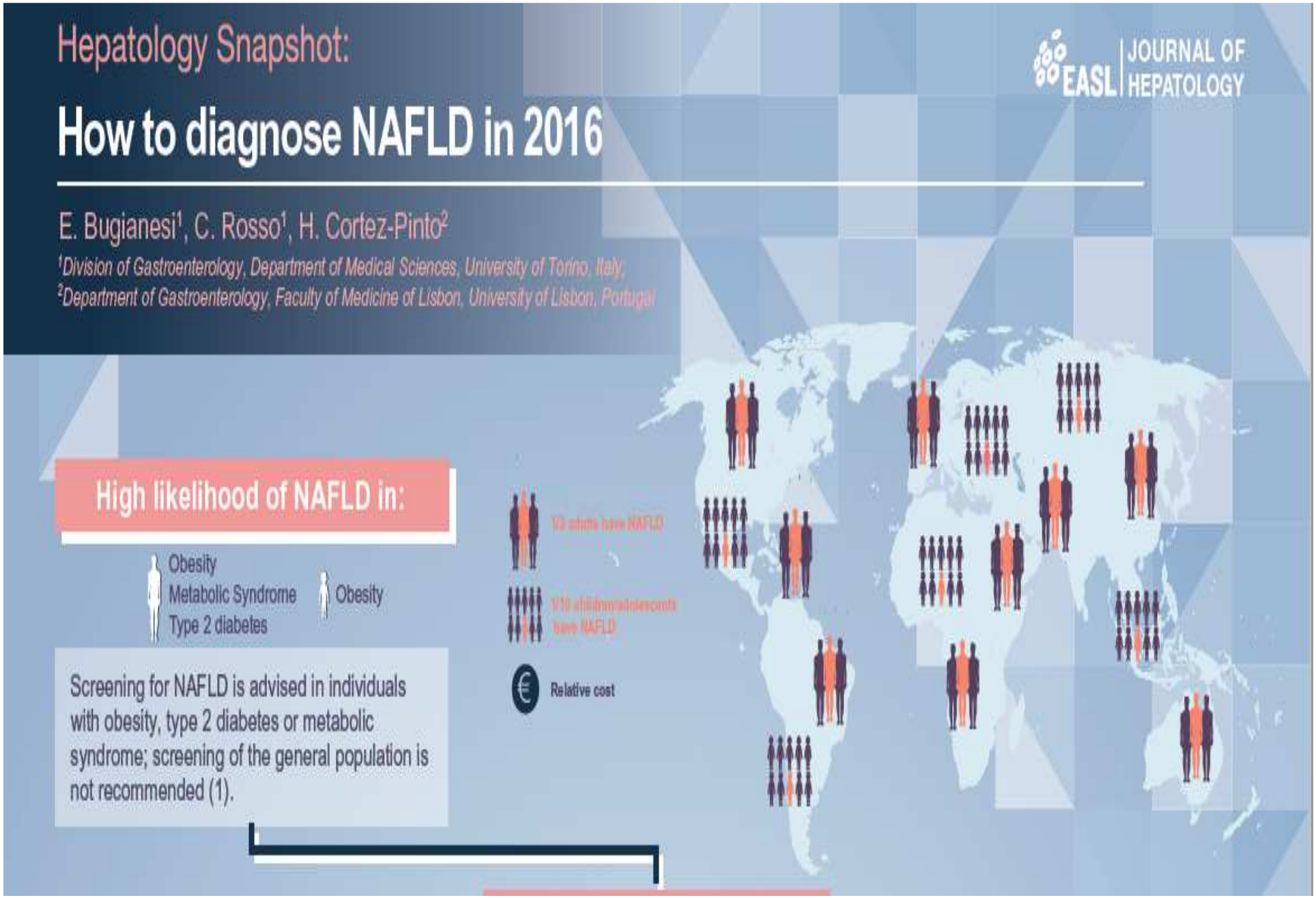
O FANTASMA DA ESTEATOSE HEPÁTICA

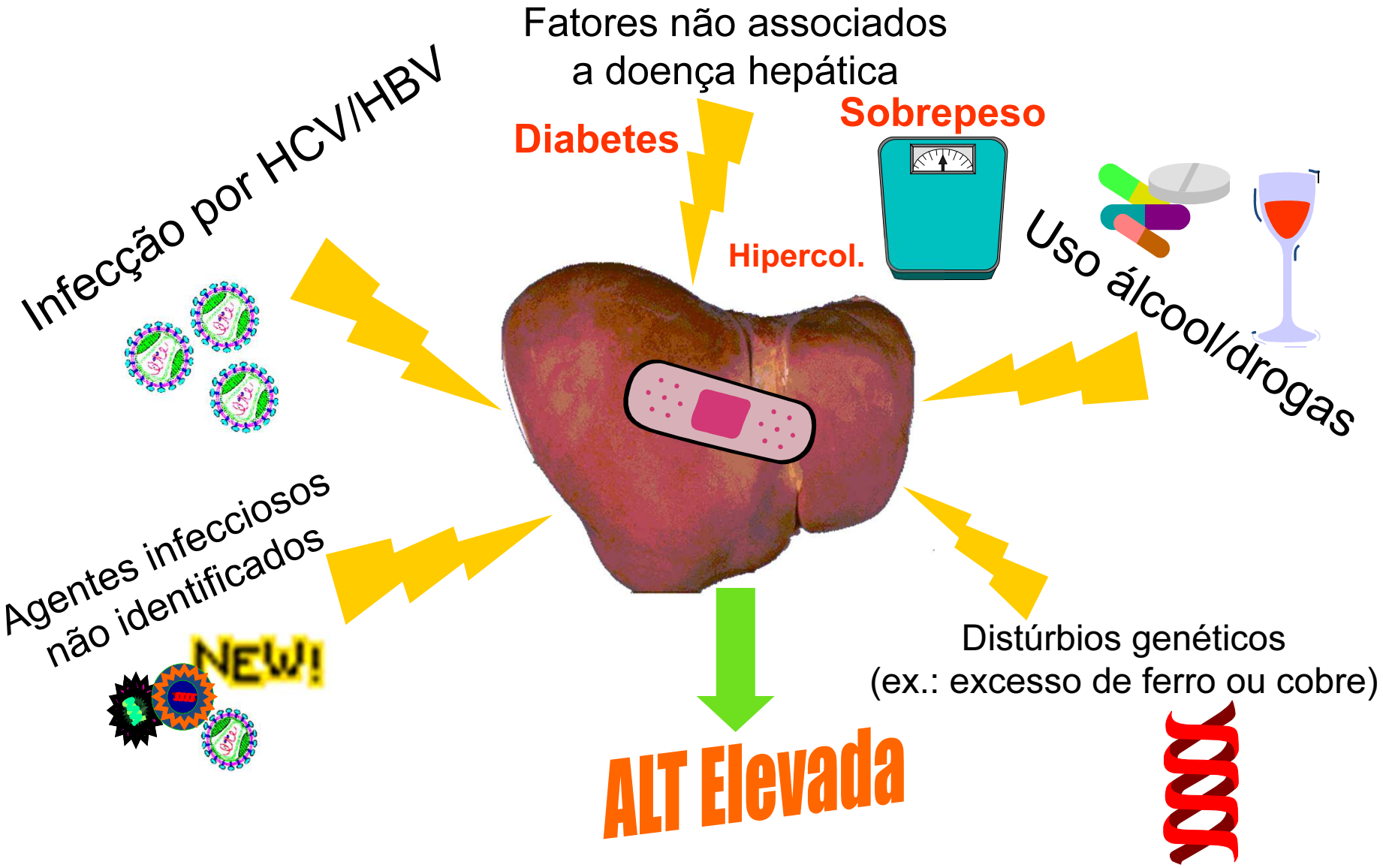
Nilma Lúcia Sampaio Ruffeil

São Paulo
14/09/2016

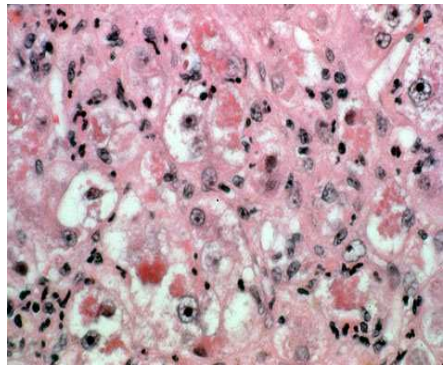


Journal of Hepatology **2016** vol. 65 | 643-644

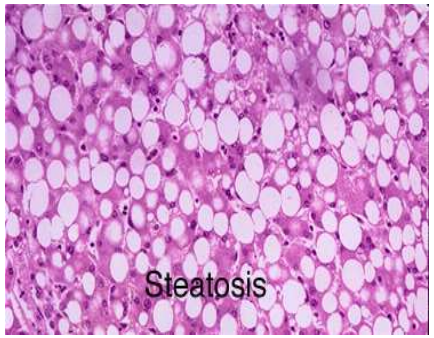
Fatores que podem lesar o fígado



Doença Hepática Gordurosa Não Alcoólica



•Ludwig et al., 1980 - **esteato-hepatite não alcoólica** (NASH) esteatose com inflamação e balonização dos hepatócitos, com ou sem fibrose, na ausência de alcoolismo e hepatite viral que justifiquem o quadro**.**



NASH e esteatose não alcoólica (EH) apresentam muitos pontos em comum (pacientes obesos, diabéticos e hiperlipêmicos, além de fatores patogênicos) - **DHGNA**

•EH pura apresenta maior prevalência e parece ser uma doença auto-limitada, NASH potencial evolutivo para cirrose (20%-30% casos.)

•Em 1990 houve primeiro relato de HCC relacionado com **DHGNA**

Insulin resistance index (HOMA-IR) in the differentiation of patients with non-alcoholic fatty liver disease and healthy individuals

(Arq Gastroenterol 2010*)*

Salgado AL, Carvalho L, Leite-Mor M, Santos VN, Uezato NT, Vieira J G, Parise ER

Characteristics	Control Group	NAFLD Group	P
N	88	116	
Age	42.3 ± 11.7	41.2 ± 11.0	0.488
Male gender	54	86	0.075
BMI	20.41 ± 0.31	30.05 ± 0.51	<0.001
Glucose	84.7 ± 6.8	94.5 ± 9.9	<0.001

FIGURE 1A. Comparative values for glucose levels during oral tolerance test in control and NAFLD groups

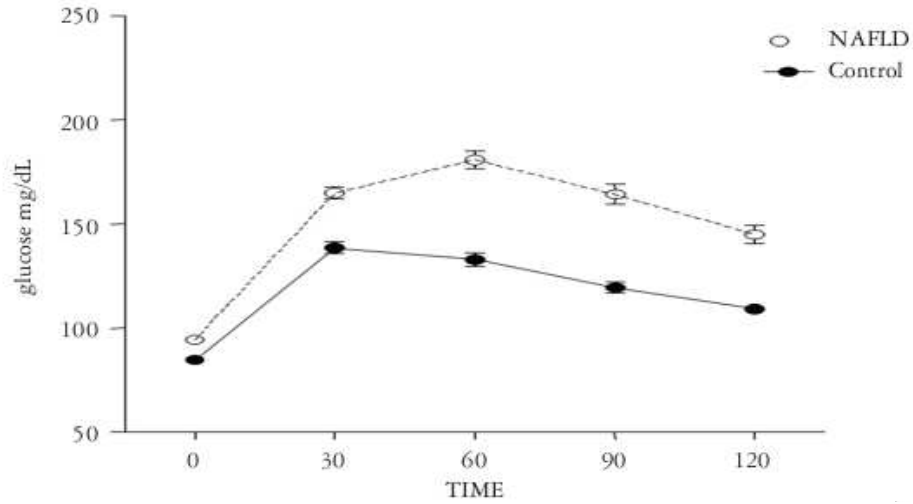
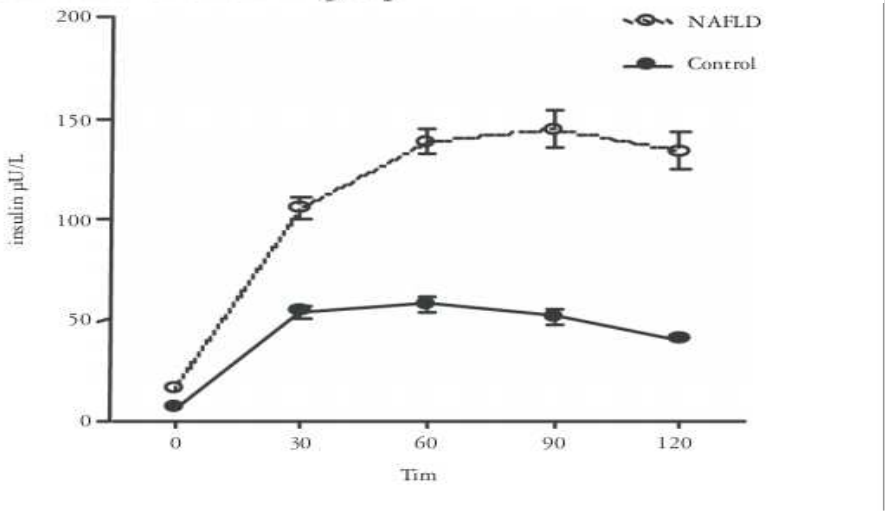
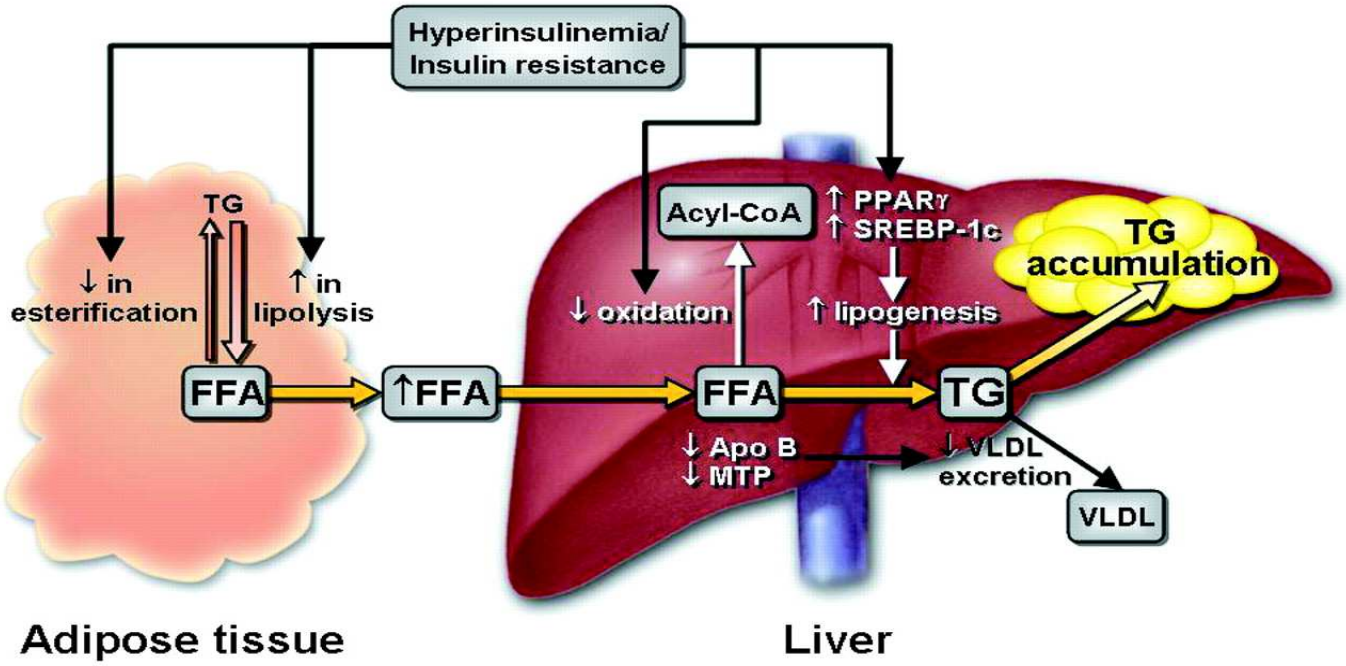


