

Paris Mash Meeting 2024, Institut Pasteur

Are rates of development of MASLD and type 2 diabetes altered by HCV treatment ?

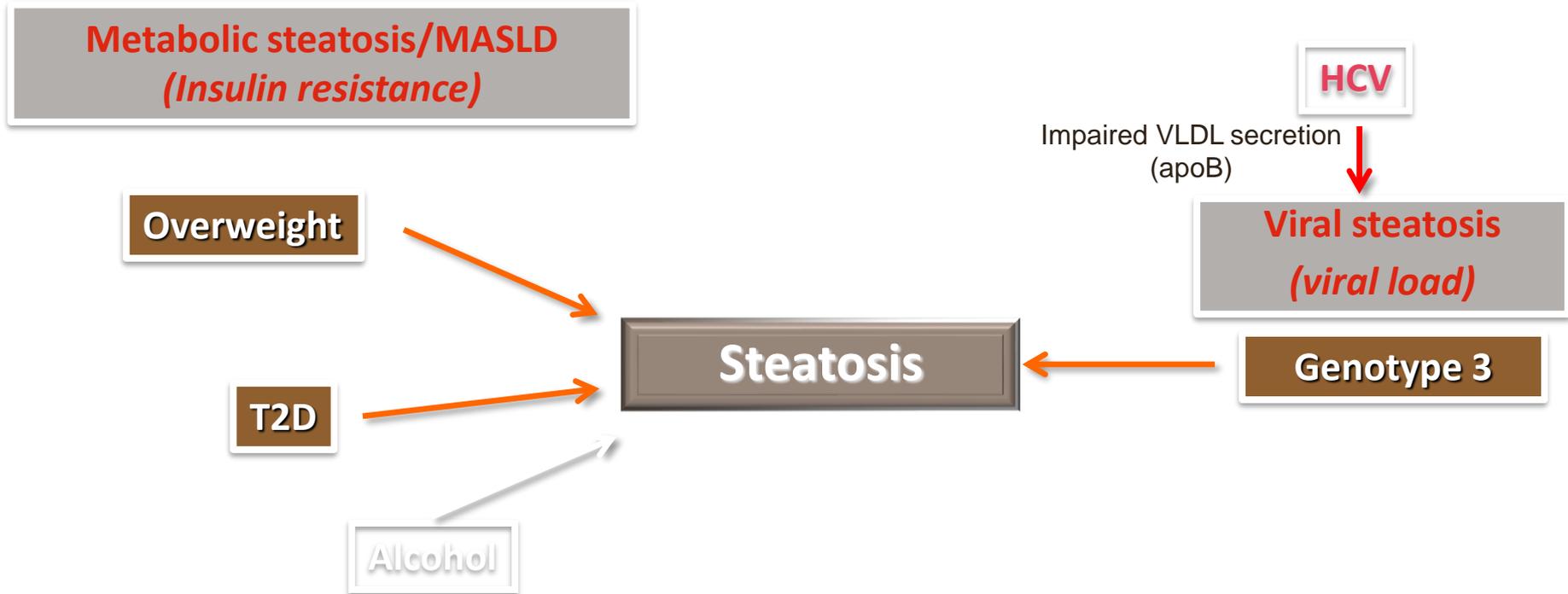
Lawrence Serfaty

*Hôpitaux Universitaires de Strasbourg
INSERM UMR_S938, Sorbonne Université, France*

