SORVEGLIANZA DELL'EPATOPATIE CRONICHE E DELLE LESIONI FOCALI

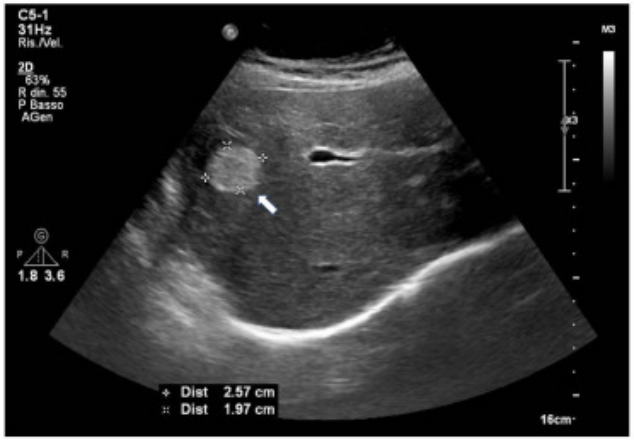
Prof. Fabio Farinati

elluno, 21/10/2023

FNOMCeO
Federazione Nazionale degli Ordini
dei Medici Chirurghi e degli Odontoiatri

Non ho conflitti di interesse sull’argomento.

Lesioni focali



LESIONI FOCALI EPATICHE

BENIGNE
Emangioma
Iperplasia focale nodulare (FNH)
Cisti
Adenoma epatocellulare (HCA)

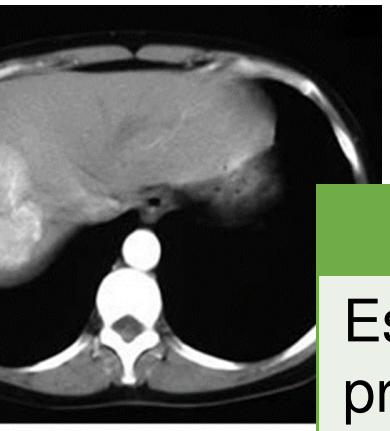
MALIGNE
Epatocarcinoma (HCC)
Colangiocarcinoma (cC

CISTI EPATICHE?

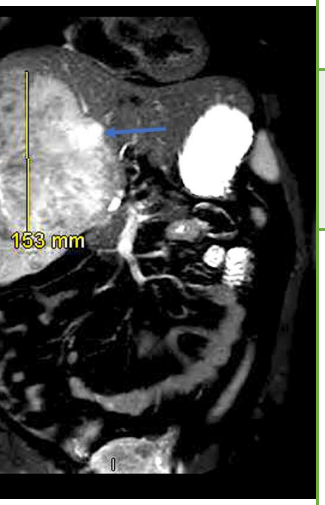
Recommendations

It is not recommended to follow asymptomatic patients because of simple hepatic cysts, biliary hamartomas or peribiliary cysts **(LoE 3, strong recommendation, 96% consensus).**

