Actualités en Hépatologie

NAFLD et Alcool

Dr Jérôme Boursier

XIXe Symposium D'Hépato-gastroentérologie

17 juin 2011

Actualité en Hépatologie
NAFLD et Alcool

- **Prise en charge**
  - Hépatique
  - Extra-hépatique
- **Traitement**

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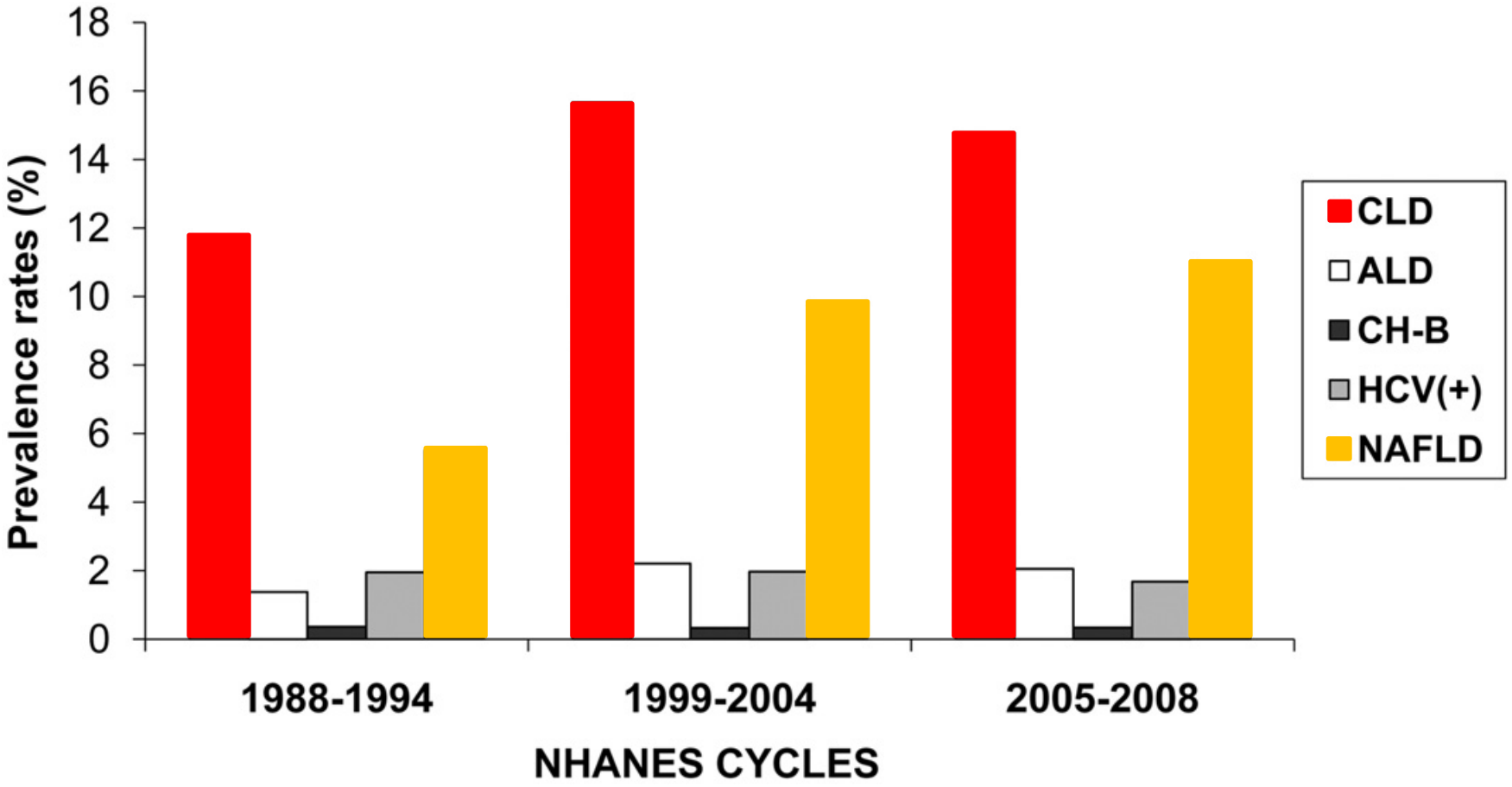
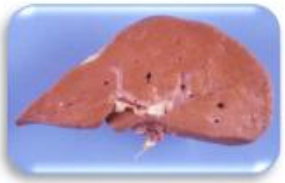
Prévalence des hépatopathies chroniques aux Etats-Unis



Younossi, Clin Gastroenterol Hepatol 2011

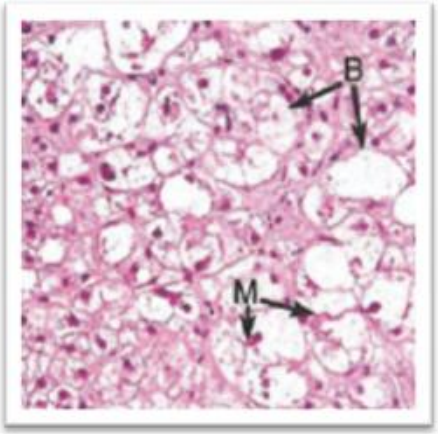
Histoire Naturelle de la NAFLD



Foie normal

Steatose → Accumulation de triglycérides

Stéatohépatite (NASH)