Disclosures: None

The history of steatosis in chronic hepatitis C

Two types of steatosis in chronic hepatitis C

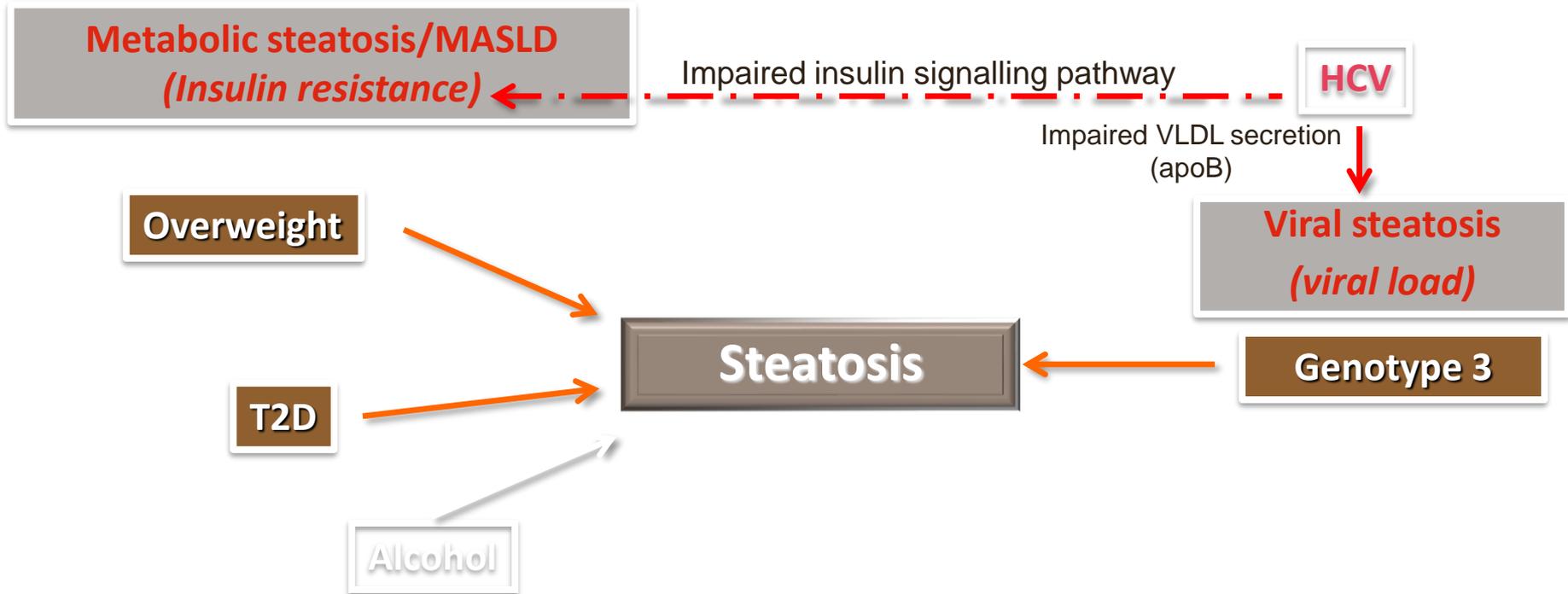


Rubbia-Brandt et al, *J Hepatol* 2000
Serfaty et al, *Am J Gastroenterol* 2002

Adinolfi et al, *Hepatology* 2001
Monto et al, *Hepatology* 2002

Serfaty et al, *J Hepatol* 2001
Poynard et al, *Hepatology* 2003

Two types of steatosis in chronic hepatitis C



Serfaty et al, *Liver Intern* 2009

Rubbia-Brandt et al, *J Hepatol* 2000

Serfaty et al, *Am J Gastroenterol* 2002

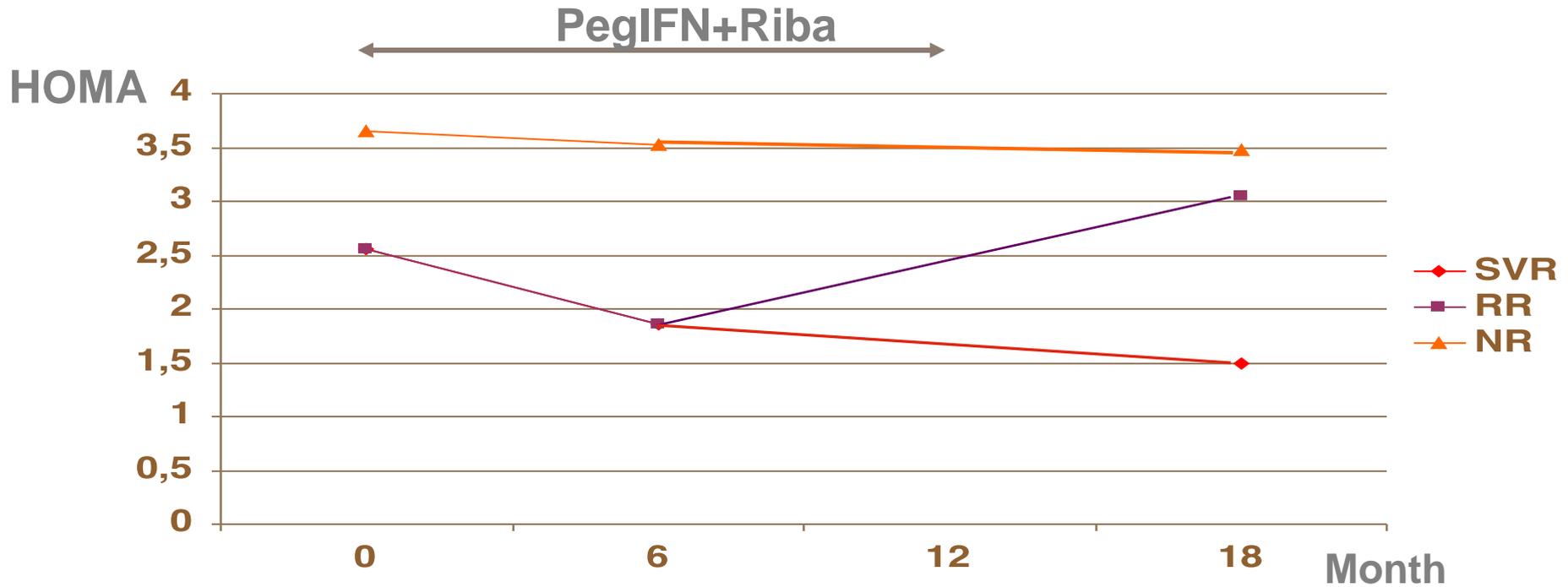
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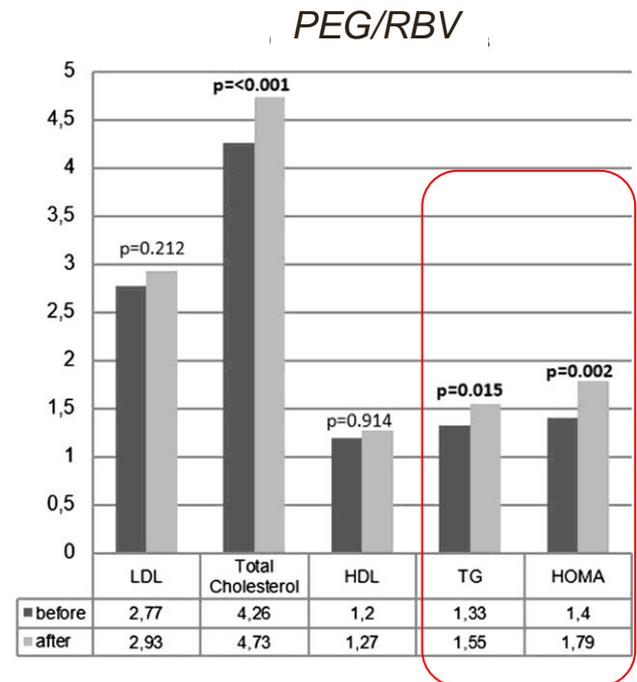
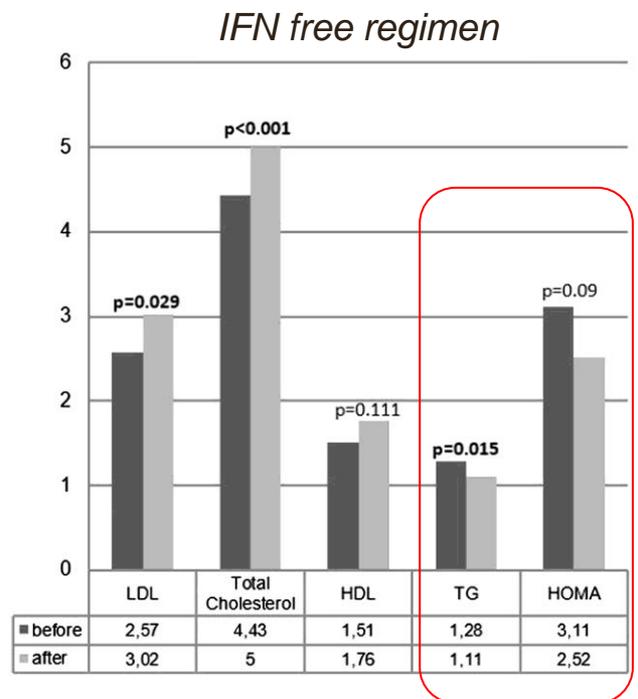
Improvement of insulin resistance following HCV eradication in patients treated with PEG/RBV