LESIONI EPATICHE BENIGNE



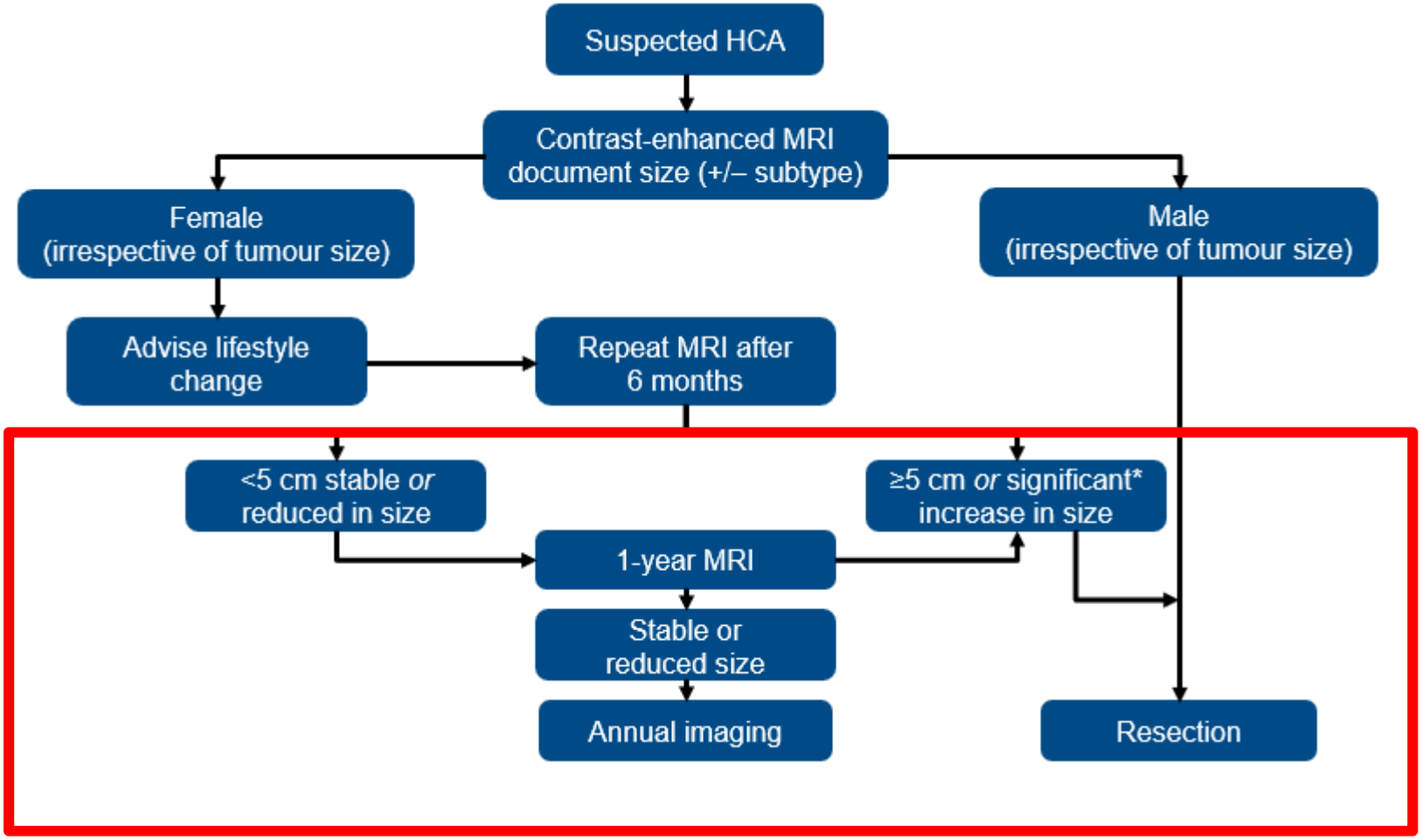
Hyperplasia



	Haemangioma	FNH	HCA
Estimated prevalence	Common ~5%*	Less common 0.03%	Rare ≤0.004%
Age	30–50 years	20–40 years	All ages
Gender	F > M	F ~ M	F >> M
US	Hyperechoic	Varied	Varied
CT/CEUS	Centripetal enhancement	Central scar	Varied
MRI	Centripetal enhancement Hyperintense T2-w	Central scar	Varied
Surveillance	Not required	Not required (?)	Required

EASL CPG benign liver tumours. J Hepatol, 2016.

ADENOMA SORVEGLIANZA



Resection irrespective of size is recommended in men and in all cases of proven β-catenin mutation

EASL CPG benign liver tumours. J Hepatol, 2016.

BACKGROUND

LESIONI FOCALI EPATICHE

MALIGNE
Epatocarcinoma (HCC)
Colangiocarcinoma (cCA)

BENIGNE
Emangioma
Iperplasia focale nodulare (FNH)
Cisti
Adenoma (HCA)

Sorveglianza epatopatie

EPATOPATIA CRONICA

- STEATOSI
- CIRROSI
- EPATITE CRONICA

CIRROSI EPIDEMIOLOGIA

In the GBD Study 2017, the estimated number of people with compensated cirrhosis was 112 million worldwide, corresponding to an age-standardized global prevalence of compensated cirrhosis of 1,395 cases per 100,000 population[12].