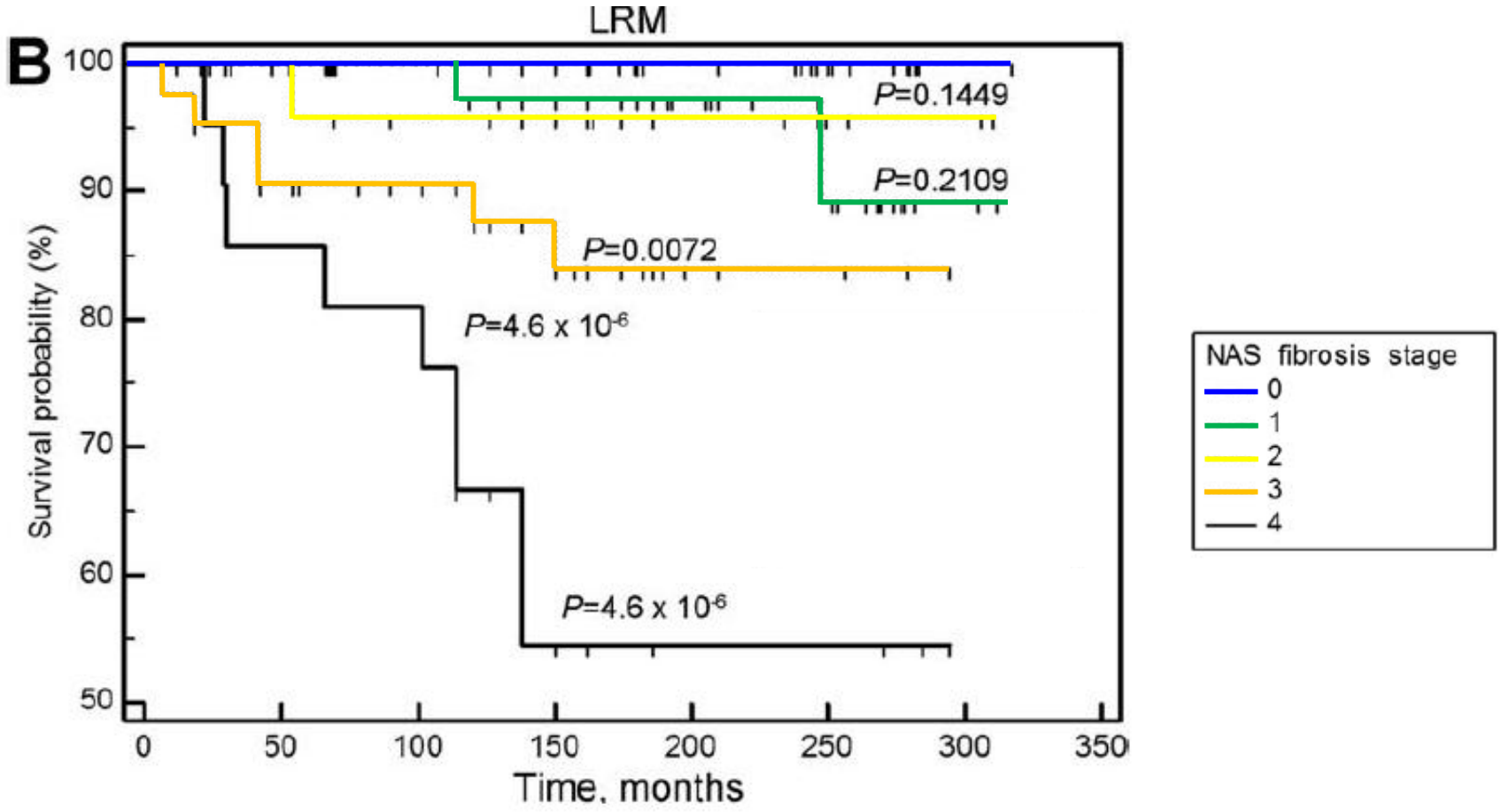


Inflammation
Corps de Mallory
Ballonnisation

Fibrose

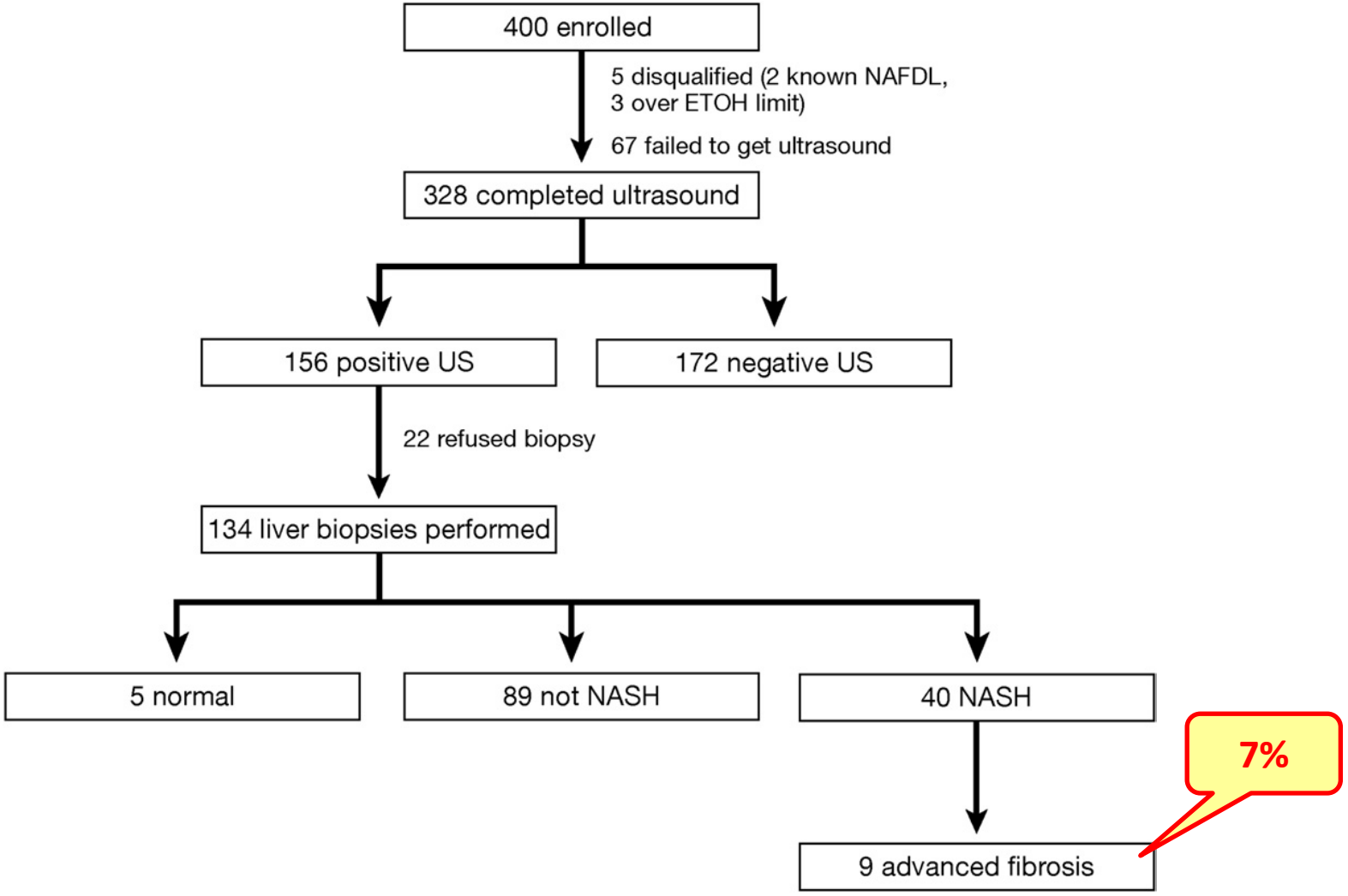
Cirrhose

Stades de fibrose et décès de cause hépatique



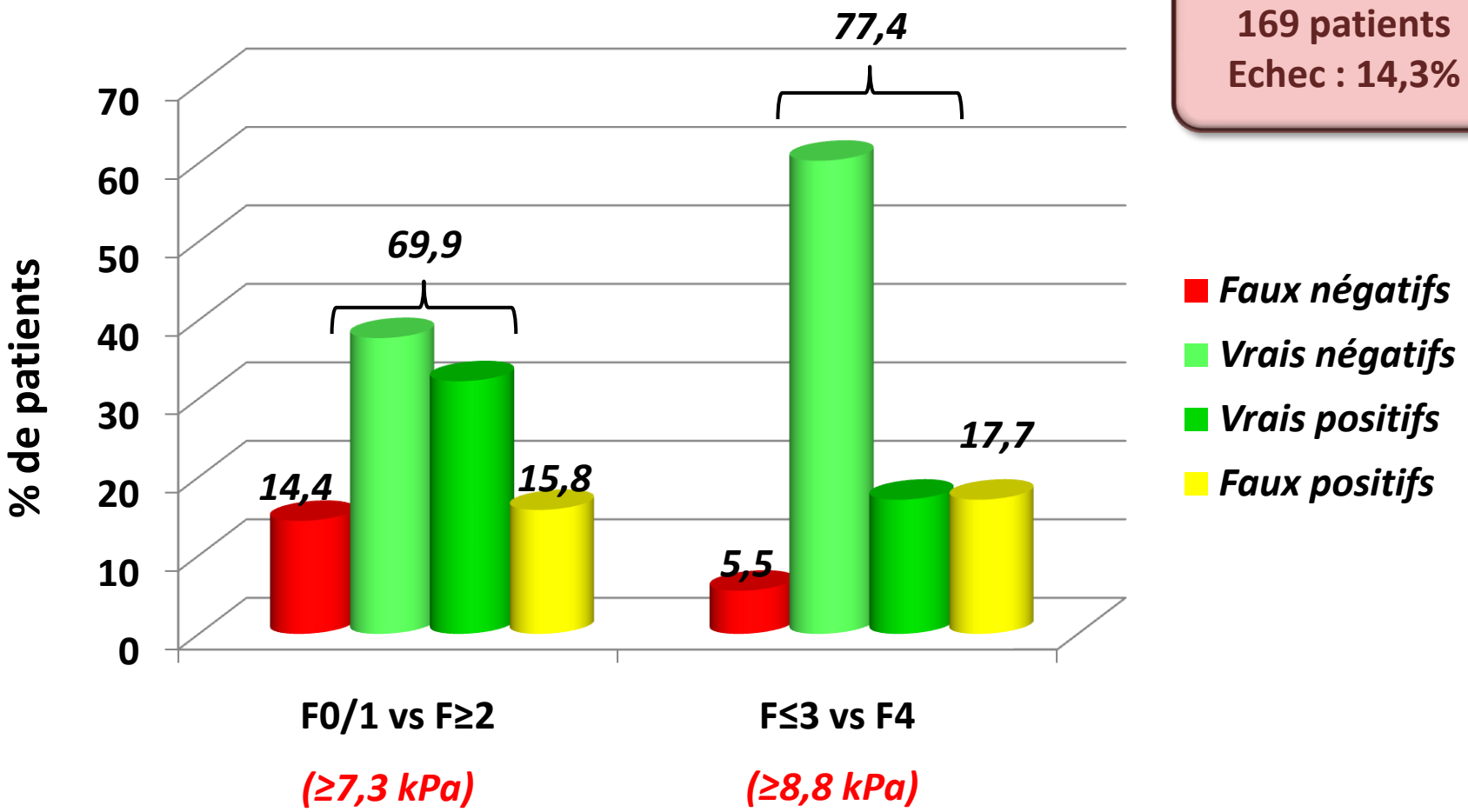
Younossi, Hepatology 2011

Epidémiologie de la NAFLD



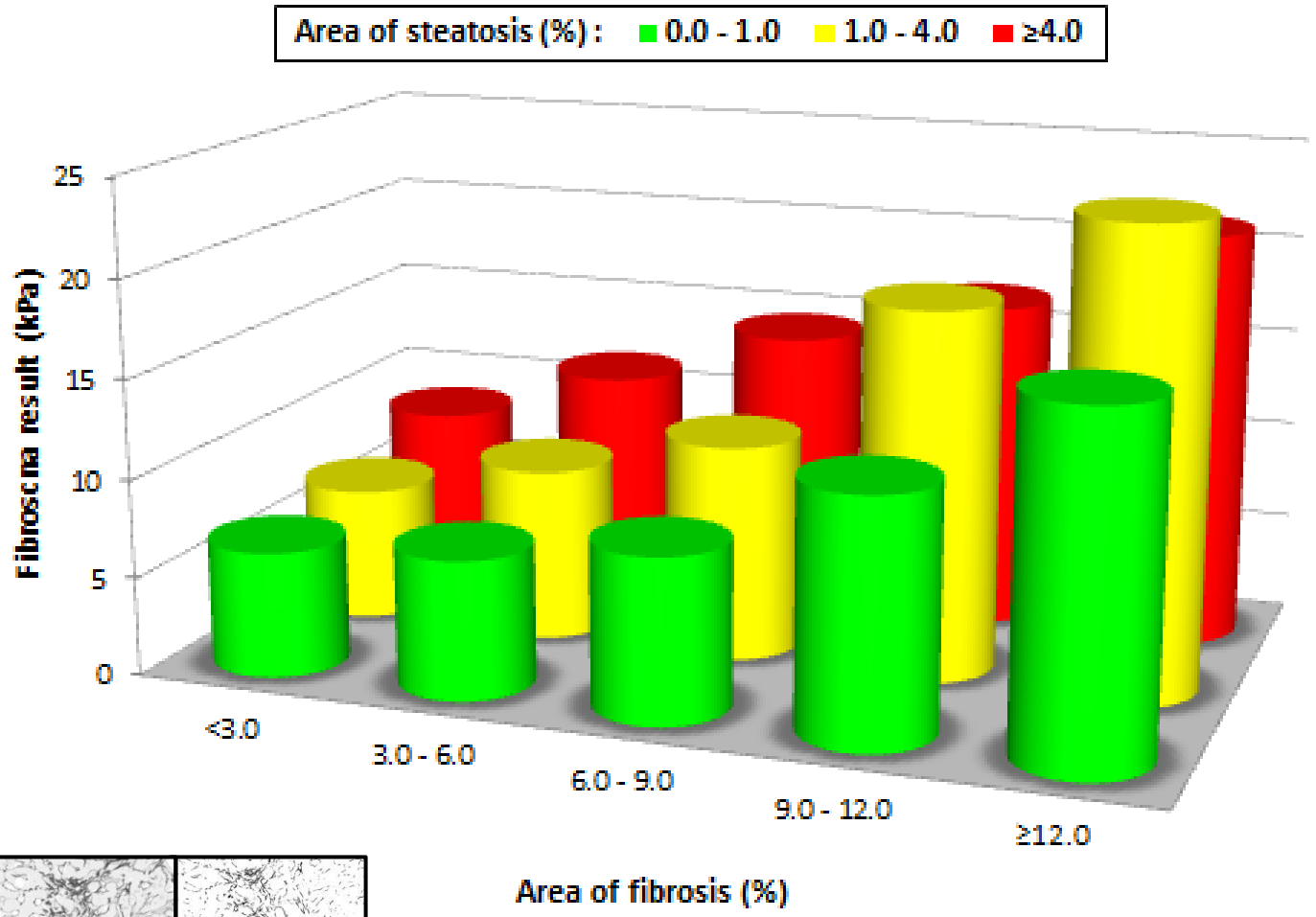
Williams, Gastroenterology 2011

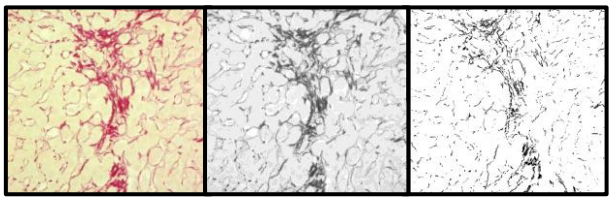
Performance du Fibroscan dans la NAFLD



Petta, Aliment Pharmacol Ther 2011

Fibroscan et stéatose hépatique

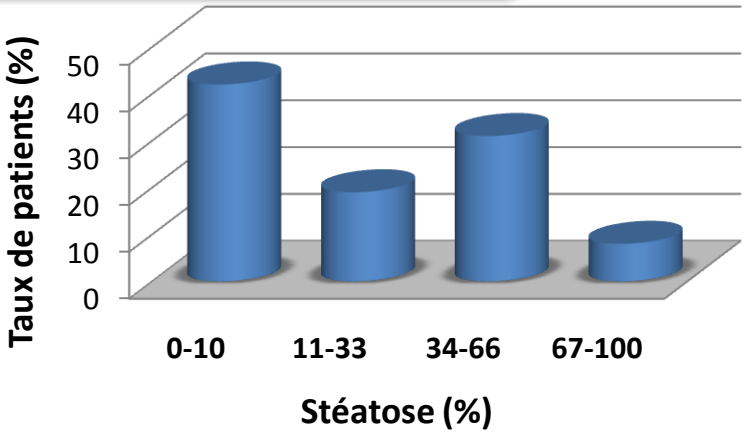


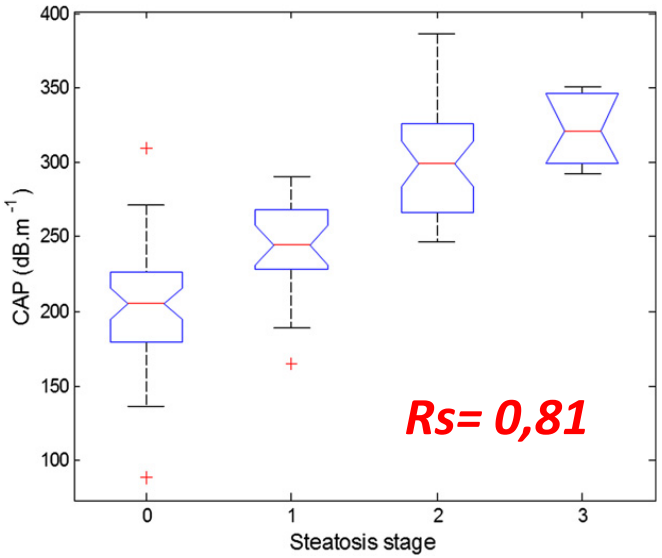


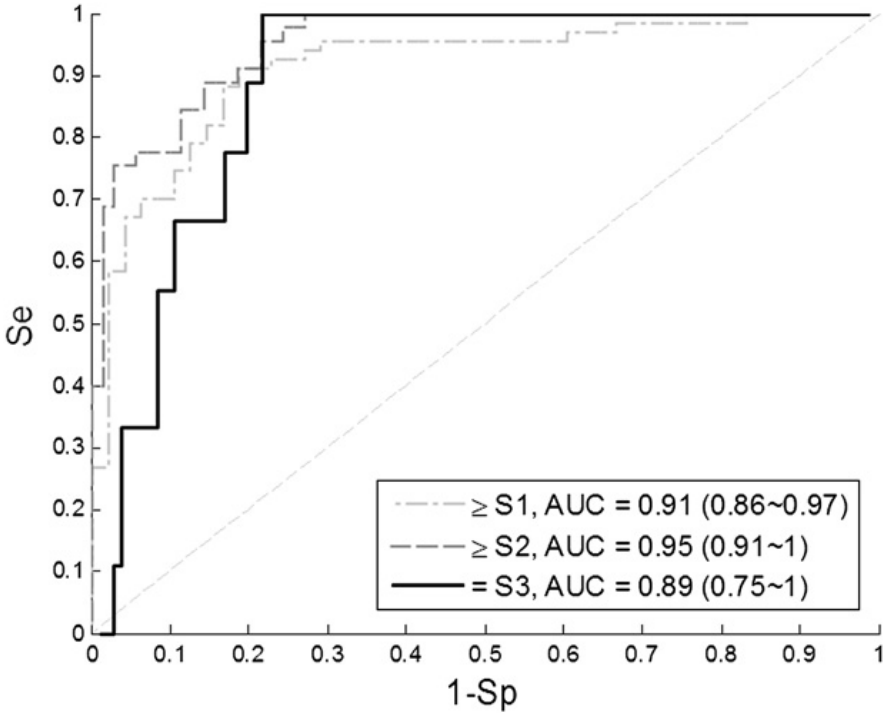
Boursier, AASLD 2010

Controlled Attenuation Parameter (CAP)