Effect of IFN free regimen on metabolic change in HCV patients

Different metabolic change according to antiviral regimen: IFN-based vs IFN-free

- 178 SVR patients treated with IFN free regimen vs PEG/RBV, 1 yr follow-up
- More cirrhotic in group 1



Steatosis change following DAA treatment

Author, yr	n	Follow-up	Method	Steatosis change	Predictors
Tada, 2018	198 (G1,G2)	24w after EOT	PDFF	70% decrease /no 30% increase	None
Kobayashi, 2018	57 (G1,G2)	24w after EOT	CAP	Overall: no Fatty liver at BL: decrease	ND
Shimizu, 2018	70 (G1/G2)	12w after EOT	CAP	Decrease (100% fatty liver at BL)	High HDL, low HbA1c
Cespati, 2021	794 (G1-G4)	36w after EOT	CAP	29% de novo 30% resolution	Male, BMI, TG
Rout, 2019	160 (G3-G4)	52w after EOT	CAP	66% increase 32% decrease	Low albumin
Ogasawara, 2018	214 (G1)	72w after EOT	CAP	Increase	ND

Tada T et al. AP&T 2018

Kobayashi N et al. Eur J Gastroenterol Hepatol 2018

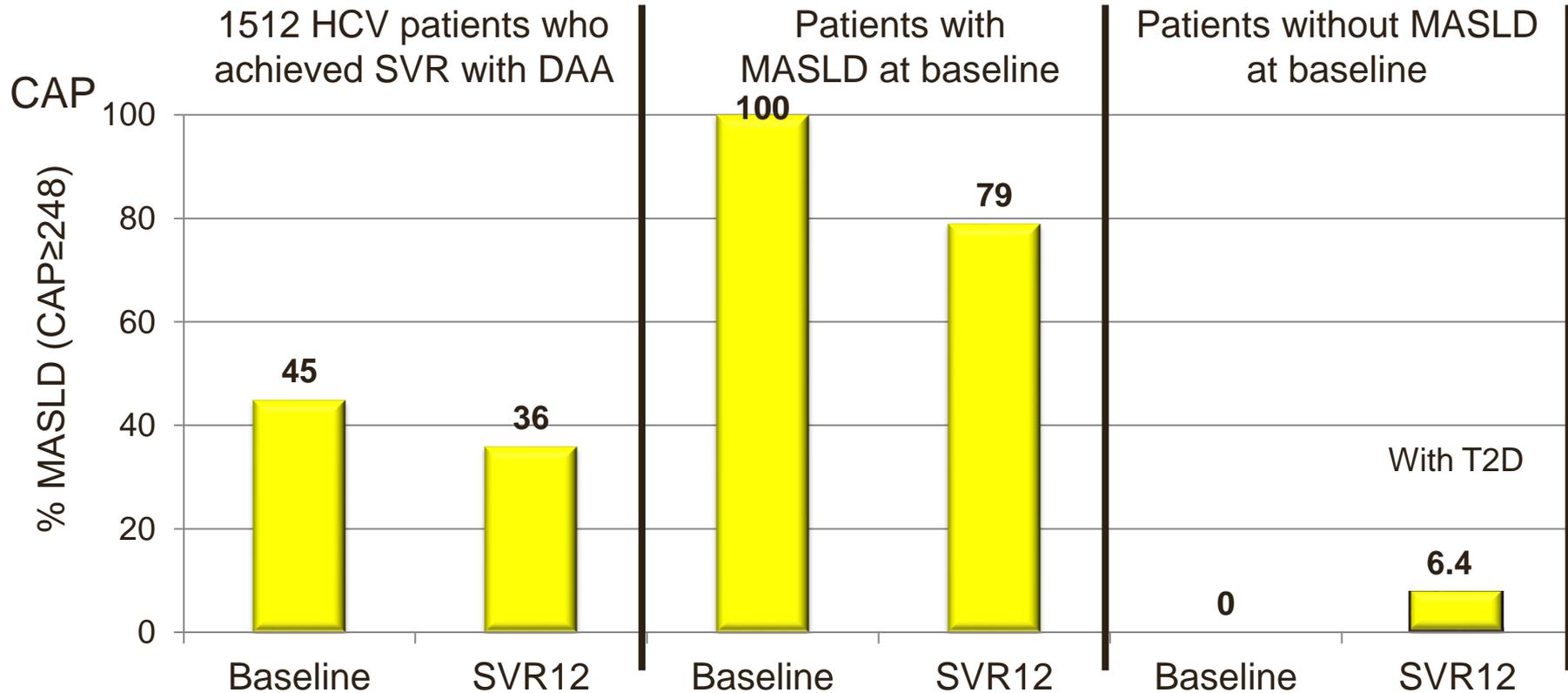
Shimizu K et al. Sci Rep 2018

Cespiati A, et al. Dig Liver Dis 2021

Rout G, et al. J Clin Exp Hepatol. 2019

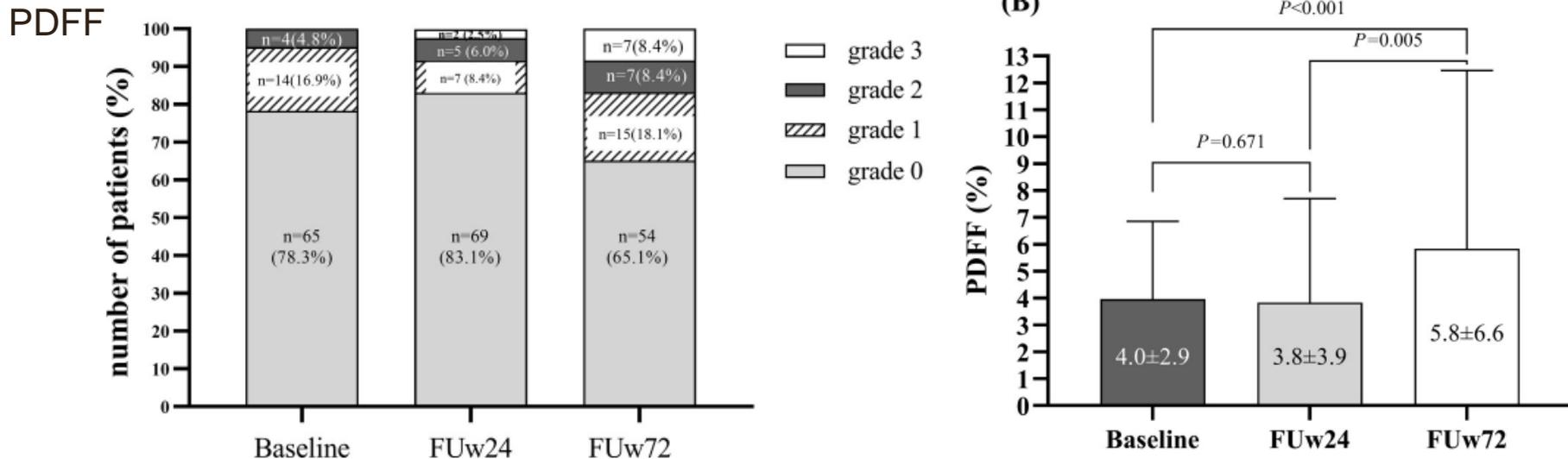