FIGURE 1B. Comparative values for insulin levels during oral tolerance test in control and NAFLD groups



ESTEATOSE HEPÁTICA NA DHGNA

Mecanismo de ação da insulina



Prevalência Esteatose

- População urbana EUA
- Esteatose avaliada por RM espectroscopia
- N=2287

Table 2. Hepatic Triglyceride Content and Percent of Subjects With Hepatic Steatosis in the Three Major Ethnic Groups

Ethnicity	n	Hepatic Triglyceride Content, %	Hepatic Steatosis, %
Hispanic			
Men	172	4.6 (2.7–11.9)	45
Women	229	4.6 (2.6–9.9)*	45*
All	401	4.6 (2.6–10.7)	45
White			
Men	375	4.4 (2.4–8.6)	42
Women	359	3.0 (1.9–5.3)	24
All	734	3.6 (2.1–7.3)	33
Black			
Men	499	3.2 (2.0–5.3)†	23†
Women	606	3.3 (1.9–5.3)	24
All	1105	3.2 (2.0–5.3)	24
All	2,287	3.6 (2.1–6.6)	31

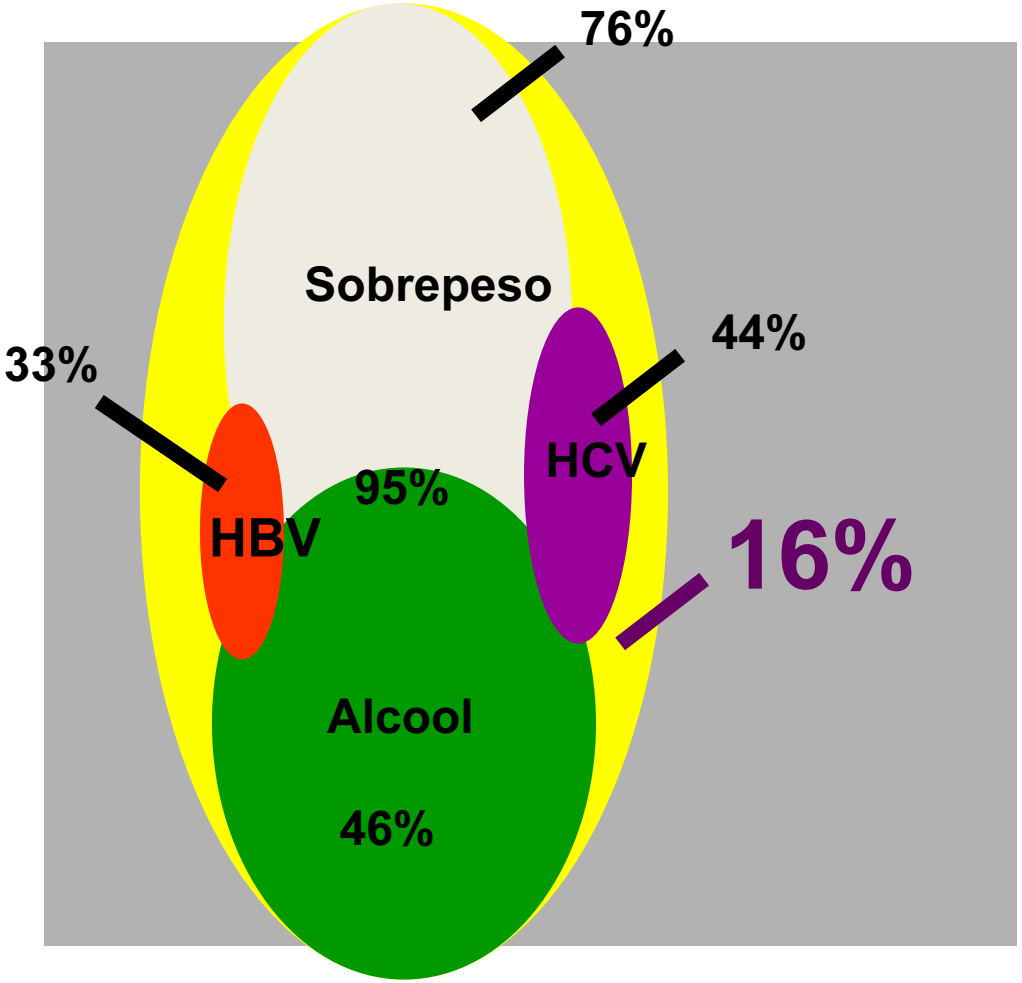
NOTE. Medians are presented with interquartile ranges in parentheses. Other values indicate prevalence.

*Significantly different from women in the other ethnic groups.

†Significantly different from men in the other ethnic groups.

Browning et al. Hepatology,2004

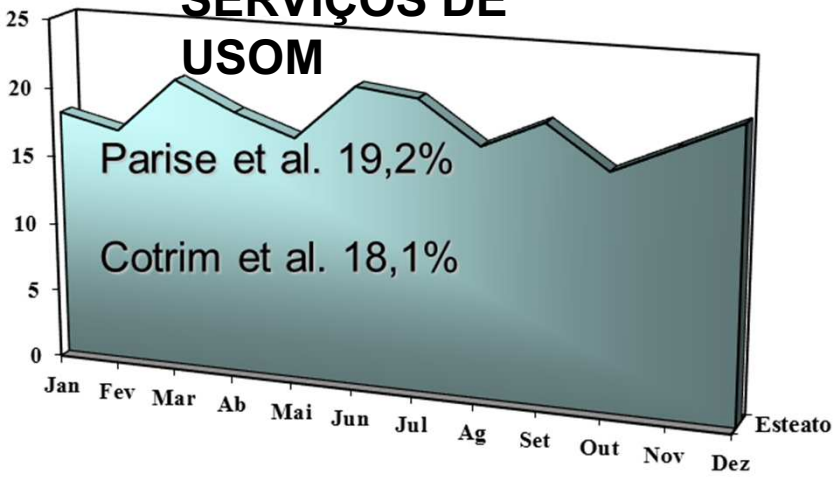
Prevalência de Esteatose (ultra-som)



Bellentani, Dionysos Study, J Hepatol 2001

Prevalência de DHGNA NO BRASIL

SERVIÇOS DE USOM



NÚMERO DE EXAMES

= 9345 *Parise et al. 2001*

= 11474 *Cotrim et al 2009*

Parise et al. Arq Gastroenterol 2001
Cotrim HP et al.. Gaz Med Bahia/2011

14000 EXECUTIVOS

35% ESTEATOSE

15%

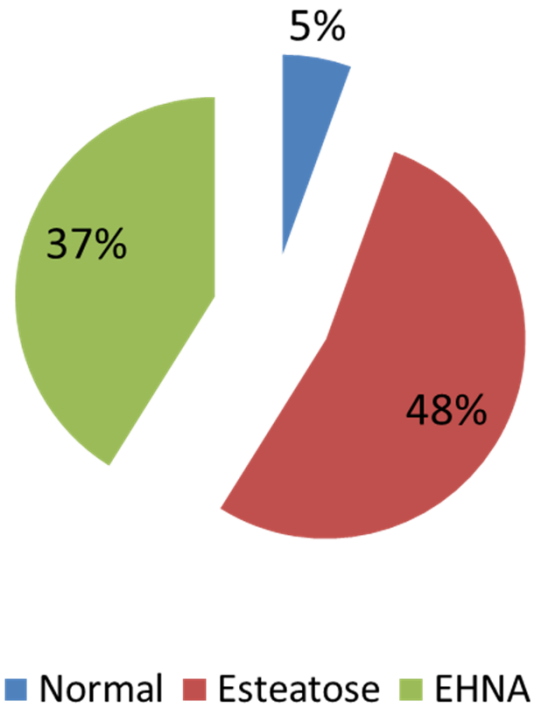
AUDIT>8+ HCV

28% ESTEATOSE NÃO ALCOOL.