115 patients
hépatopathie chronique





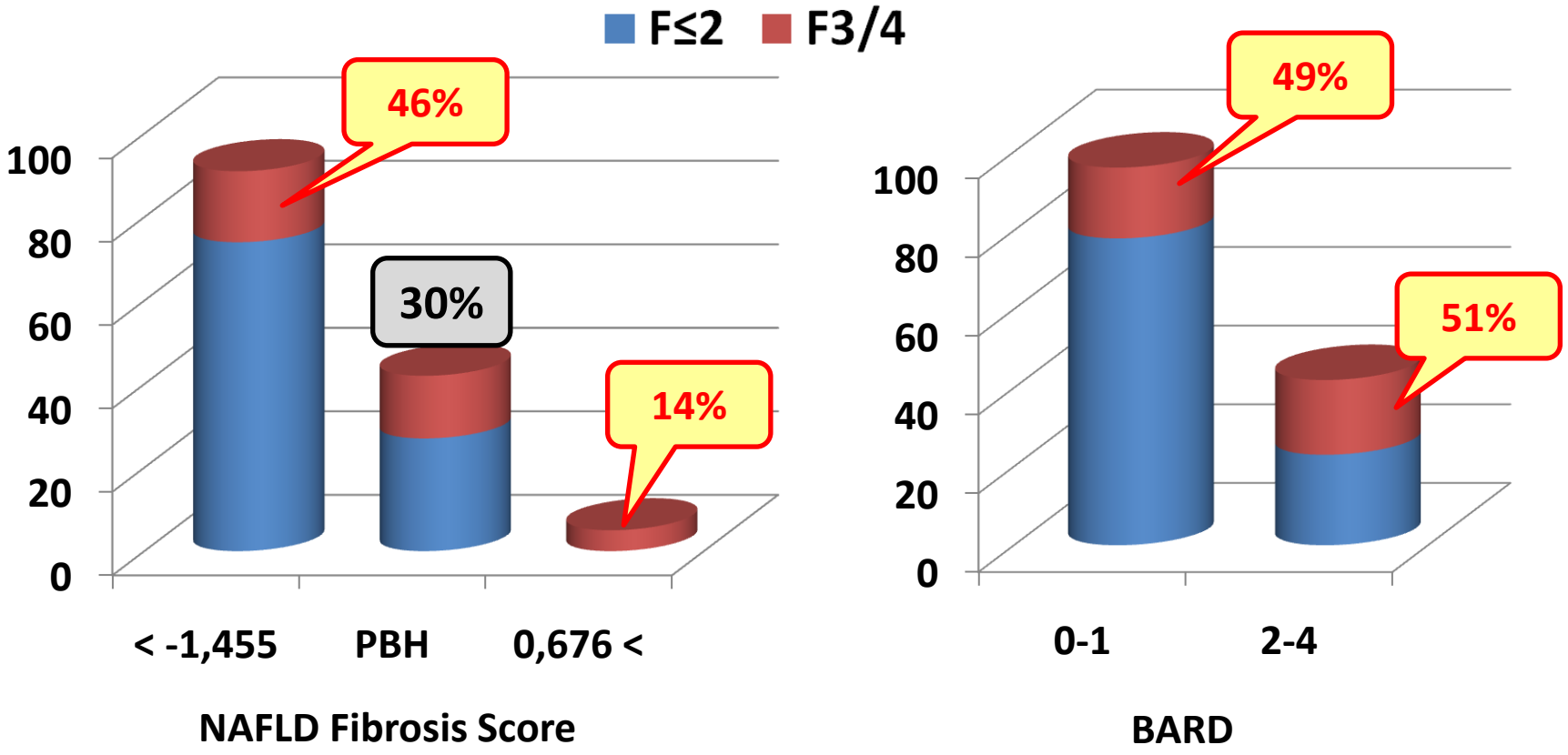


Sasso, Ultrasound Med Biol 2010

Performance des tests sanguins dans la NAFLD

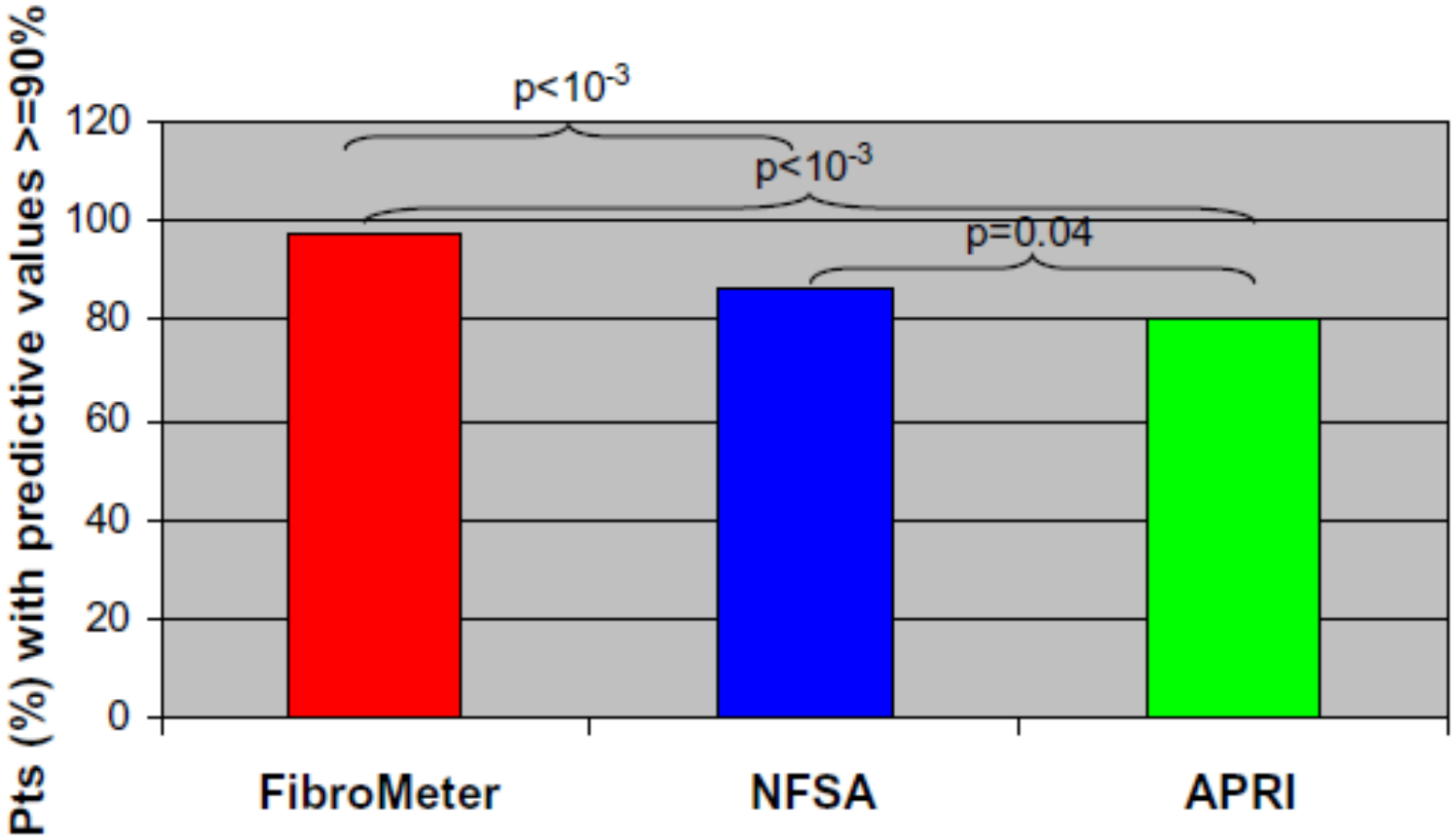
BARD (0-4) : ASAT/ALAT ≥2 = 2; BMI ≥28 = 1, diabète = 1

NFSA : 0,037*age + 0,094*BMI + 1,13*IFG/diabetes + 0,99*AST/ALT – 0,013*platelets – 0.66 albumin + 1,675



Ruffillo, J Hepatol 2011

Performance des tests sanguins dans la NAFLD

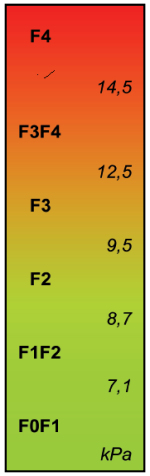


Calès, J Hepatol 2009

Combinaison de tests ?

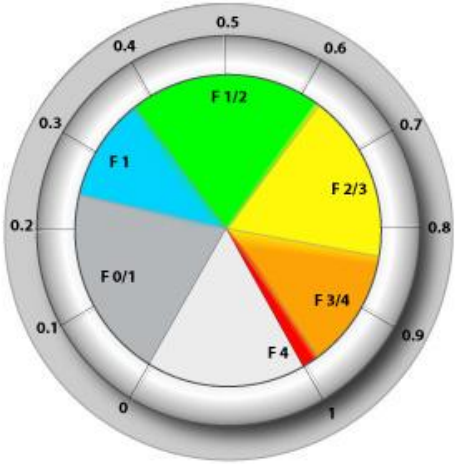
Fibroscan

FibroMeter



Fibroscan Result (kPa)

FibroMeter result (0-1)