Ogasawara N, et al. Journal of medical virology. 2018

Short term effect of DAA on MASLD prevalence



Long term effect of DAA on metabolic steatosis

55 HCV G1 and 28 HCV G1-HIV patients treated with DAA



Independent parameters associated with PDFF increase:

- Diabetes at BL (OR 6.72 (1.62–27.83))
- BMI increase (OR 4.48 (1.40–14.32))
- PNPLA3

Weight gain in IFN free regimen treated patients

<i>Author, yr</i>	n	Follow-up	Weight gain	Predictors
<i>Do A et al, 2020</i>	11 469 VA	2 yrs post SVR	19.8%>4.5kg	Young age, high BMI, alcohol, cirrhosis, SVR
<i>El kassas M et al, 2019</i>	162	12 w post SVR	+1.6±10 %	ND
<i>Chen CH et al, 2024</i>	735	2 yrs post SVR	15.1%	Young age, low BMI, FIB4 reduction
<i>Schlevogt B et al, 2021</i>	5111	3 yrs post SVR	22%>5kg	Low BMI
<i>Nkwocha et al, 2022</i>	122	12 w post SVR	Yes	High BMI

El Kassas, M.et al. Turk J Gastroenterol 2019; 30: 708–713.

Do, A et al. J Gen Intern Med 2020; 35: 2025–2034.

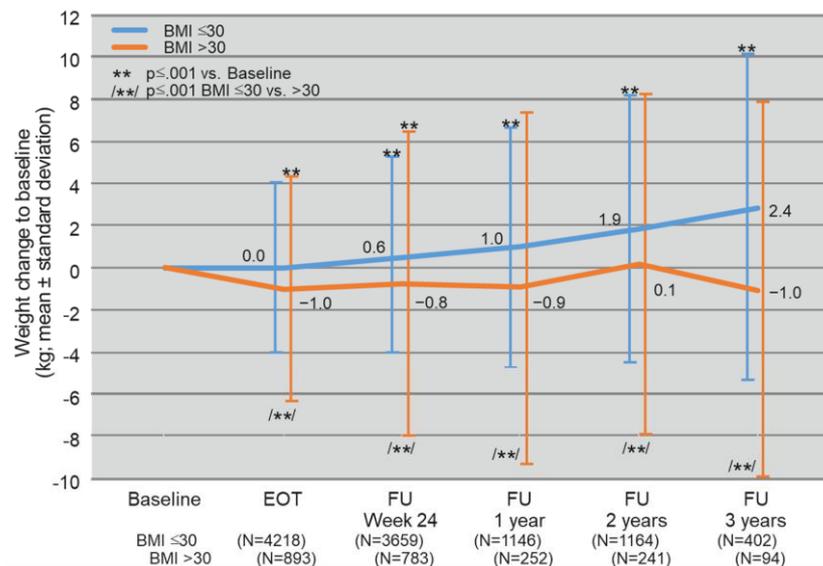
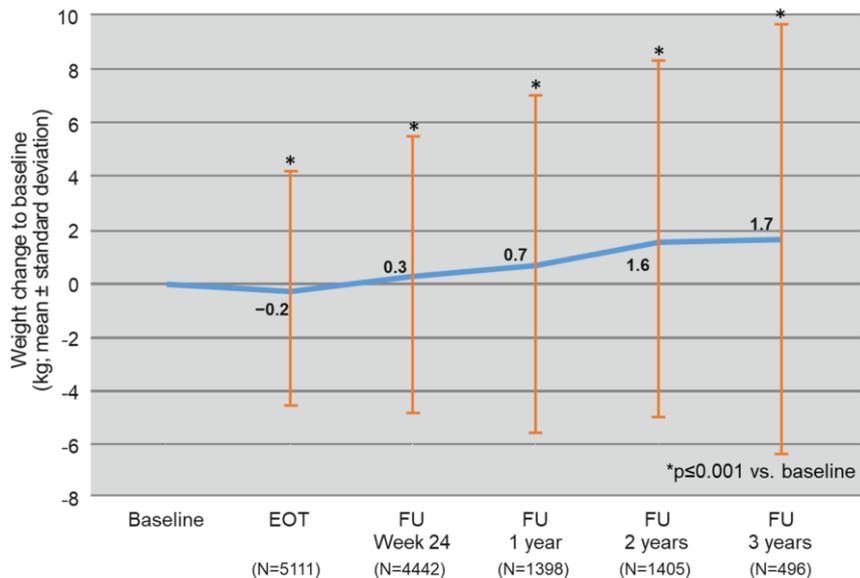
Schlevogt B.et al. Biomedicines 2021; 9: 1495.

