

PRIMER FORO
InmunoDerma2025

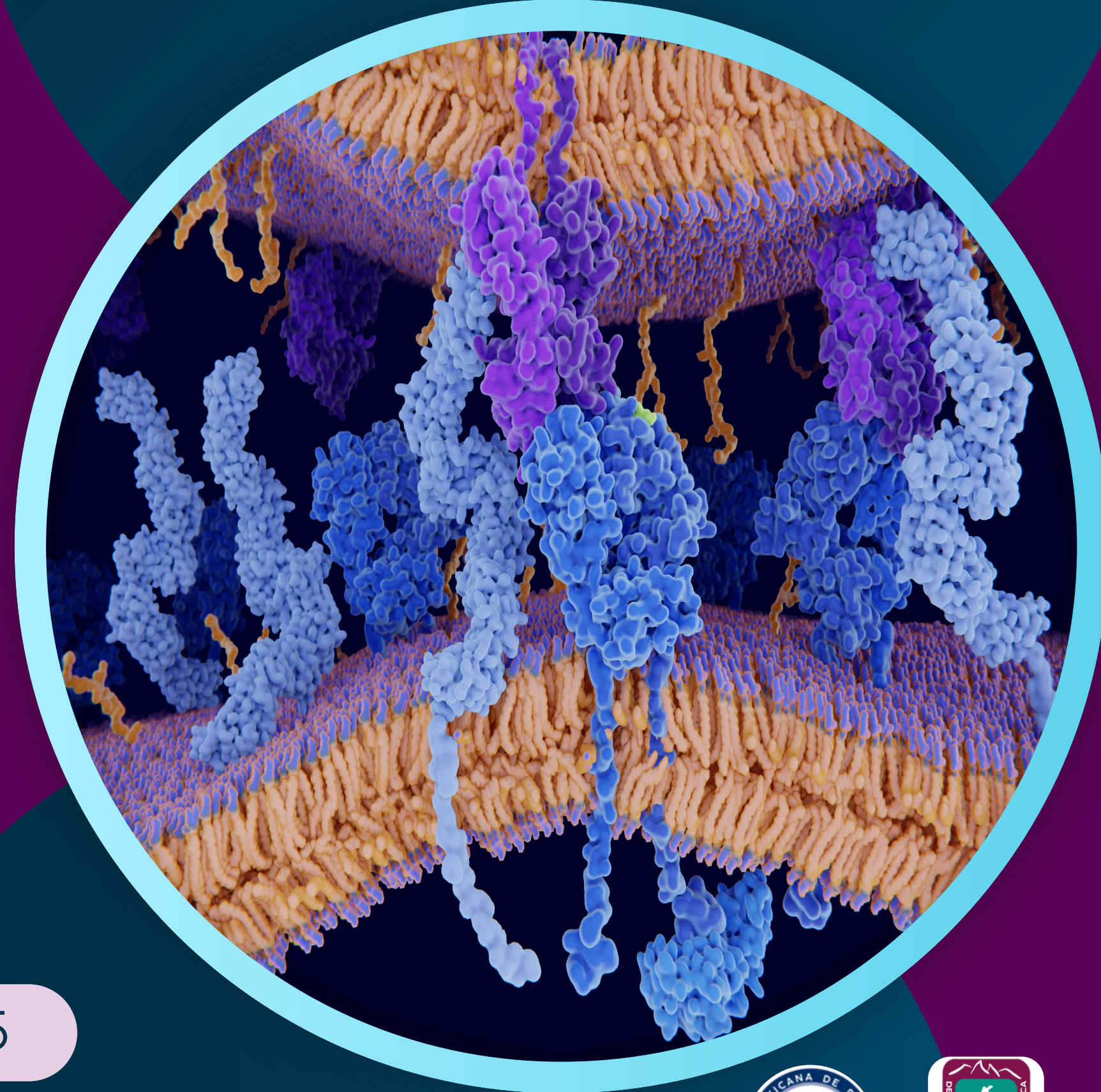
CANCÚN, MX

Hígado graso e inflamación cutánea: Una mirada Hepato- dermatológica

INNOVACIÓN & CONEXIONES EN
INMUNODERMATOLOGÍA

Ponente: Sergio Muñoz Martínez

3/OCT/25



Conflictos de interés

- Consultor, speaker y miembro del Advisory Board: ROCHE y Astrazeneca
- Speaker fees from Bayer and travel funding from Gilead, Madrigal, Bayer, Eisai, and MSD
- Grant support from Bristol Myers Squibb and Celgene for the "Title of Expert in Immuno-Oncology, VII Edition" organized by the University of Navarra, Spain
- Participación previa en ensayos clínicos de fase 2 y 3: Gilead, Madrigal, Novo Nordisk, Boehringer, MSD, Janssen, Pfizer, Bristol Myers Squibb, ROCHE, AstraZeneca

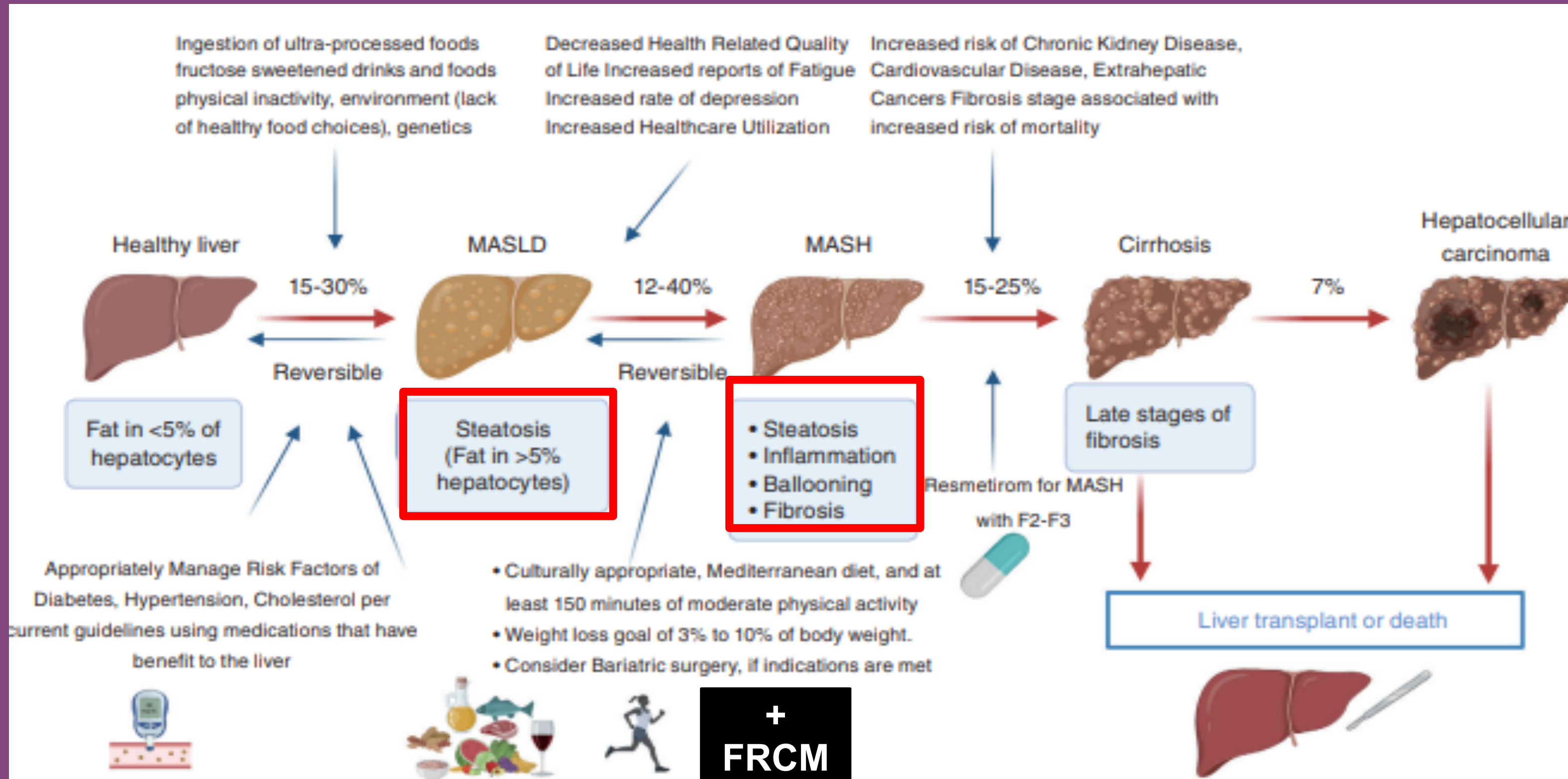


Agenda de trabajo

- Hígado graso: MASLD y MASH
- Importancia de **detección** de MASLD y **estadiaje** de fibrosis
- **MASLD y psoriasis**
 - Epidemiología
 - Mecanismo fisiopatológico compartido: “**Eje Hepato-dérmico**”
 - Dianas potenciales



¿Qué es MASLD?



Nomenclatura nueva

PRIMER FORO
InmunoDerma2025

CANCÚN, MX

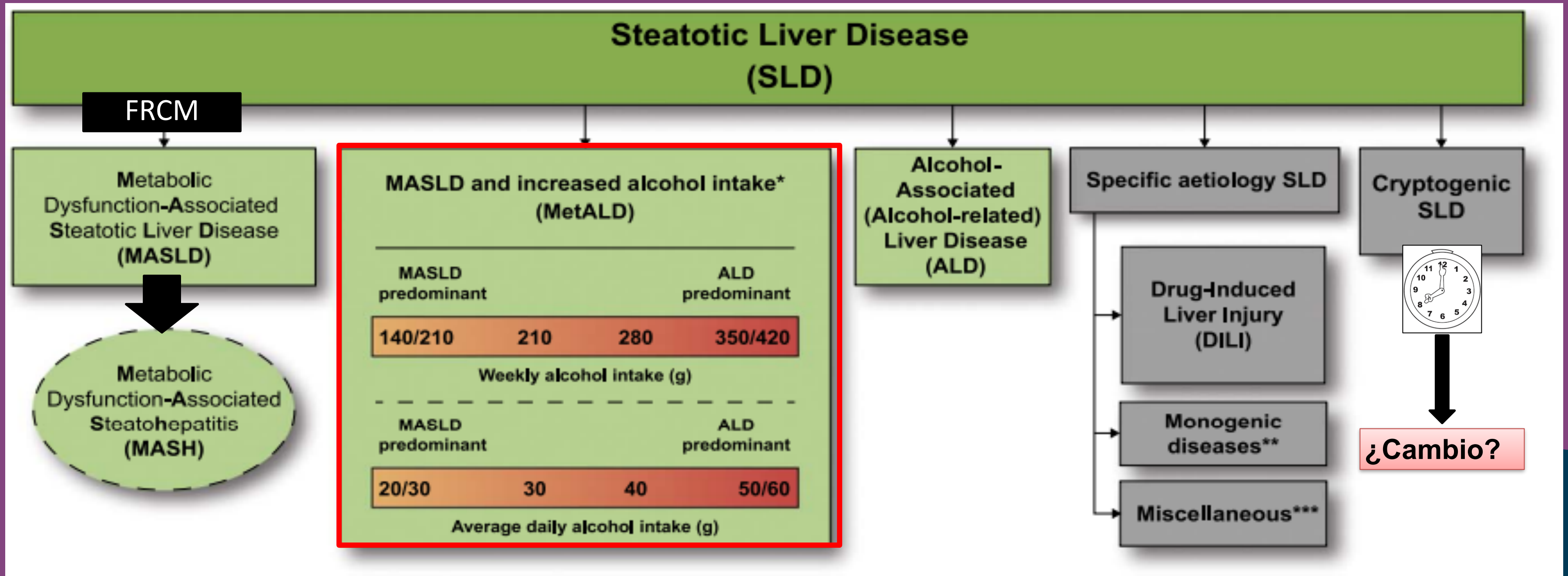
- Consenso internacional: 236 panelistas / 56 países
- Previamente: NAFLD y NASH
- Confusores excluyentes
- Lenguaje estigmatizante (“Fatty”, “non-alcoholic”)
- Cambio en nomenclatura y en la definición
- Consideración a consumo de enol



*Cardiometabolic criteria

Adult Criteria	Paediatric Criteria
At least 1 out of 5:	At least 1 out of 5:
☐ BMI ≥ 25 kg/m ² [23 Asia] OR WC > 94 cm (M) 80 cm (F) OR ethnicity adjusted equivalent	☐ BMI $\geq 85^{\text{th}}$ percentile for age/sex [BMI z score $\geq +1$] OR WC > 95 th percentile OR ethnicity adjusted equivalent
☐ Fasting serum glucose ≥ 5.6 mmol/L [100 mg/dL] OR 2-hour post-load glucose levels ≥ 7.8 mmol/L [≥ 140 mg/dL] OR HbA1c $\geq 5.7\%$ [39 mmol/L] OR type 2 diabetes OR treatment for type 2 diabetes	☐ Fasting serum glucose ≥ 5.6 mmol/L [≥ 100 mg/dL] OR serum glucose ≥ 11.1 mmol/L [≥ 200 mg/dL] OR 2-hour post-load glucose levels ≥ 7.8 mmol [140 mg/dL] OR HbA1c $\geq 5.7\%$ [39 mmol/L] OR already diagnosed/treated type 2 diabetes OR treatment for type 2 diabetes
☐ Blood pressure $\geq 130/85$ mmHg OR specific antihypertensive drug treatment	☐ Blood pressure age < 13y, BP $\geq 95^{\text{th}}$ percentile OR $\geq 130/80$ mmHg (whichever is lower); age $\geq 13y$, 130/85 mmHg OR specific antihypertensive drug treatment
☐ Plasma triglycerides ≥ 1.70 mmol/L [150 mg/dL] OR lipid lowering treatment	☐ Plasma triglycerides age < 10y, ≥ 1.15 mmol/L [≥ 100 mg/dL]; age $\geq 10y$, ≥ 1.70 mmol/L [≥ 150 mg/dL] OR lipid lowering treatment
☐ Plasma HDL-cholesterol ≤ 1.0 mmol/L [40 mg/dL] (M) and ≤ 1.3 mmol/L [50 mg/dL] (F) OR lipid lowering treatment	☐ Plasma HDL-cholesterol ≤ 1.0 mmol/L [≤ 40 mg/dL] OR lipid lowering treatment

Nomenclatura nueva



Nomenclatura nueva • MetALD

Mediana FU: 70 meses (IQR 53-94)

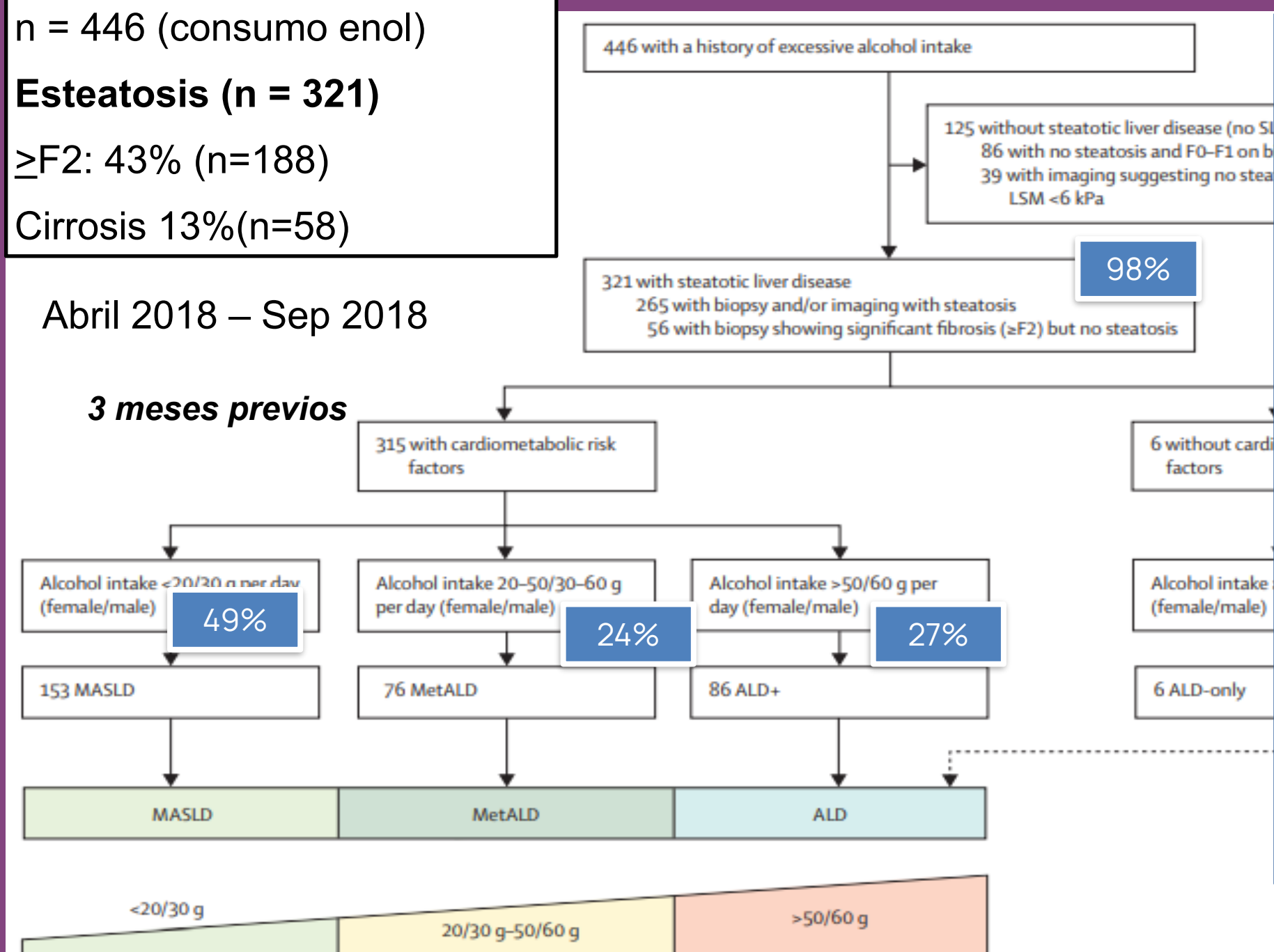
n = 446 (consumo enol)

