/L)	230 ± 62	248 ± 51	208 ± 69	0.001*
IgA (g/L)	3.26 ± 1.50	2.95 ± 1.32	3.7 ± 1.65	0.05*
IgG (g/L)	10.9 ± 3.1	11.2 ± 3.3	10.5 ± 2.7	0.4*
Ferritin	194 ± 218	199 ± 205	187 ± 237	0.81*
AST/ALT ratio	0.81 ± 0.30	0.74 ± 0.29	0.89 ± 0.29	0.01*
FIB-4 score	1.79 ± 1.39	1.36 ± 0.62	2.33 ± 1.69	0.001*
NAFLD score	-0.77 ± 1.38	-1.35 ± 1.08	-0.07 ± 1.40	<0.001*

Variable	cOR (95% CI)[a] Fibrosis Regression vs No Change	*P* Value	Fibrosis Progression vs No Change	*P* Value
First Model: Clinical and Histologic (n = 216)[b]				
Baseline clinical and histologic features				
Age at biopsy (per 10 y)	0.7 (0.5-1.0)	.05	1.3 (0.9-1.8)	.10
Current smoker	0.1 (0.0-0.5)	.009	2.4 (0.8-7.2)	.12
AST (per 10 U/L)	0.6 (0.4-0.7)	<.001	1.3 (1.1-1.5)	.002
HOMA-IR (per 5 U)	0.5 (0.4-0.8)	.003	1.1 (0.9-1.3)	.25
Portal inflammation	0.4 (0.2-0.9)	.02	1.4 (0.7-2.7)	.36
Fibrosis stage	3.0 (1.8-4.8)	<.001	0.6 (0.4-0.8)	.007
Change[c]				
ΔALT (per 10 U/L)	0.7 (0.5-0.9)	.002	1.0 (0.9-1.2)	.93
ΔAST (per 10 U/L)	0.9 (0.6-1.2)	.47	1.3 (1.0-1.6)	.02
Years between biopsies	1.1 (0.9-1.3)	.56	1.2 (1.0-1.4)	.04

McPherson et al, J Hepatol 2015

Kleiner et al, JAMA Network Open 2019

CAMBIOS EN EL SEGUIMIENTO

	Progressive Fibrosis (n = 29)	Nonprogressive Fibrosis (n = 41)	P
Age (years)	61.1 ± 11.0	60.1 ± 11.1	NS
Follow-up time (years)	14.0 ± 1.0	13.7 ± 1.3	NS
Sex (male)	21 (72%)	29 (71%)	NS
BMI (kg/m^2)	29.6 ± 3.3	28.3 ± 5.3	NS
BMI > 25	28 (97%)	34 (83%)	NS
Weight gain > 5 kg	16 (55%)	10 (24%)	.02
IGT	7 (24%)	7 (17%)	NS
Diabetes	15 (52%)	24 (58%)	NS
Hypertension	28 (97%)	38 (93%)	NS
Metabolic syndrome	18 (62%)	21 (51%)	NS
Alcohol consumption (g/week)	46 ± 44	28 ± 36	NS
ALT (U/L)	75 ± 44	51 ± 25	.005
AST (U/L)	42 ± 17	31 ± 13	.003
AST/ALT ratio	0.6 ± 0.2	0.7 ± 0.4	NS
ALP (U/L)	61 ± 21	67 ± 51	NS
Bilirubin (mg/dL)	0.8 ± 0.4	0.7 ± 0.2	NS
Albumin (g/dL)	4.2 ± 0.4	4.1 ± 0.4	NS
Platelet count (× 10^9/L)	205 ± 59	252 ± 62	.003
Prothrombin (INR)	1.0 ± 0.1	1.0 ± 0.09	NS
Ferritin (μg/L)	207 ± 193	174 ± 125	NS
Glucose (mg/dL)	124 ± 32	127 ± 44	NS
IR_{HOMA}	5.2 ± 5.3	2.9 ± 1.5	.04
Triglycerides (mg/dL)	167 ± 96	144 ± 84	NS
Cholesterol (mg/dL)	201 ± 44	205 ± 43	NS
HDL (mg/dL)	48 ± 11	55 ± 25	NS
LDL (mg/dL)	123 ± 38	127 ± 35	NS