Nkwocha CL et al. Antivir Ther 2022, 27, 13596535221115253.

Chen CH, et al. Diagnostics 2024

Course of weight in IFN free regimen treated patients

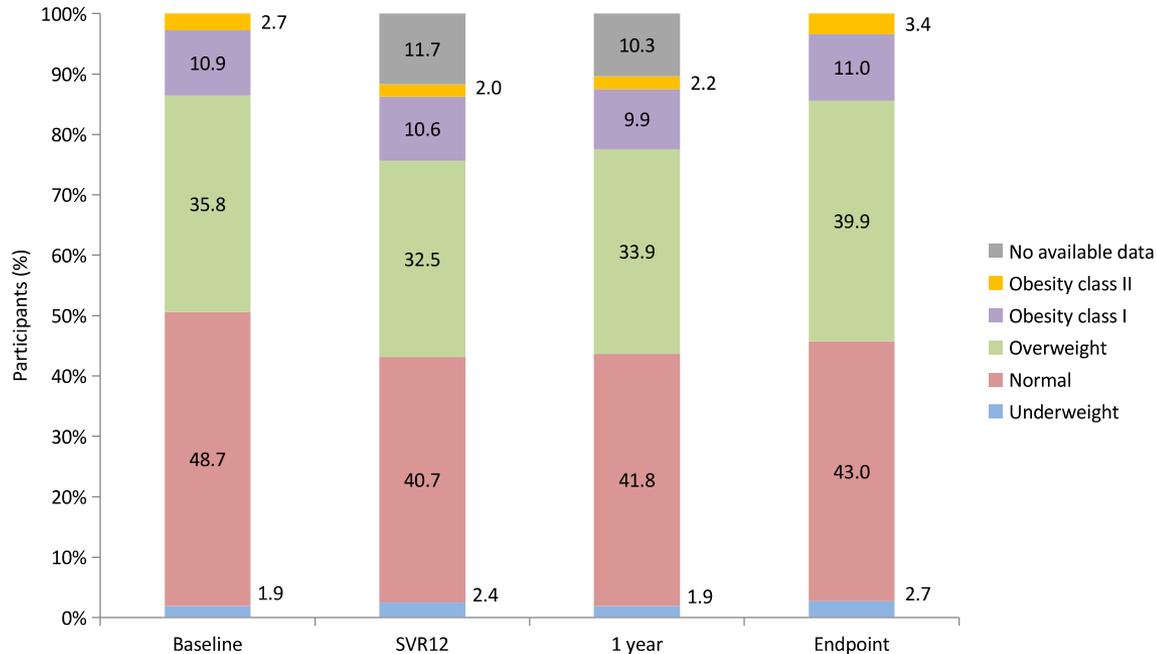
5111 HCV patients treated with IFN free regimen, 3 yrs FU post SVR



Change of BMI distribution in DAA treated patients

735 HCV patients who achieved SVR with DAA, 2yrs FU

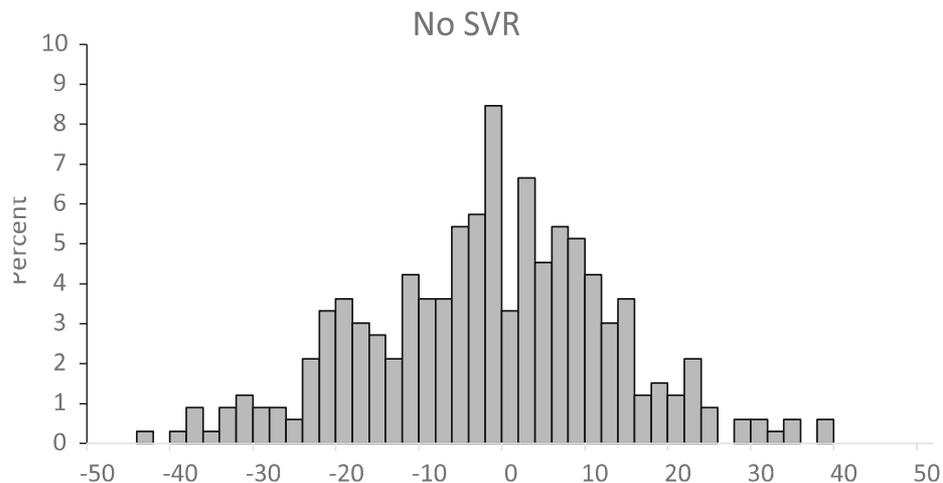
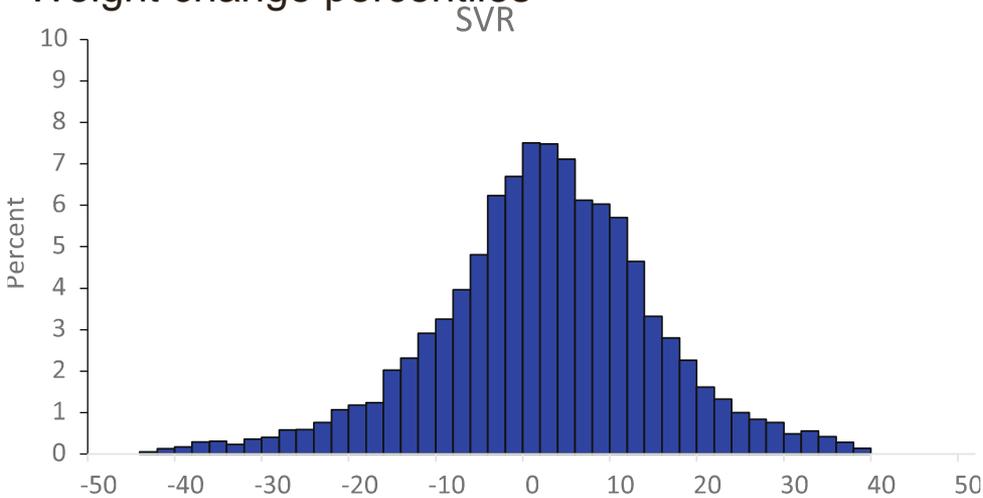
Mean BMI : 25.56 ± 4.07 at baseline vs 25.77 ± 4.29 at end point ($p = 0.005$)