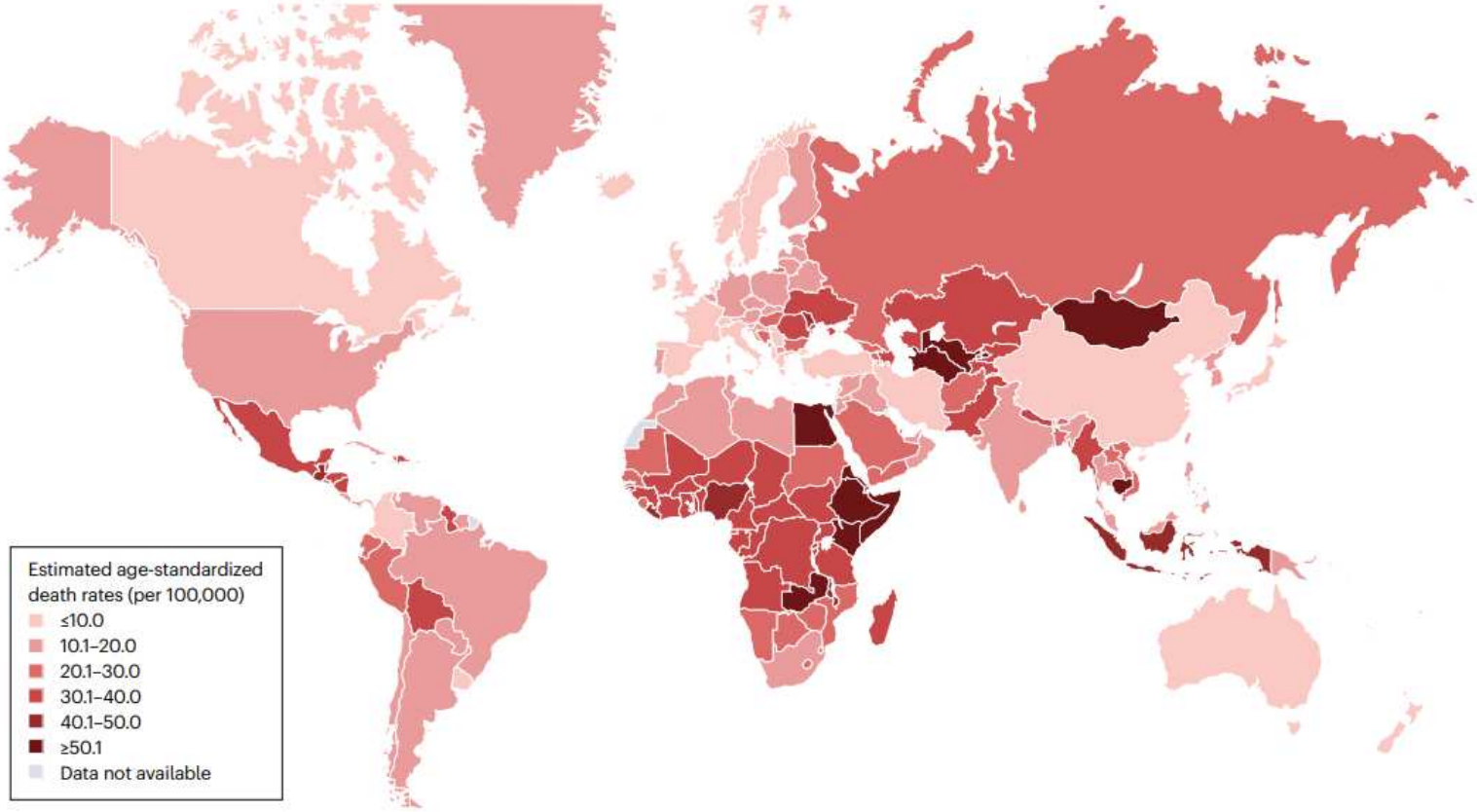


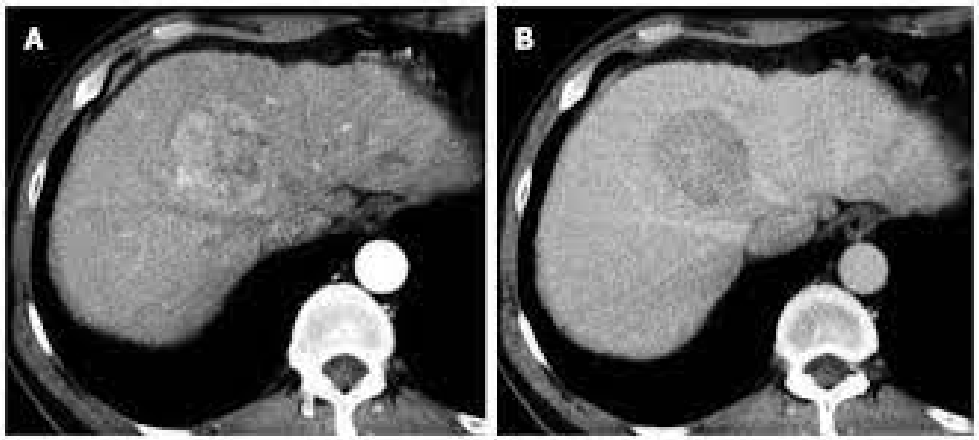
Fig. 2 | Estimated age-standardized death rates due to cirrhosis in 2019 by country. Data for the age-standardized death rate in 2019 were estimated in the Global Burden of Disease Study 2019 and these data were obtained from the GBD Results Tool[27]. Where data for countries or regions were unavailable, the Global Burden of Disease Study 2019 results depended on modelling and past trends, potentially resulting in discrepancies in the accuracy of the data.

Huang, D.Q. et al, Nat Rev Gastroenterol Hepatol, 2023.