Fatores Associados
Sdme Metabólica
Idade >45 a
IMC>25

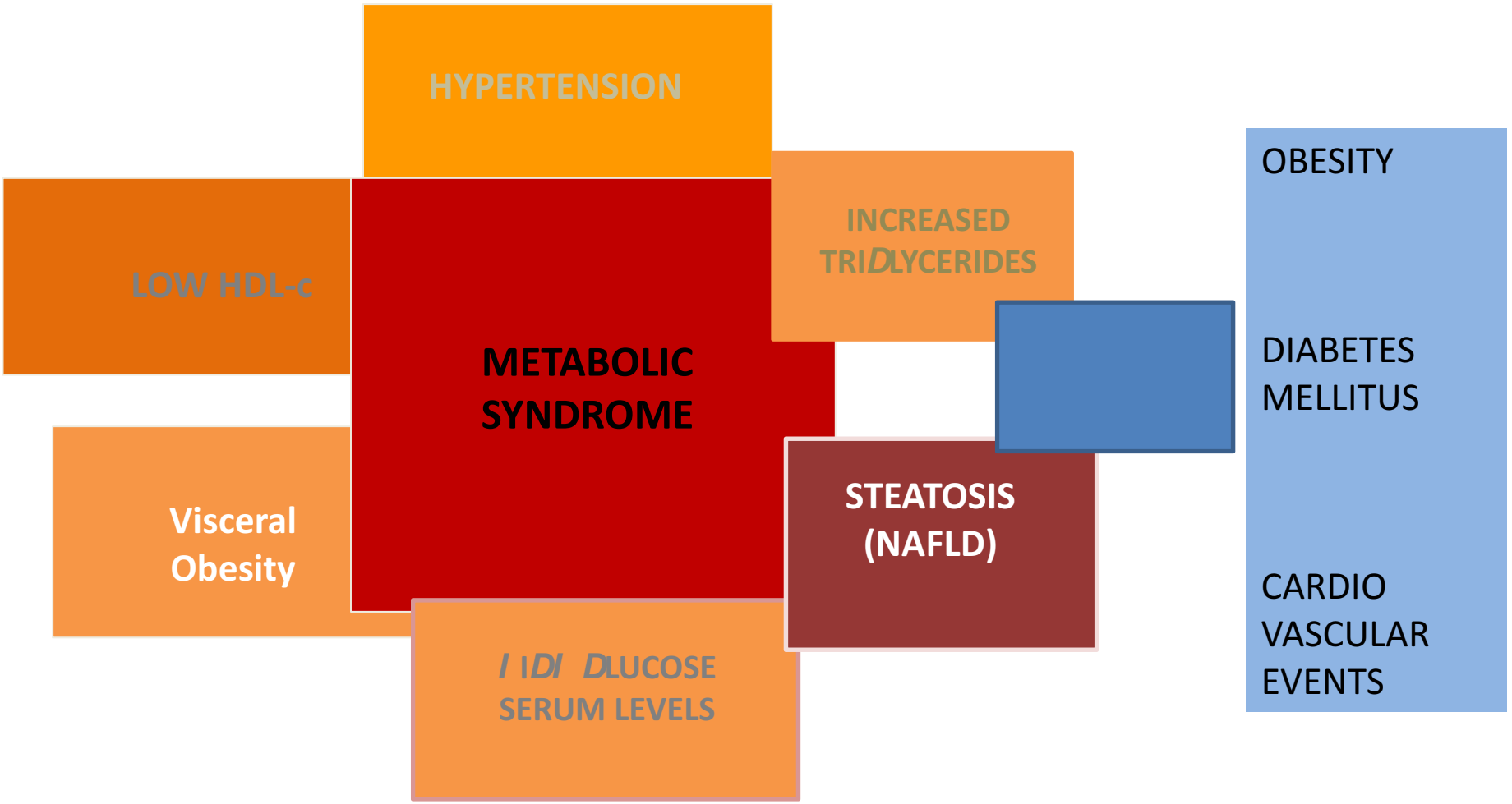
Conceição et al 2007

Cirurgia Bariátrica n= 400



Congresso SBH 2009

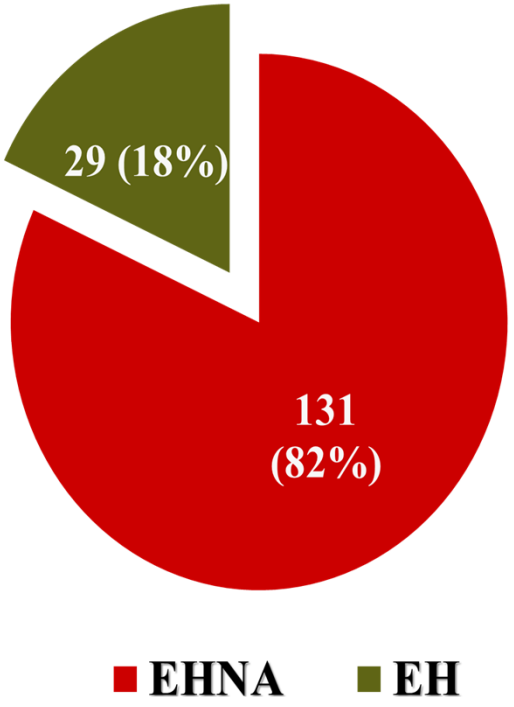
NAFLD – The Hepatic Manifestation of Metabolic Syndrome



Características da População Estudada (n= 263)

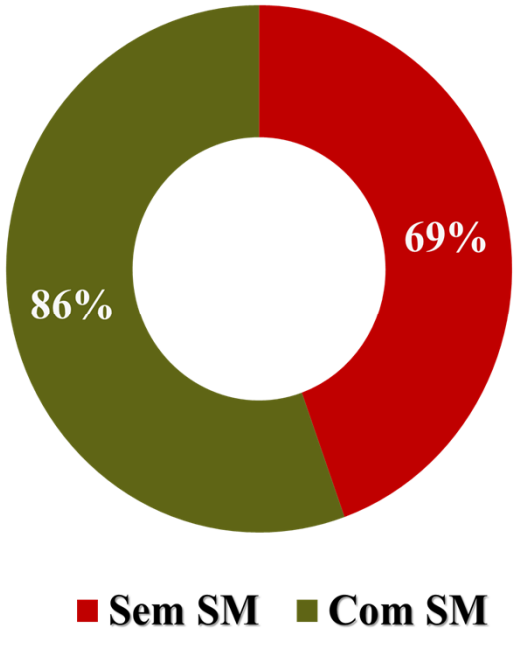
Parâmetro avaliado	Resultado
Idade (anos: média ± DP)	55,8 ± 10,5
Gênero Feminino	68%
Presença de SM	79%
Biópsia Hepática	61%
EH histológica	18%
EHNA	82%

Classificação Histológica da DHGNA



*C*ongresso SBH
2015

Prevalência de SM nos Pacientes com EHNA



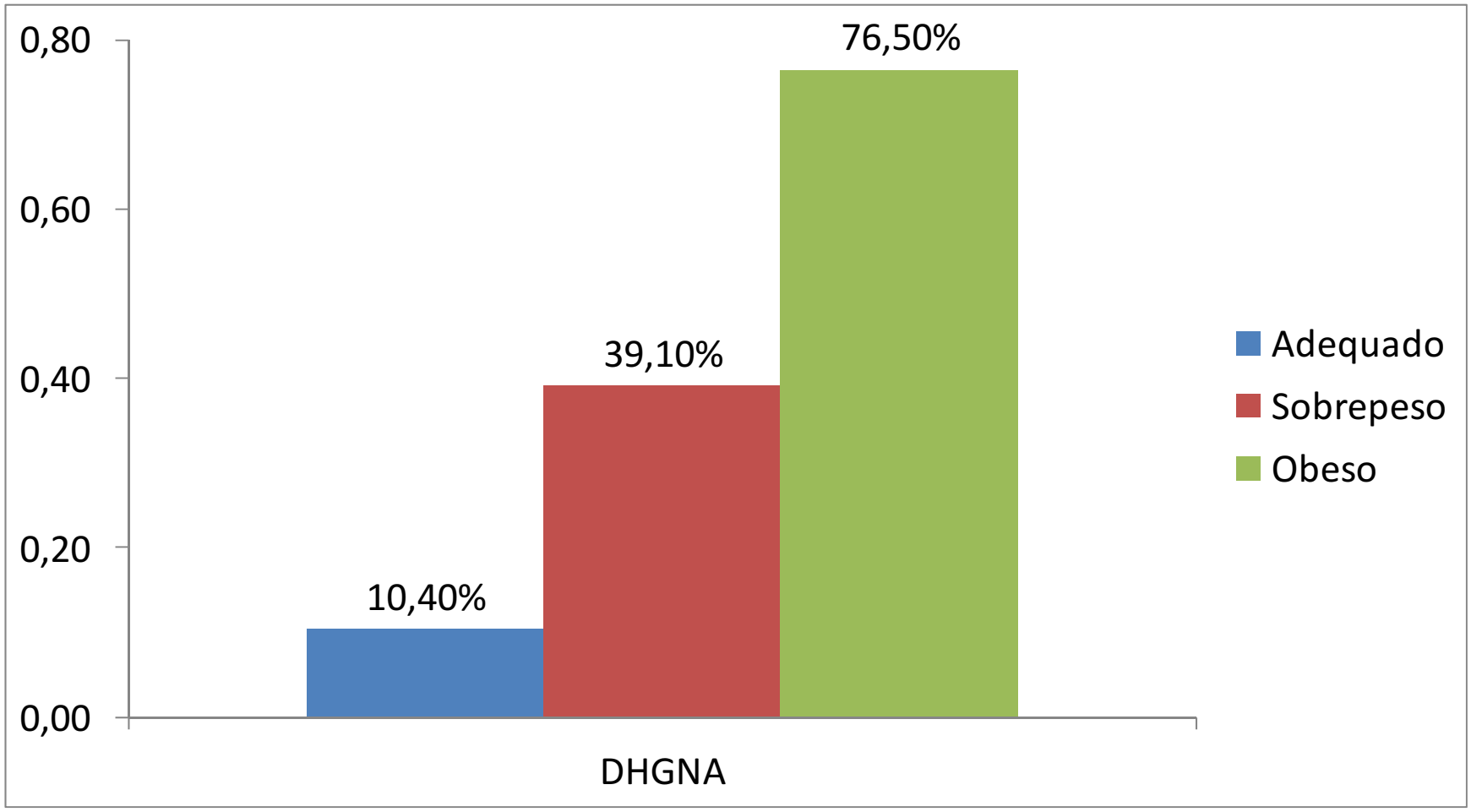
Changes in the Prevalence of the Most Common Causes of Chronic Liver Diseases in the United States from 1988 to 2008

Younossi ZM ,et al. **Clin Gastroenterol Hepatol**. *2011*

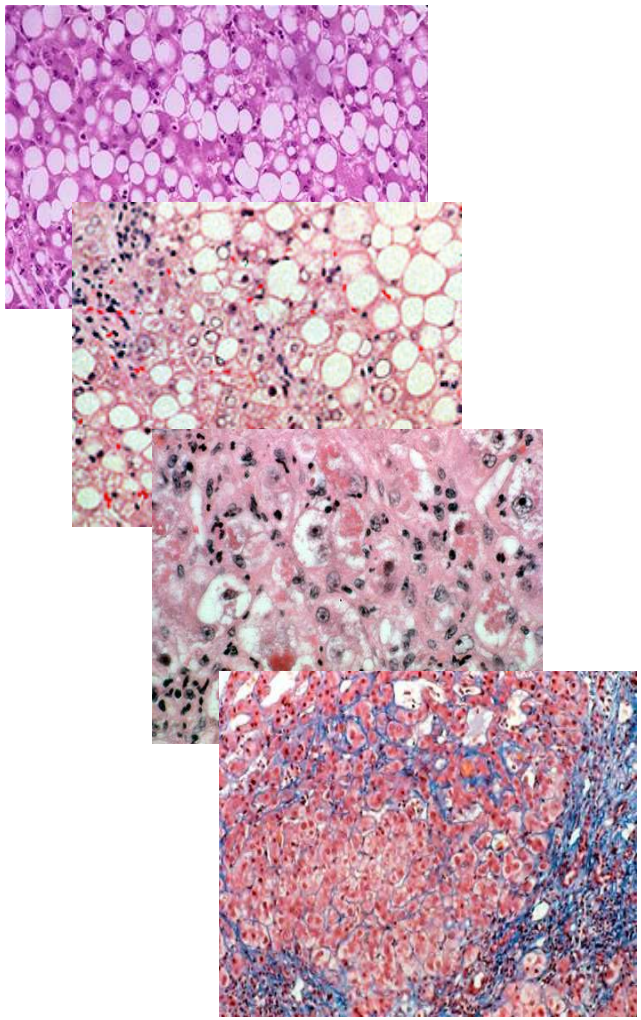
Prevalência	1988-1994	1999-2004	2005-2008
Hepatopatia cronica	11.78%	15.66%	14.78%
Hepatite B	0.36%	0.33%	0.34%
Hepatite C	1.95%	1.97%	1.68%
Álcool	1.38%	2.21%	2.05%
DHGNA	5.51%	9.84%	11.01%

Serologic and clinical data were used to establish the diagnoses of CLDs in 39,500 adults.

ESTEATOSE x ÍNDICE MASSA CORPORAL



EVOLUÇÃO DA NAFLD



***FATORES GENÉTICO* = PNPLA3**

***FATORES ADQUIRIDOS* = DIETA E MICROBIOTA INTESTINAL**

POLIMORFISMO GENÉTICO

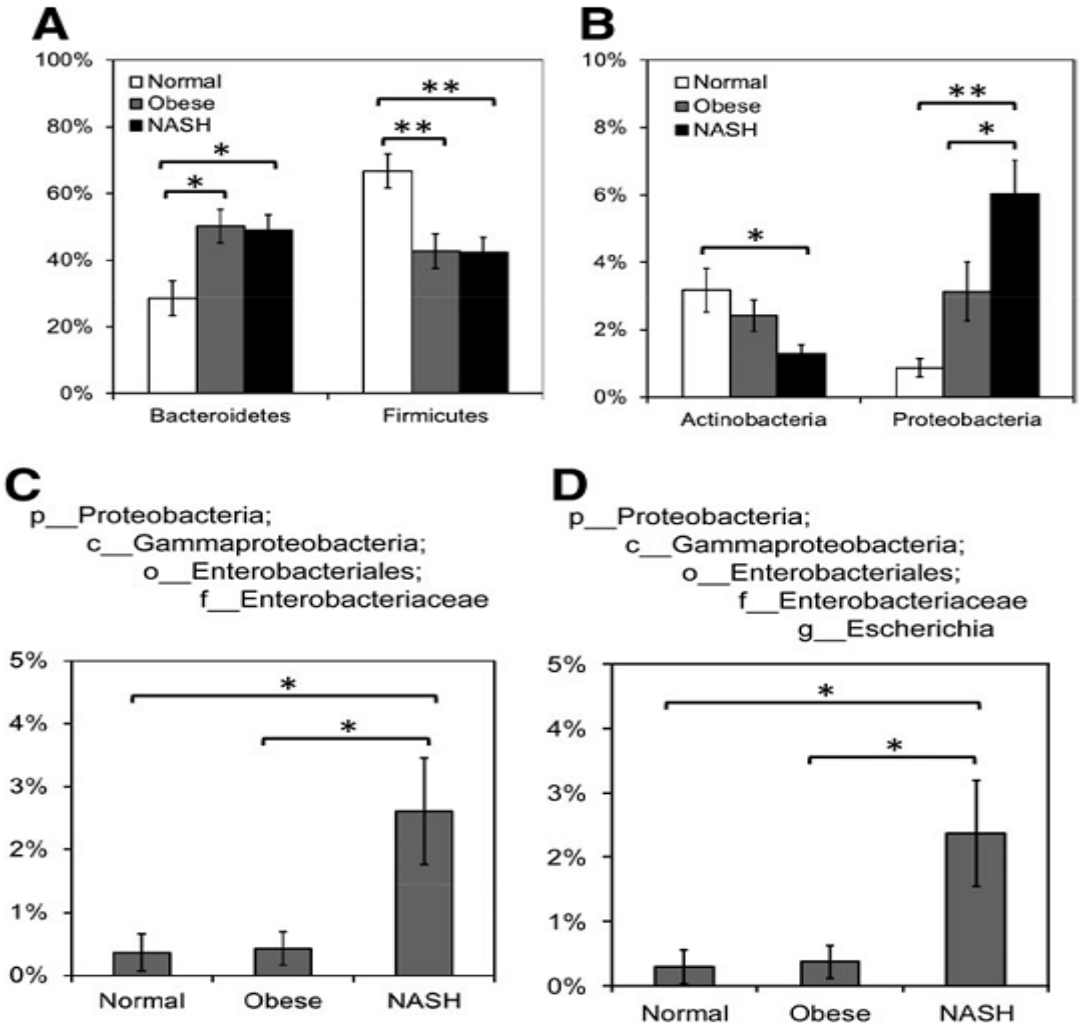
- **Journal of Hepatology**
  Volume 61, Issue 1, Pages 75–81, July 2014

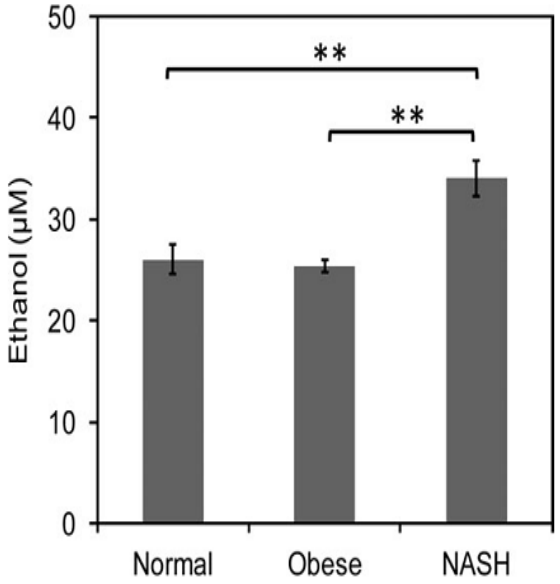
  Carriage of the *PNPLA3* rs738409 C >G polymorphism is not only associated with greater risk of progressive steatohepatitis and fibrosis but also of HCC. If validated, these findings suggest that *PNPLA3* genotyping has the potential to contribute to multi-factorial patient-risk stratification, identifying those to whom HCC surveillance may be targeted.