Weight change according to treatment response

11,469 VA with HCV and treated with DAA, FU 2yrs post SVR12

Weight change percentiles



Mean weight change: $+0.56 \pm 12.8$

vs

-3.43 ± 14.6

$p < 0.0001$

Patients with weight gain: 52.9%

vs

40.9%

$p < 0.0001$

Hypothetical mechanisms of weight gain post DAA

- Chronic inflammation removal
- Increased nutritional intake
- Improved hepatic anabolic function

Short term improvement of glycemic control following DAA

2435 diabetic patients treated with IFN free regimen, FU 12 mo post tt

Table 2—Impact of HCV eradication (SVR) on HbA_{1c} (%)

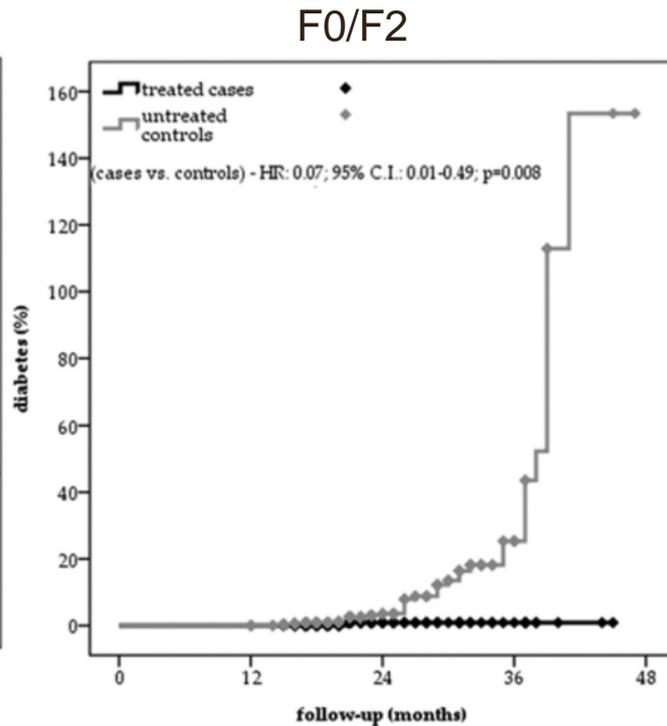
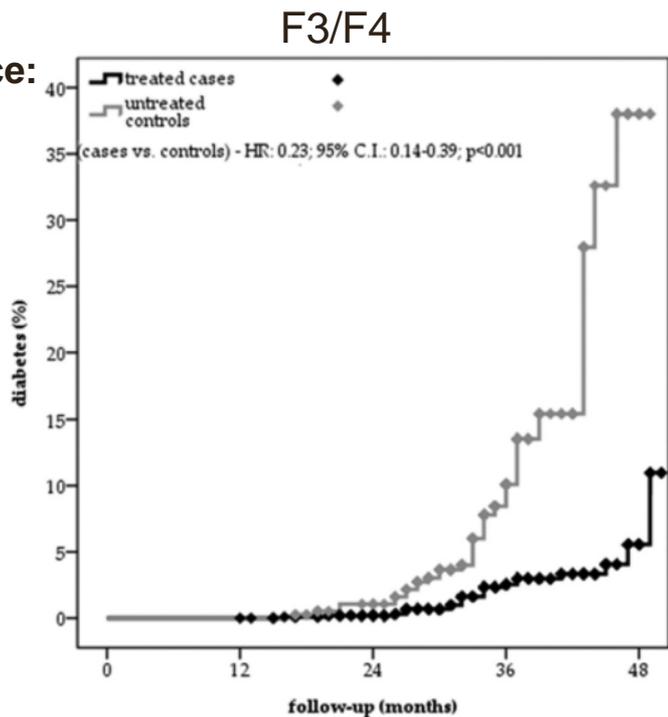
	Pretreatment HbA _{1c}	Post-treatment HbA _{1c}	Absolute change in HbA _{1c} (post-treatment from pretreatment)	Mean difference in HbA _{1c} drop in SVR vs. no SVR groups	P value	Adjusted* mean difference in HbA _{1c} drop in SVR vs. no SVR	P value
All patients							
No SVR	7.27 (1.6)	7.08 (1.5)	-0.19 (1.3)	-0.18	0.03	-0.13	0.1
SVR	7.20 (1.5)	6.82 (1.3)	-0.37 (1.2)				
Patients with pretreatment HbA_{1c} >7.2%							
No SVR	8.54 (1.2)	7.89 (1.6)	-0.65 (1.5)	-0.33	0.02	-0.34	0.02
SVR	8.54 (1.2)	7.56 (1.3)	-0.98 (1.4)				
Patients with pretreatment HbA_{1c} ≤7.2%							
No SVR	6.1 (0.7)	6.4 (1.06)	0.22 (0.9)	-0.15	0.04	-0.05	0.5
SVR	6.2 (0.6)	6.3 (0.9)	0.07 (0.8)				
Patients with cirrhosis							
No SVR	7.2 (1.5)	6.9 (1.4)	-0.27 (1.35)	-0.02	0.8	0.05	0.7
SVR	7.1 (1.5)	6.8 (1.3)	-0.30 (1.29)				
Patients without cirrhosis							
No SVR	7.4 (1.6)	7.3 (1.6)	-0.09 (1.3)	-0.33	0.005	-0.31	0.01
SVR	7.2 (1.4)	6.8 (1.2)	-0.42 (1.2)				

Values are reported as mean (SD) unless otherwise indicated. *Adjusted by multiple linear regression for age, sex, race/ethnicity, cirrhosis, platelet count, hemoglobin level, creatinine, bilirubin, albumin, INR, BMI, and FIB-4 score.