LESIONI FOCALI MALIGNE

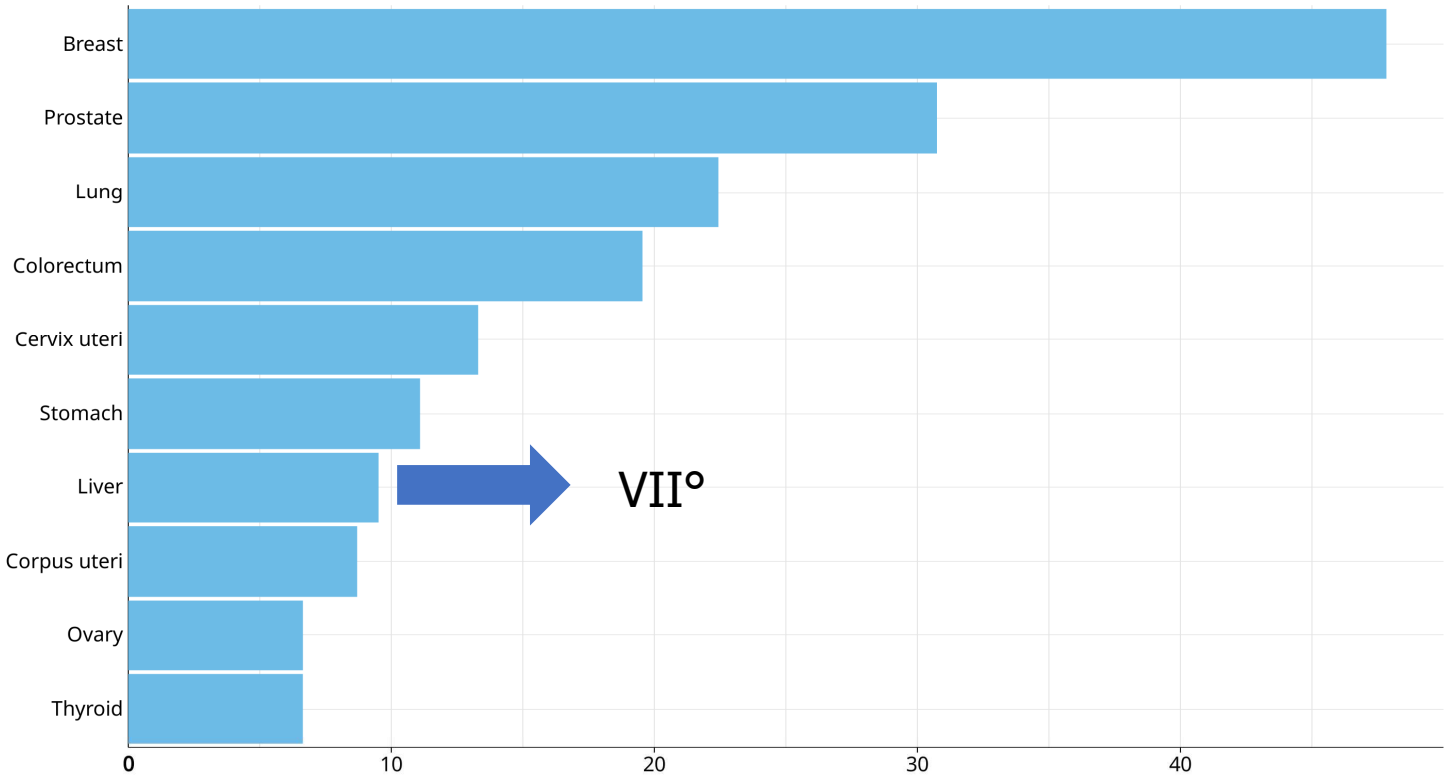
- HCC
  - Accounts for approximately 90% of primary liver cancers
- **Cirrhosis is an important risk factor for HCC**
  - Multiple causes, including viral hepatitis, chronic alcohol use, NAFLD
  - Up to 90% of HCC arises on a background of cirrhosis in the Western world[1]

EASL CPG HCC. J Hepatol 2018.