Esteatosis (n = 321)

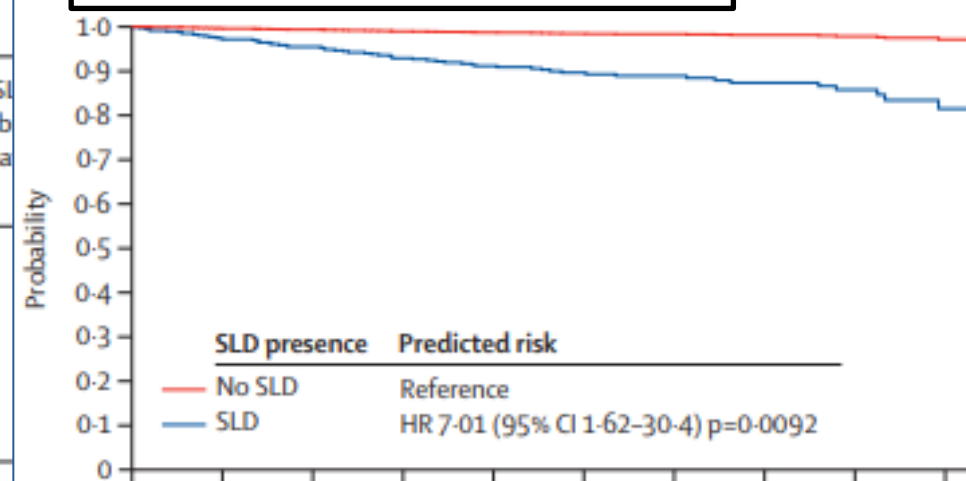
≥F2: 43% (n=188)

Cirrosis 13%(n=58)

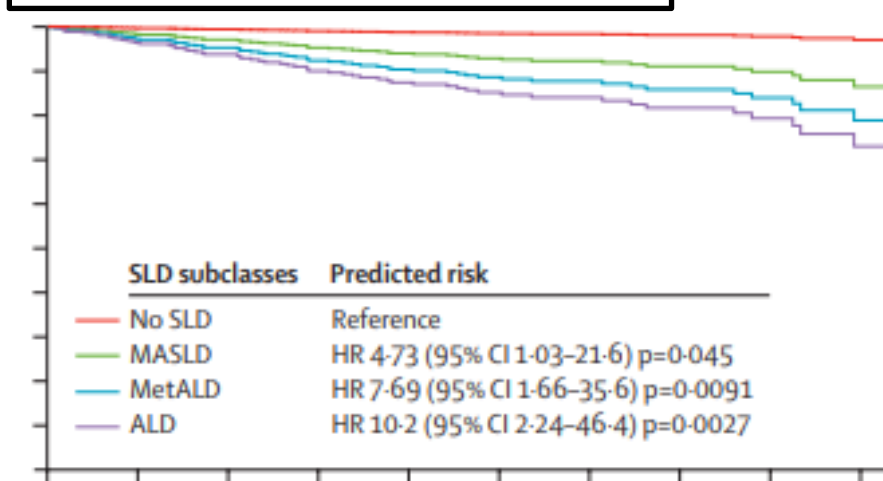
Abril 2018 – Sep 2018



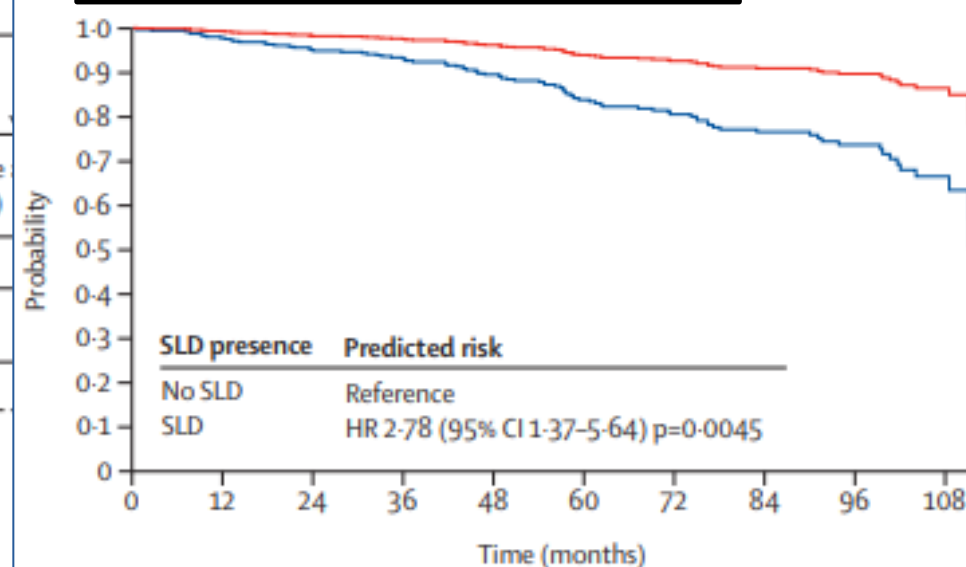
Descompensación



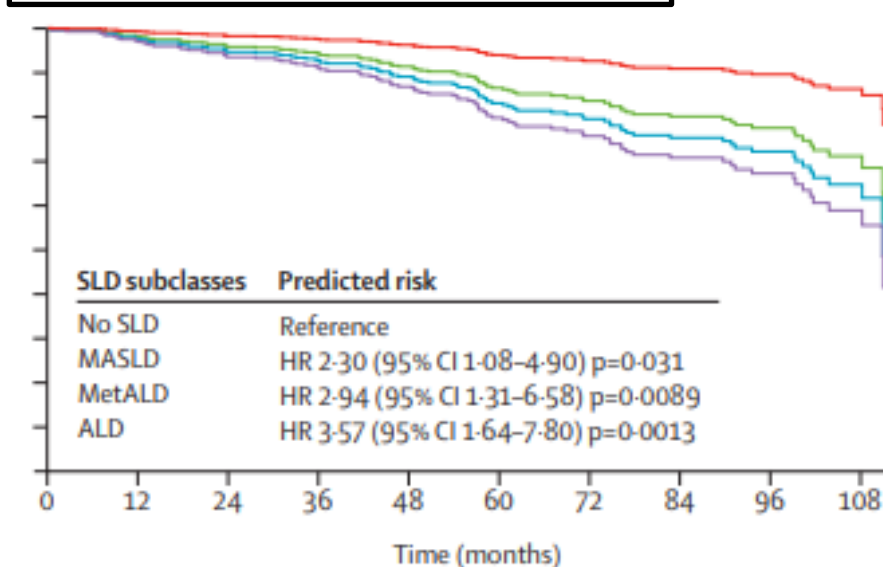
Descompensación



Supervivencia global



Supervivencia global



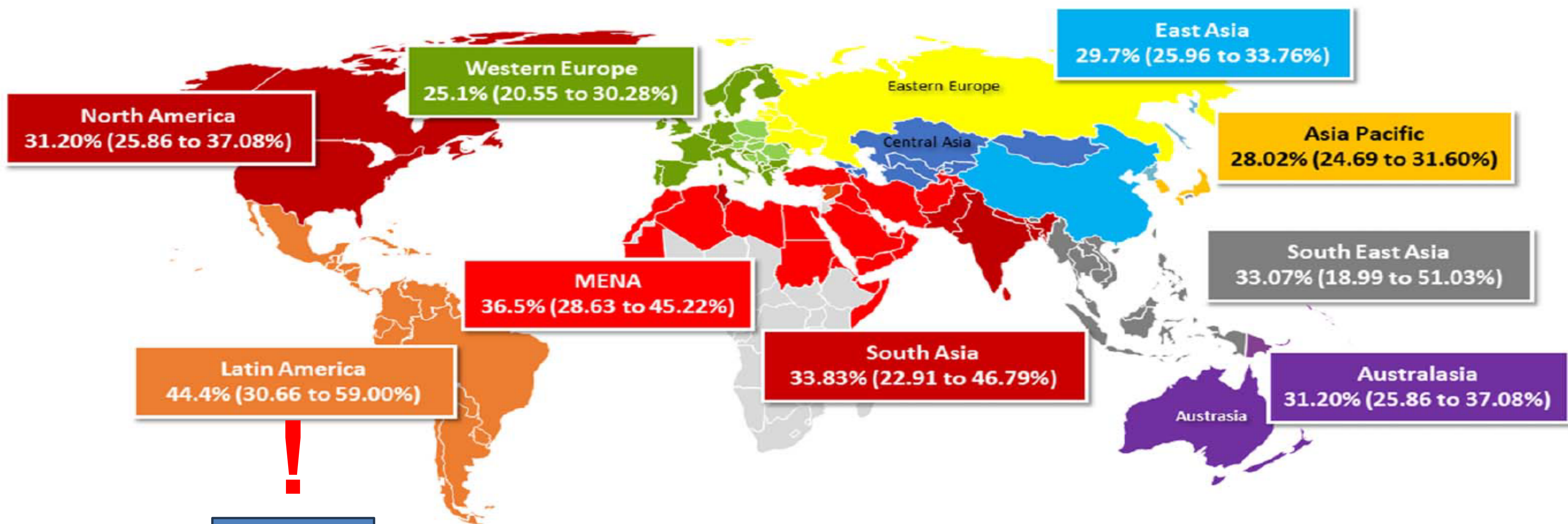
Independiente de edad, sexo o LSM

Epidemiología: MASLD

PRIMER FORO
InmunoDerma2025

CANCÚN, MX

Pooled Prevalence of NAFLD: **30.05%** (95% confidence interval: 27.88 to 32.32%)



DM2: 63%

Geographical regions are based on epidemiological similarities and geographical proximity from the GBD study

Epidemiología: MASLD

- Revisión sistemática: 1990 – 2019
- 92 estudios (n = 9,361,716)
 - Aumento de prevalencia NAFLD un +50.4%
25.7% (<2006) $\square$ 38% (2016-2019)

Mortalidad

	Studies with ultrasound or FLI (n = 3)	Studies with ultrasound, FLI, or biopsy (n = 5)
	Rate per 1000 person-years (95% CI)	
Total NAFLD cases	8153	19,340
Total person-years	104,470	263,947
All-cause mortality	12.6 (6.68–23.67)	17.05 (10.31–28.05)
Cause-specific death		
Cardiac specific	4.20 (1.34–7.05)	5.54 (2.72–8.35)
Extrahepatic cancer specific	2.83 (0.78–4.88)	4.21 (1.94–6.48)
Liver specific	0.92 (0.00–2.21)	1.75 (0.58–2.91)

Abbreviation: FLI, fatty liver index.



Importancia: MASLD / MASH

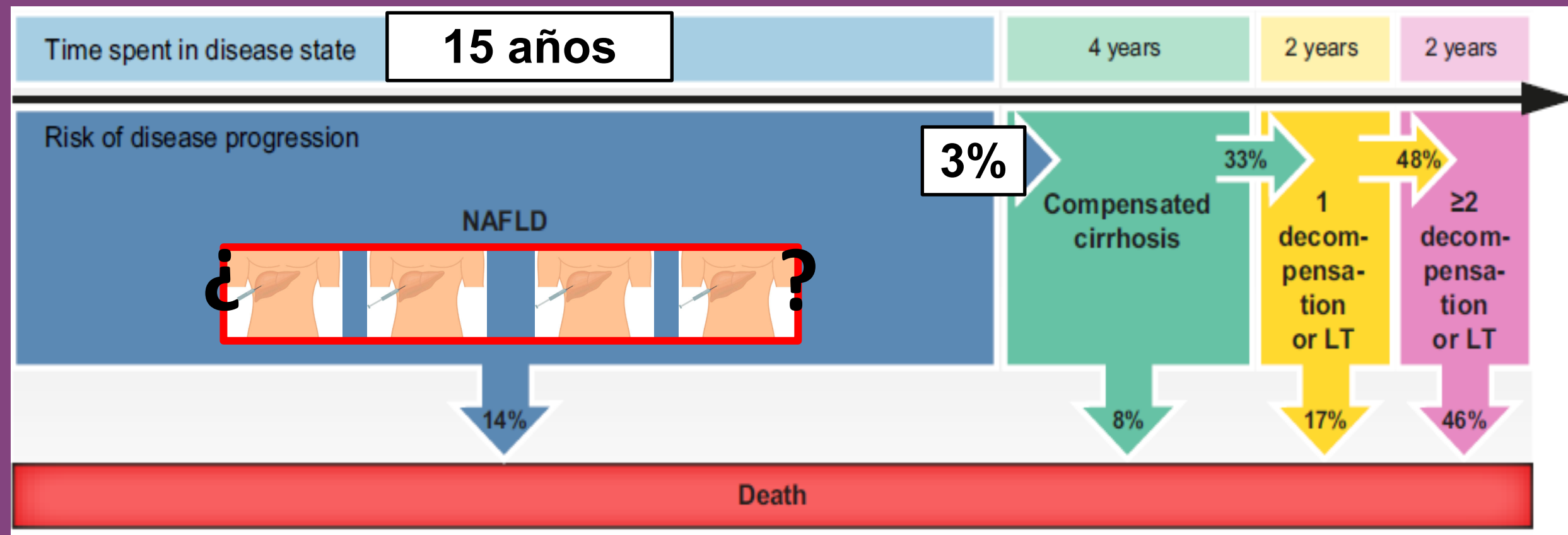
n = 5,123 NAFLD (cirrosis basal 1.8%) – Seguimiento de 23 años

Historia Natural

Estadía enfermedad:

- NASH
- Fibrosis

Limitantes biopsia hepática:



SUMMARY GUIDANCE STATEMENT OF IMAGING-BASED NILDA

- Recognizing that liver histology is an imperfect reference standard, prior to considering a liver biopsy to assess fibrosis staging in patients with CLD, AASLD recommends using blood and imaging-based NILDA as the initial tests to detect significant (F2-4) to advanced fibrosis (F3-4) and cirrhosis (F4). (ungraded statement)

CAP
MRI-PDFF

NIS4
FAST

ELF / FibroTest / ProC3 / FIB-4 / APRI / NFS
Elastografía / MRE



Diagnóstico y
seguimiento

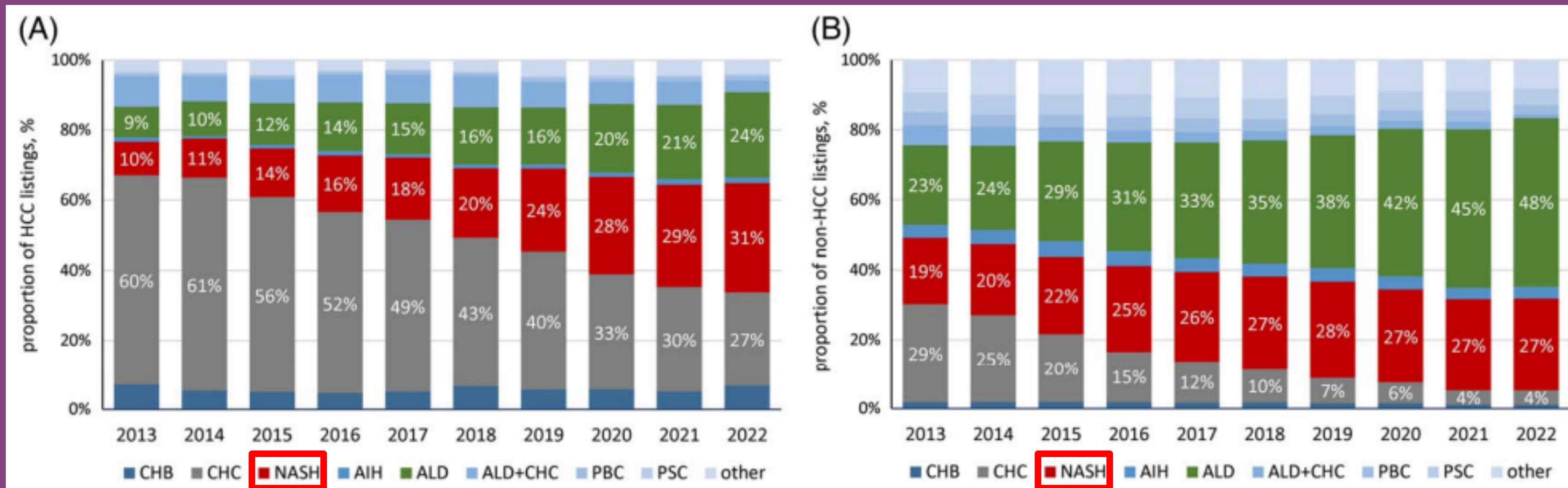
Importancia: MASLD / MASH

Etiología hepatopatía en THO (USA)

PRIMER FORO
InmunoDerma2025

CANCÚN, MX

Etiología emergente



Importancia: MASLD / MASH

Etiología emergente

Age-standardized prevalence (per 100,000 inhabitants) of the leading causes of chronic liver disease in Latin America (2019); data were collected from the Global Burden of Disease database [13].