Characterization of Gut Microbiomes in Nonalcoholic Steatohepatitis (NASH) Patients: A Connection Between Endogenous Alcohol and NASH

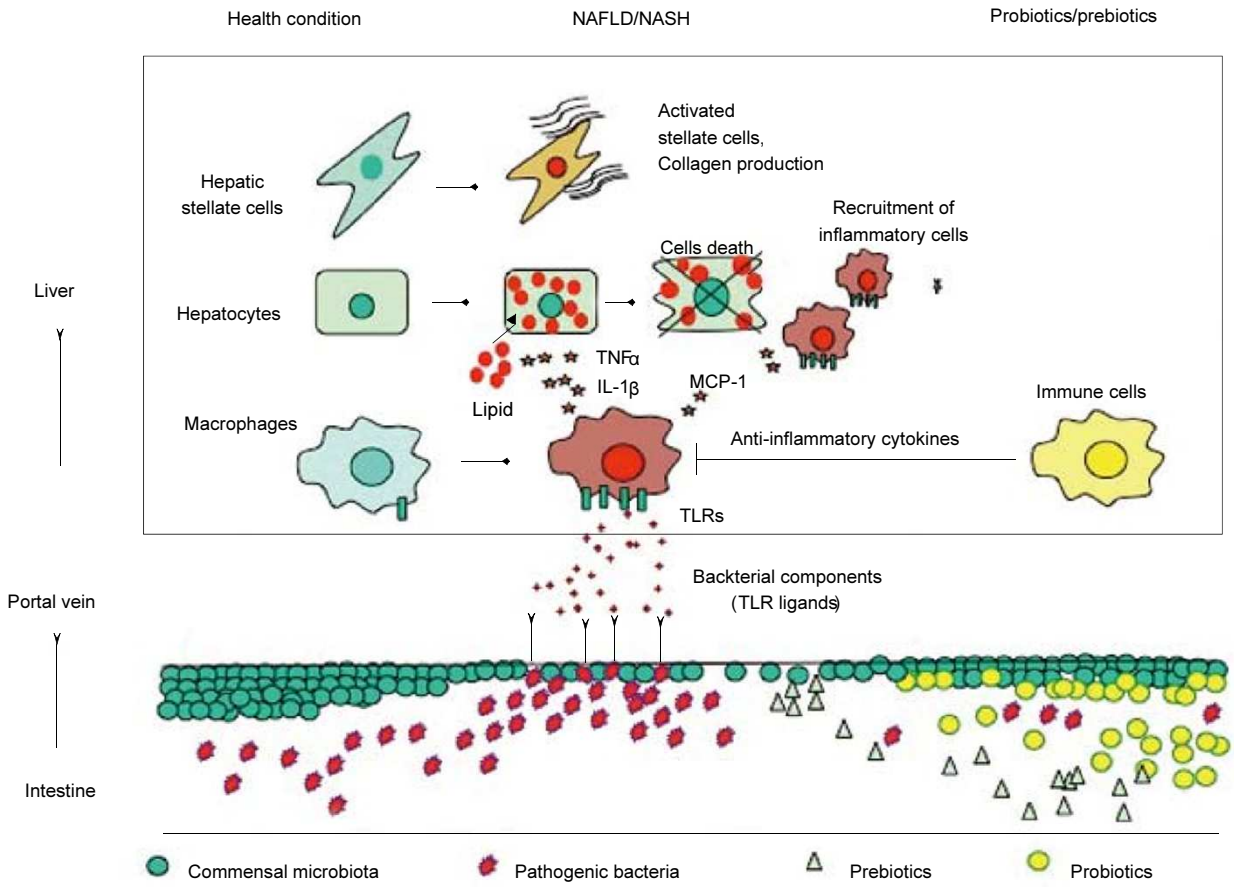
Lixin Zhu,[1] Susan S. Baker,[1] Chelsea Gill,[2] Wensheng Liu,[1] Razan Alkhouri,[1] Robert D. Baker,[1]

(HEPATOLOGY 2013;57:601-609)





MICROBIOTA INTESTINAL



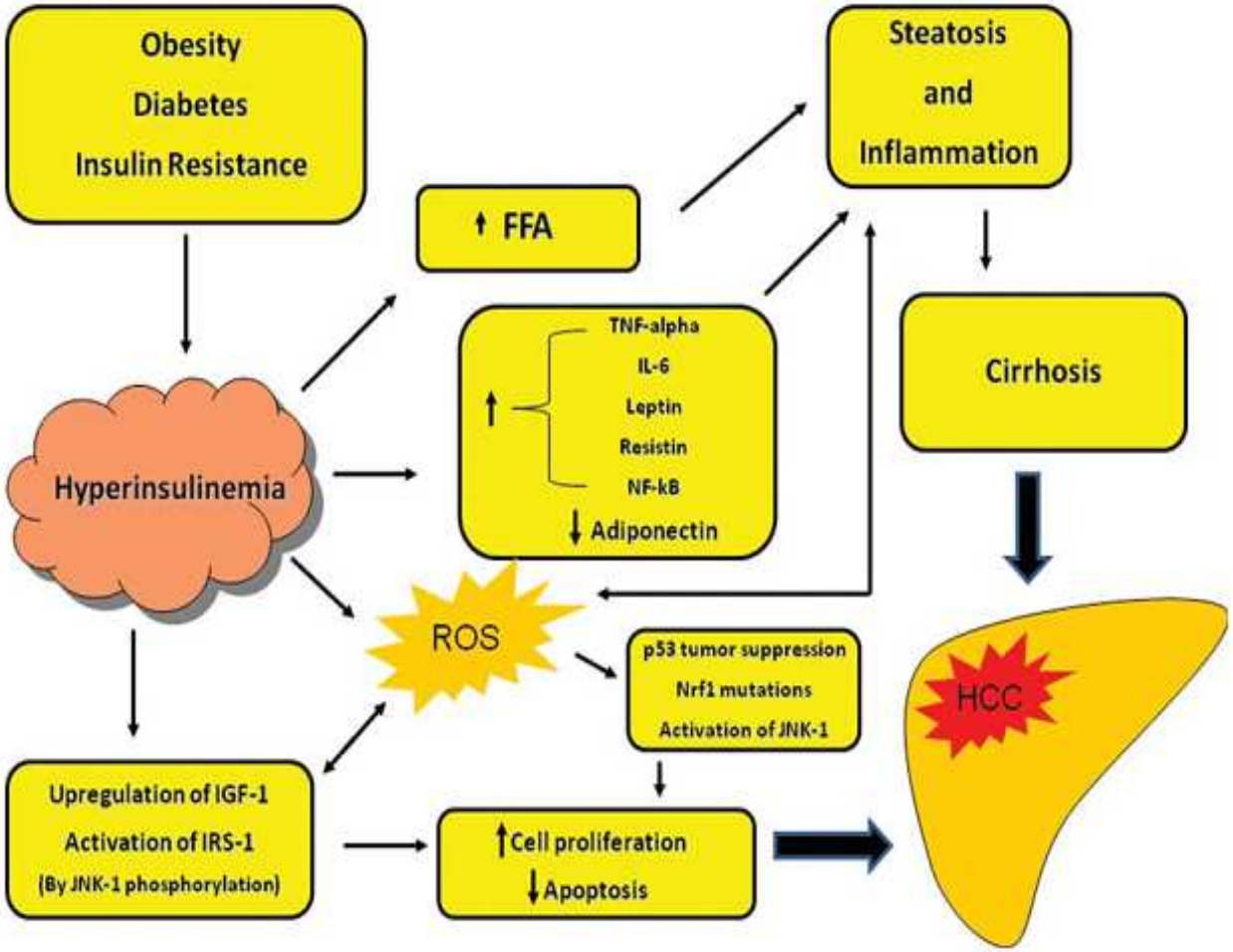
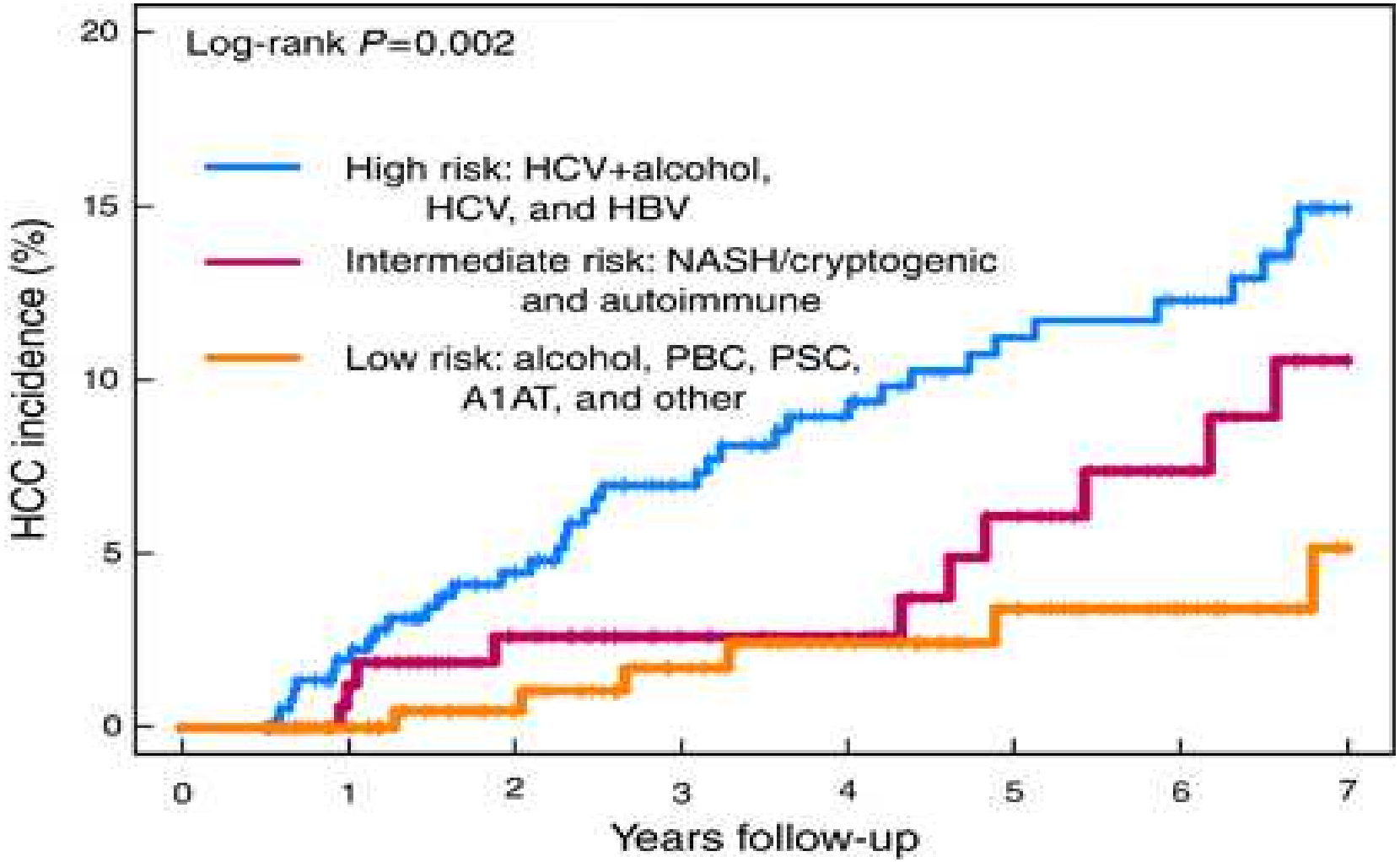