Ekstedt et al, Hepatol 2006

Factors	Fibrosis progression	No fibrosis progression	p
N	14	38	
Age (years)	45±10	44±9	0.72
Male gender, n (%)	9 (64)	25 (66)	0.92
Diabetes mellitus, n (%)	6 (43)	20 (53)	0.53
Hypertension, n (%)	9 (64)	17 (45)	0.21
Metabolic syndrome, n (%)	8 (57)	27 (71)	0.34
Body mass index (kg/m^2)	27.7±4.4	27.3±3.4	0.70
Change in body mass index (kg/m^2)*	1.1±2.2	−0.5±1.4	0.018
Waist circumference (cm)	92.9±12.4	92.5±7.7	0.91
Change in waist circumference (cm)*	4.0±6.3	−3.3±6.4	0.001
ALT (IU/l)	51 (35 to 96)	63 (40 to 106)	0.35
Change in ALT (IU/l)*	−1 (−14 to 36)	−17 (−48 to 8)	0.069
Fasting glucose (mmol/l)	6.9±3.7	6.6±2.6	0.78
Insulin (pmol/l)	88 (51 to 158)	106 (63 to 176)	0.35
HOMA-IR (%)	1.7 (0.9 to 3.0)	2.1 (1.3 to 3.5)	0.36
Total cholesterol (mmol/l)	5.8±1.9	5.2±0.9	0.24
HDL-cholesterol (mmol/l)	1.3±0.2	1.3±0.3	0.54
LDL-cholesterol (mmol/l)	3.5±1.1	2.8±1.0	0.046
Triglycerides (mmol/l)	1.8 (1.1 to 2.4)	2.0 (1.2 to 2.9)	0.48

Wong et al, Gut 2010

Table 3. Overall Fibrosis Progression Rate by Baseline Fibrosis Stage in Patients With NAFLD, NAFL Alone, and NASH Alone

		Final fibrosis stage					Total stages of fibrosis progressed	Person-years of follow-up evaluation	Fibrosis progression rate (95% CI)	Time taken to progress by 1 stage (95% CI)
NAFLD (11 studies)										
		0	1	2	3	4				
Baseline fibrosis stage	0 (131)	79	28	13	7	4	+91	968	0.13 (0.07–0.18)	7.7 (5.5–14.8)
	1 (119)	26	44	32	15	2	+43	628.4	0.10 (0.04–0.16)	10.0 (6.2–25.0)
	2 (61)	9	17	14	13	8	−6	331.8	NA	-
	3 (34)	2	5	10	7	10	−16	153.4	NA	-
	4 (21)	0	0	1	6	14	−8	63.8	NA	-
	Overall (366)						+104	2145.4	NA	-
	Stage 0 plus stage 1 fibrosis (250)						+134	1596.4	0.12 (0.07–0.16)	8.3 (6.2–14.3)
NAFL (6 studies)										
		0	1	2	3	4				
Baseline fibrosis stage	0 (81)	52	16	8	4	1	+48	751.3	0.07 (0.02–0.11)	14.3 (9.1–50.0)
	1 (39)	6	13	14	6	0	+20	112.6	0.15 (-0.09 to 40)	NA
	2 (13)	2	3	5	2	1	−3	40.7	NA	-
	3 (0)	0	0	0	0	0	0	0	NA	-
	4 (0)	0	0	0	0	0	0	0	NA	-
	Overall (133)						+75	904.6	NA	-
	Stage 0 plus stage 1 fibrosis (120)						+68	863.9	0.09 (0.04–0.14)	11.1 (7.1–25.0)
NASH (7 studies)										
		0	1	2	3	4				
Baseline fibrosis stage	0 (21)	10	7	2	1	1	+18	115.5	0.14 (0.07–0.21)	7.1 (4.8–14.3)
	1 (49)	9	25	9	5	1	+13	396.6	0.08 (-0.01 to 0.17)	NA
	2 (25)	3	10	4	4	4	−4	222.3	NA	
	3 (16)	0	4	4	2	6	−6	95.8	NA	
	4 (5)	0	0	0	1	4	−1	12.6	NA	
	Overall (116)						+20	842.8	NA	
	Stage 0 plus stage 1 fibrosis (70)						+31	512.1	0.10 (0.03–0.17)	10.0 (5.9–33.3)