Country	Alcohol-related liver disease ^a	Metabolic dysfunction-associated steatotic liver disease ^a	Hepatitis B virus infection ^a	Hepatitis C virus infection ^a	Hepatocellular carcinoma ^b
Argentina	201.9	8022.4	323.8	490.0	2.0
Bolivia	306.6	13,039.9	597.9	1183.0	4.6
Brazil	227.2	15,300.1	3066.9	2334.8	2.4
Chile	300.6	9434.0	430.6	590.0	3.0
Colombia	142.5	13,262.8	2347.1	1654.6	2.5
Costa Rica	282.0	12,719.3	664.1	2142.2	5.1
Cuba	183.8	17,035.3	303.9	1471.9	2.3
Dominican Republic	295.8	14,866.0	661.6	1971.6	4.6
Ecuador	343.3	20,749.4	509.1	1007.6	3.4
El Salvador	316.8	16,079.7	677.5	2367.9	2.0
Guatemala	430.7	18,643.6	1294.2	3035.6	4.5
Haiti	223.3	13,719.5	1659.9	2595.3	4.1
Honduras	300.6	18,973.7	1266.4	3180.1	14.8
Mexico	455.0	17,687.8	170.3	1636.8	3.5
Nicaragua	339.7	16,539.1	814.4	3117.0	3.8
Panama	199.3	16,681.5	540.6	1596.8	2.9
Paraguay	178.2	13,079.9	3058.7	1956.6	2.1
Peru	301.3	10,452.5	492.5	997.2	2.6
Uruguay	124.0	11,239.6	240.4	415.3	2.3
Venezuela	187.4	17,166.7	704.2	1841.1	2.3



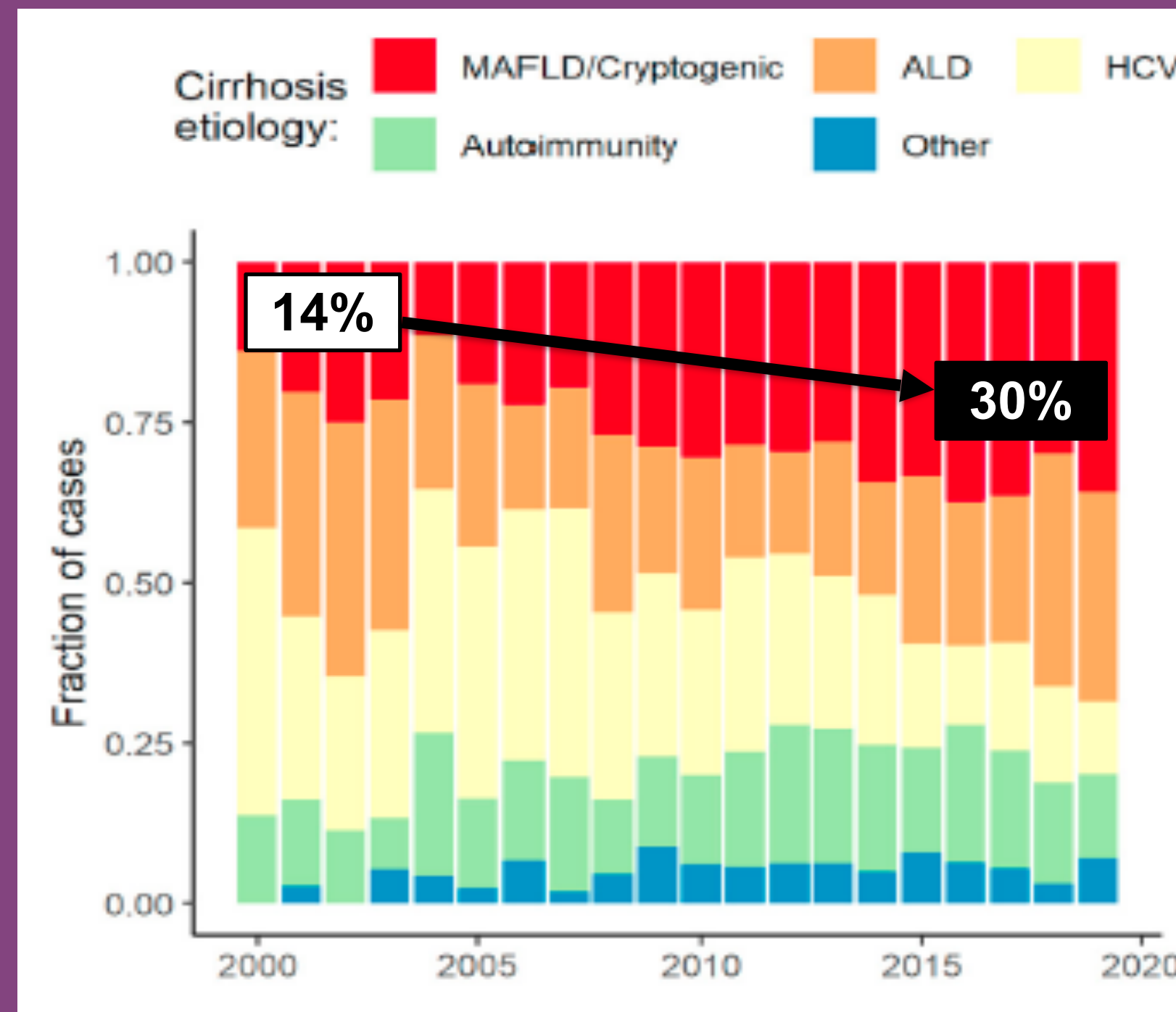
Importancia: MASLD / MASH

Etiología emergente

Retrospectivo

n = 4584

- Adultos
- Dx Cirrosis 2000 – 2019
- 6 centros CDMX / Edo Mex



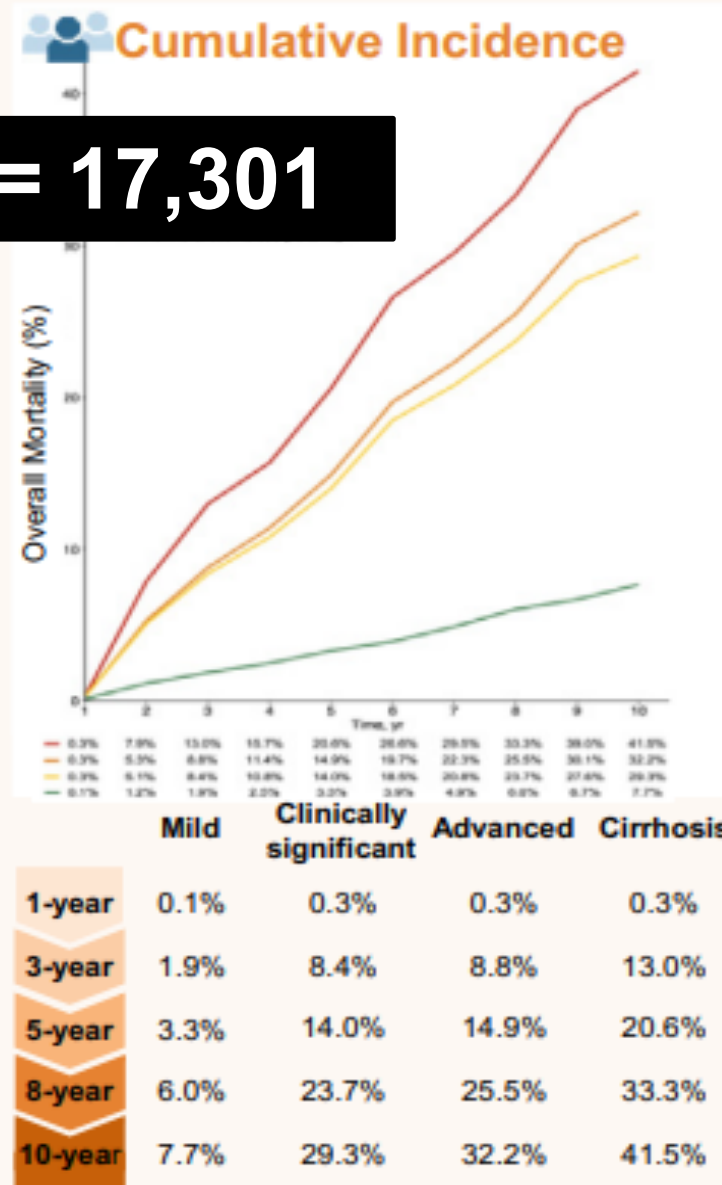
Importancia: MASLD / MASH

FIBROSIS

Meta-análisis: Mortalidad por estadio de fibrosis por MASLD vs. F0 (Biopsia)



n = 17,301



All-Cause Mortality

Compared to F0	F2	HR: 1.46 (CI: 1.08 - 1.98, p=0.01)
	F3	HR: 1.96 (CI: 1.41 - 2.72, p<0.01)
	F4	HR: 3.66 (CI: 2.65 - 5.05, p<0.01)
	F1 - F4	HR: 1.99 (CI: 1.47 - 2.71, p<0.01)
	F1- F2	HR: 1.33 (CI: 1.05 - 1.70, p=0.02)

Fibrosis clínicamente significativa **HR 2.06**

Clinically significant fibrosis compared to non-clinically significant fibrosis resulted in a significant increase in mortality (HR: 2.06, CI: 1.52 - 2.81, p<0.01).

Liver-Related Mortality

Compared to F0	F2	HR: 4.07 (CI: 1.44 - 11.5, p<0.01)
	F3	HR: 7.59 (CI: 2.80 - 20.5, p<0.01)
	F4	HR: 15.1 (CI: 5.27 - 43.4, p<0.01)
	F1 - F4	HR: 4.15 (CI: 1.77 - 9.73, p<0.01)
	F1- F2	HR: 2.39 (CI: 0.93 - 6.18, p=0.07)

Fibrosis clínicamente significativa **HR 6.49**

fibrosis (HR: 6.49, 3.30 - 12.8, p<0.01).

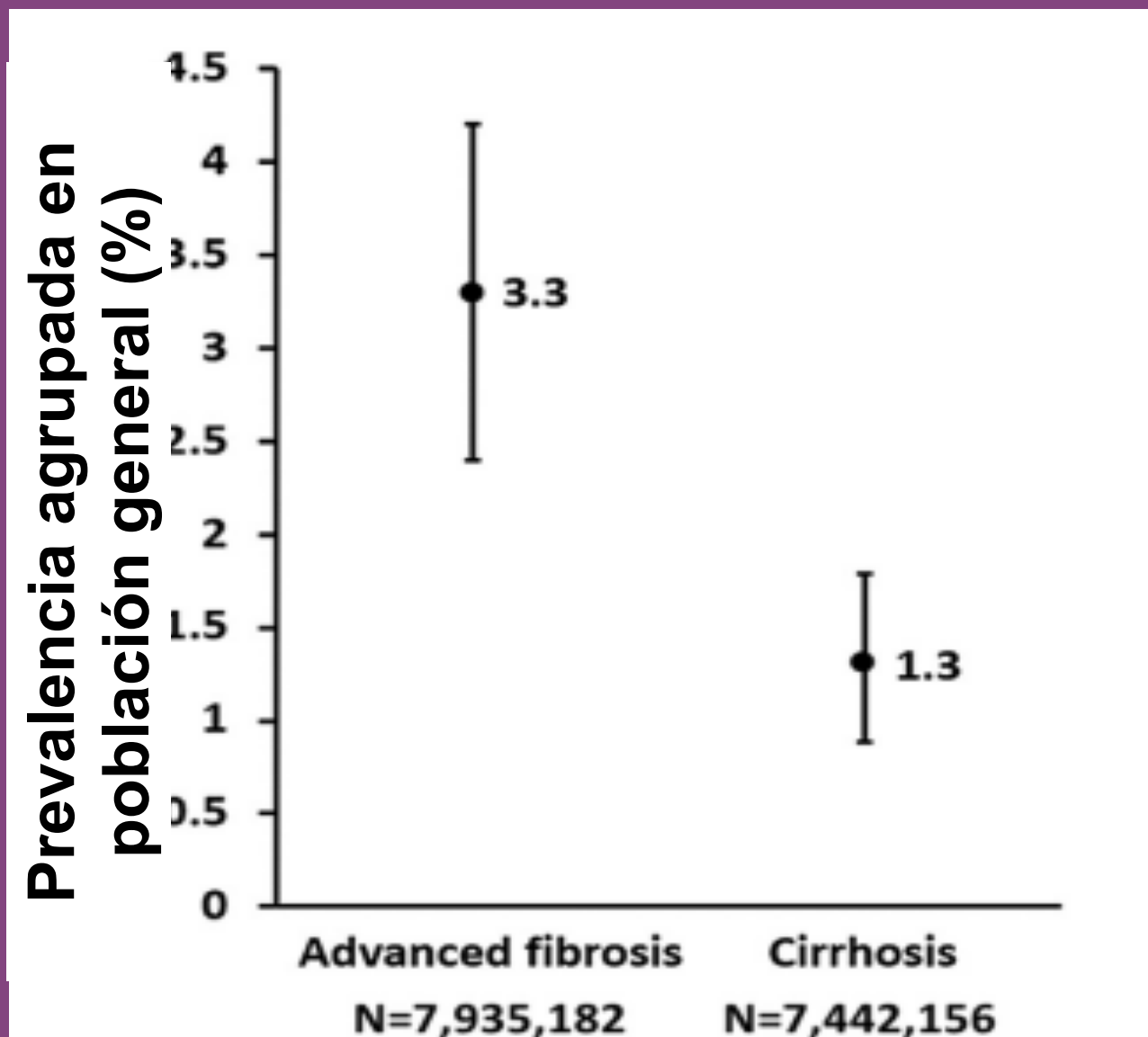
Clinical Gastroenterology and Hepatology