Computerization

Fibroscan classification

Diagnostic accuracy: ***58.7%***

FibroMeter classification

Diagnostic accuracy: ***68.7%***

CSF/SF classification

Diagnostic accuracy: ***86.7%***

Boursier, AJG 2011

Genome Wide Association Studies

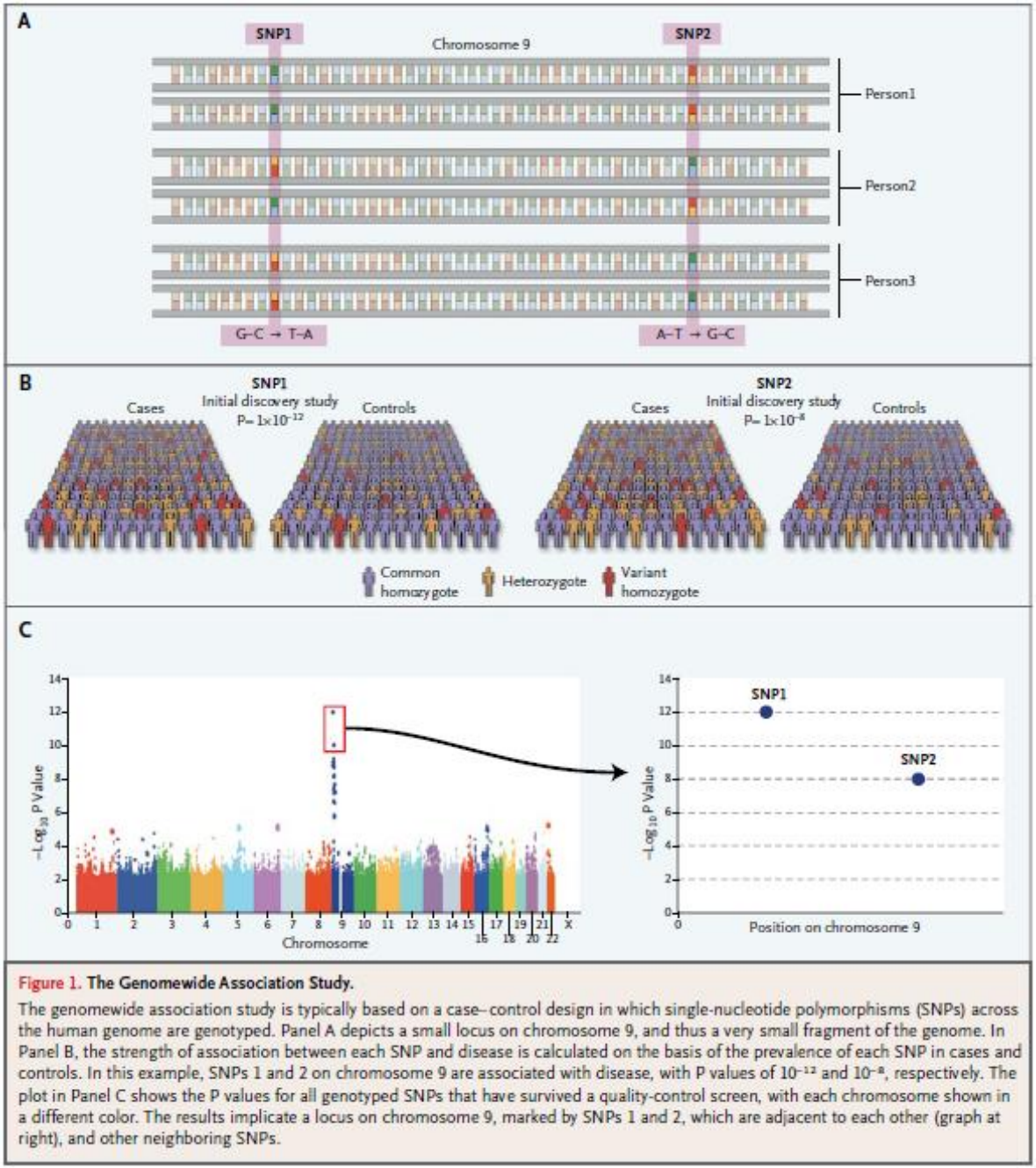
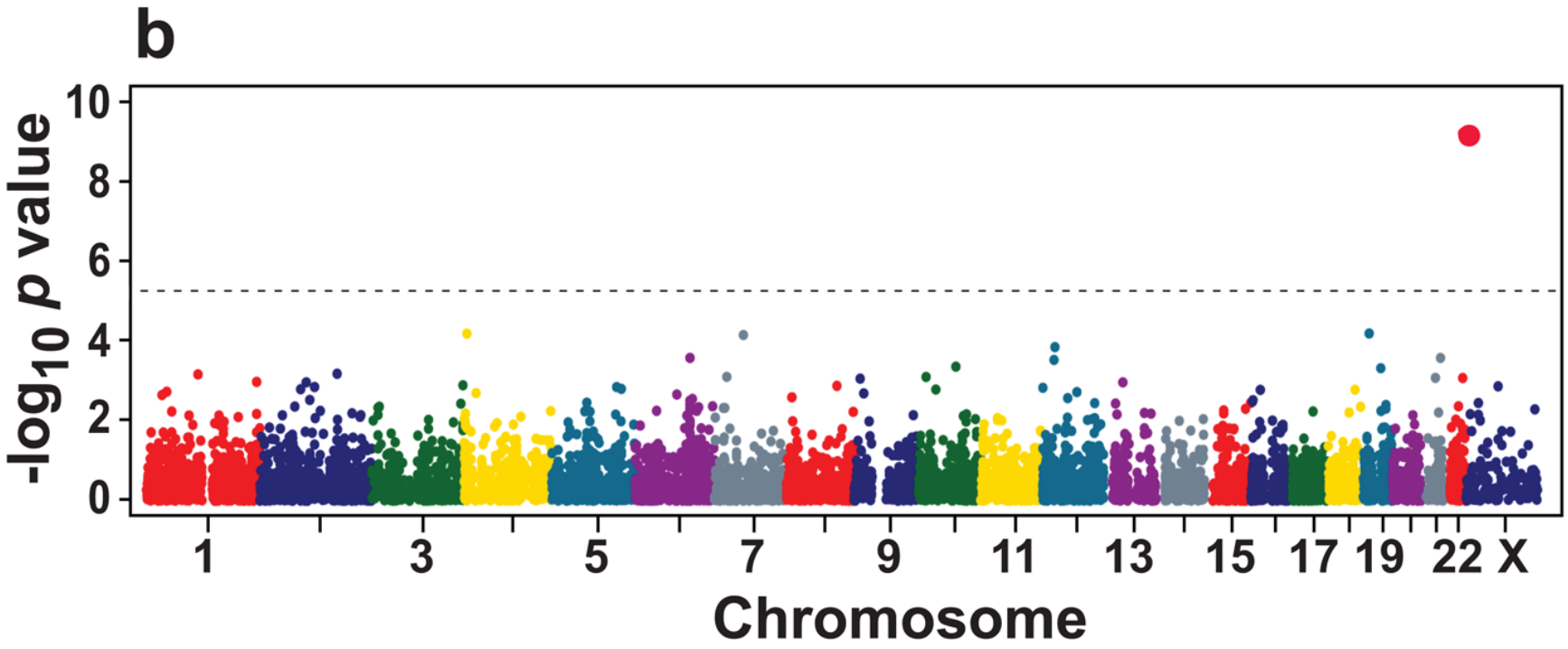


Figure 1. The Genomewide Association Study.

The genomewide association study is typically based on a case–control design in which single-nucleotide polymorphisms (SNPs) across the human genome are genotyped. Panel A depicts a small locus on chromosome 9, and thus a very small fragment of the genome. In Panel B, the strength of association between each SNP and disease is calculated on the basis of the prevalence of each SNP in cases and controls. In this example, SNPs 1 and 2 on chromosome 9 are associated with disease, with P values of 10^{-12} and 10^{-8}, respectively. The plot in Panel C shows the P values for all genotyped SNPs that have survived a quality-control screen, with each chromosome shown in a different color. The results implicate a locus on chromosome 9, marked by SNPs 1 and 2, which are adjacent to each other (graph at right), and other neighboring SNPs.

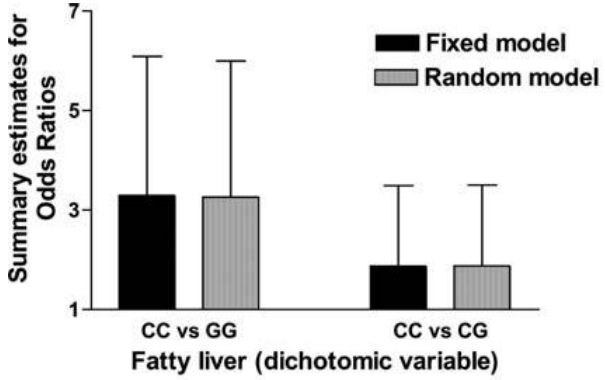
Manolio, NEJM 2010

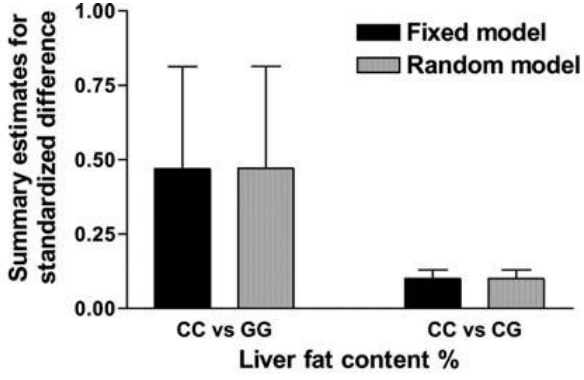
Polymorphisme du gène PNPLA3

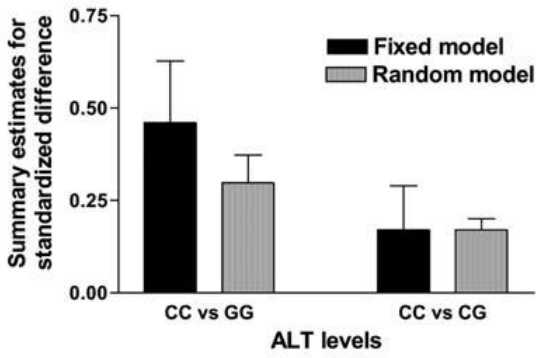


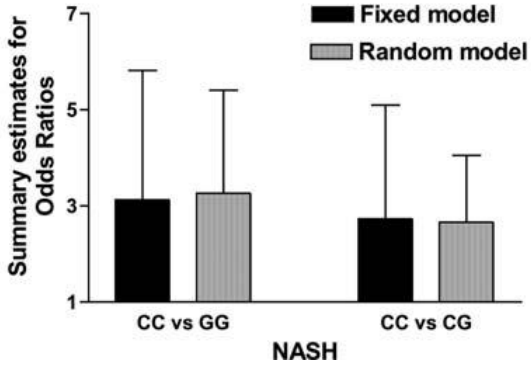
Romeo, Nat Genet 2008

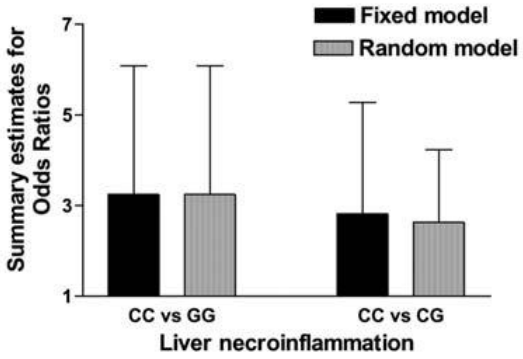
Polymorphisme du gène PNPLA3 et sévérité de la NAFLD

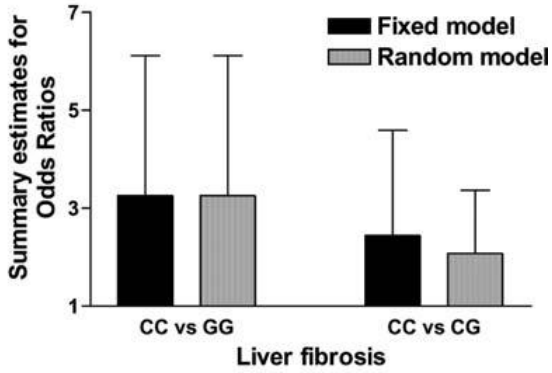












Sookoian, Hepatology 2011

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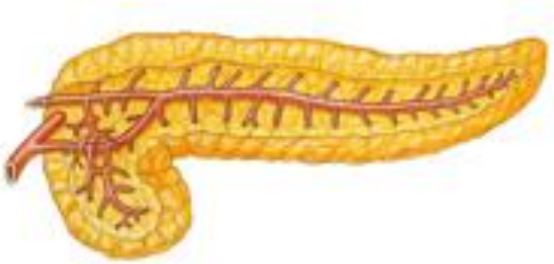
Maladie métabolique