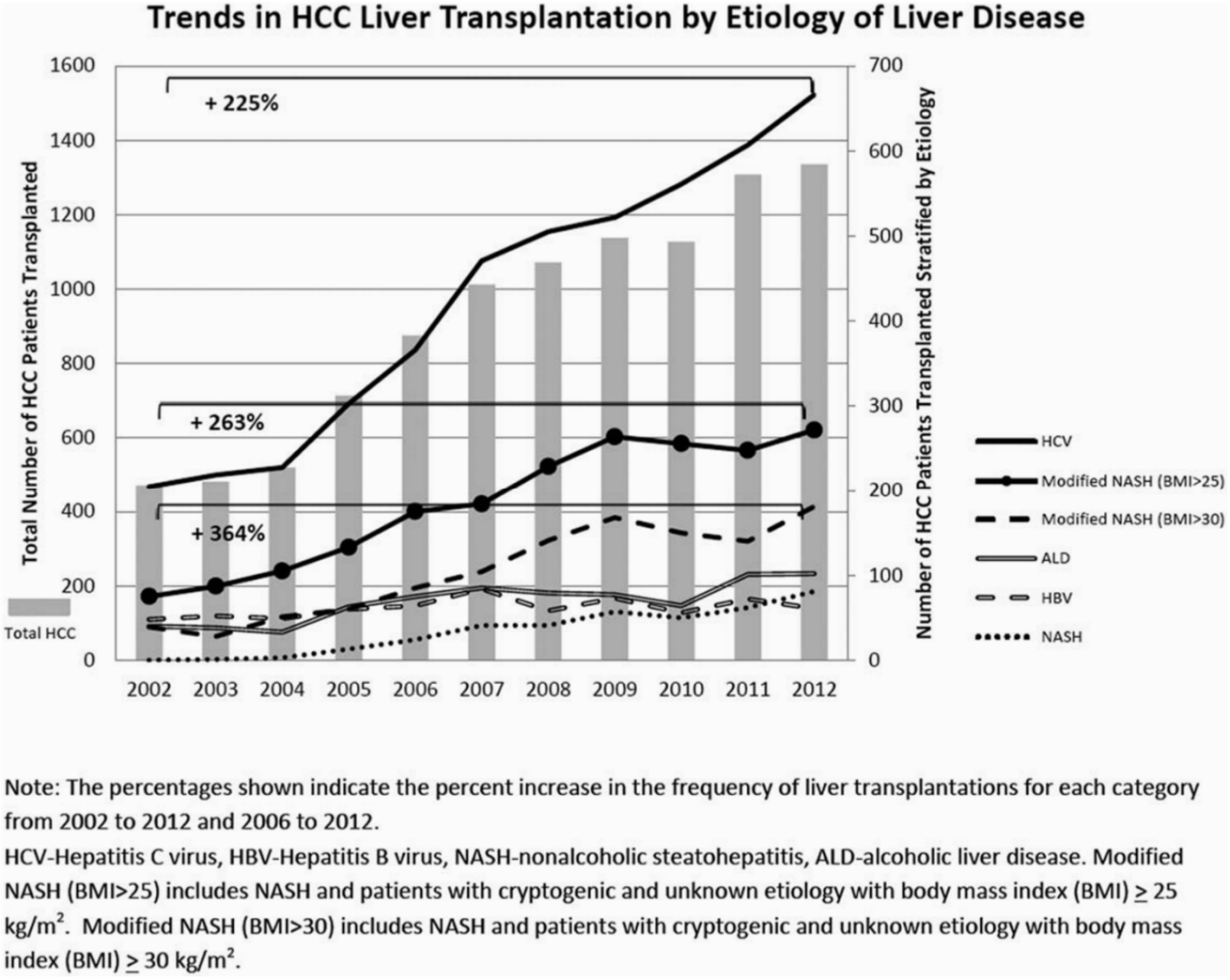
Fig. 4. Proposed pathogenesis of HCC in NASH.

insulin-like growth factor-1 (IGF1) insulin receptor substrate-1 (IRS-1) Nuclear respiratory factor-1 (Nrf1) c-Jun amino-terminal kinase 1 (JNK1)

NASH e RISCO DE HCC



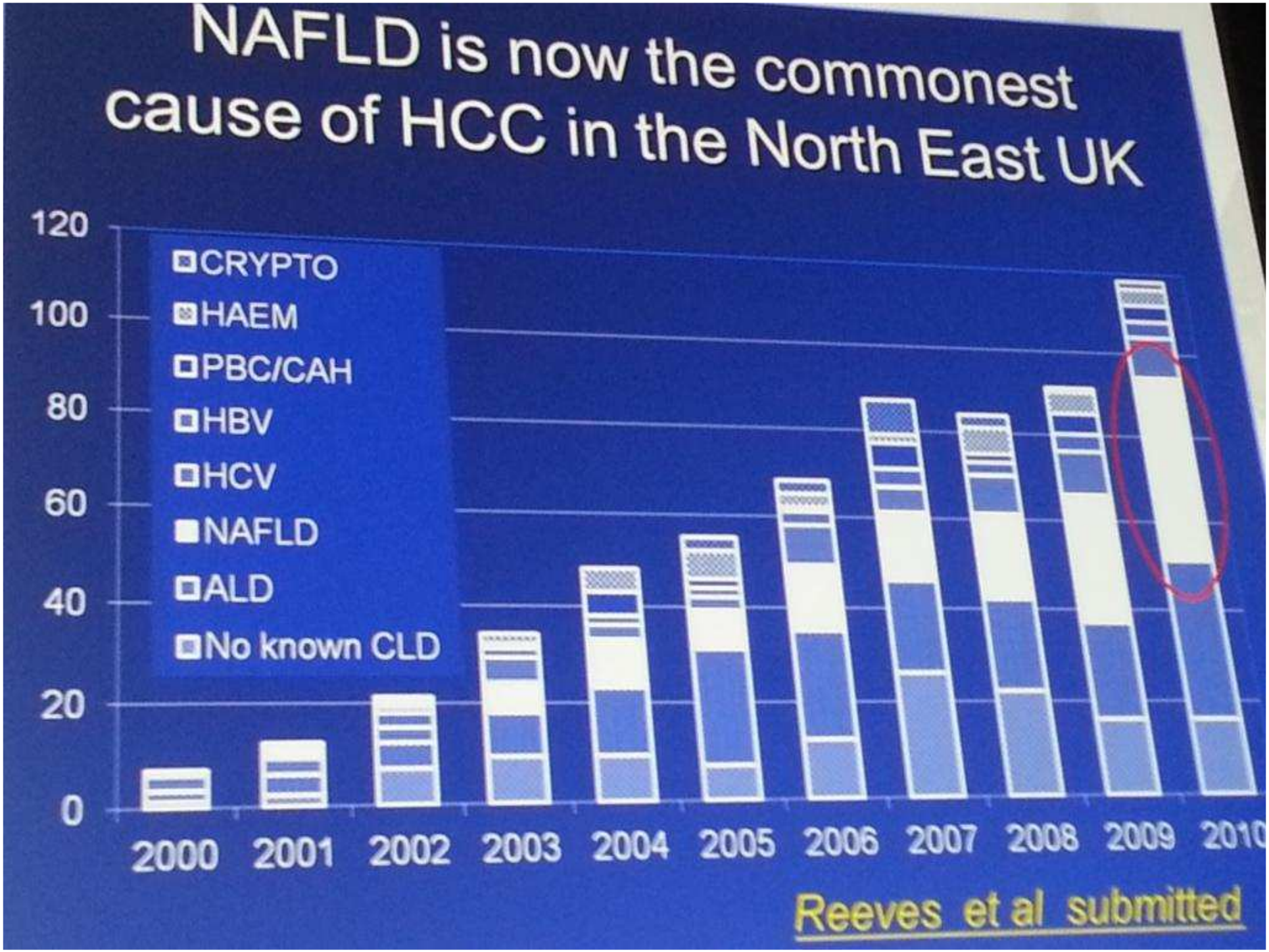
HCC POR NASH – 2a CAUSA DE TRANSPLANTE NOS EUA



Note: The percentages shown indicate the percent increase in the frequency of liver transplantations for each category from 2002 to 2012 and 2006 to 2012.

HCV-Hepatitis C virus, HBV-Hepatitis B virus, NASH-nonalcoholic steatohepatitis, ALD-alcoholic liver disease. Modified NASH (BMI>25) includes NASH and patients with cryptogenic and unknown etiology with body mass index (BMI) $\geq$ 25 kg/m^2. Modified NASH (BMI>30) includes NASH and patients with cryptogenic and unknown etiology with body mass index (BMI) $\geq$ 30 kg/m^2.

HEPATOLOGY 2014, VOL 59, N6,VOL 14


NAFLD is now the commonest cause of HCC in the North East UK
120
100
80
60
40
20
0
CRYPTO
HAEM
PBC/CAH
HBV
HCV
NAFLD
ALD
No known CLD
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
Reeves et al submitted

HÁ TRATAMENTO PARA O PACIENTE COM DHGNA??

QUEM TRATAR ?

1- PACIENTE COM DHGNA SEM ESTEATOEPATITE
2- PACIENTE COM EHNA
3- PACIENTE COM EHNA E FIBROSE AVANÇADA

O QUE TRATAR ?

1- TRATAMENTO DO PACIENTE COM SDME METABÓLICA, IG, RI
2- TRATAMENTO DA DOENÇA HEPÁTICA
3- PREVENÇÃO DE COMPLICAÇÕES

COMO TRATAR?

1- MUDANÇA ESTILO DE VIDA (DIETA E EXERCÍCIOS)
2- SENSIBILIZADORES DE INSULINA (metformina, glitazonas)
3- ANTIOXIDANTES (vitamina E)
4-CIRURGIA BARIÁTRICA (?)
5 -NOVAS DROGAS(Elafibranor, Ac. Obeticolico)

Marcadores Não Invasivos em DHGNA

NAFLD Fibrosis Score (Angulo et al, Hepatology,2007)

- Escore : -1,675 + 0,037 X (51) + 0,094 X **IMC** (30,1) + 1,13 X **IG/Diabetes** (0) + 0,99 X **AST/ALT(0,78)** – 0,013 X **Plaquetas** (256) – 0,66 X **Albumina** (4)

= -1,675+ 1,887+ 2,829 +1,13+ 0,772- 3,328-2,64 = -1,205

Table 3. Predictive Value of the Scoring System Obtained from the Estimation Group (n = 480)

	Low cutoff point (< −1.455)	Indeterminate (−1.455-0.676)	High cutoff point (> 0.676)	Total
Total	295	114	71	480
No significant fibrosis (stage 0-2)	273	75	7	355
Significant fibrosis (stage 3-4)	22	39	64	125
Sensitivity	82%		51%	
Specificity	77%		98%	
Positive predictive value	56%		90%	
Negative predictive value	93%		85%	
Likelihood ratio (+)	3.567		25.966	
Likelihood ratio (−)	0.229		0.498	
Interpretation	Absence of significant fibrosis (93% certainty)		Presence of significant fibrosis (90% certainty)	

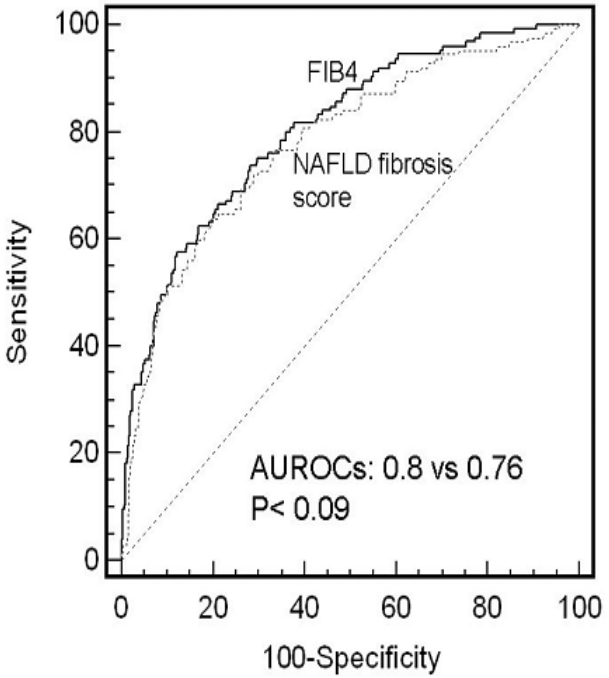
NOTE. Prevalence of advanced fibrosis of 26% in the estimation group.