Importancia: MASLD / MASH

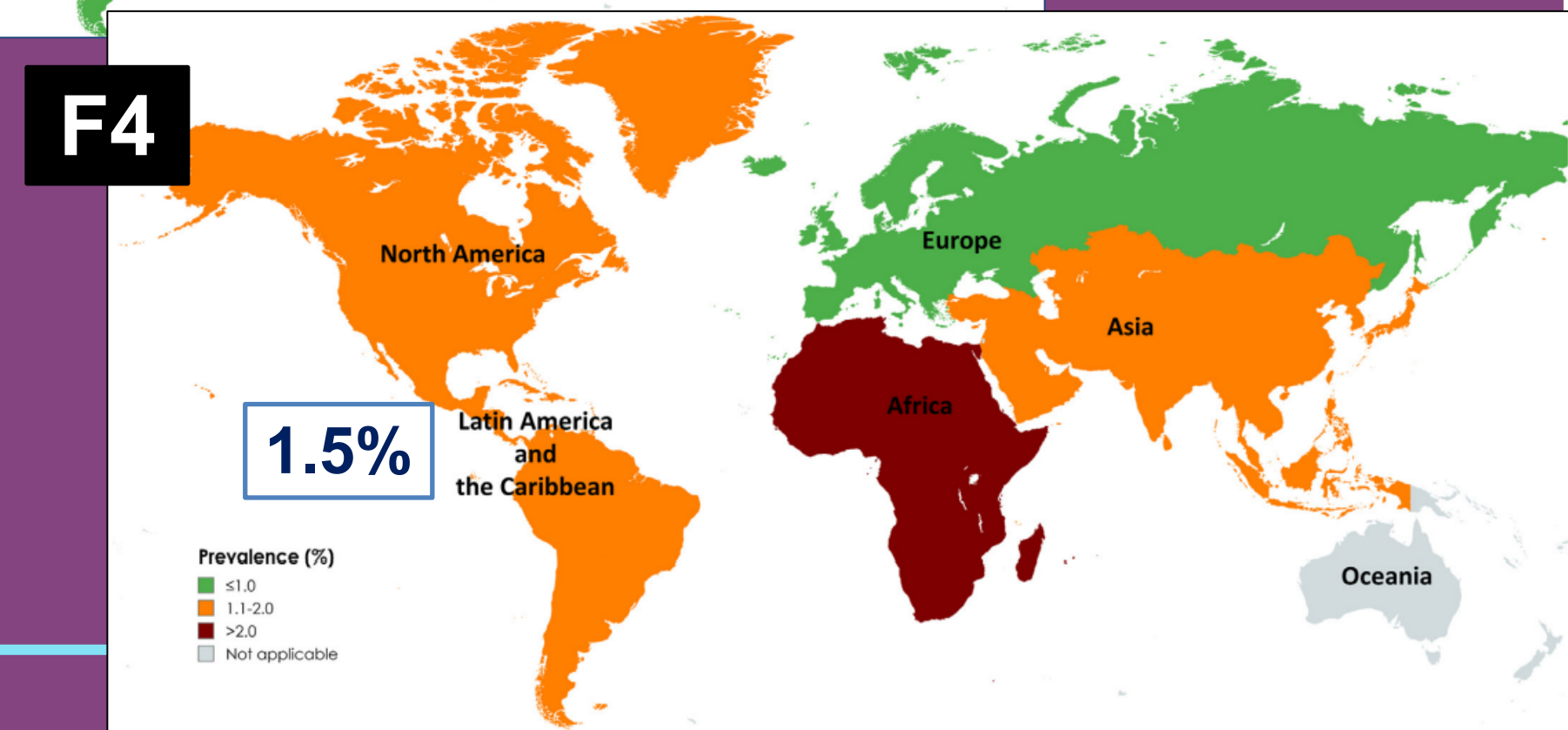
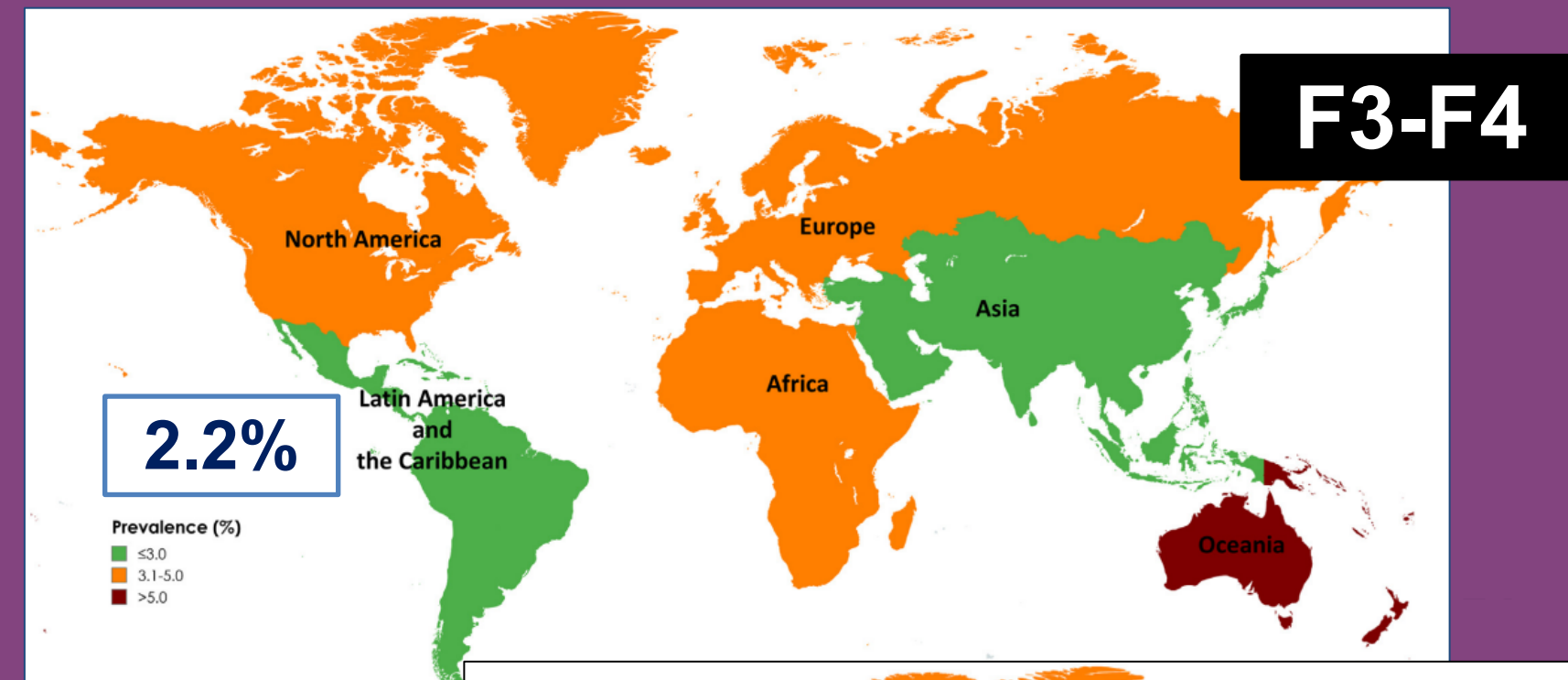
46 estudios (21 países)

n = 8 millones

- Fibrosis: Imagen, sangre y/o biopsia



FIBROSIS

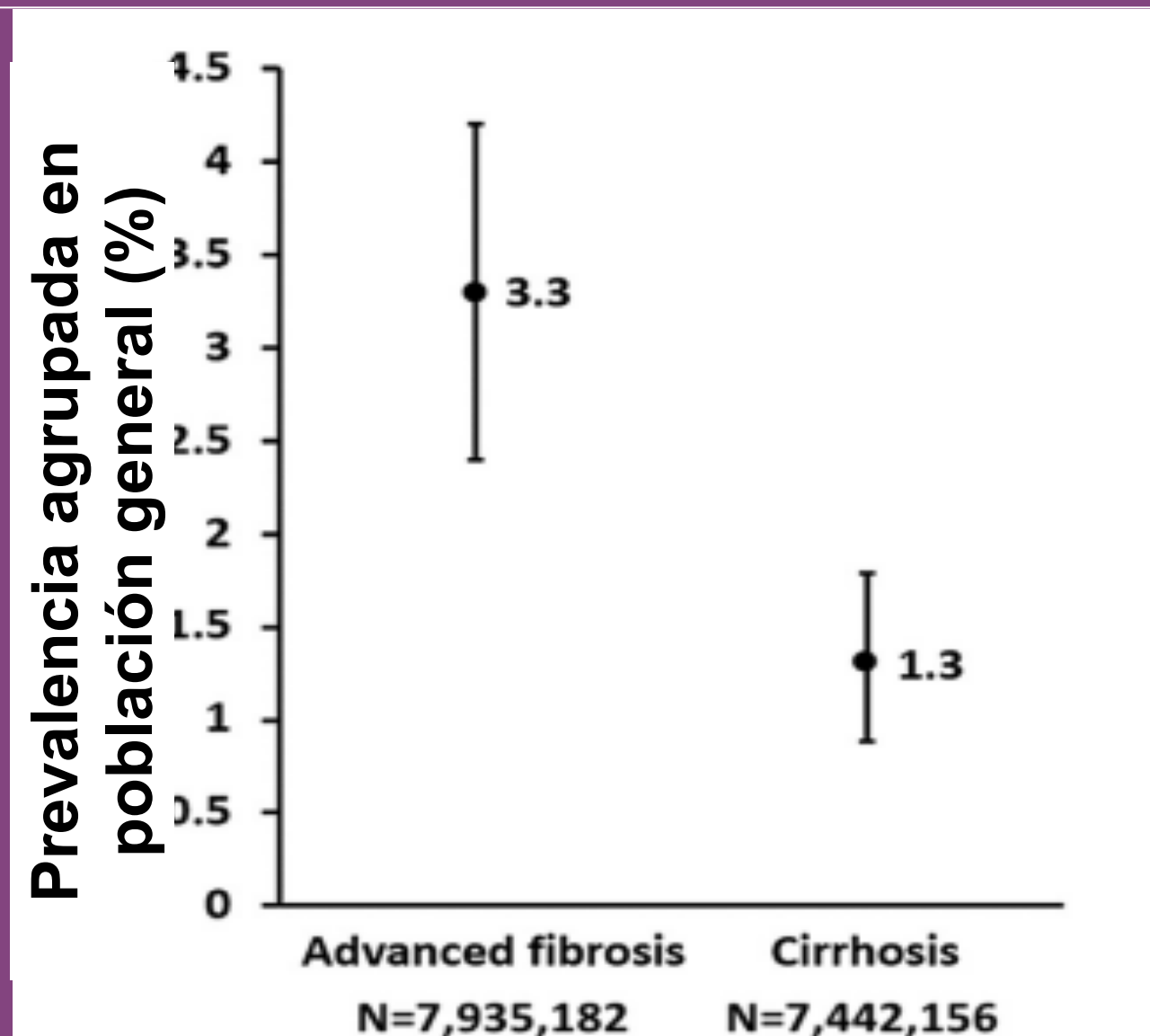


Importancia: MASLD / MASH FIBROSIS

46 estudios (21 países)

n = 8 millones

- Fibrosis: Imagen, sangre y/o biopsia

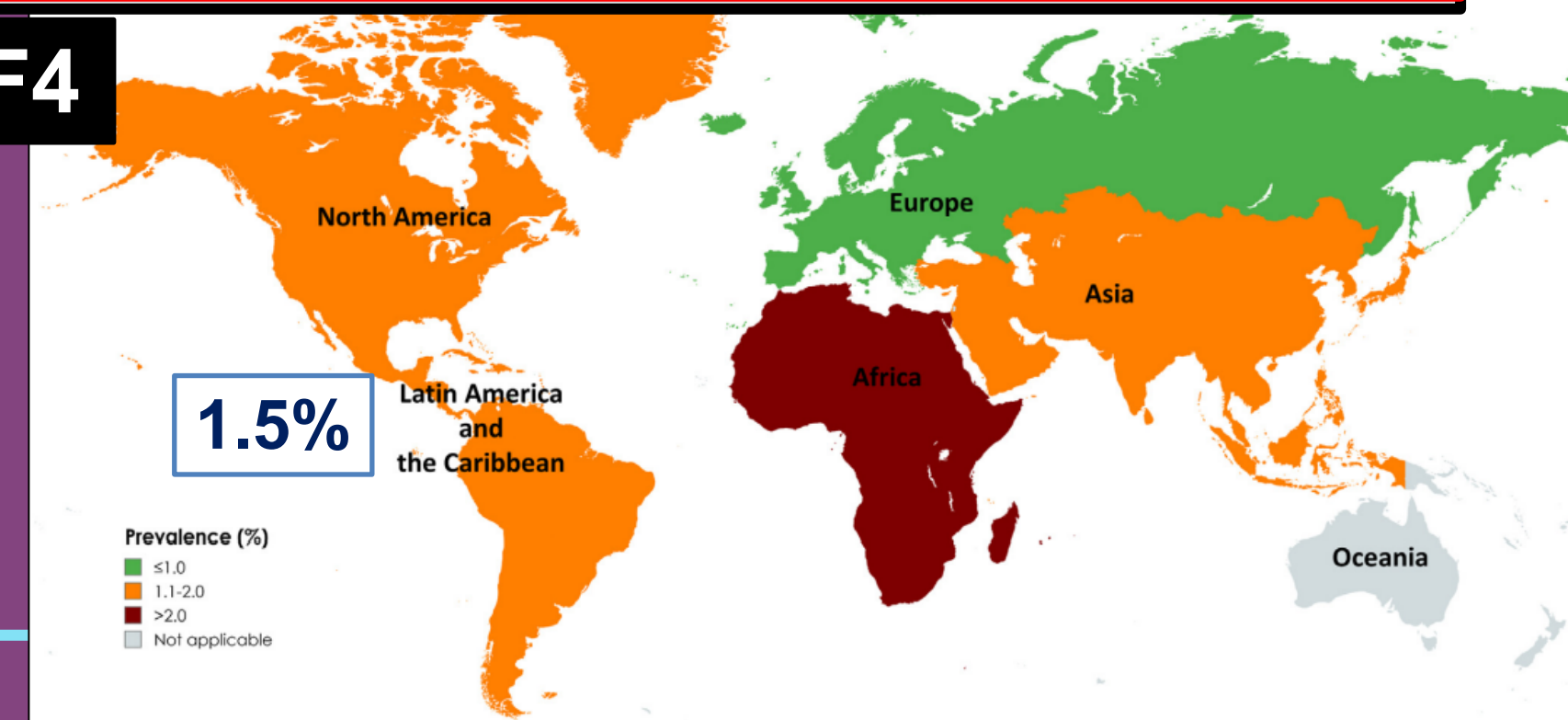


F3-F4

Table 1. Pooled Prevalence of Advanced Liver Fibrosis in the General Population According to Different Subgroups

Subgroups	No. of studies	No. of participants	Prevalence of advanced fibrosis, % (95% CI)	I ²	P-value for heterogeneity	P-value for interaction
Overall	39	7,935,182	3.3 (2.4-4.2)	100.0%	< .0001	NA
Study year ^a						
<2010	5	1,069,267	2.0 (1.0-3.0)	99.9%	< .0001	0.004
2010-2016	9	1,606,663	2.0 (1.3-2.7)	98.9%	< .0001	
>2016	20	5,988,299	4.7 (3.2-6.2)	99.9%	< .0001	