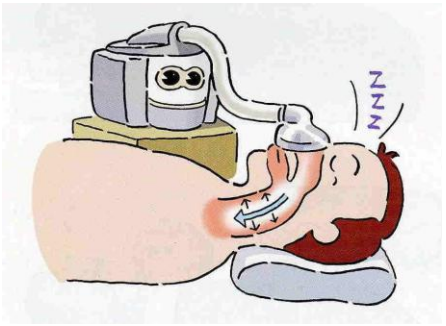
Diabète

Stéatose

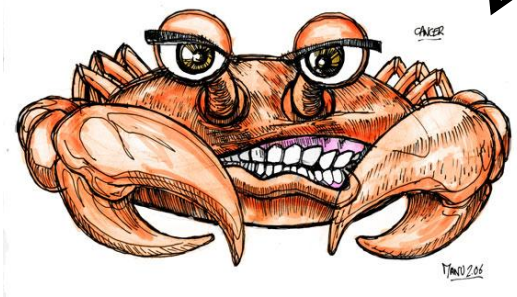
NASH

Fibrose

Cirrhose



Syndrome d'apnée du sommeil



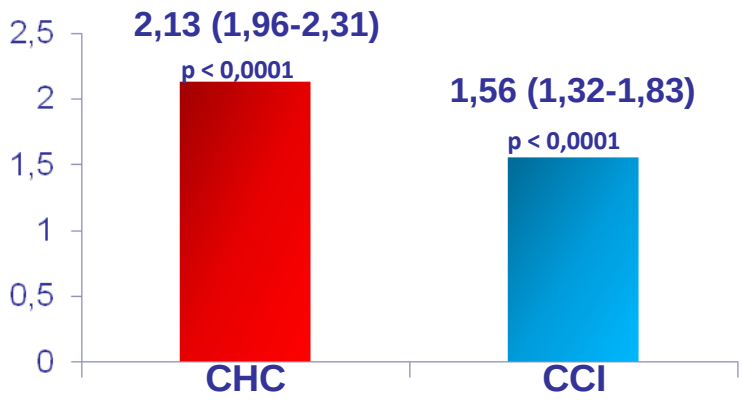
Cancer

Cardio-Vasculaires

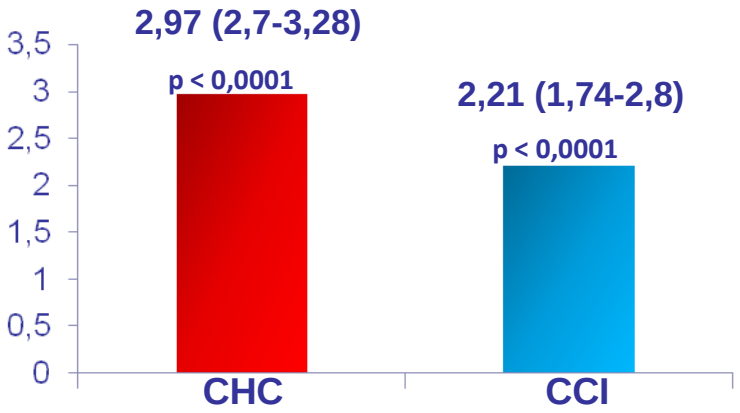
CHC, cholangiocarcinome intrahépatique et syndrome métabolique

CHC 3 649 sujets ; CCI 743 sujets
Contrôles (sans cancer) 195 953 sujets

Risque relatif attribuable au syndrome métabolique



Risque relatif attribuable au tabac

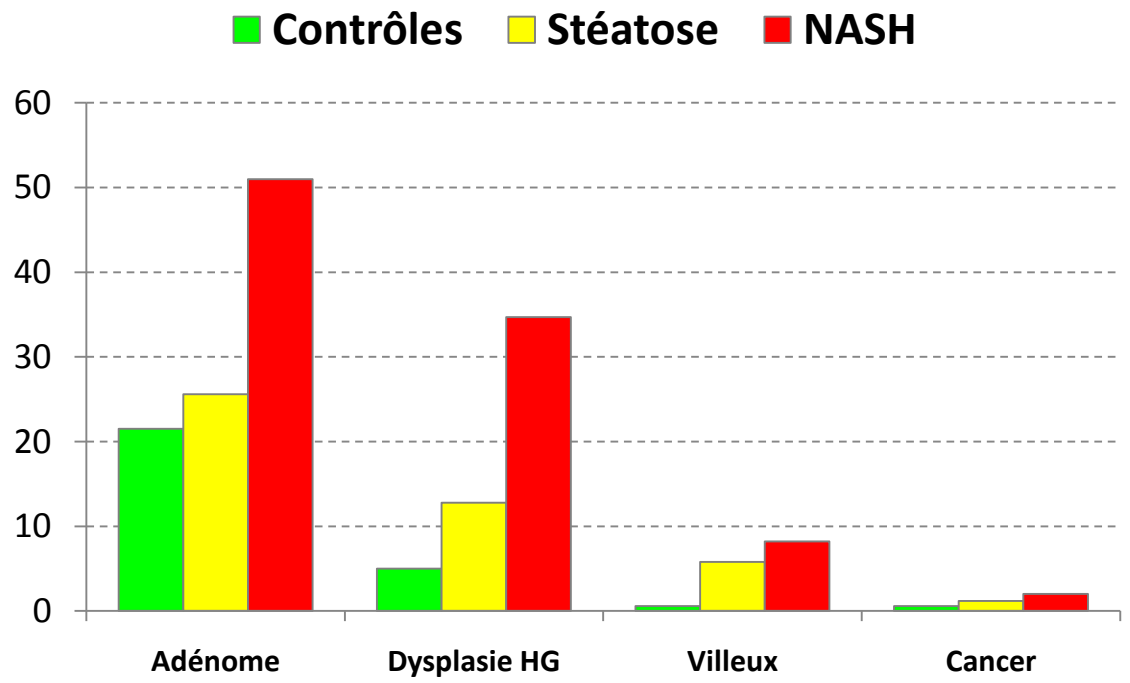


➔ Le syndrome métabolique est un facteur de risque significatif des deux types de cancer primitif du foie et pourrait expliquer certains CHC et CCI “idiopathiques”

Welzel, EASL 2011

NAFLD et Cancer du Colon

- **245 patients population générale : 181 contrôles, 64 avec stéatose (spectro-RM)**
- **135 NAFLD avec biopsies**



NAFLD : facteur indépendant de polype avancé (OR 3,04) mais pas de polype colorectal
NASH : facteur indépendant de polype avancé (OR 5,3) ou de polype colorectal (OR 4,9)

Wong, Gut 2011

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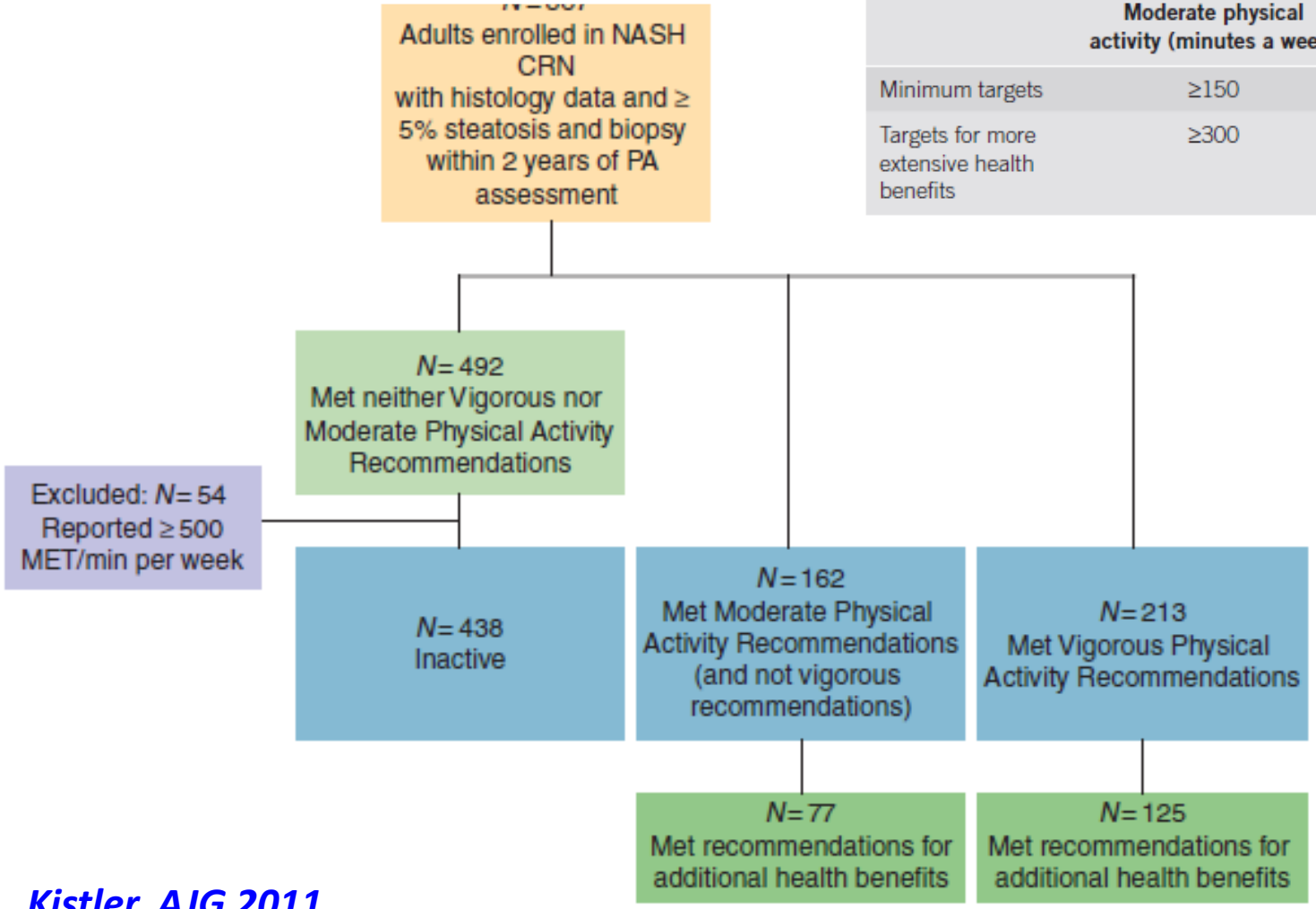
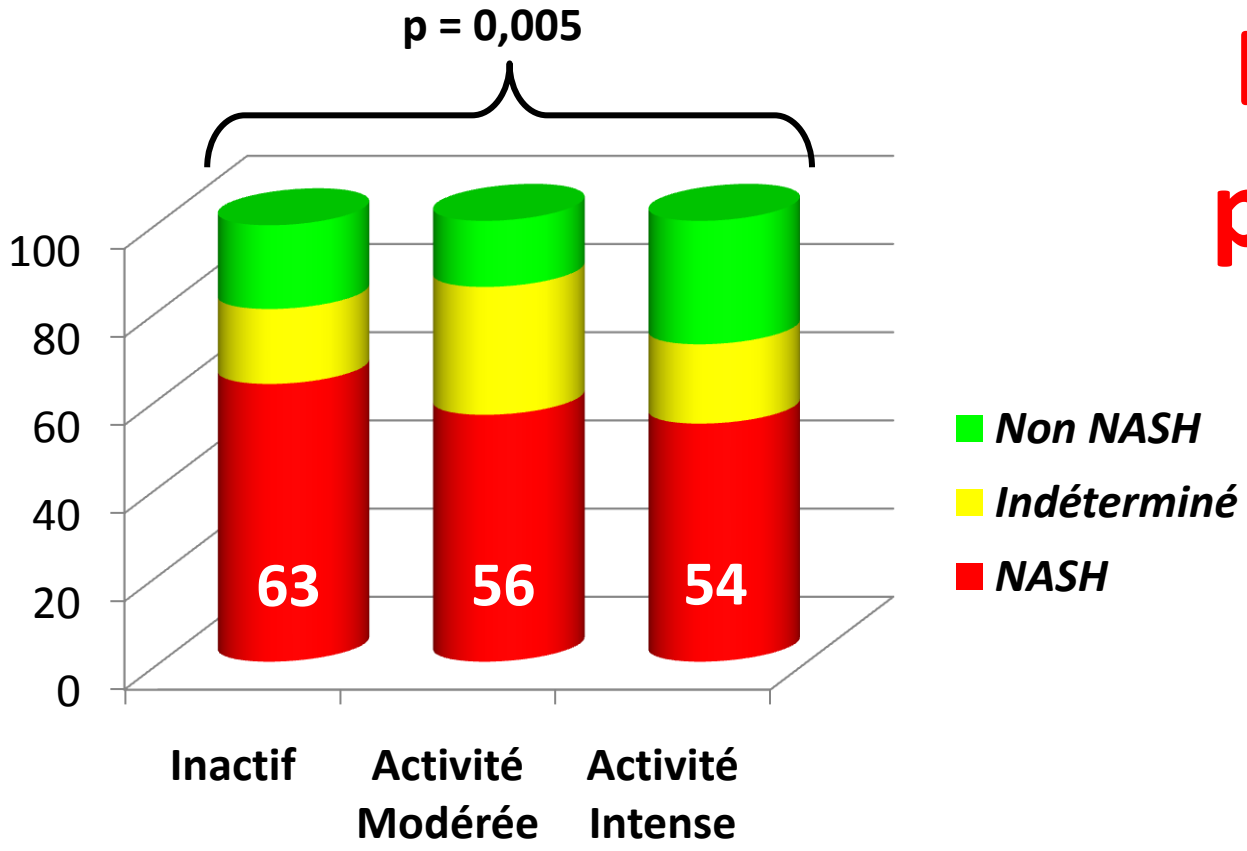
Exercice physique