Singh et al, Clin Gastroenterol Hepatol 2015

¿Cómo monitorizar a los pacientes?

Mirando la bola de cristal

MONITORIZACIÓN DE FIBROSIS HEPÁTICA

¿Existen datos?

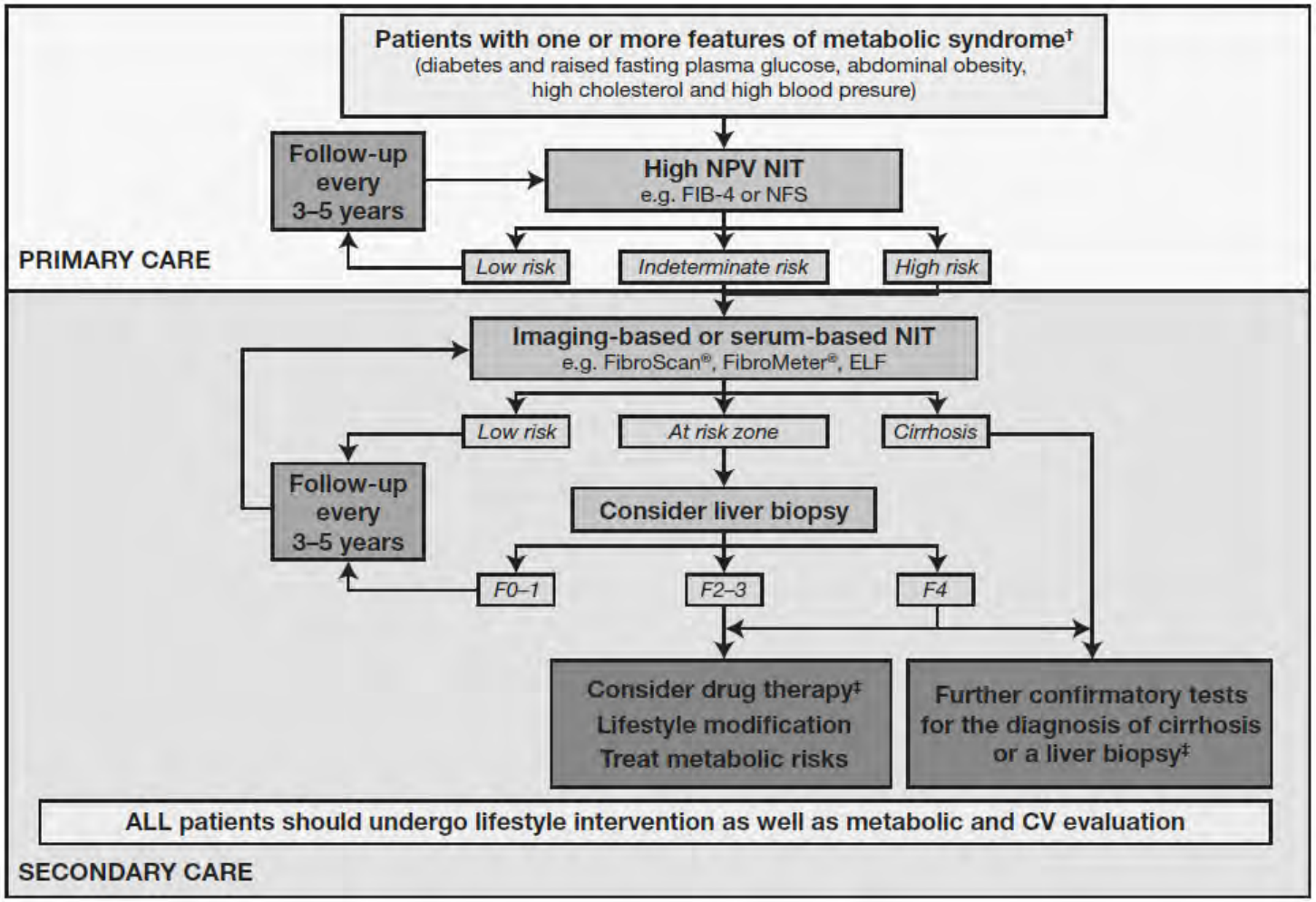
HOSPITALES UNIVERSITARIOS Virgen del Rocío