F4



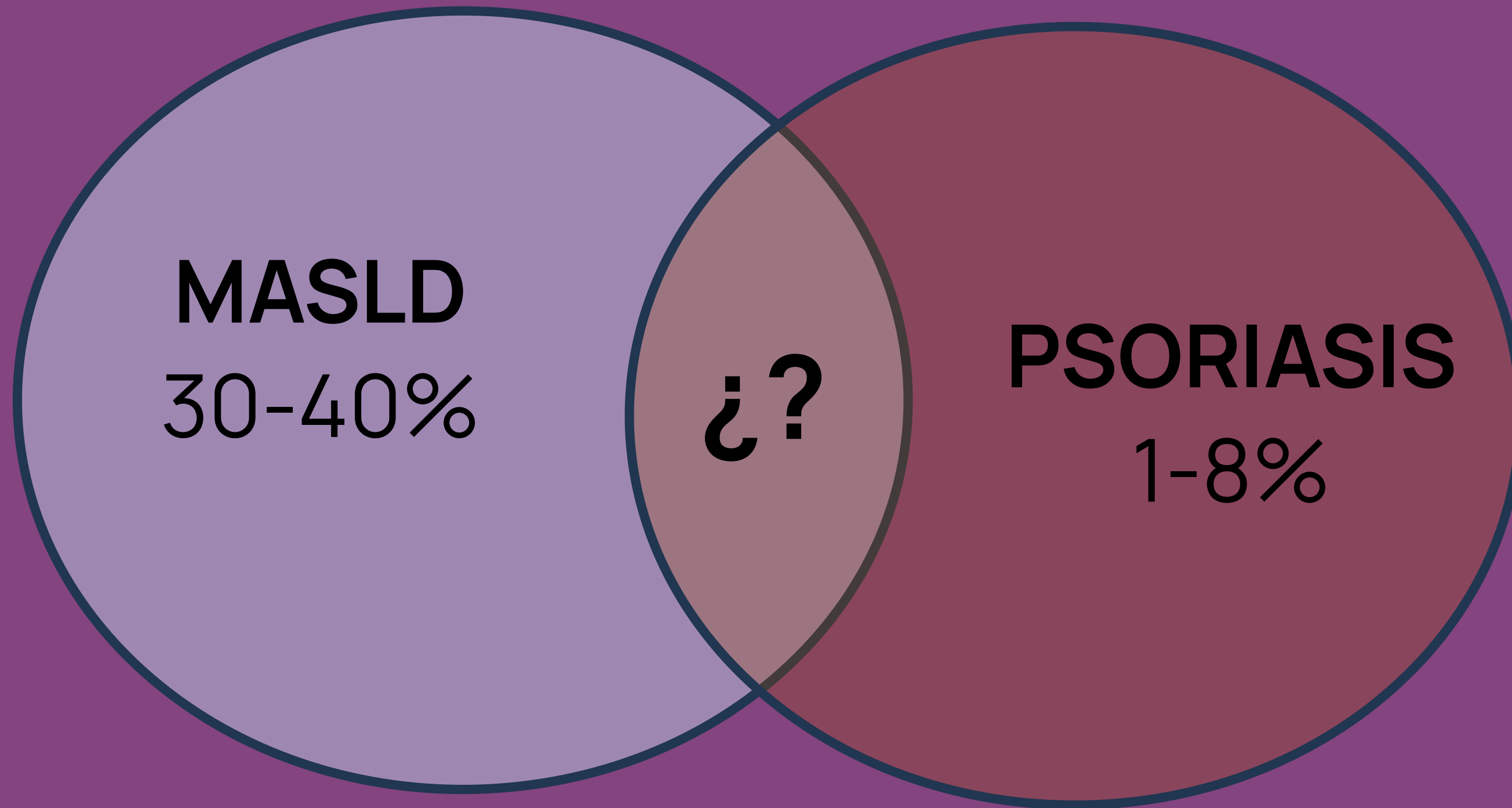
Importancia: MASLD / MASH

FIBROSIS

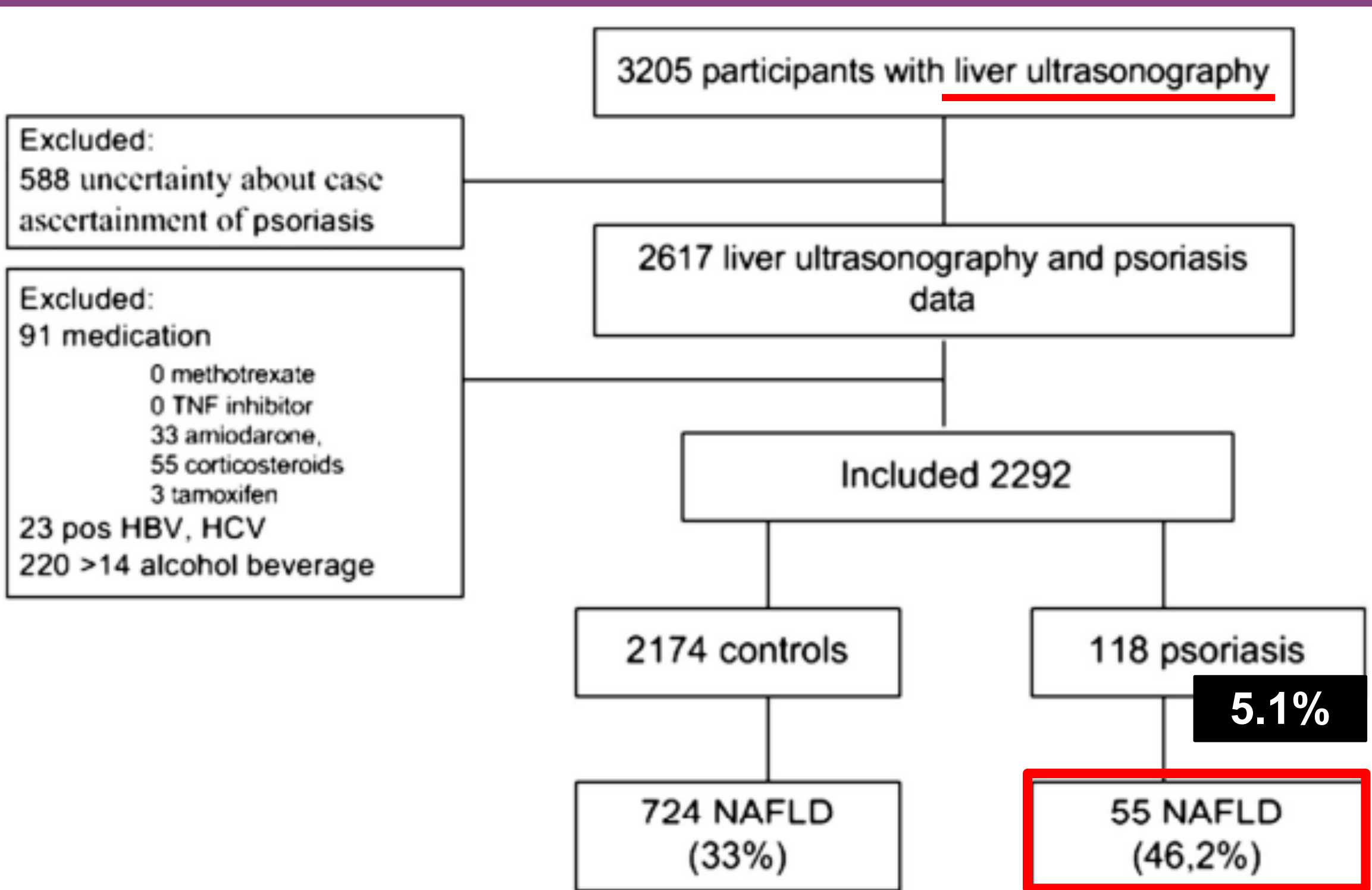
Table 3. Pooled Adjusted ORs^a for Potential Risk Factors for Advanced Liver Fibrosis and Cirrhosis

Variables	Advanced fibrosis				Cirrhosis			
	No. of studies	OR (95% CI)	I ²	P-value for heterogeneity	No. of studies	OR (95% CI)	I ²	P-value for heterogeneity
Age (per 10 years)	3	3.09 (1.08–5.10)	95.8%	< .0001	NA	NA	NA	NA
Diabetes	5	2.33 (1.49–3.16)	38.6%	.164	2	1.99 (1.94–2.04)	0.0%	.690
Dyslipidemia	4	0.99 (0.63–1.35)	96.0%	< .0001	NA	NA	NA	NA
Excessive alcohol intake	4	1.43 (1.25–1.61)	0.0%	.670	2	2.01 (1.18–3.42)	3.2%	.310
Hepatic steatosis	3	1.35 (1.12–1.57)	46.2%	.156	NA	NA	NA	NA
Hypertension	3	1.08 (0.42–1.74)	89.5%	< .0001	NA	NA	NA	NA
Obesity	4	1.87 (1.14–2.61)	55.7%	.079	2	1.98 (1.93–2.03)	0.0%	.842
Sex (men)	5	1.69 (1.28–2.11)	56.1%	.043	4	1.56 (1.20–1.92)	64.4%	.038
Smoking	2	0.86 (0.61–1.11)	0.0%	.699	NA	NA	NA	NA
Viral hepatitis (B or C) ^b	3	7.89 (4.17–11.61)	0.0%	.649	2	1.81 (1.19–2.42)	0.0%	.622

MASLD y Psoriasis



MASLD y Psoriasis: Epidemiología



	Crude/adjusted OR (95% CI)	P value
Crude univariate model*		
<u>Psoriasis</u>	<u>1.70 (1.17-2.46)</u>	.005
Age and sex adjusted		
<u>Psoriasis</u>	<u>1.70 (1.17-2.47)</u>	.006
Multivariable adjusted†		
Age, y	0.98 (0.96-1.00)	.01
Sex, female	1.19 (0.96-1.48)	.10
Metabolic syndrome	3.51 (2.86-4.32)	<.001
Smoking		.2
Never	1	
Past	0.88 (0.67-1.15)	.34
Current	0.99 (0.96-1.01)	.07
Pack years	1.01 (1.01-1.02)	<.001
Alcoholic beverages weekly	0.99 (0.96-1.01)	.35
ALT, U/L	1.01 (1.01-1.02)	<.001
<u>Psoriasis</u>	<u>1.70 (1.13-2.58)</u>	.01

¿LEPTINA?

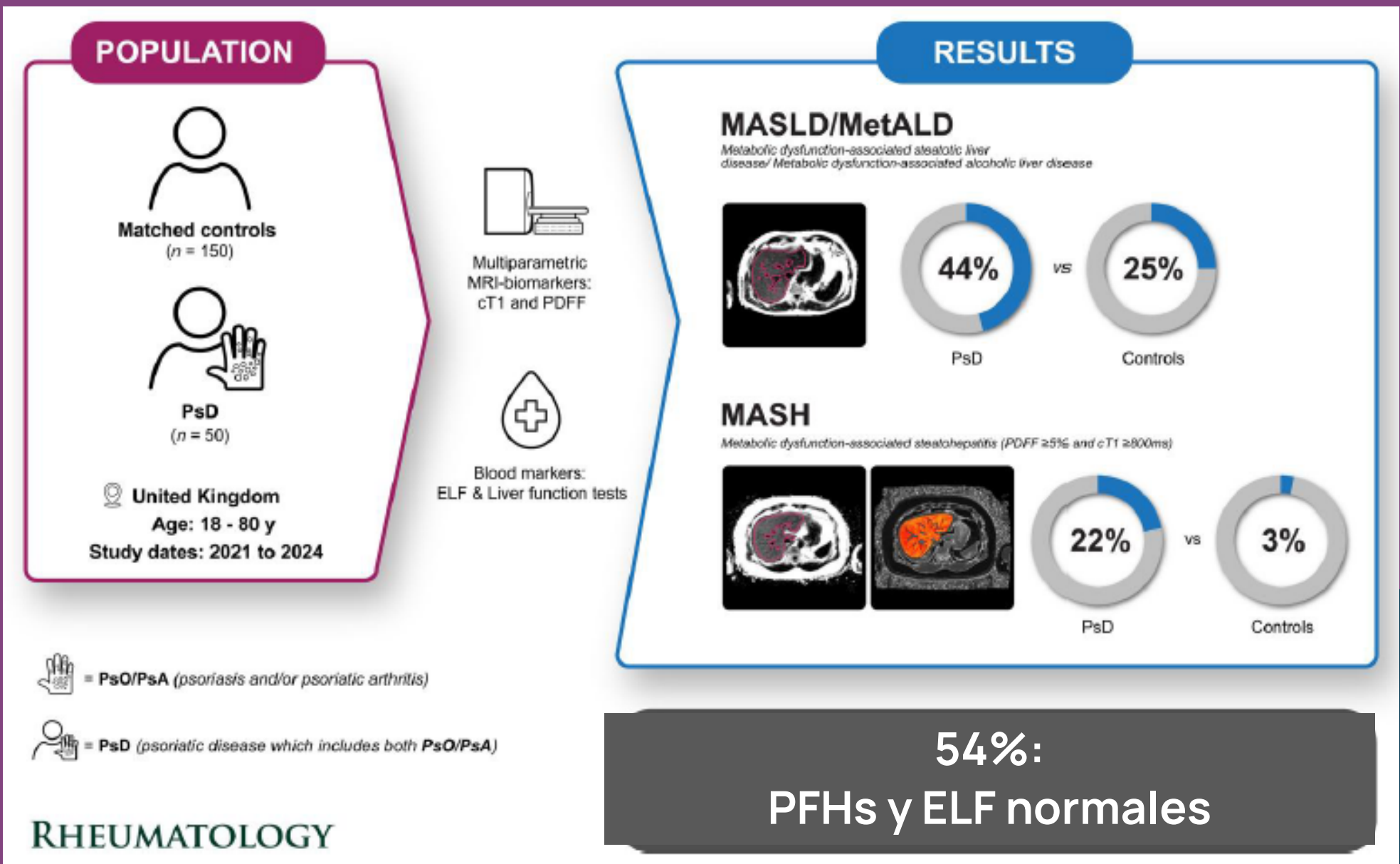
MASLD y Psoriasis: Epidemiología

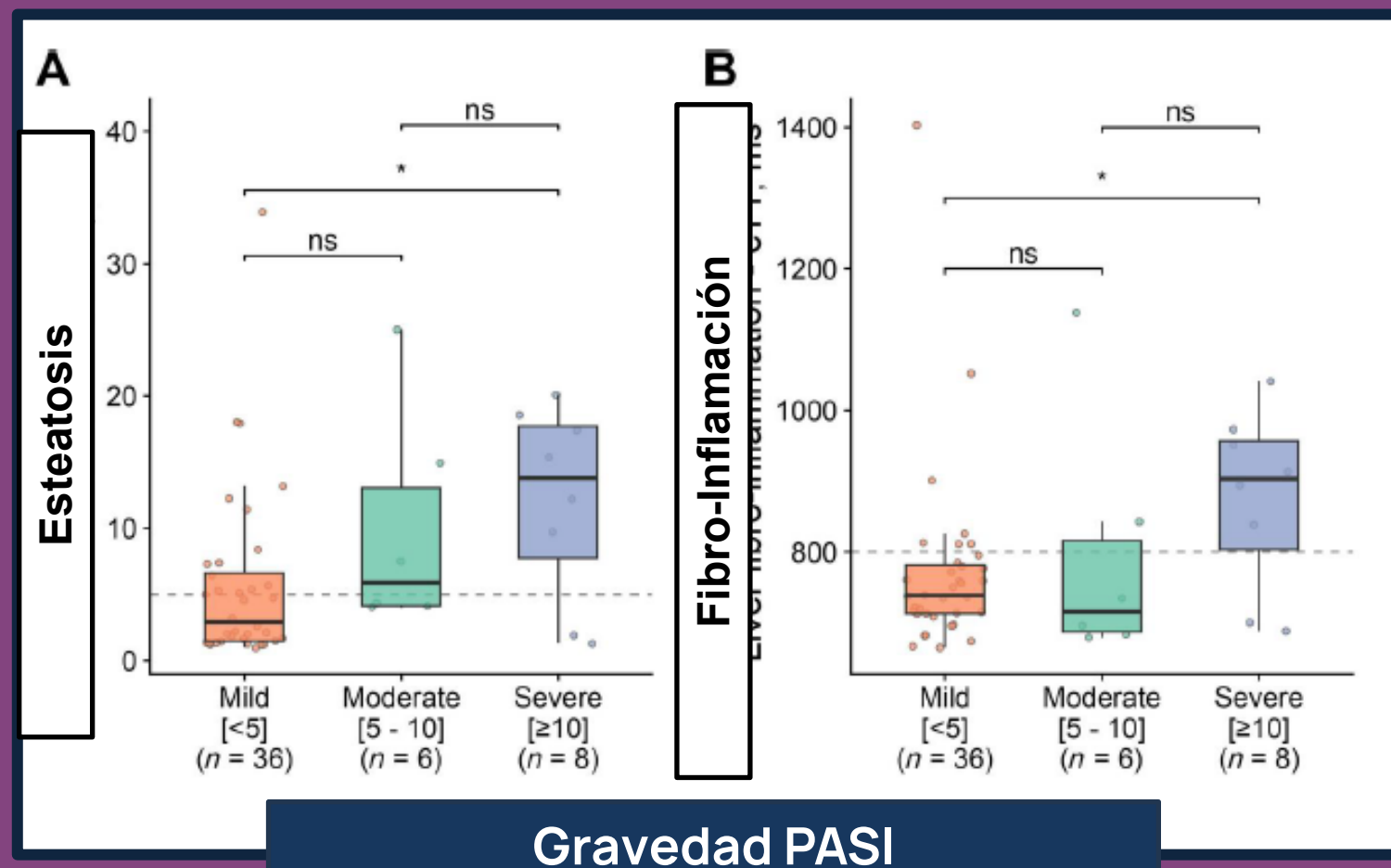
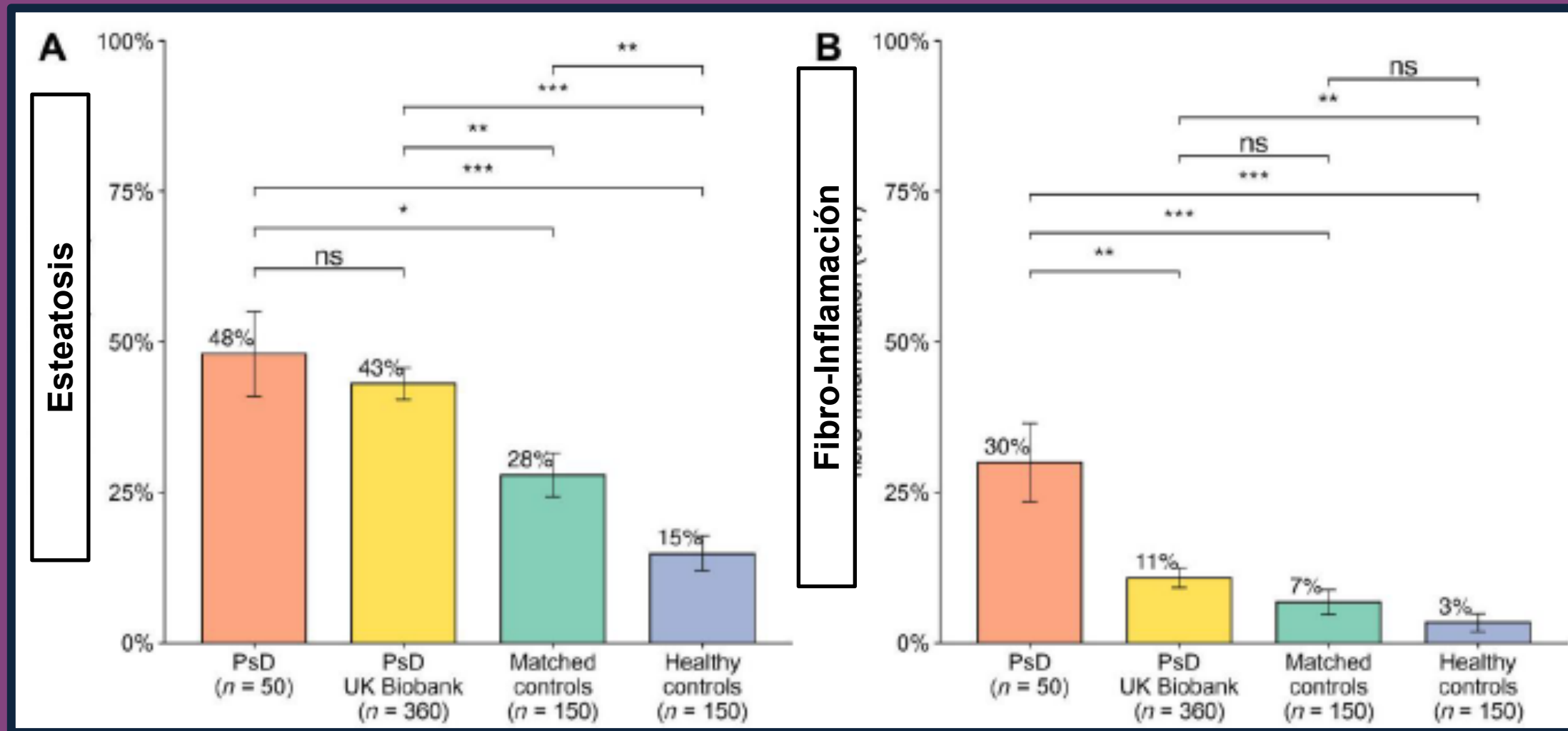
COLIPSO study (Co-prevalence of Liver Disease in Psoriatic Disease)