	Moderate physical activity (minutes a week)	Vigorous physical activity (minutes a week)
Minimum targets	≥150	≥75
Targets for more extensive health benefits	≥300	≥150

Kistler, AJG 2011

Exercice physique



Odd Ratios (ajustés) :

	Activité Modérée		Activité Intense	
	Minimum	« Etendue »	Minimum	« Etendue »
NASH	NS	NS	0,65	0,56
Fibrose F≥3	NS	NS	NS	0,53

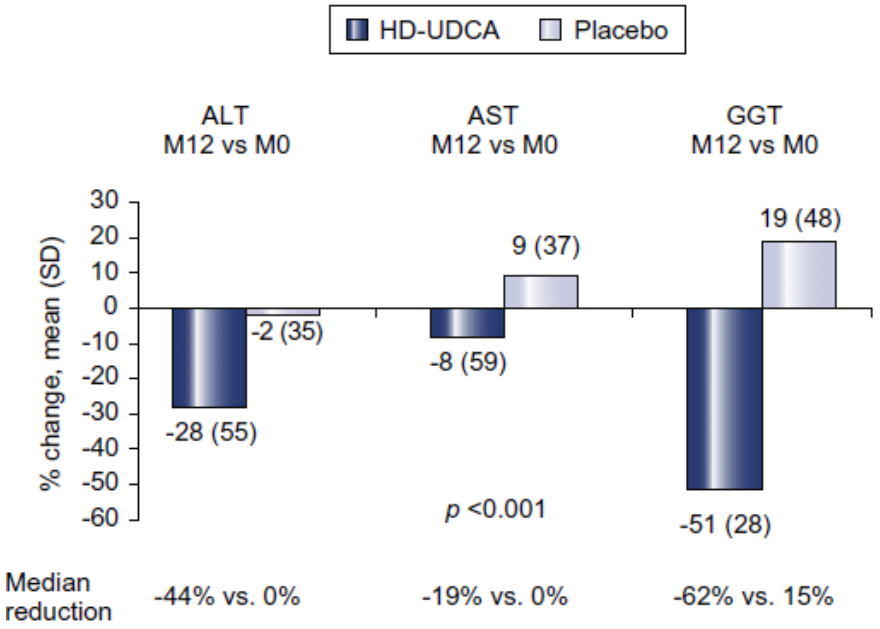
Kistler, AJG 2011

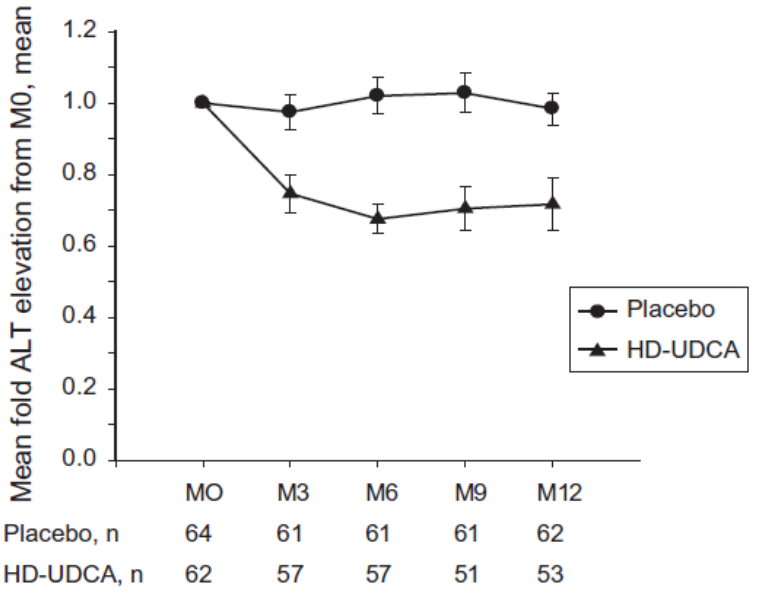
Traitements médicamenteux

- **Glitazones**
- **Vitamine E**
- **Sartan**
- **AUDC**
- **…**

- **Autres :**
  - Alcool
  - Café
  - Tabac

Acide UrsoDésoxycholique



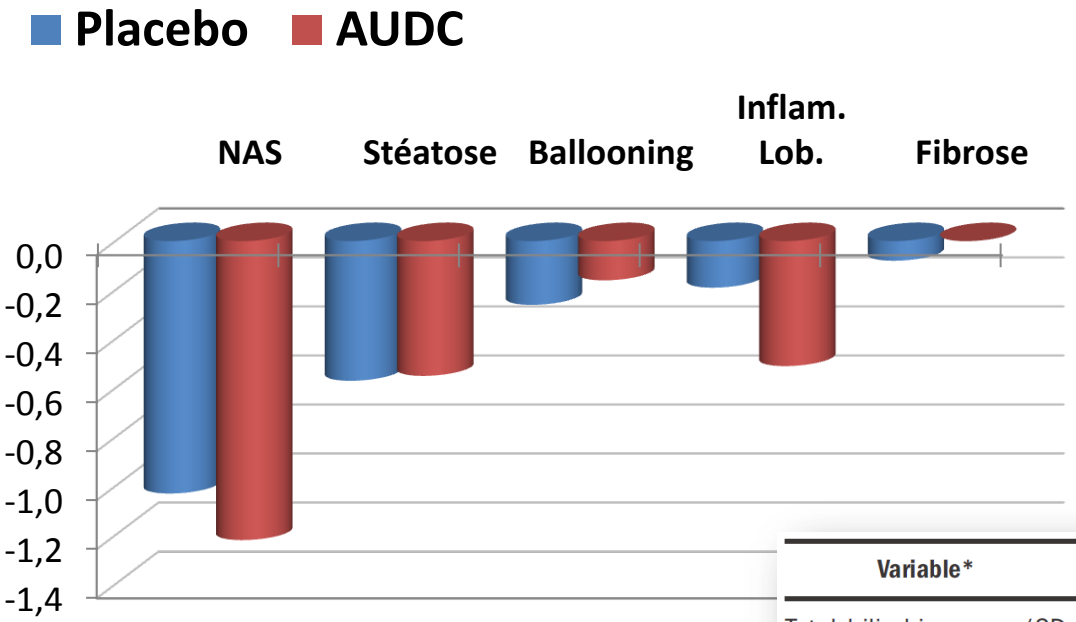


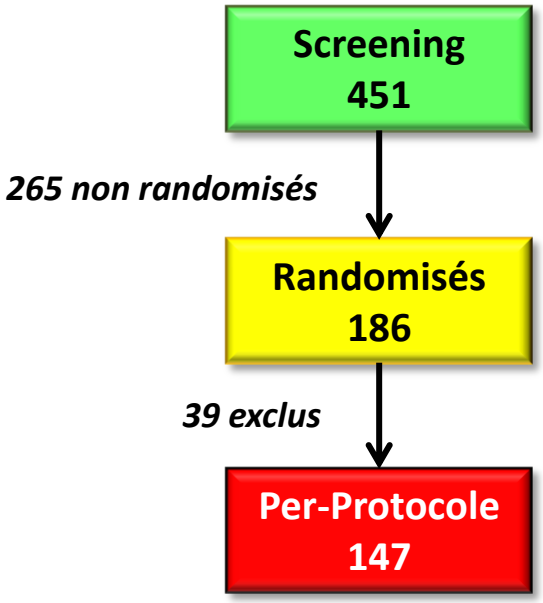
Parameter	HD-UDCA	Placebo	*p*
Serum glucose level	-2.2	+3.9	0.002
HbA1c level	-2.3	+5.2	<0.001
Insulin level	-19	-0.2	0.038
HOMA score	-20	+6	<0.009

*Percent relative change between baseline median values and M12.

Ratziu, J Hepatol 2011

Acide UrsoDésoxycholique





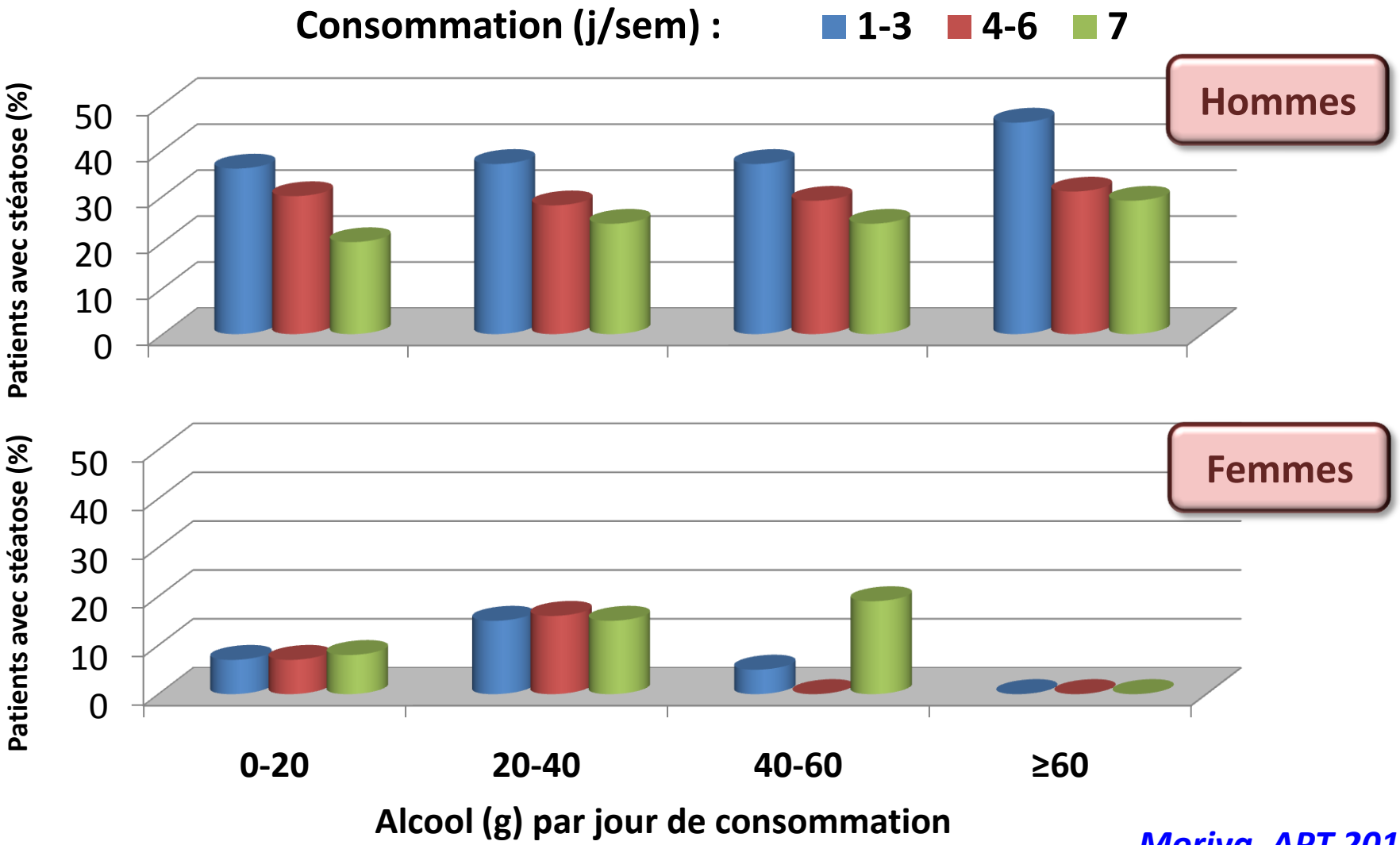
Variable*	UDCA	Placebo	*P* Value
Total bilirubin, mean/SD	0.15/0.89	−0.24/0.91	0.061
AST, mean/SD	−16.46/30.83	−14.30/28.84	0.917
ALT, mean/SD	−40.63/58.37	−38.15/62.60	0.851
AP, mean/SD	−10.52/47.65	−9.43/43.88	0.792
GGT, mean/SD	−52.42/64.19	−16.84/53.98	<0.0001
Albumin, mean/SD	0.22/3.62	−0.66/4.26	0.289
Triglycerides, mean/SD	−0.18/1.19	−0.17/1.21	0.828
Cholesterol, mean/SD	−85.09/109.04	−88.29/105.53	0.973
Glucose, mean/SD	−0.19/2.24	−0.08/2.49	0.193
Iron, mean/SD	−0.31/7.83	−0.58/7.50	0.530