CANCRO AL FEGATO: INCIDENZA

Estimated age-standardized incidence rates (World) in 2020, World, both sexes, all ages (excl. NMSC)



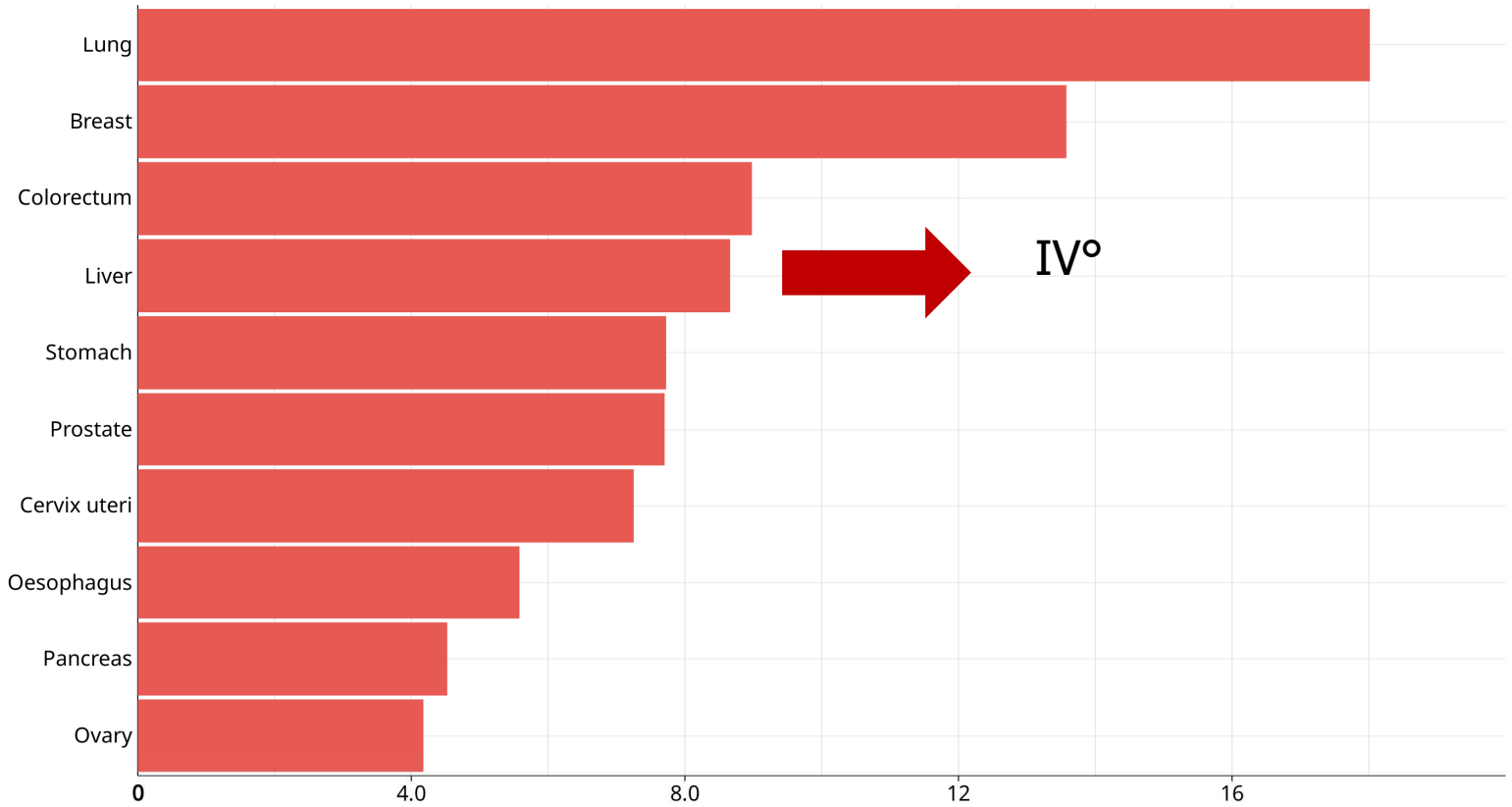
Data source: Globocan 2020
Graph production: Global Cancer Observatory (http://gco.iarc.fr)

International Agency for Research on Cancer
World Health Organization

GLOBACAN, 2020.

CANCRO AL FEGATO: MORTALITÀ

Estimated age-standardized mortality rates (World) in 2020, World, both sexes, all ages (excl. NMSC)