- Multicéntrico, vida real y observacional
- Psoriasis moderada – grave (n=50) vs controles (n=150)

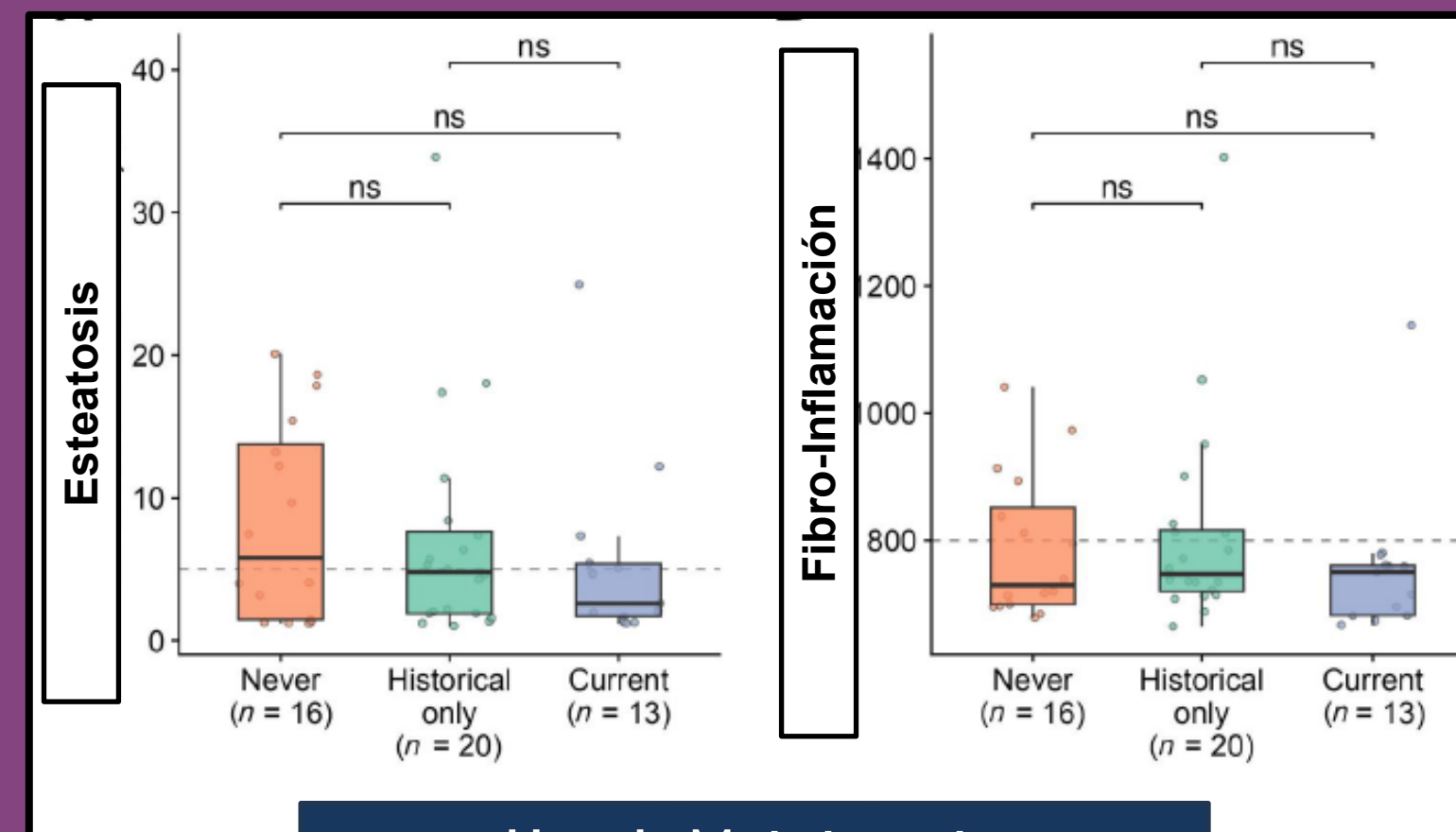
MRI
PDFF + cT1

	PsD from secondary care (COLIPSO) (n = 50)	Matched controls without PsD (n = 150)
Demographics		
Age, mean (s.d.), years	48 (14)	50 (13)
Sex (male), n (%)	29 (58)	87 (58)
BMI, mean (s.d.), kg/m ²	29 (5)	27 (5)
Categories, n (%)		
Lean (<25 kg/m ²)	10 (20)	49 (33)
Overweight (≥25–<30 kg/m ²)	24 (48)	57 (38)
Obese (≥30 kg/m ²)	16 (32)	44 (29)
PsA, n (%)	34 (68)	—
PsO, n (%)	16 (32)	—
Type 2 diabetes, n (%)	1 (2)	4 (3)
Type 1 diabetes, n (%)	2 (4)	16 (11)
Hypertension, n (%)	10 (20)	38 (25)
Hyperlipidaemia, n (%)	9 (18)	43 (29)
Cardiometabolic risk factor, n (%)	43 (86)	111 (74)
High alcohol use, n (%)	3 (6)	9 (6)





Gravedad PASI



Uso de Metotrexate

MASLD y Psoriasis

Meta-análisis: 7 estudios de casos-contróles

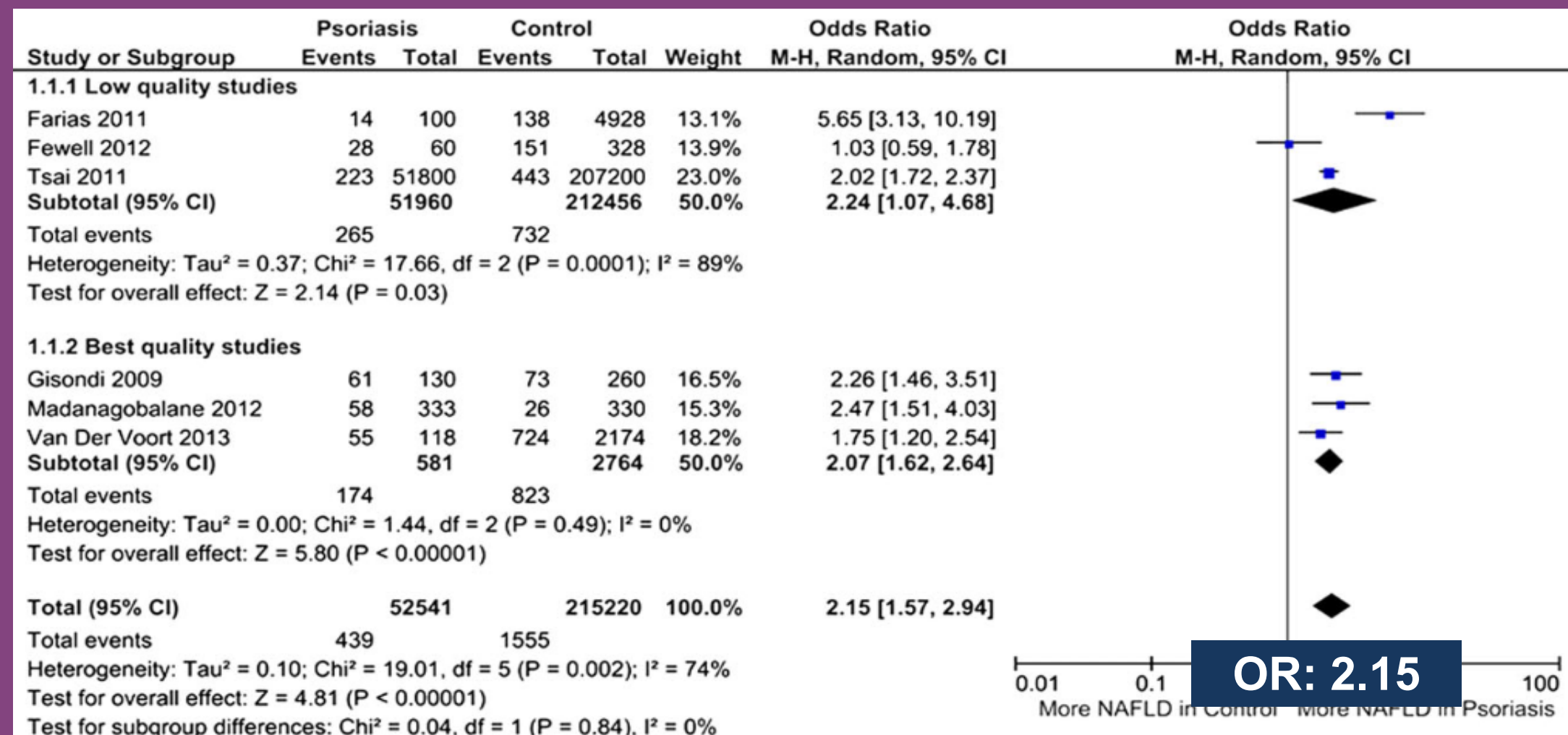
- Asociación entre MASLD y Psoriasis
- ¿Screening MASLD en pacientes con Psoriasis?

Study	n (psoriasis/ control)	Age ($\pm$ SD), years	Country of origin	Characteristics of control group	Diagnosis of NAFLD
Farias <i>et al.</i> ¹⁵	100/4928	43 ($\pm$ 19)	Chile	National Health Survey	Not described
Gisondi <i>et al.</i> ¹⁶	130/260	51.2 ($\pm$ 13.4)	Italy	Healthy volunteers	US, liver test, exclusion of other liver diseases
Fewell <i>et al.</i> ¹⁸	60/328	53.2 ($\pm$ 13.3)	USA	Outpatients recruited in a military medical centre	US, liver test, exclusion of other liver diseases
Madanagobalane <i>et al.</i> ¹⁹	333/330	46.2 ($\pm$ 11.5)	India	Outpatients recruited in a Dermatological centre	US, liver test, exclusion of other liver diseases
Miele <i>et al.</i> ^{20*}	142/125	50.1 ($\pm$ 15)	Italy	Outpatients recruited in a Dermatological centre	US, liver test, exclusion of other liver diseases
Tsai <i>et al.</i> ²¹	51 800/207 200	46.4 ($\pm$ 18.6)	Taiwan	National Health Insurance Research Database	ICD-9-CM code: 571.8†
Van Der Voort, <i>et al.</i> ^{22,23}	118/2174	76.2 ($\pm$ 6)	Netherlands	Population-based (Rotterdam Study)	US, liver test, exclusion of other liver diseases

MASLD y Psoriasis

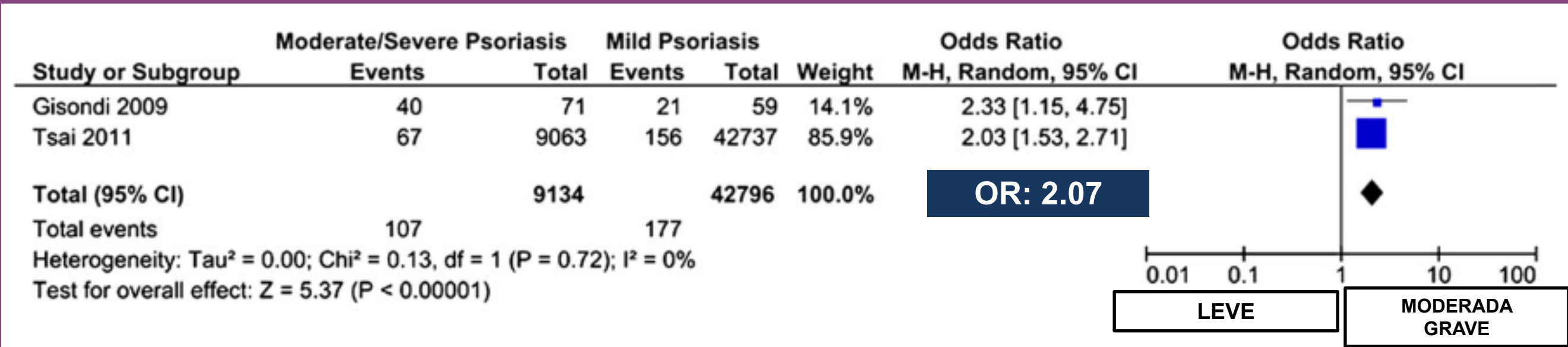
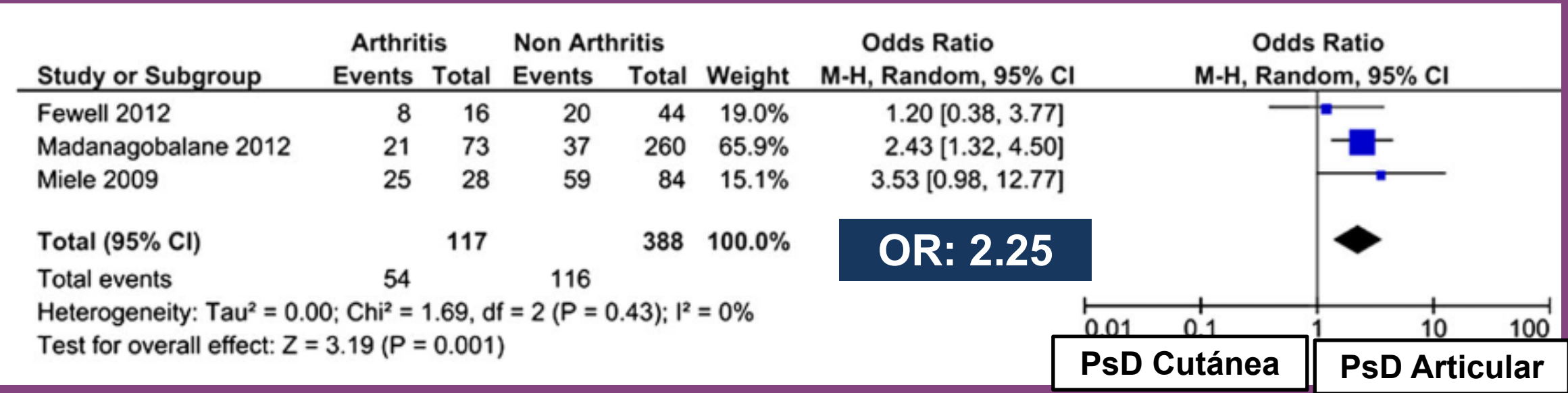
Meta-análisis: 7 estudios de casos-contrroles

- Asociación entre MASLD y Psoriasis
- ¿Screening MASLD en pacientes con Psoriasis?