Long term risk of incident diabetes following DAA

1327 non diabetic HCV patients who achieved viral eradication with DAA vs 1099 untreated HCV
 Median FU 30 months

T2D incidence:

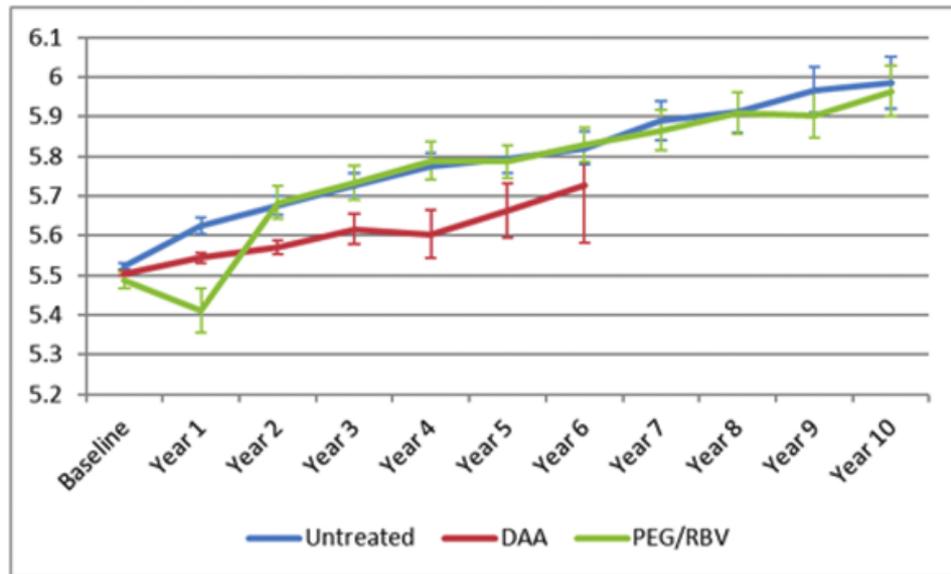


Long terms change of HbA1c following DAA

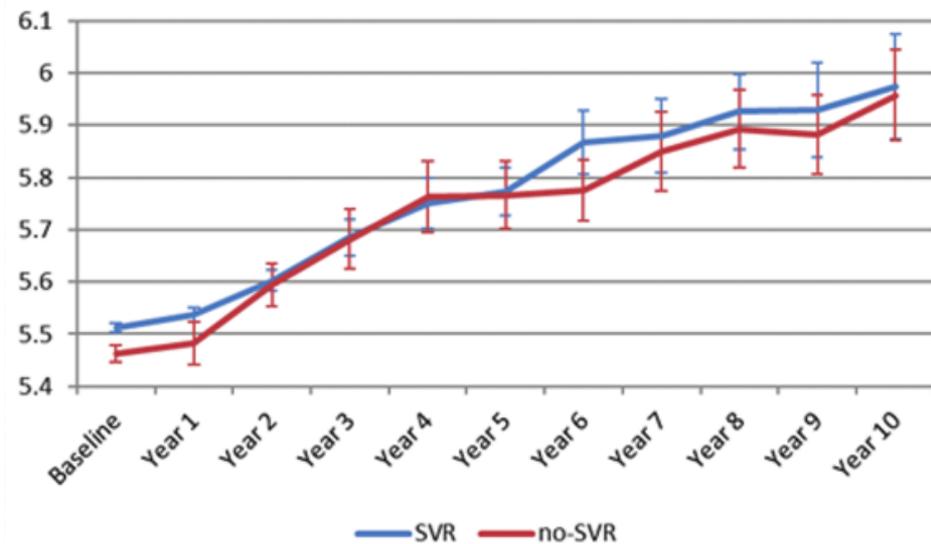
(VA) n=21279 DAA and n=4764 PEG/RBV, non-diabetic

Diabetes incidence rates: 9.89 vs 19.8 per 1000 person-years

HbA1c



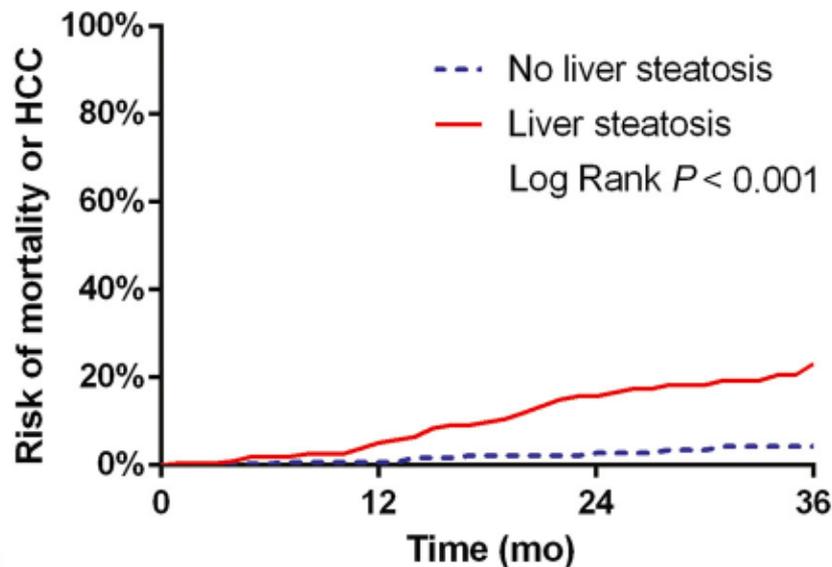
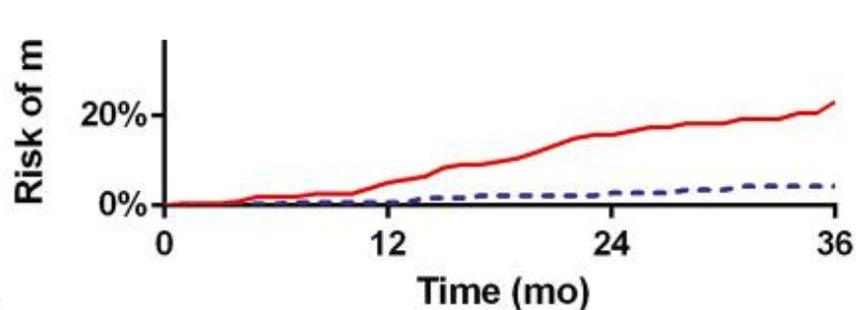
HbA1c