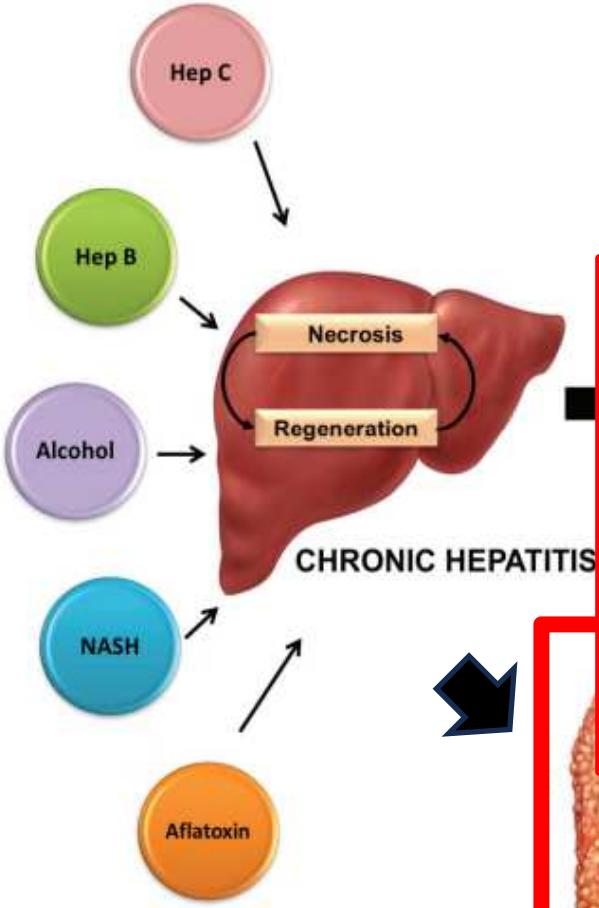


Data source: Globocan 2020
Graph production: Global Cancer Observatory (http://gco.iarc.fr)

International Agency for Research on Cancer
World Health Organization

GLOBACAN, 2020.

SORVEGLIANZA



Insieme di azioni e comportamenti che si propongono di identificare la malattia in stadio iniziale, quello in cui sono maggiori le possibilità di cura e guarigione.

SORVEGLIANZA

Dhanasekaran R et al, *F1000Research,* 2016.

SORVEGLIANZA

WHO?

WHY ?

WHEN (HOW OFTEN)?

HOW?

C’È UN IDENTIKIT DEL PAZIENTE DA SOTTOPORRE A SORVEGLIANZA?

WHO?

Surveillance is recommended in specific target populations

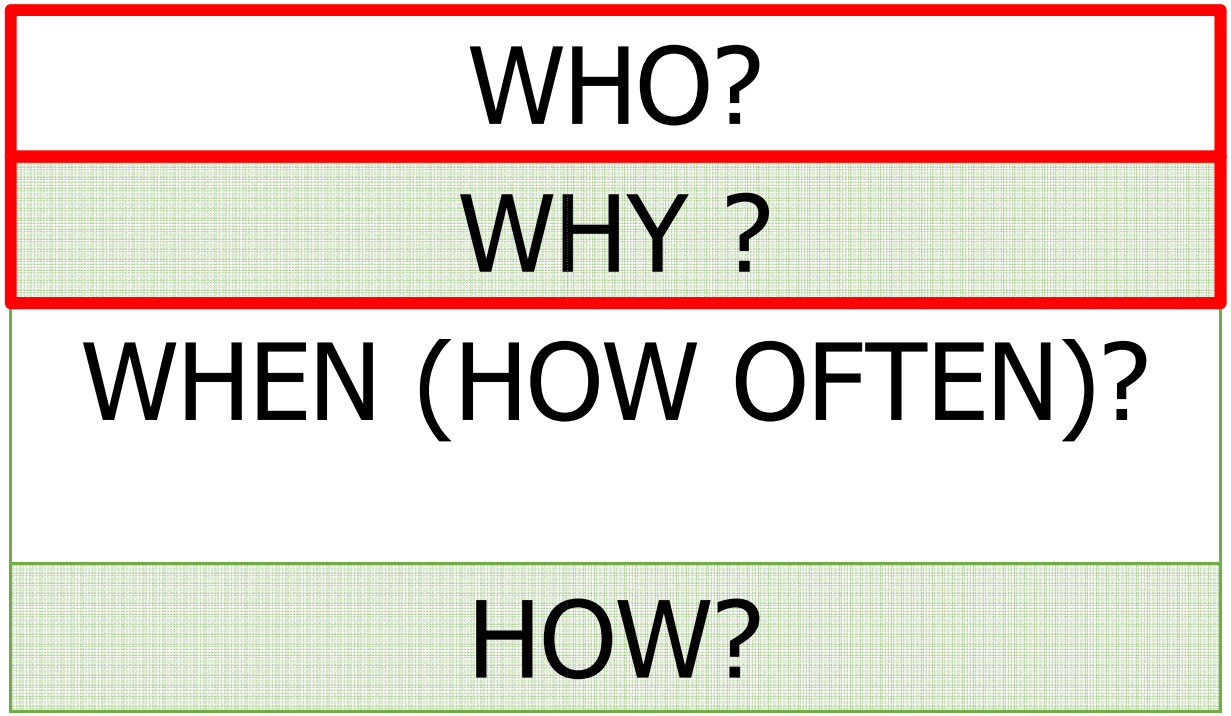
ecommendations		
Cirrhotic patients, **Child–Pugh stage A and B**	Low	Strong
Cirrhotic patients, **Child–Pugh stage C awaiting LT**	Low	Strong
Non-cirrhotic HBV patients at intermediate or high risk of HCC* (according to PAGE-B† classes for Caucasian subjects, respectively 10–17 and ≥18 score points)	Low	Weak
Non-cirrhotic F3 patients, based on an individual risk assessment	Low	Weak

MAFLD?