MASLD y Psoriasis

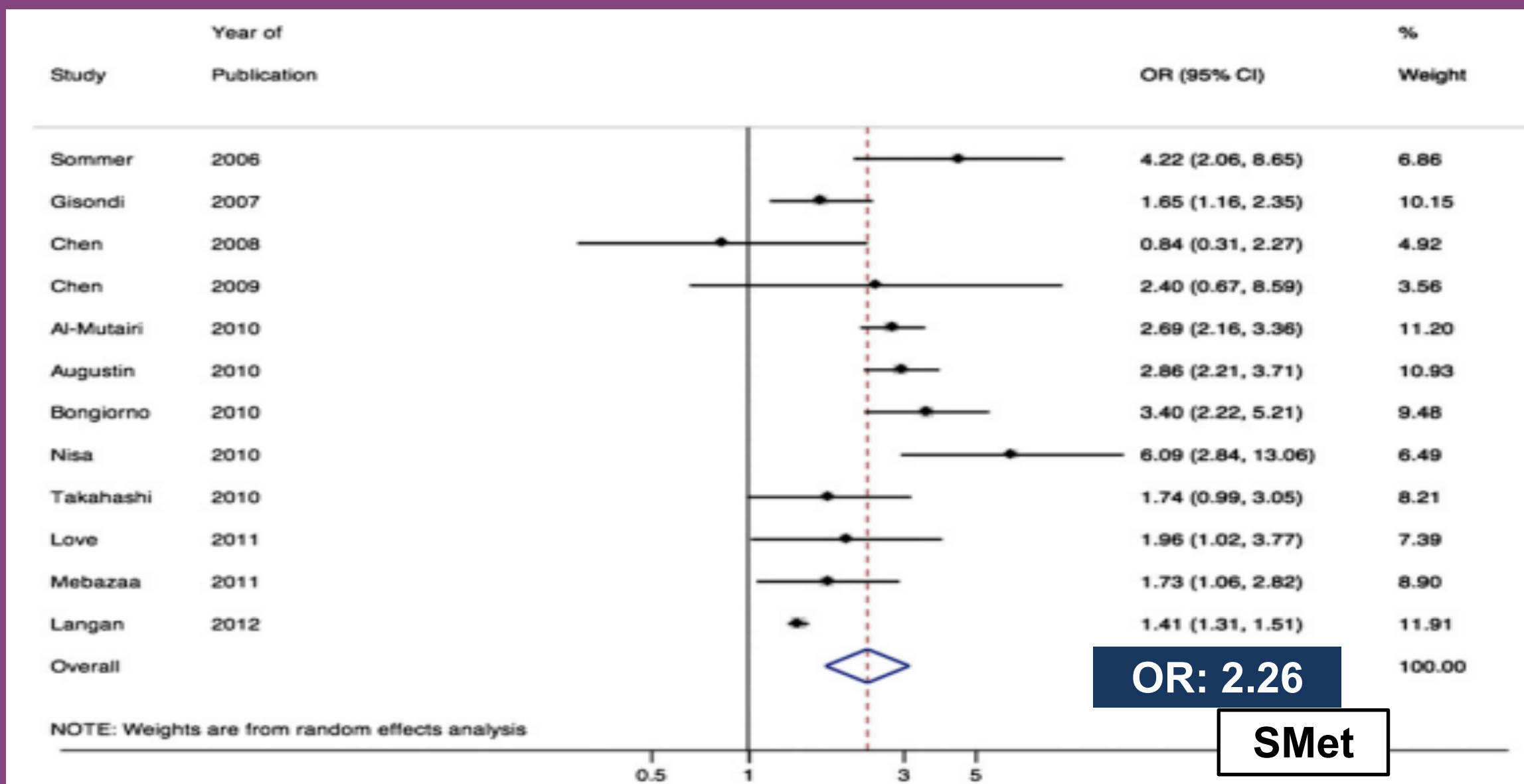
- Meta-análisis: 7 estudios de casos-contrroles
- Asociación entre MASLD y Psoriasis
 - ¿Screening MASLD en pacientes con Psoriasis?



MASLD y Psoriasis

Meta-análisis: 12 estudios observacionales (casos y controles / transversales)

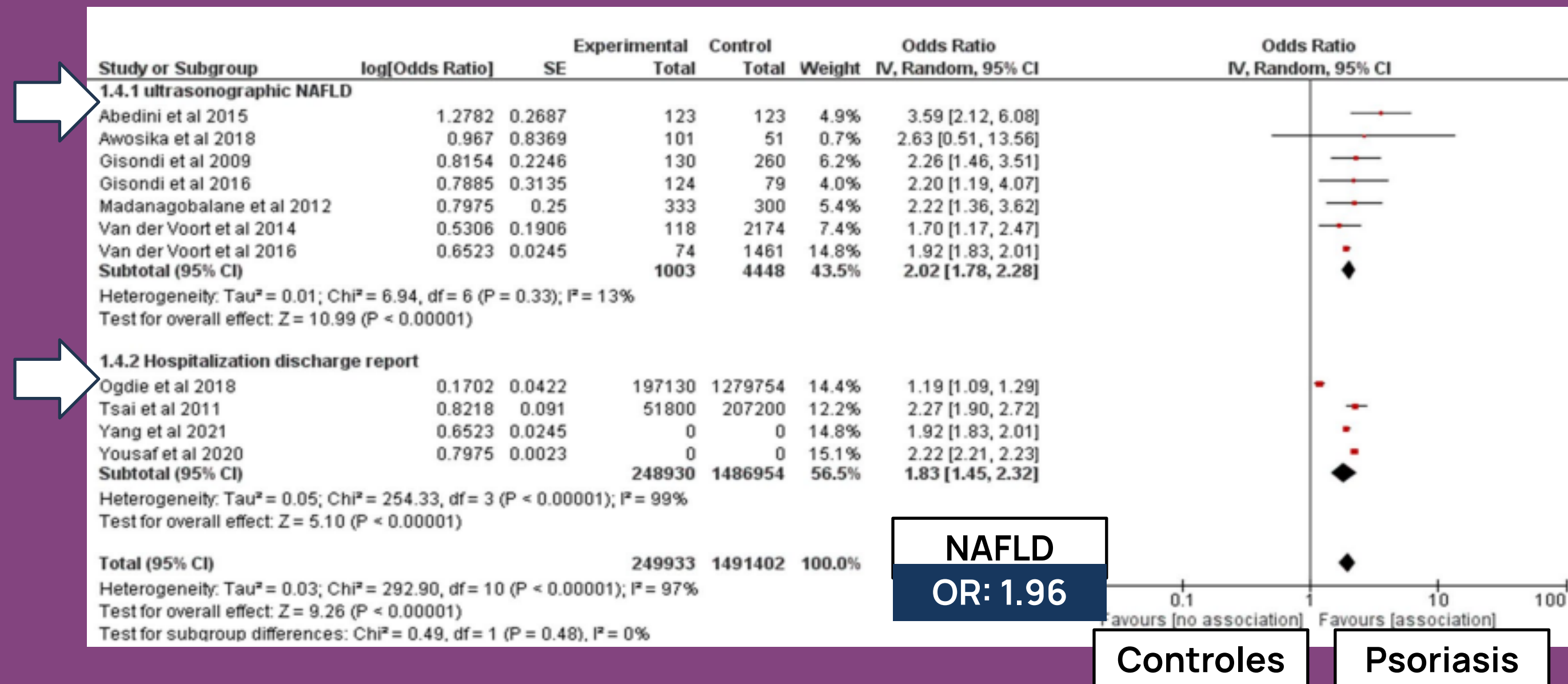
- n = 1.4 millones (Psoriasis: 41,853)
- Asociación entre MetS = Psoriasis vs población general



MASLD y Psoriasis •

Meta-análisis: 15 estudios observacionales (casos y controles / transversales)

- n = 249,933 Psoriasis (49% NAFLD) / 1,491,402 Controles (36% NAFLD)
- Asociación entre NAFLD y Psoriasis placa crónica (Dx imagen)



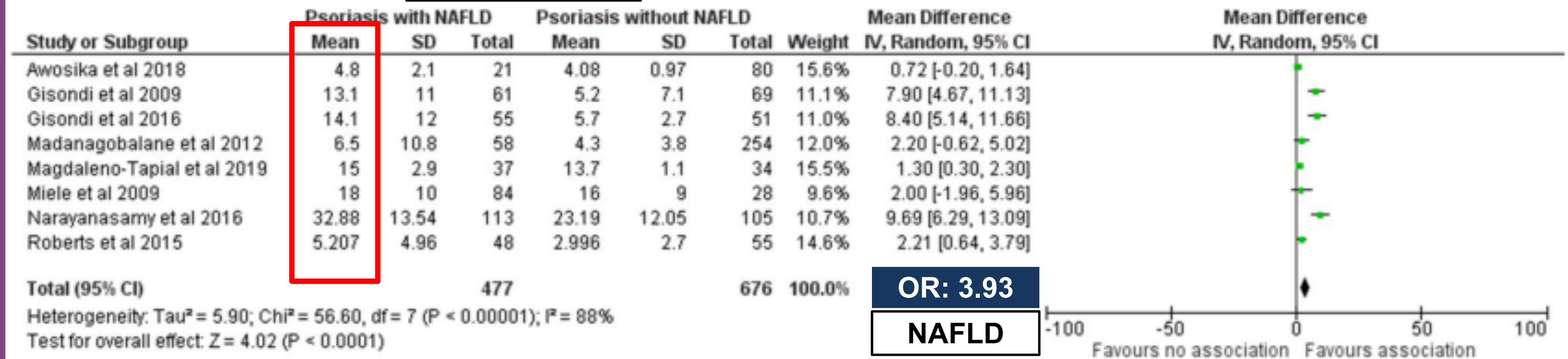
MASLD y Psoriasis



Meta-análisis: 15 estudios observacionales (casos y controles / transversales)

- n = 249,933 Psoriasis (49% NAFLD) / 1,491,402 Controles (36% NAFLD)
- Asociación entre NAFLD y Psoriasis placa crónica (Dx imagen)

Mediana PASI



PSORIASIS:

↑ Prevalencia SMet y MASLD

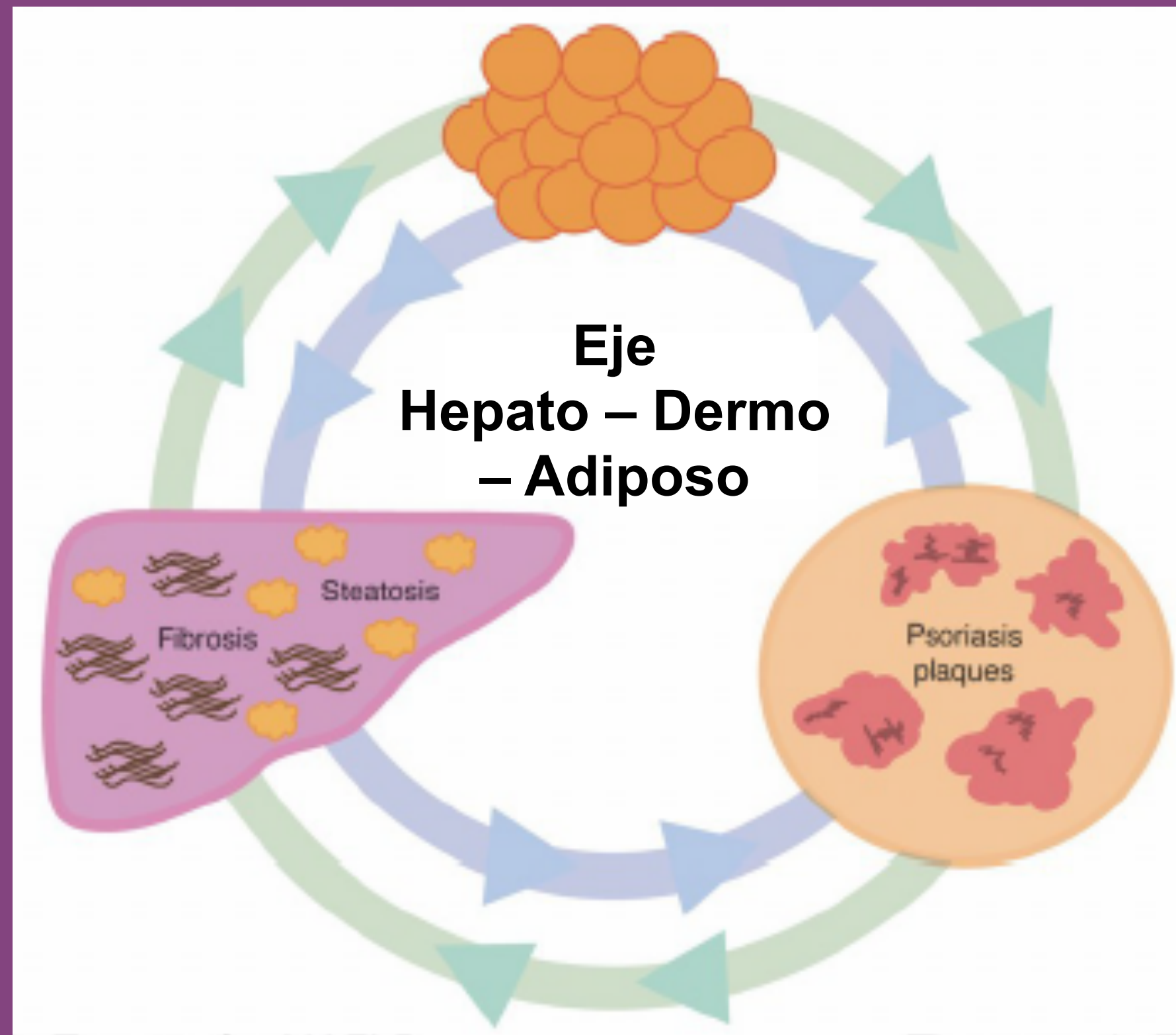
↑ Esteatosis hepática (independiente FRCM)

↑ Gravedad Psoriasis = ↑ MASLD



MASLD y Psoriasis

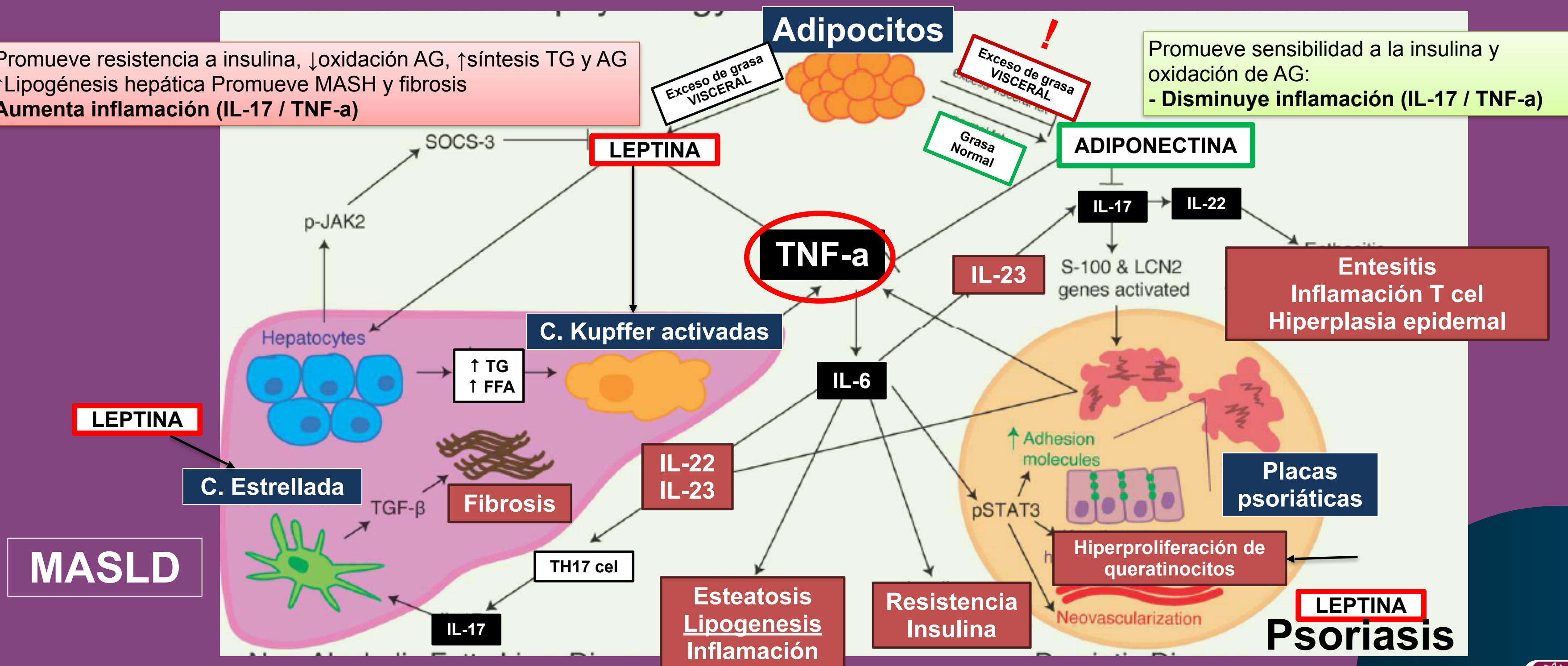
PRIMER FORO
InmunoDerma2025
CANCÚN, MX



MASLD y Psoriasis: Mecanismo fisiopatológico compartido

Promueve resistencia a insulina, ↓ oxidación AG, ↑ síntesis TG y AG
↑ Lipogénesis hepática Promueve MASH y fibrosis
Aumenta inflamación (IL-17 / TNF-α)