USE OF THE FIB4 INDEX FOR NON-INVASIVE EVALUATION OF FIBROSIS IN NONALCOHOLIC FATTY LIVER DISEASE

Clin Gastroenterol Hepatol. 2009

Amy G Shah, M.D.[1], **Alison Lydecker, M.P.H.**[2], **Karen Murray, M.D.**[3], **Brent N. Tetri, M.D.**[4], **Melissa J. Contos, M.D.**[5], **Arun J. Sanyal, M.D.**[1], and **NASH Clinical Research Network**

$$\text{(Age[years]} \times \text{AST[U/L])/(platelet [10}^9\text{]} \times \sqrt{\text{ALT[U/L]}})$$

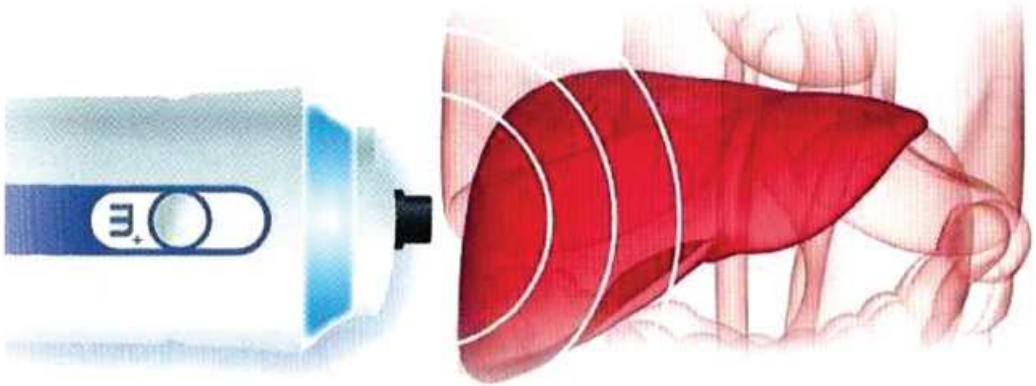


Predictive Values of FIB-4 Index Scores for Advanced Fibrosis (stage 3–4)*

	Low cutoff point (<1.30)	Indeterminate (1.30–2.67)	High cutoff point (>2.67)	Total
Total	327	163	51	541
No advanced fibrosis	294	112	10	416
Advanced fibrosis	33	51	41	125
Sensitivity	74%		33%	
Specificity	71%		98%	
Positive predictive value	43%		80%	
Negative predictive value	90%		83%	
Interpretation	Absence of advanced fibrosis		Presence of advanced fibrosis	

A rigidez hepática determina o estado patológico

Fígado macio = normal



Fígado rígido = estado patológico

FibroScan® mede a rigidez hepática que é sujeita a variação devido a inflamação e grau de fibrose. Quanto mais fibrose presente, mais rígido o fígado fica.

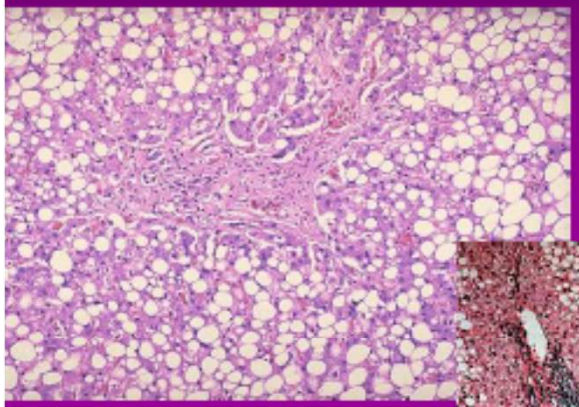
PONTOS DE CORTE DHGNA

F ≥ 1→ 5,8 KPa
F ≥ 2 →7,0 KPa
F ≥ 3 → 8,7 KPa
F 4 → 10,4 KPa ou Cirrose

Hepatology 2010;51:454-62

DOENÇA HEPÁTICA GORDUROSA NÃO ALCOÓLICA

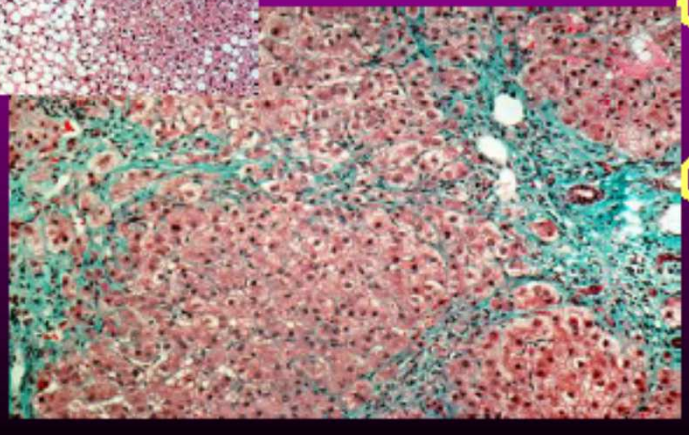
Esteatose

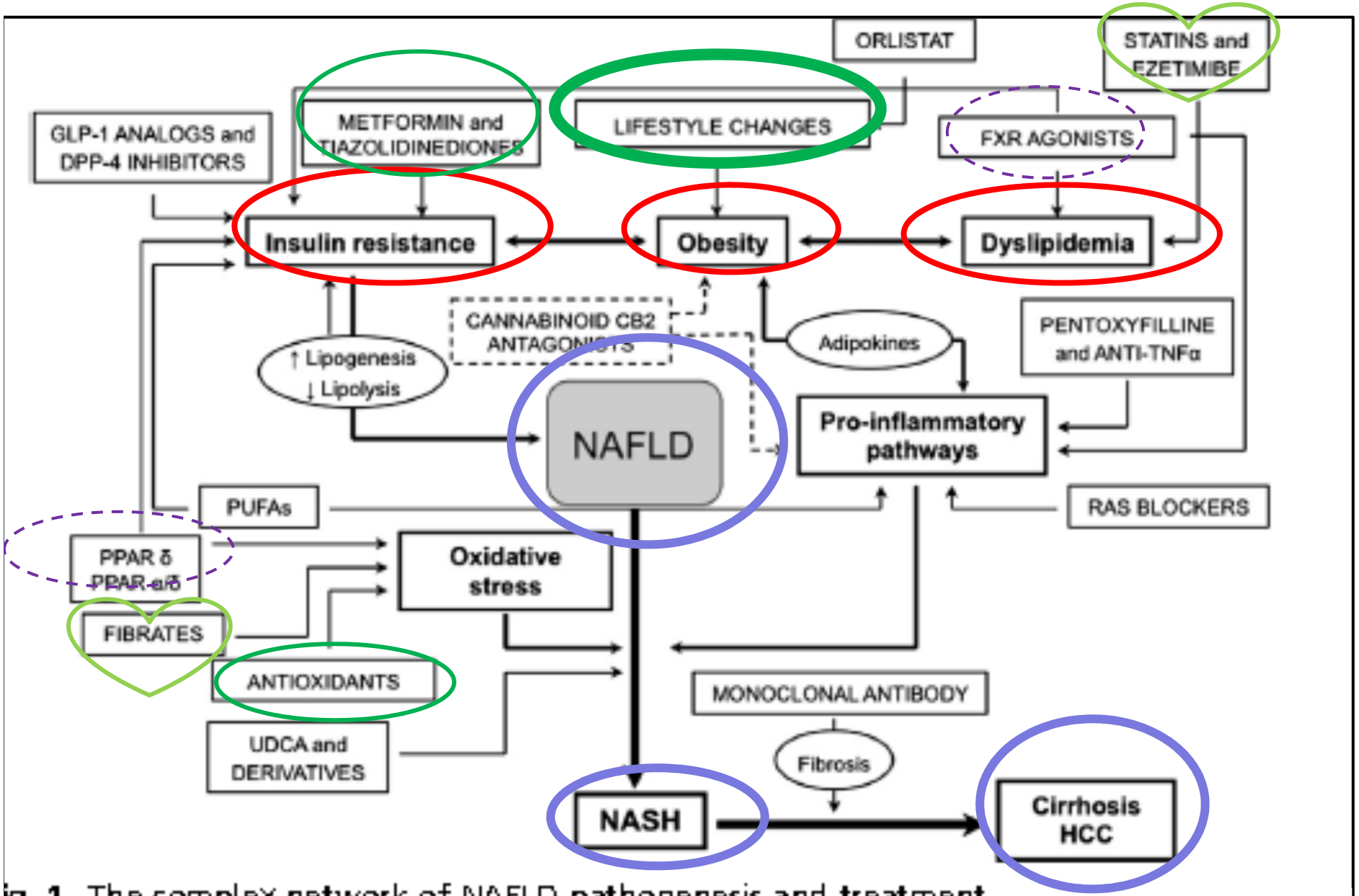


Esteato- Hepatite

Cirrose

CHC





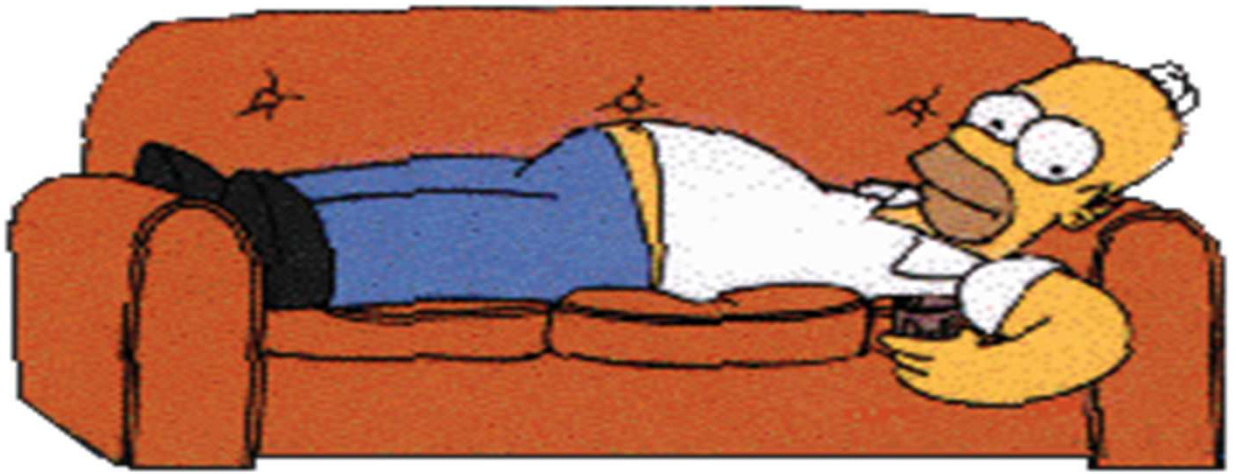
ig. 1. The complex network of NAFLD pathogenesis and treatment.

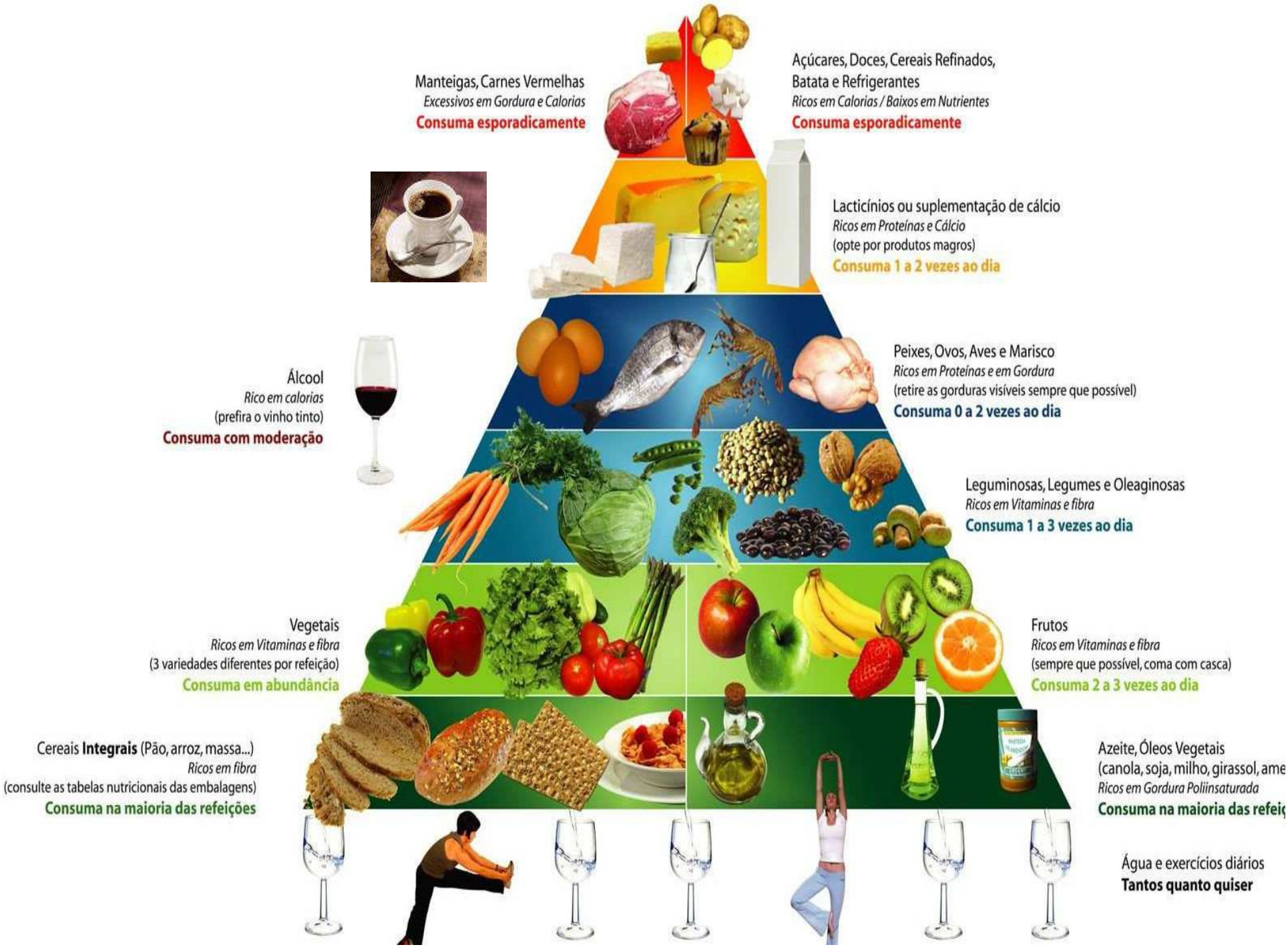
Clin Liver Dis 18 (2014) 73–89

PHYSICAL ACTIVITY

From the perspective of NAFLD patients, weekly or daily performance of walking, swimming, or cycling might seem as simple as jumping of the cliff.