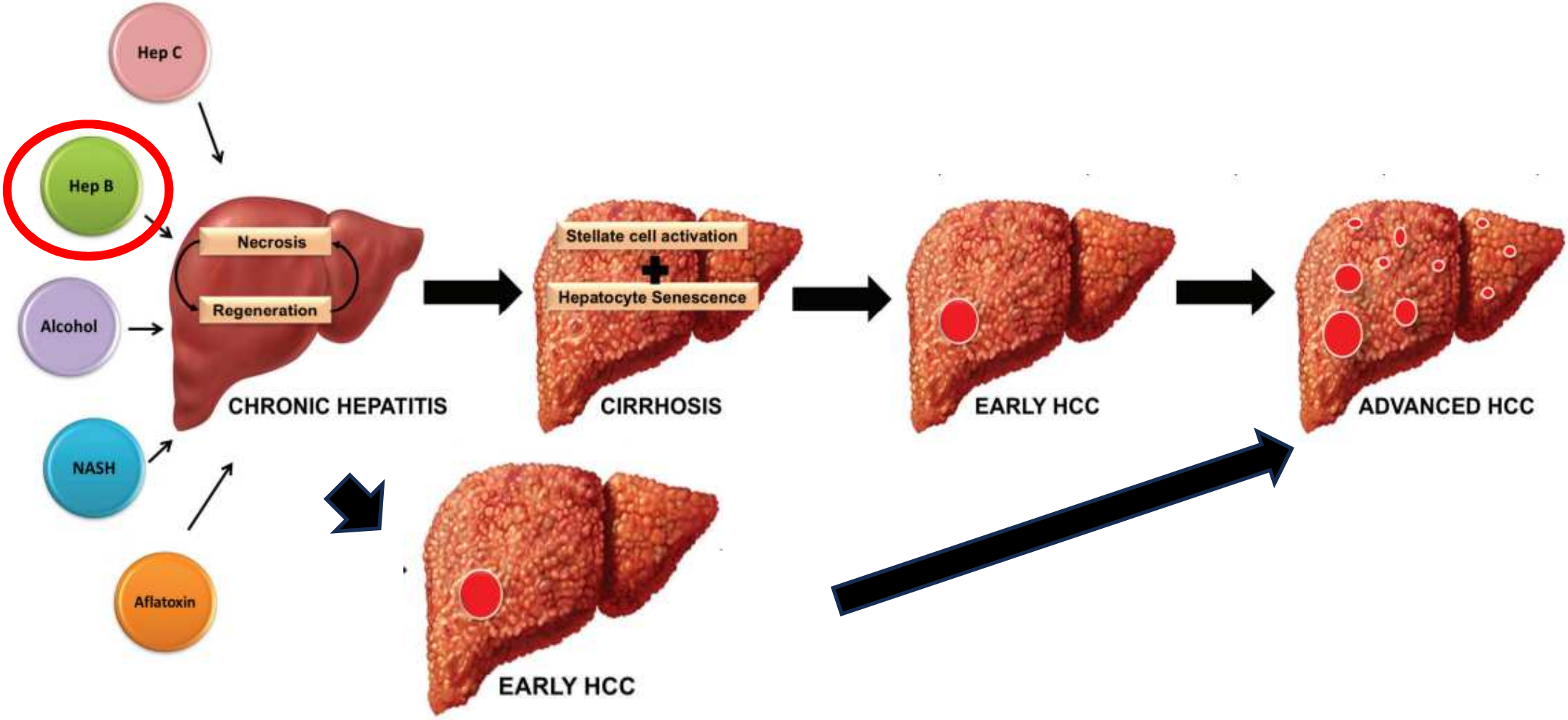
Recommendations	Level of evidence	Grade of recommendation
Role of **surveillance for patients with NAFLD** without cirrhosis is **unclear**	Low	

EASL CPG HCC. J Hepatol 2018.