Promueve sensibilidad a la insulina y oxidación de AG:
- Disminuye inflamación (IL-17 / TNF-α)

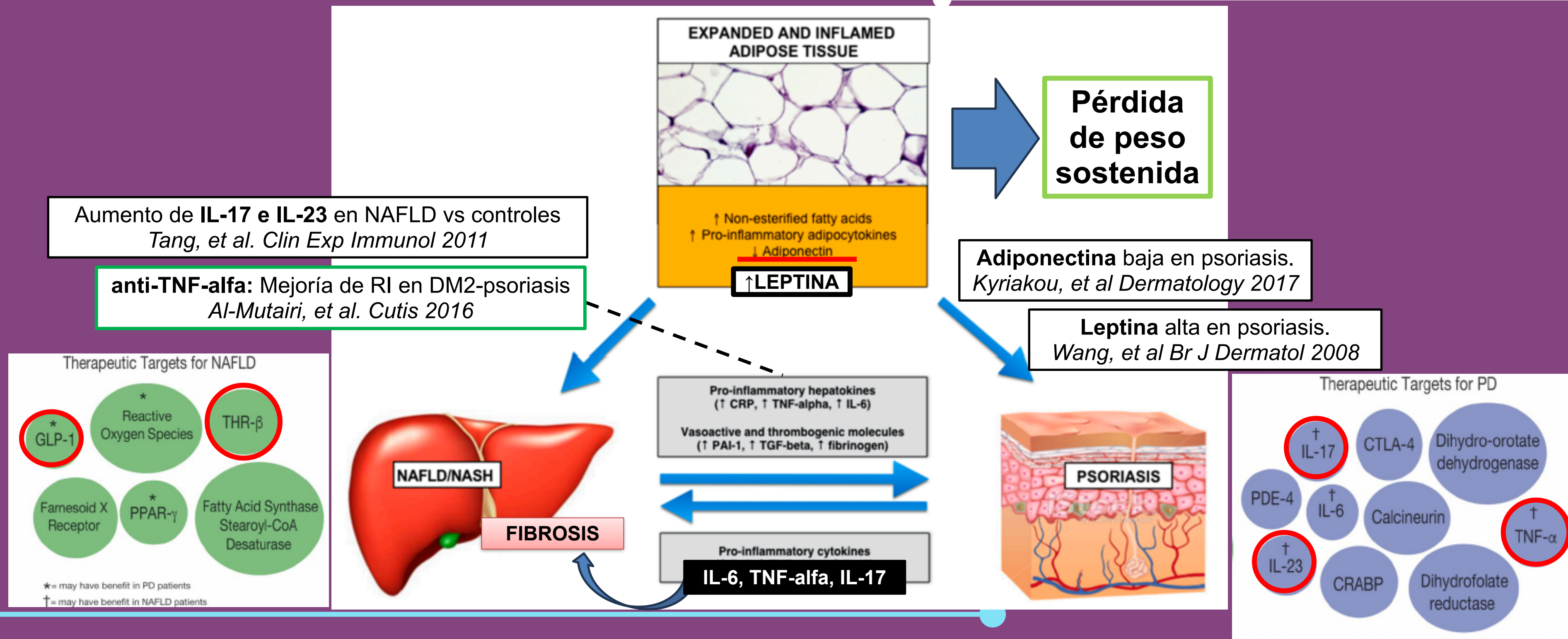


MASLD y Psoriasis:

Dianas terapéuticas potenciales

PRIMER FORO
InmunoDerma2025
CANCÚN, MX

“Eje Hepato – Dérmico”



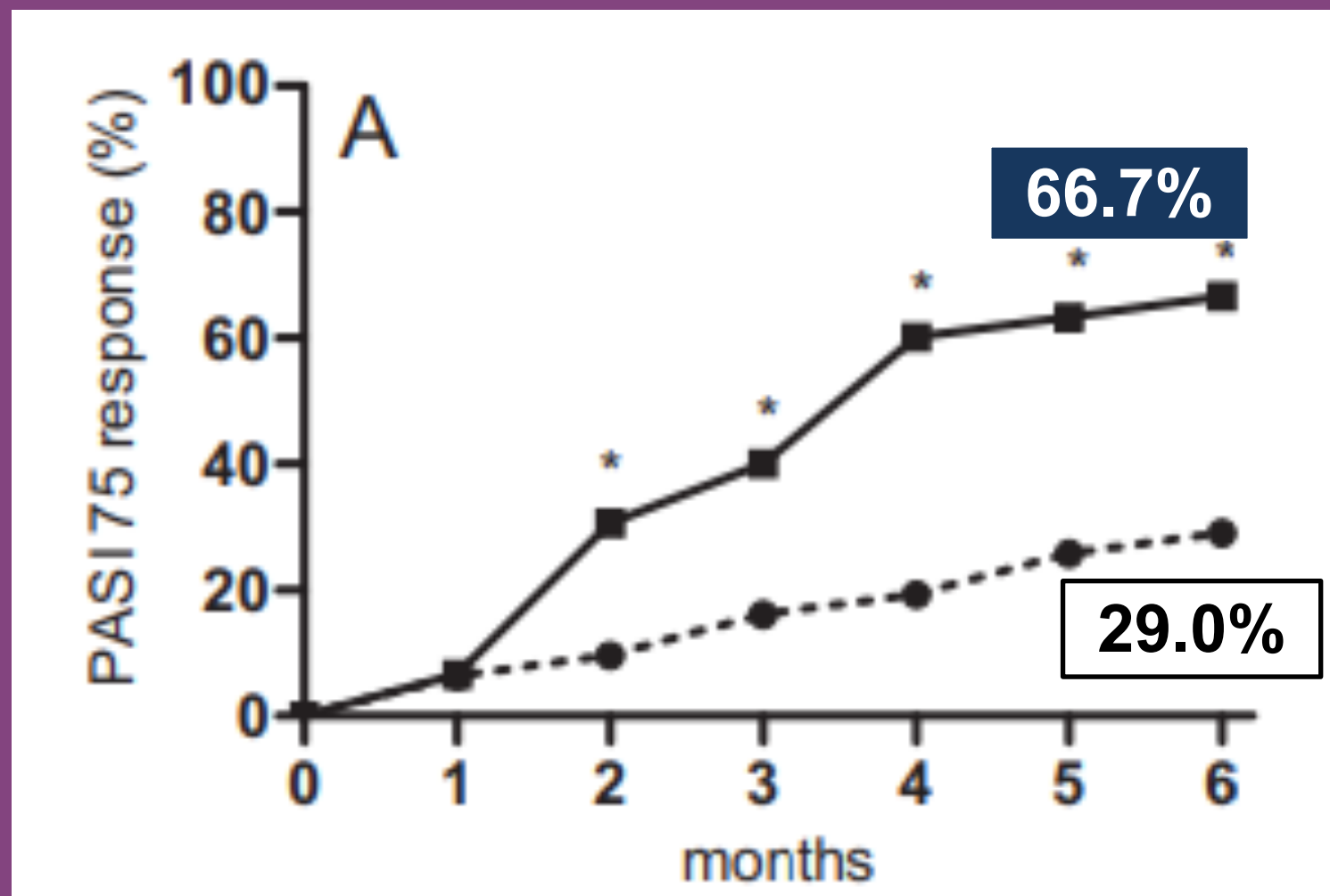
MASLD y Psoriasis: Dianas terapéuticas potenciales

“Eje Hepato – Dérmico”

Ensayo clínico:

- ¿Pérdida de peso (5-10%) mejoría en respuesta a dosis baja de CyA?
- n=30: 2.5 mg/kg/d CsA + dieta hipocalórica / n=31: CsA (control)
- Objetivo 1º: Mejoría de PASI $\geq 75\%$ del basal a las 24w

- 11.2% peso



MASLD y Psoriasis: Dianas terapéuticas potenciales

“Eje Hepato – Dérmico”

Meta-análisis (14 estudios):

- Psoriasis + MASLD / Fibrosis hepática
- **Tto inhibidores de IL-17 o IL-23**

CANCÚN, MX

- Psoriasis + MASLD / Fibrosis hepática
- **Tto inhibidores de IL-17 o IL-23**

“Eje Hepato – Dérmico”



MASLD y Psoriasis:

Dianas terapéuticas potenciales

Meta-análisis (14 estudios):

- Psoriasis + MASLD / Fibrosis hepática
- Tto inhibidores de IL-17 o IL-23

IL-17: 11 estudios

- 6: Neutro
- 5: Mejoría en PFHs

IL-23: 3 estudios

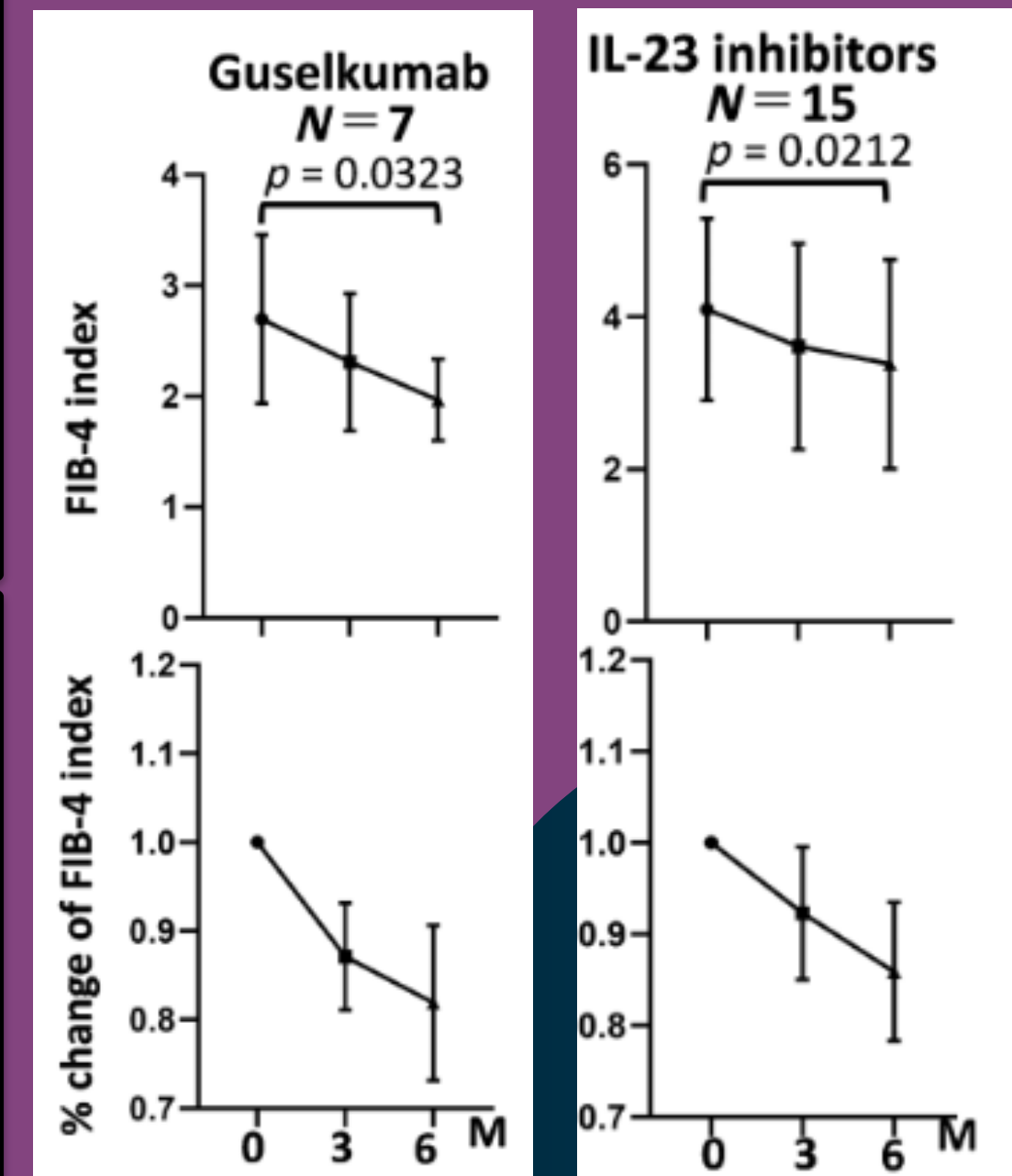
- 1: Neutro
- 1: Mejoría de FIB-4 a 6m
- 1: Reclutamiento (NCT06586281: Guselkumab / Objetivo: MRI PDFF)

Conclusión:

Inhibidores de IL-17 e IL-23 podrían tener efectos beneficios en MASLD y fibrosis hepática en pacientes con psoriasis. Faltan estudios con mayor diseño y mayor n

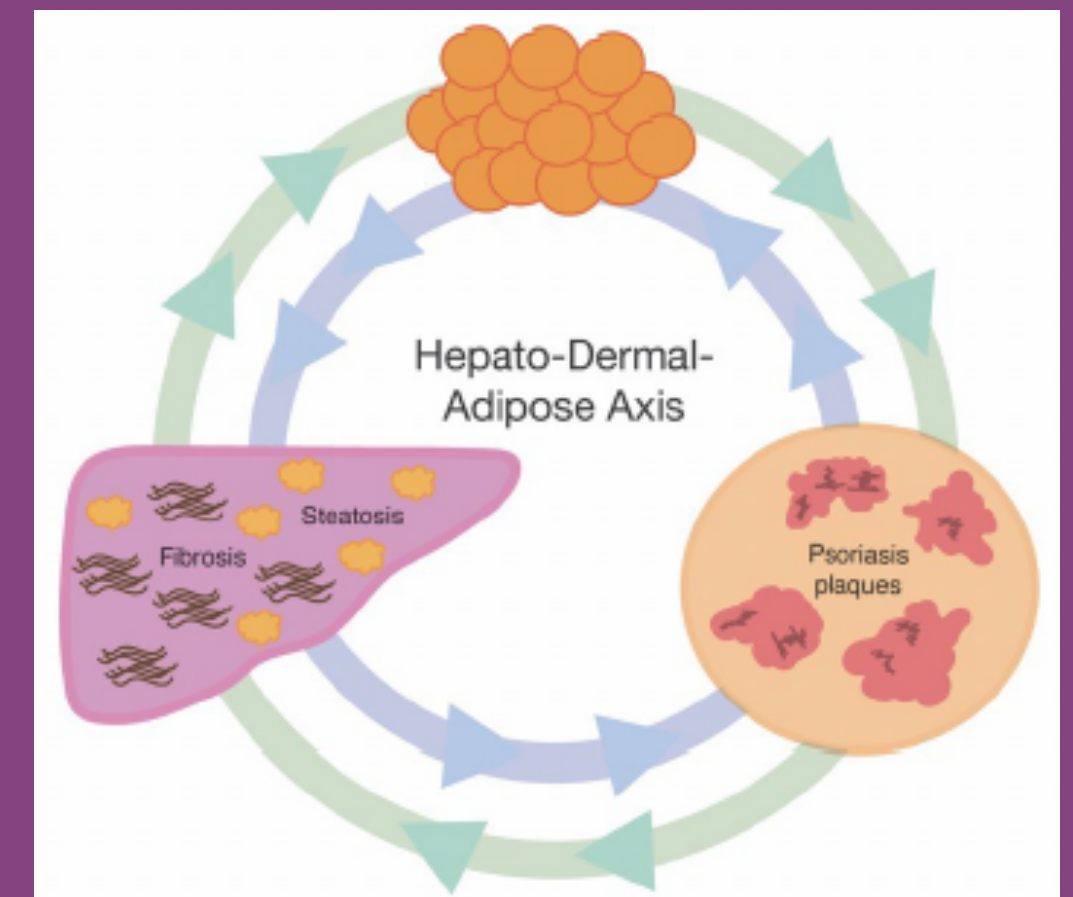
Takeshima, et al. J Dermatol 2024

“Eje Hepato – Dérmico”



CONCLUSIONES

- Pacientes con psoriasis: Tamizaje para Smet y MASLD (¿Fibrosis?)
- Psoriasis: Más prevalencia para Smet y MASLD vs población general
- **Fibrosis hepática:** Riesgo de progression rápida
- La **inflamación es clave** en ambas entidades
¿Dianas terapéuticas en el Eje Hepato-Dermatológico?



GRACIAS POR SU ATENCIÓN



@dr.sergiogmm



dr.sergiogmm@gmail.com



PRIMER FORO
InmunoDerma2025

CANCÚN, MX