Zelber-Sagi S *et al*.




Manteigas, Carnes Vermelhas
Excessivos em Gordura e Calorias
Consuma esporadicamente
Açúcares, Doces, Cereais Refinados,
Batata e Refrigerantes
Ricos em Calorias / Baixos em Nutrientes
Consuma esporadicamente
Lacticínios ou suplementação de cálcio
Ricos em Proteínas e Cálcio
(opte por produtos magros)
Consuma 1 a 2 vezes ao dia
Álcool
Rico em calorias
(prefira o vinho tinto)
Consuma com moderação
Peixes, Ovos, Aves e Marisco
Ricos em Proteínas e em Gordura
(retire as gorduras visíveis sempre que possível)
Consuma 0 a 2 vezes ao dia
Leguminosas, Legumes e Oleaginosas
Ricos em Vitaminas e fibra
Consuma 1 a 3 vezes ao dia
Vegetais
Ricos em Vitaminas e fibra
(3 variedades diferentes por refeição)
Consuma em abundância
Frutos
Ricos em Vitaminas e fibra
(sempre que possível, coma com casca)
Consuma 2 a 3 vezes ao dia
Cereais Integrais (Pão, arroz, massa...)
Ricos em fibra
(consulte as tabelas nutricionais das embalagens)
Consuma na maioria das refeições
Azeite, Óleos Vegetais
(canola, soja, milho, girassol, ame
Ricos em Gordura Poliinsaturada
Consuma na maioria das refeiç
Água e exercícios diários
Tantos quanto quiser

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Applied nutritional investigation

Effect of 6-month nutritional intervention on non-alcoholic fatty liver disease

Maria Cristina Elias M.S. [a,*], Edison Roberto Parise M.D., Ph.D [a], Luciana de Carvalho Ph.D. [a], Denis Szejnfeld M.D. [b], João Prola Netto M.D. [b]

[a] Department of Medicine, Division of Gastroenterology and Hepatology, Federal University of São Paulo, São Paulo, Brazil
[b] Department of Diagnostic Image, Abdominal Division, Federal University of São Paulo, São Paulo, Brazil

Liver enzyme levels at baseline and after 6 mo of nutritional intervention*

	Adherent (n = 17)			Non-adherent (n = 14)		
	Baseline	Final	P	Baseline	Final	P
AST (IU/L)	32.4 ± 11.6	30.4 ± 11.6	0.82	38.3 ± 17.3	40.3 ± 26.5	1.00
ALT (IU/L)	46.1 ± 27.7	33.1 ± 13.4	0.050	57.6 ± 32.8	53.8 ± 33.2	0.57
GGT (IU/L)	67.6 ± 66.1	45.2 ± 29.5	<0.05	91.1 ± 58.0	94.9 ± 98.3	0.55

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, γ-glutamyl transferase

* Values are expressed as mean ± SD. $P \leq 0.05$ (Wilcoxon's test).

Comparison of degree of hepatic density and visceral and subcutaneous adiposity assessed by magnetic resonance parameters, at the beginning of the study and after 6 mo of nutritional intervention in the groups studied*

	Adherent (n = 17)			Non-adherent (n = 14)		
	Baseline	Final	P	Baseline	Final	P
Visceral fat	105.0 ± 47.7	66.3 ± 35.9	0.011	102.9 ± 30.2	93.7 ± 24.7	0.575
Subcutaneous fat	167.5 ± 70.5	150.5 ± 76.1	0.278	182.8 ± 95.5	214.1 ± 77.2	0.508
Total fat	272.5 ± 69.3	216.8 ± 85.9	0.011	293.2 ± 103.8	298.5 ± 82.7	0.878
Liver density†	41.6 ± 11.6	47.8 ± 15.0	<0.05	45.1 ± 15.0	47.8 ± 15.9	0.507

* Values are expressed as mean ± SD. $P \leq 0.05$ (Wilcoxon's test).

† Tomographic liver density was evaluated in 16 adherent and 10 non-adherent patients.

Cardiovascular Disease and Nonalcoholic Fatty Liver Disease

Does Histologic Severity Matter?

Jeremy P. Domanski, MD, Stephen J. Park, MD,† and Stephen A. Harrison, MD**

J Clin Gastroenterol 2012

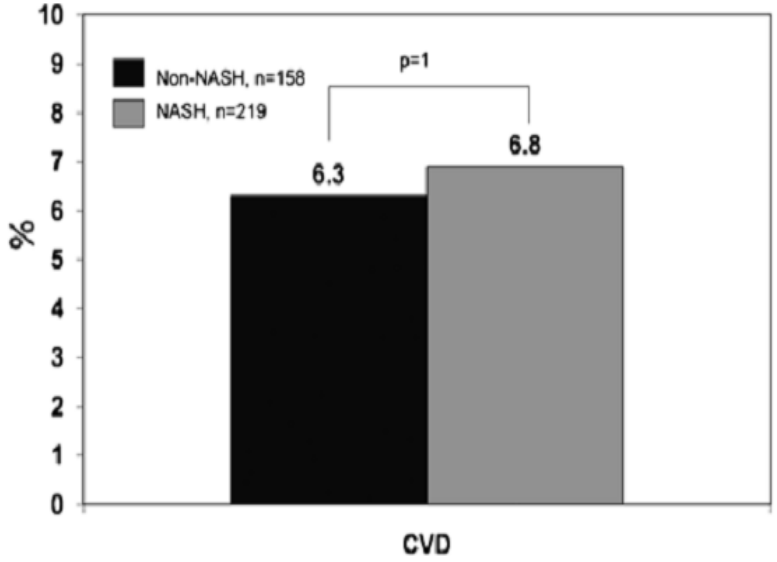


FIGURE 2. Prevalence of cardiovascular disease in nonalcoholic steatohepatitis (NASH) and non-NASH patients (CVD, cardiovascular disease—combined endpoint of congestive heart failure, unstable angina, myocardial infarction, revascularization, or stroke).

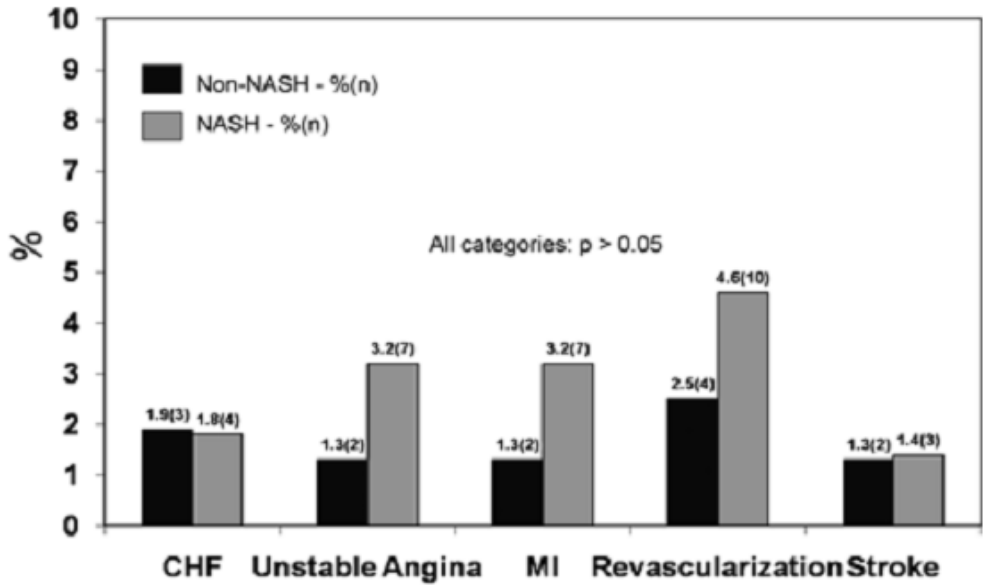
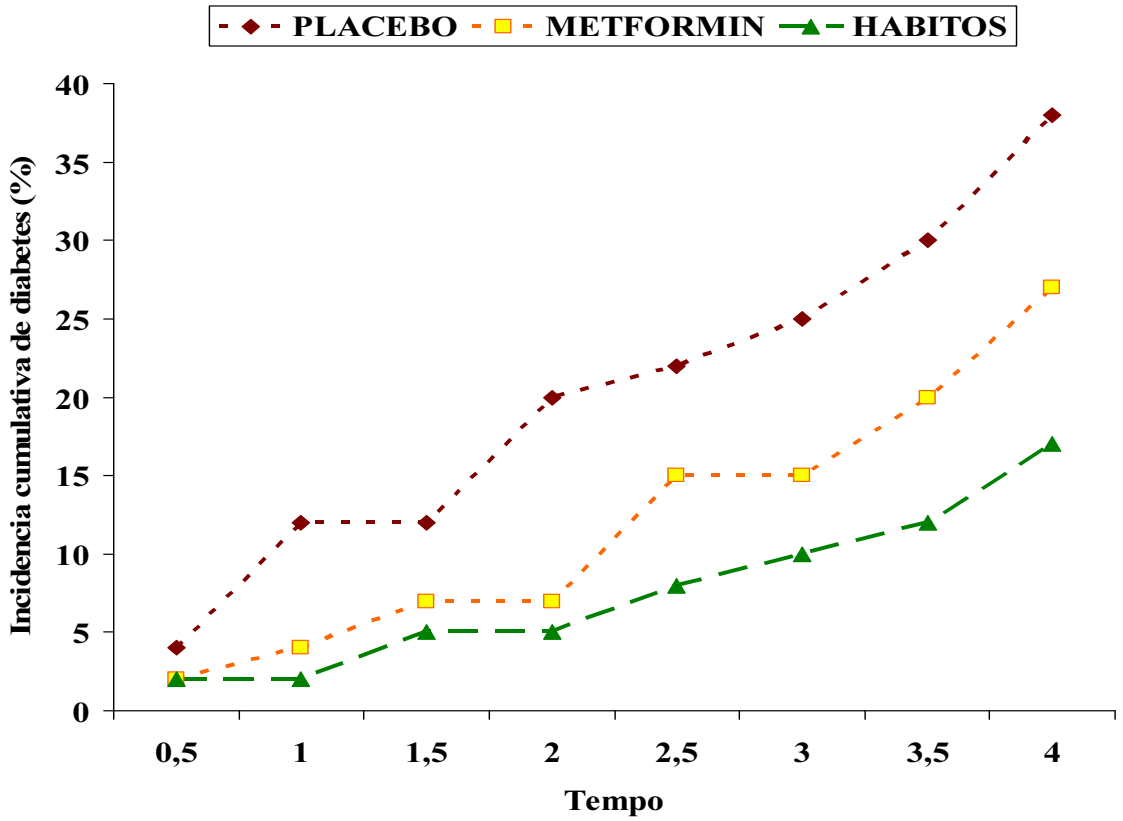


FIGURE 3. Prevalence of individual cardiovascular endpoints in nonalcoholic steatohepatitis (NASH) and non-NASH patients. CHF indicates congestive heart failure; MI, myocardial infarction.

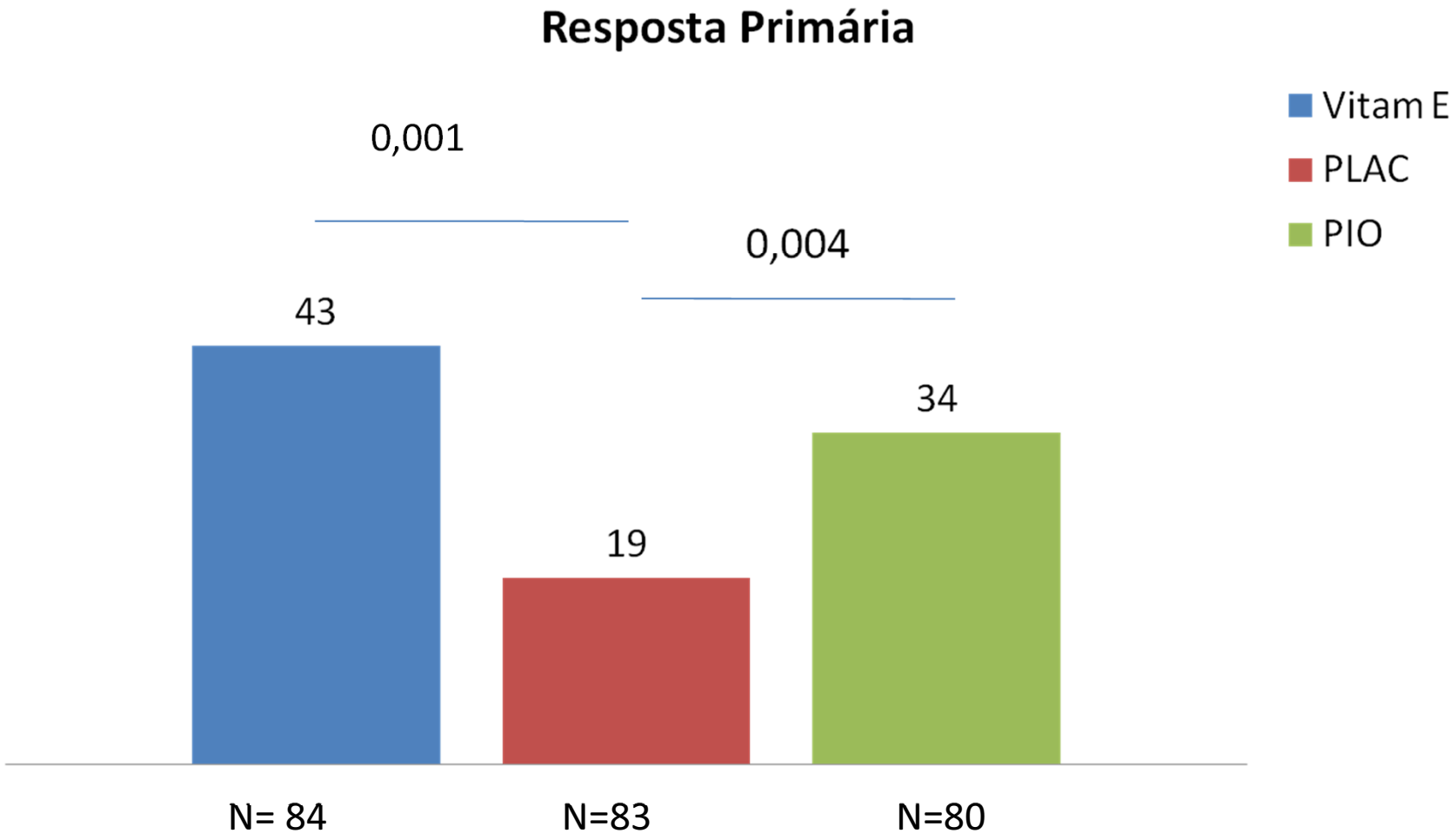
Incidência de diabetes em pacientes tratados com metformina ou placebo ou mudança hábitos de vida (Knowler et al, 2002)

•3234 pacientes não diabéticos com alteração glicose jejum ou pós-prandial.
•Grupo 1 – placebo
•Grupo 2 – metformina
•Grupo 3 – redução mínima peso 7% e , pelo menos, atividade física 150 min /semana



Pioglitazone, Vitamin E, or Placebo for Nonalcoholic Steatohepatitis.