Test	Description	Responsiveness	Feasibility	Limitations
AST:ALT ratio	AST and ALT	NA	High, as common parameters involved	Modest accuracy
AST:platelet ratio index	AST and platelet count	Modest	High, as common parameters involved	Modest accuracy
Fibrosis-4 index	Age, AST, ALT and platelet count	Modest	High, as common parameters involved	NA
NAFLD fibrosis score	Age, BMI, impaired fasting glucose and/or diabetes, AST, ALT, platelet count and albumin	Modest	High, as common parameters involved	Interpretation of BMI might differ across different ethnic groups
BARD score	AST, ALT, BMI and diabetes	NA	High, as common parameters involved	Interpretation of BMI might differ across different ethnic groups
ELF	PIIINP, hyaluronic acid, TIMP1	NA	Good prognostic factor for clinical outcomes in patients with chronic liver diseases; similar results by using fresh blood or cryopreserved blood	Not sensitive for early stages of fibrosis; age, low $CD4^+$ T cell count and other factors can affect ELF score results
FibroTest	GGT, total bilirubin, α_2m, apolipoprotein AI and haptoglobin	NA	Useful in different chronic liver disease; accurate in patients with overweight or obesity	Suboptimal for early-stage fibrosis
FibroMeter NAFLD	body weight, prothrombin index, ALT, AST, ferritin and fasting glucose	NA	Accurate for severe fibrosis in different liver diseases	High cost

Test	Description	Responsiveness	Feasibility	Limitations
FibroScan (TE)	• Mechanically induced impulse • Quantitative measurement of shear wave speed • Two probes: M and XL (for patients with BMI > 30 kg/m²)	Limited data	• Short processing time (<10 minutes) • Ambulatory clinic setting • Immediacy of results • 0–10% of measurements are failures	• Requires fasting for 2 hours • Requires a dedicated device
pSWE (ARFI)	• Ultrasound-induced focused radiation force impulse at death • Quantitative measurement of shear wave speed	Limited data	• Implemented on a regular ultrasonography machine • Enables simultaneous sonographic imaging of the liver	• Requires fasting for 2 hours • Quality criteria not well defined
2D–3D SWE	• Ultrasound-induced radiation force focus swept over depth faster than shear wave speed to create a Mach cone • Quantitative measurement of shear wave speed	Limited data	• Implemented on a regular ultrasonography machine • Enables simultaneous sonographic imaging of the liver	• Requires fasting for 2 hours • Experienced operators needed • Quality criteria not well defined
MRE	Uses a modified phase-contrast method to image the propagation of the shear wave in the liver parenchyma	High concordance with histological severity and percentage collagen area in drug trials	• Implemented on a regular MRI machine • Examination of the whole liver	• Requires an MRI facility • Time consuming • Costly

Wong et al, Nat Rev Gastroenterol Hepatol 2018

¿CÓMO MONITORIZAR PACIENTES EN RIESGO?



Augustin et al, J Gastrointestin Liver Dis 2020

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