Leuschner, Hepatology 2011

Etude de Leuschner

- Beaucoup d'exclus
- AUDC : 23 - 28 mg/kg
- Critères d'évaluation semi-quantitatifs
- Groupe placebo ?
- Effet métabolique ?

Alcool et NAFLD

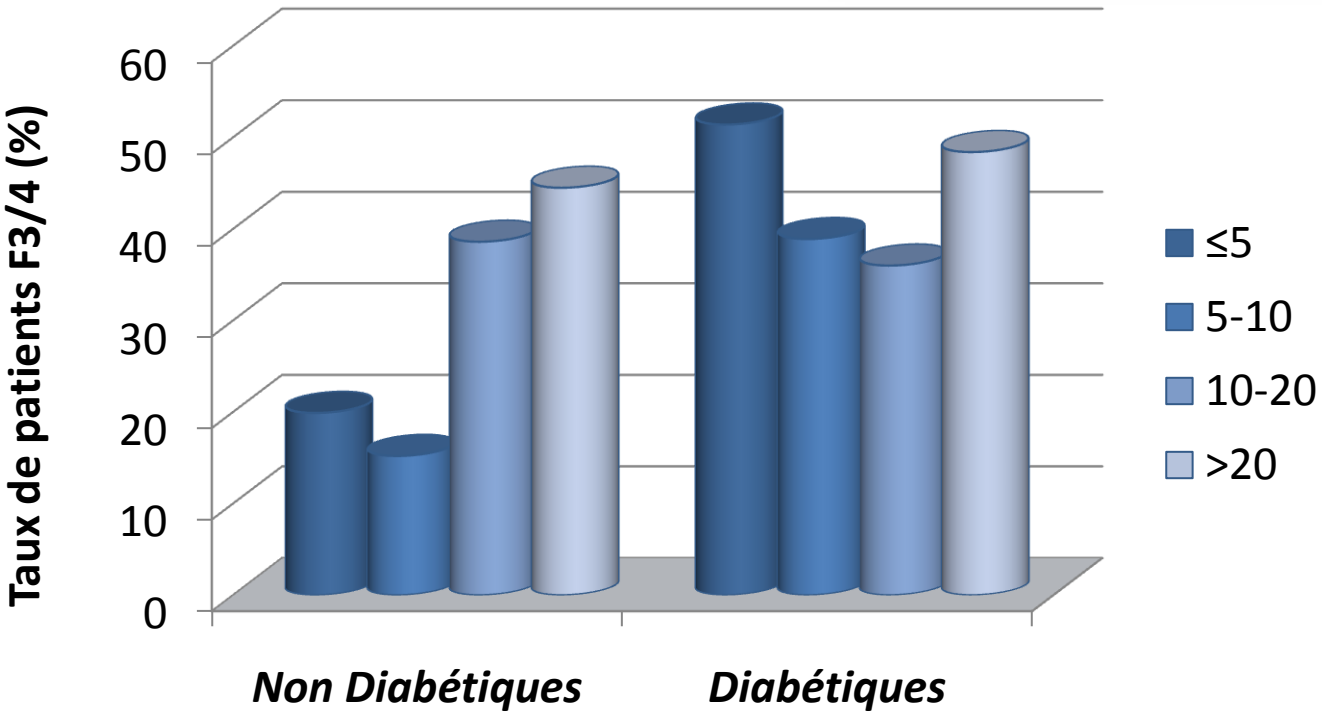


Moriya, APT 2011

Tabac et NAFLD

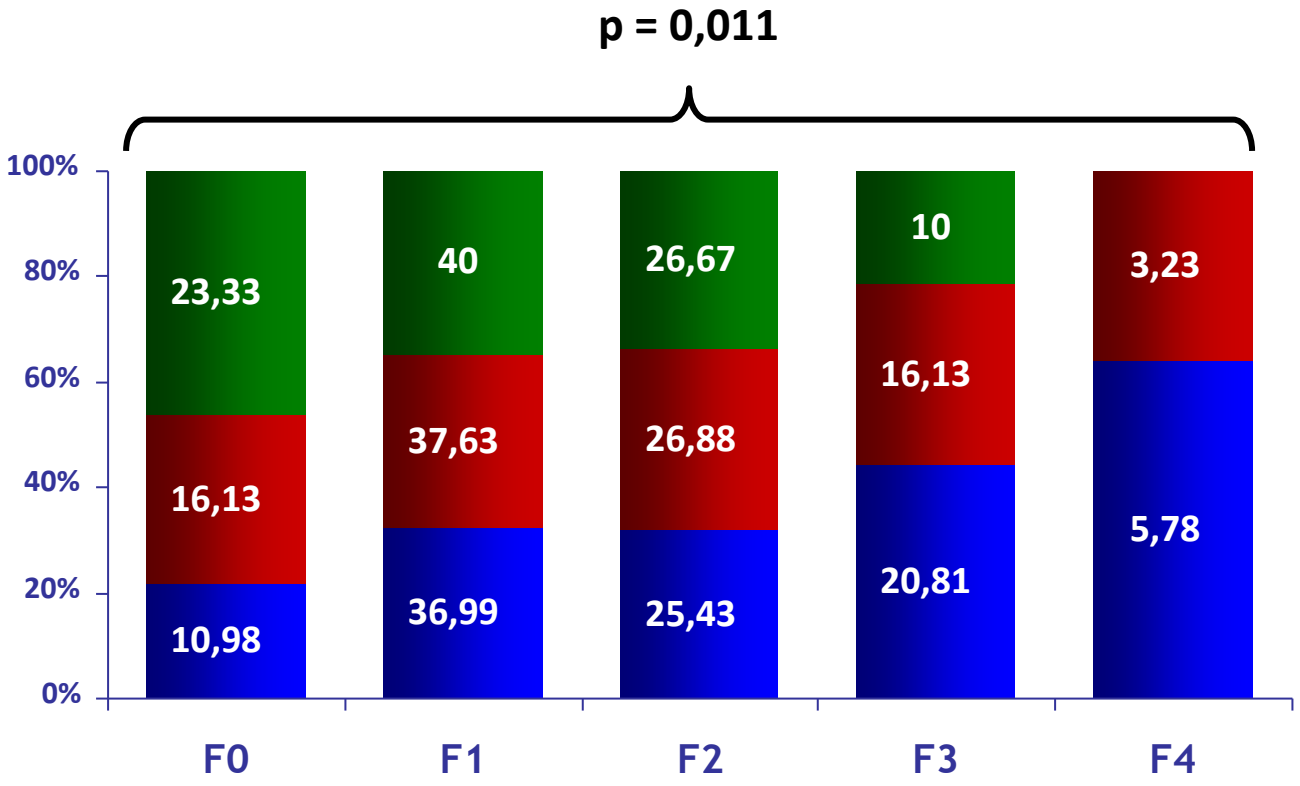
1091 patients NAFLD
Facteurs associés à F3/4

	OR (95% CI)	*p*-value
History of ≥10 vs. <10 pack-years of smoking	1.63 (1.19-2.24)	0.003
Age, years	1.06 (1.04-1.07)	<0.0001
DM, yes vs. no	2.44 (1.83-3.26)	<0.0001
Alcohol use, not lifetime abstinent versus lifetime abstinent	0.62 (0.46-0.82)	0.0008



Zein, J Hepatol 2011

Café et Fibrose dans la NAFLD



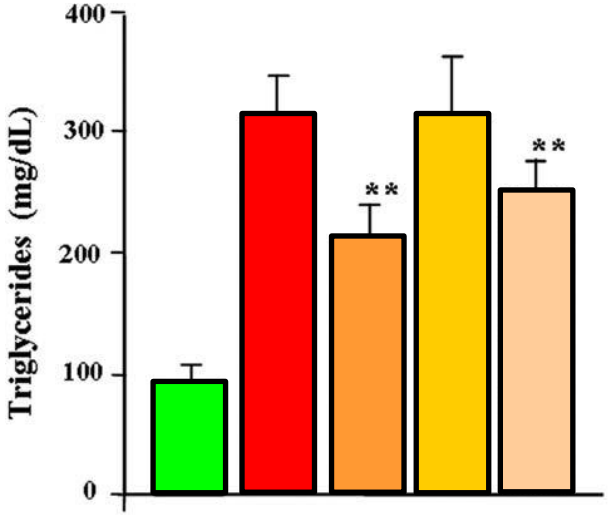
296 patients NASH

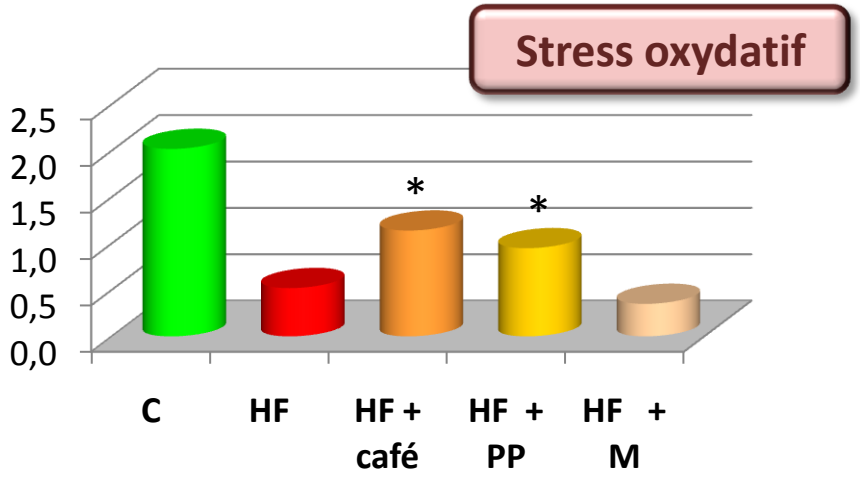
- < 7 tasses/sem.
- 7-14 tasses/sem.
- > 14 tasses/sem.