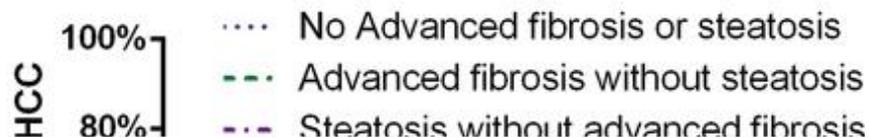
Liver outcomes in SVR patients with persistent metabolic abnormalities or steatosis following DAA

Increased risk of HCC in SVR patients with persistent steatosis following DAA treatment

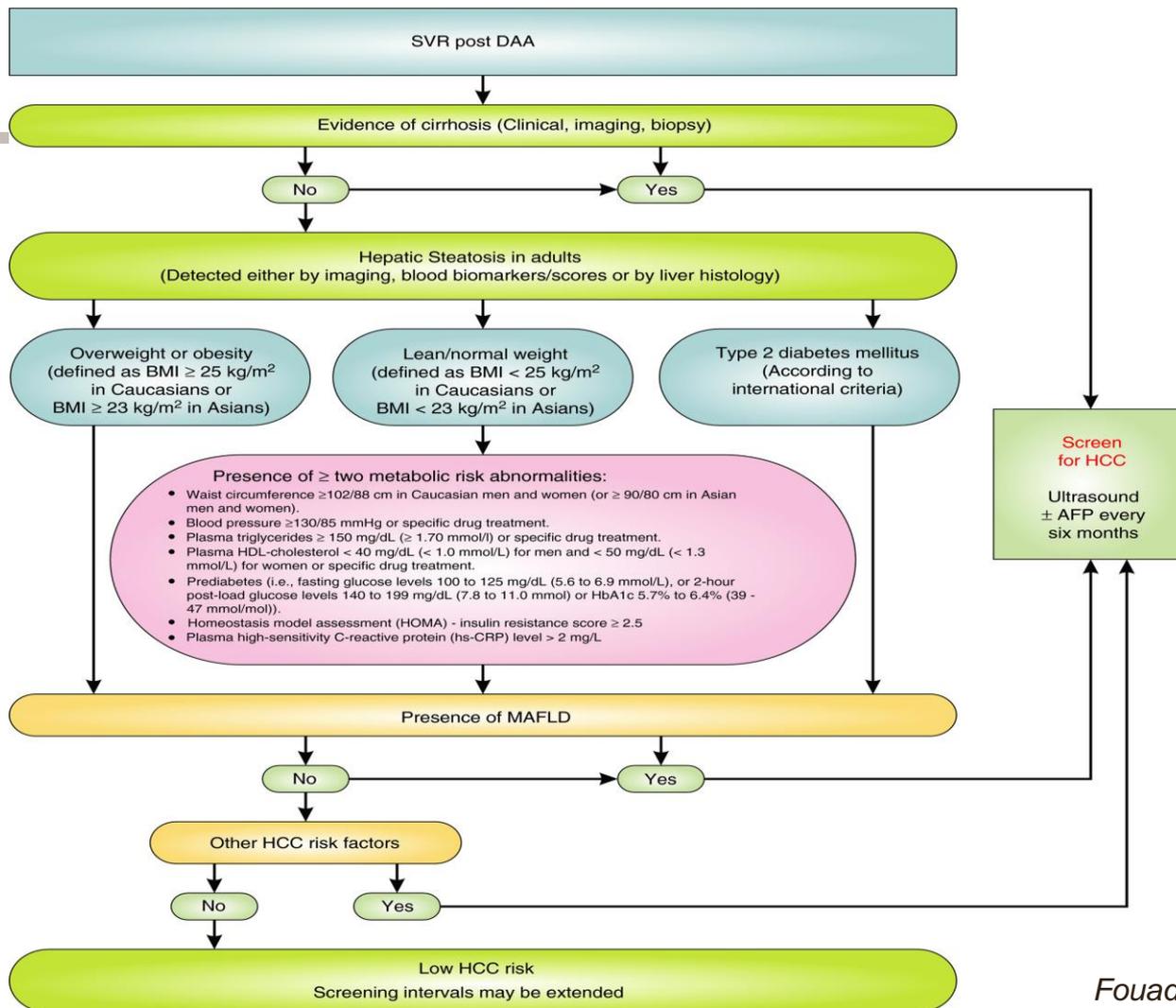
515 SVR patients following DAA, 41% with persistent steatosis, mean FU 24 mo



k:				
steatosis	211	146	105	62
no steatosis	304	212	161	84



After adjustment with components of the metabolic syndrome, LS was associated with a significant 7.5-fold increased risk of all-cause mortality and HCC



Conclusion

- Interferon based- and interferon free regimen have different impact on metabolic abnormalities in HCV patients.
- In the short term, HCV eradication following DAA is associated with glycemic control improvement and decrease of MASLD.
- In the long term, HCV eradication could be associated with weight gain and development of MASLD. Future studies are needed to better characterize the metabolic risk associated with weight gain.
- The AASLD recommends counseling on weight gain avoidance in all patients who achieve SVR.
- Persistent or *de novo* MASLD following DAA treatment is associated with increased risk of poor liver outcomes.



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Thank you