Sanyal A, et al. New England Journal of Medicine, 2010



Effect of Bariatric Surgery on Nonalcoholic Fatty Liver Disease: Systematic Review and Meta-Analysis

RAJASEKHARA R. MUMMADI,* KRISHNA S. KASTURI,* SWAPNA CHENNAREDDYGARI,* and GAGAN K. SOOD‡

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2008;6:1396–1402

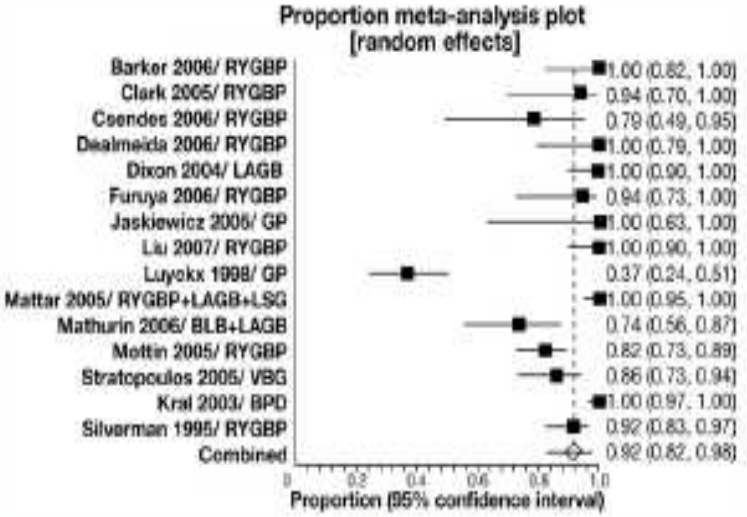


Figure 2. Forest plot showing improvement or resolution of steatosis after bariatric surgical procedures. *The left-hand column* in the Forest plot lists the names of the studies. The *squares on the right-hand column* indicate the effect measure (proportion of patients with response). The *horizontal lines* that cut through the squares indicate CIs.

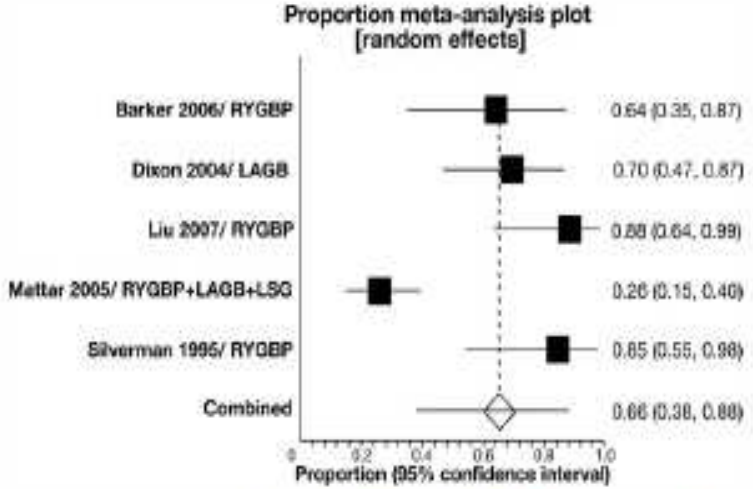
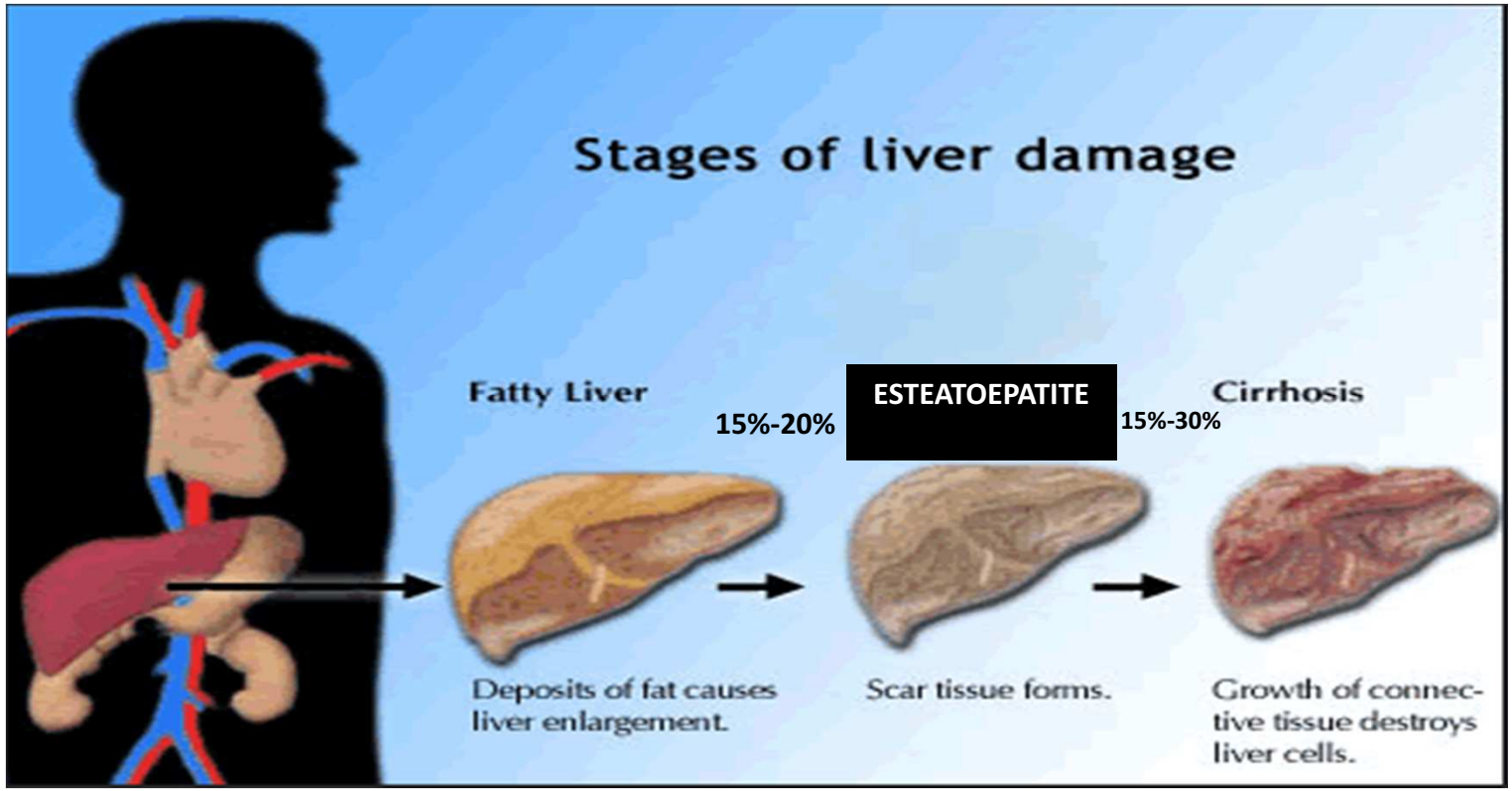


Figure 5. Forest plot showing improvement or resolution of fibrosis (subgroup analysis using studies with needle biopsies only) after bariatric surgical procedures: I^2 (inconsistency) = 88.8% (95% CI, 75%–93.5%). Random effects (DerSimonian-Laird): pooled proportion = 65.5% (95% CI, 38.2%–88.1%).

EVOLUÇÃO DA DOENÇA HEPÁTICA GORDUROSA



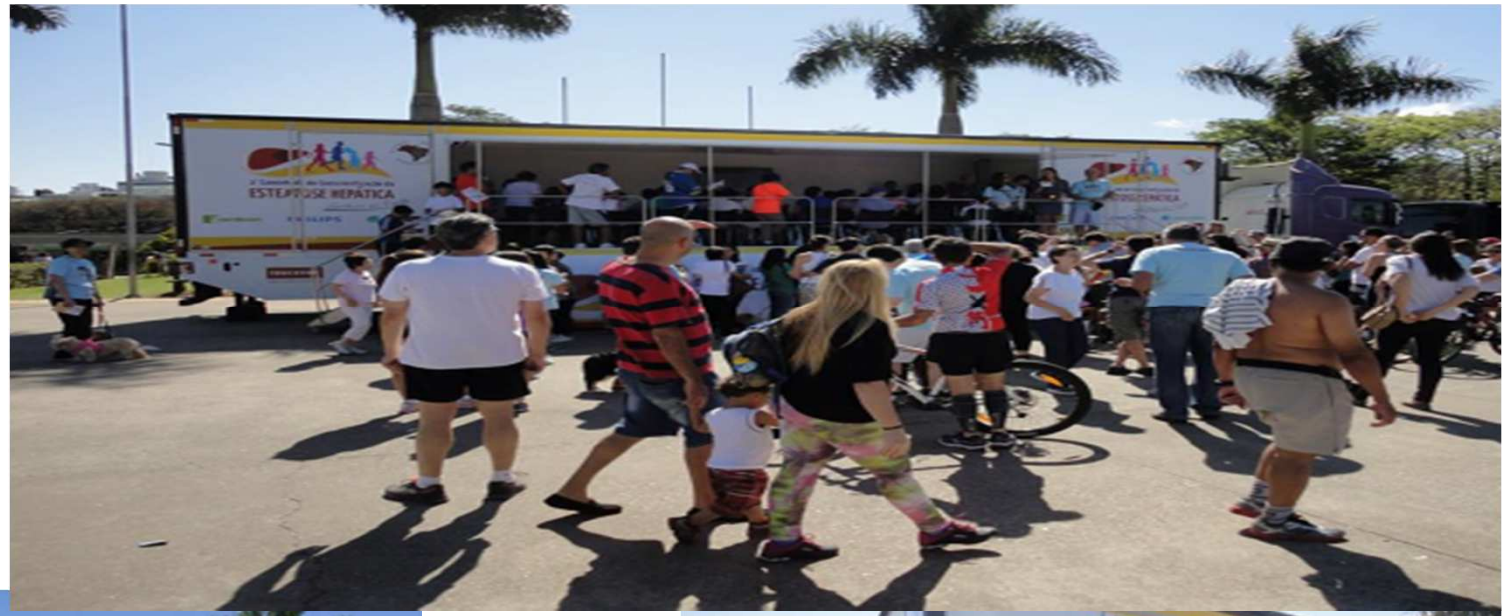
30% população 3%-4,5%popul. 0,5%-1,5%


Sociedade Brasileira de Hepatologia
1ª Caminhada de Conscientização da
ESTEATOSE HEPÁTICA
Gordura no Fígado
02 de Agosto de 2015
das 10h às 14h
Local: Parque Villa Lobos
Av. Prof. Fonseca Rodrigues, 2001
Alto dos Pinheiros, São Paulo - SP, 05461-010


TRUCKVAN


ORIENTADOR

Sociedade Brasileira de Hepatologia



A DIFICIL ARTE DE MUDAR

EQUIPE MULTIDISCPLINAR

NILMA LUCIA SAMPAIO RUFFEIL
EDISON ROBERTO PARISE
ANA CLAUDIA OLIVEIRA
ANA LUCIA AZEVEDO
AYK HELENA BARBOSA MARTINS
BARBARA FERREIRA DE MELLO BARRETO
IBRAHIN AL BACHA
JOÃO LUIZ RODRIGUES DE FARIAS
LARISSA BERTOLINI ANDREATTA
LUCIANA DE CARVALHO (IN MEMORIAN)
MARIA AMELIA SANAE OHASHI
MARIA CRISTINA ELIAS
PENELOPE MICHELE GRILLO
RENATA CRUVINEL CUMINALE
VIRGINIA NASCIMENTO DOS SANTOS

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