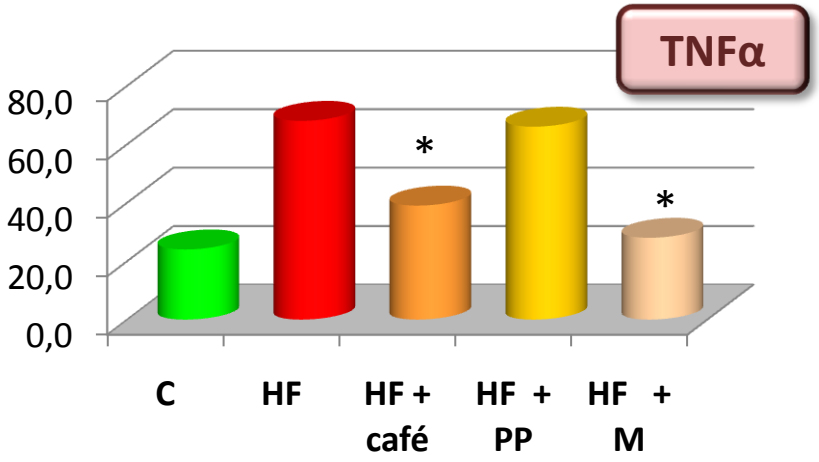
L'analyse du profil d'expression des gènes chez 48 patients a retrouvé une augmentation de l'expression de certains cytochromes (CYP 3A7, 7B1 et 26A1) et de l'enzyme UGT1 dont l'activité pourrait optimiser le métabiolisme lipidique

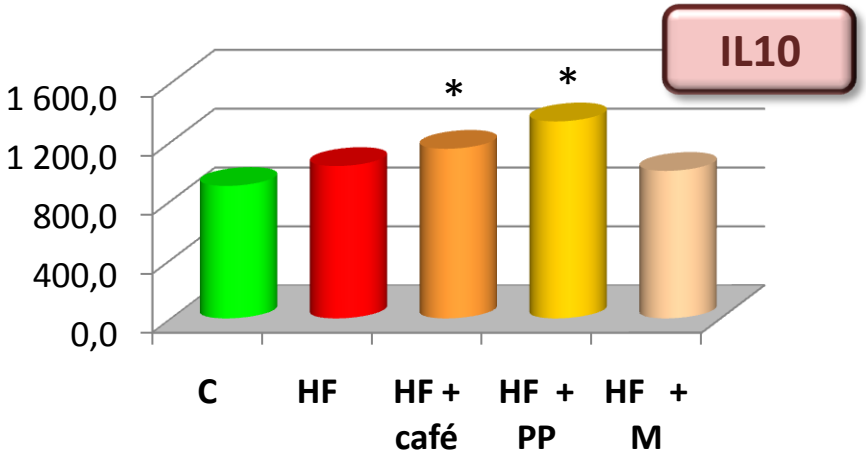
Tillman, EASL 2011

Café et NAFLD



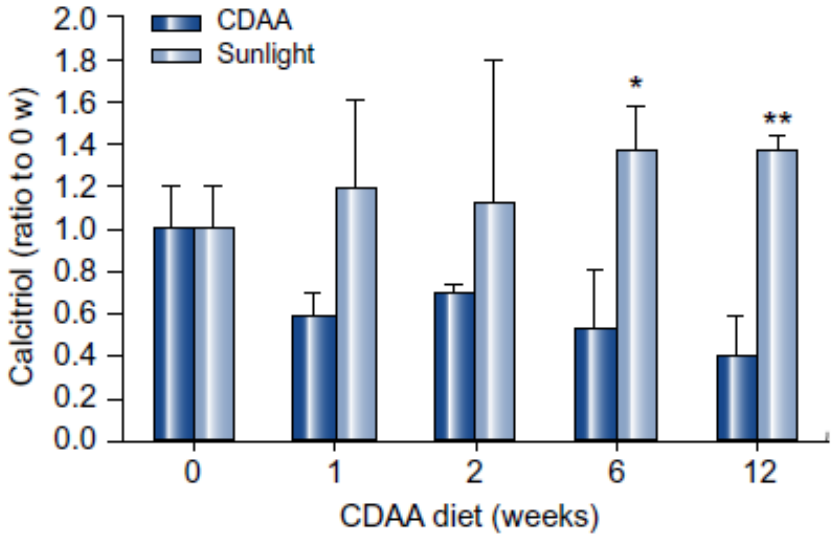


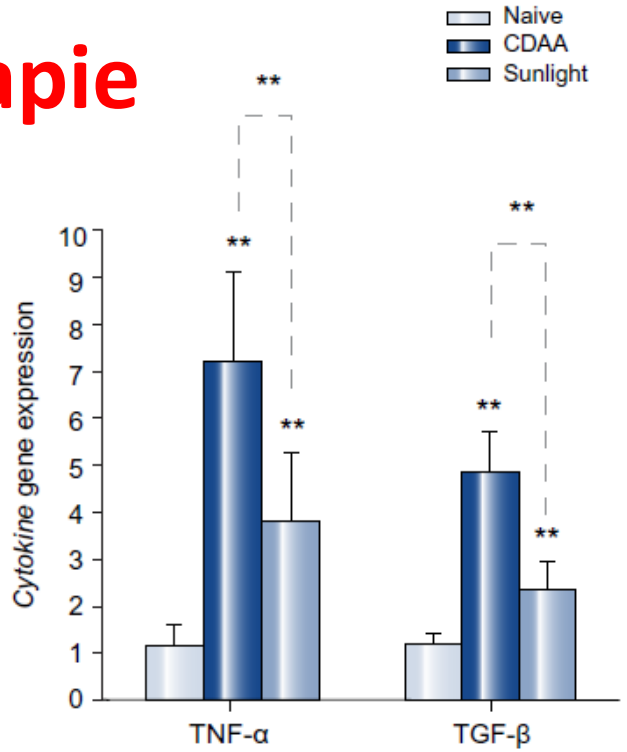


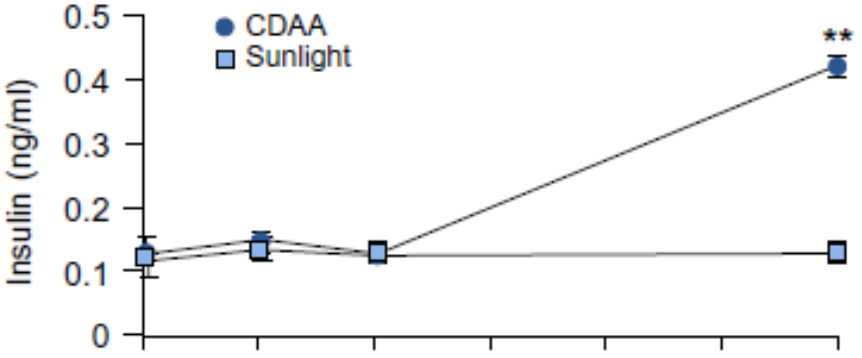


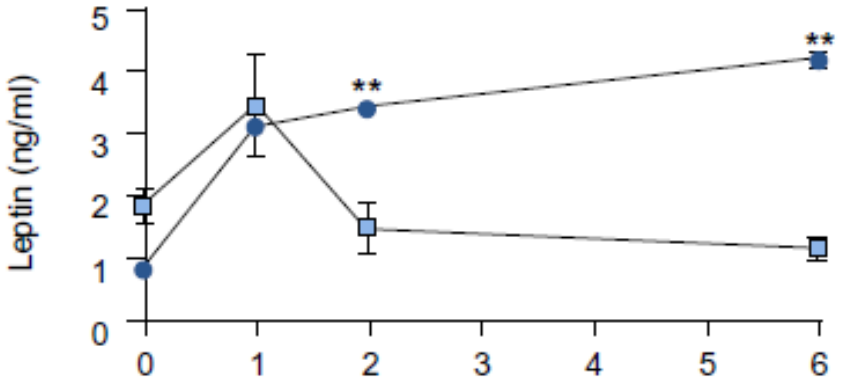
Vitaglione, Hepatology 2010

Luminothérapie









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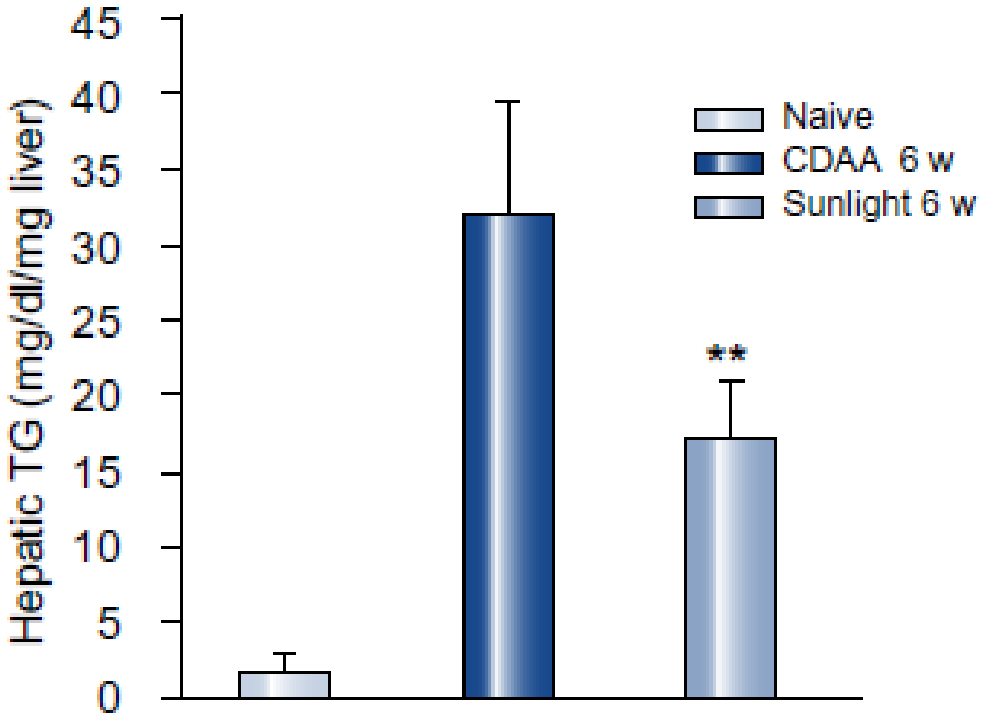

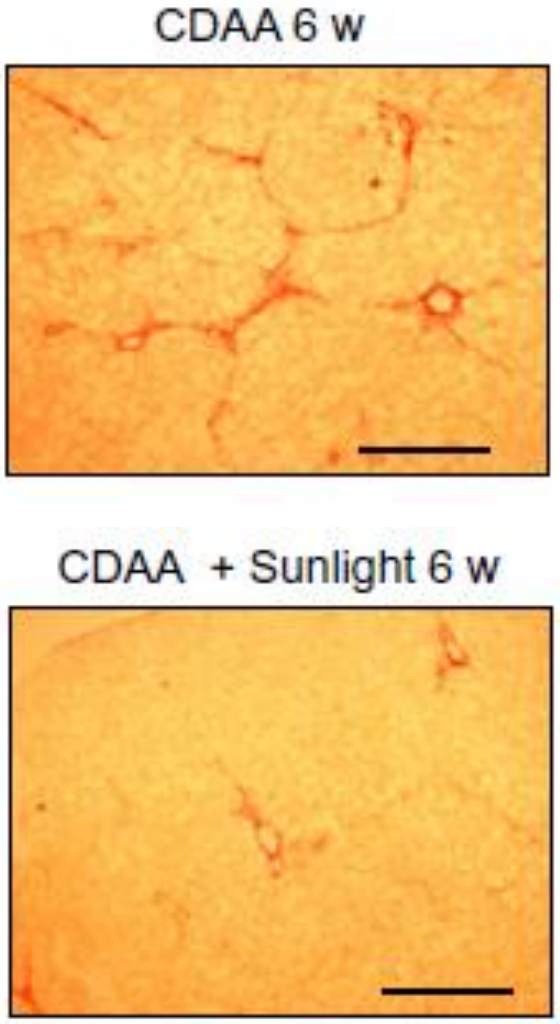

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