SORVEGLIANZA 2

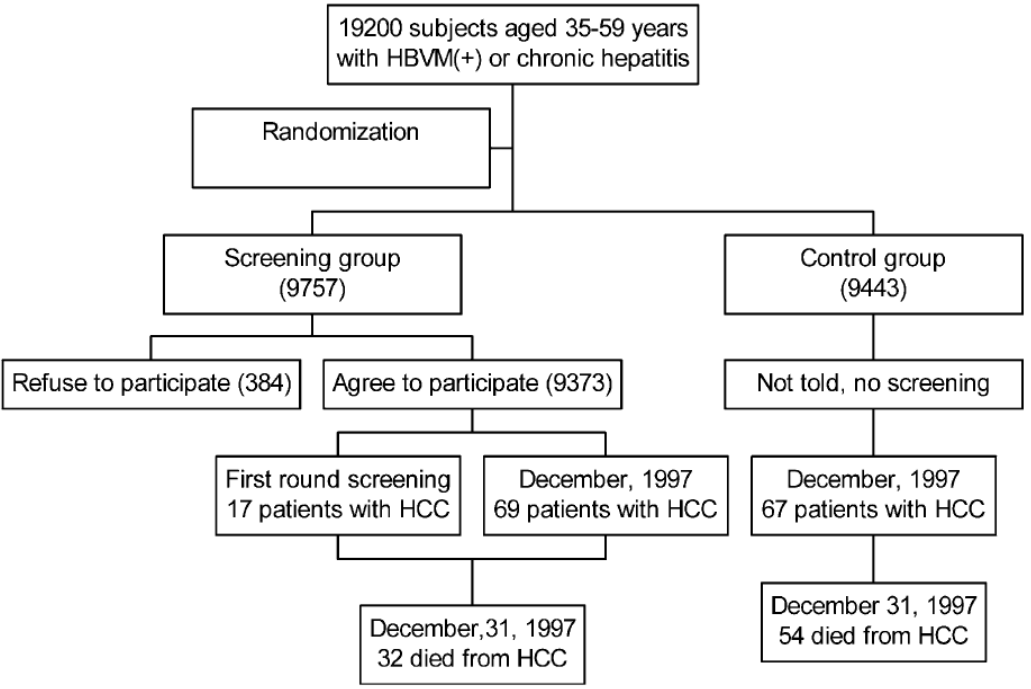


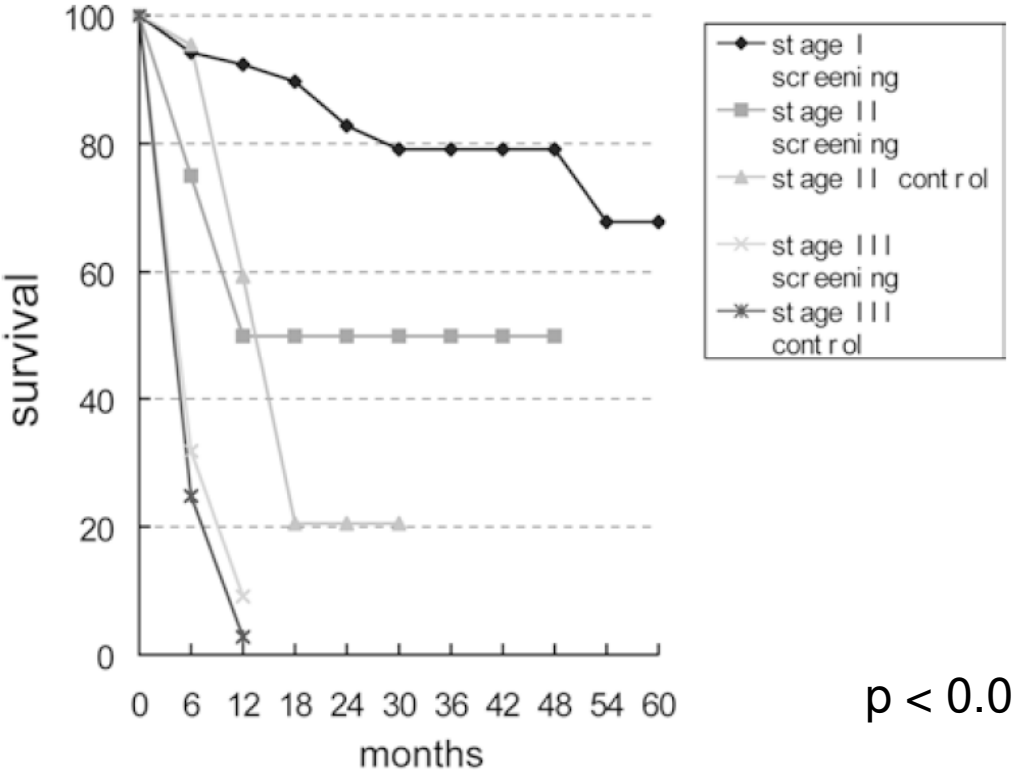
WHY?



Dhanasekaran R et al, F1000Research, 2016.

VIRUS DELL'EPATITE B





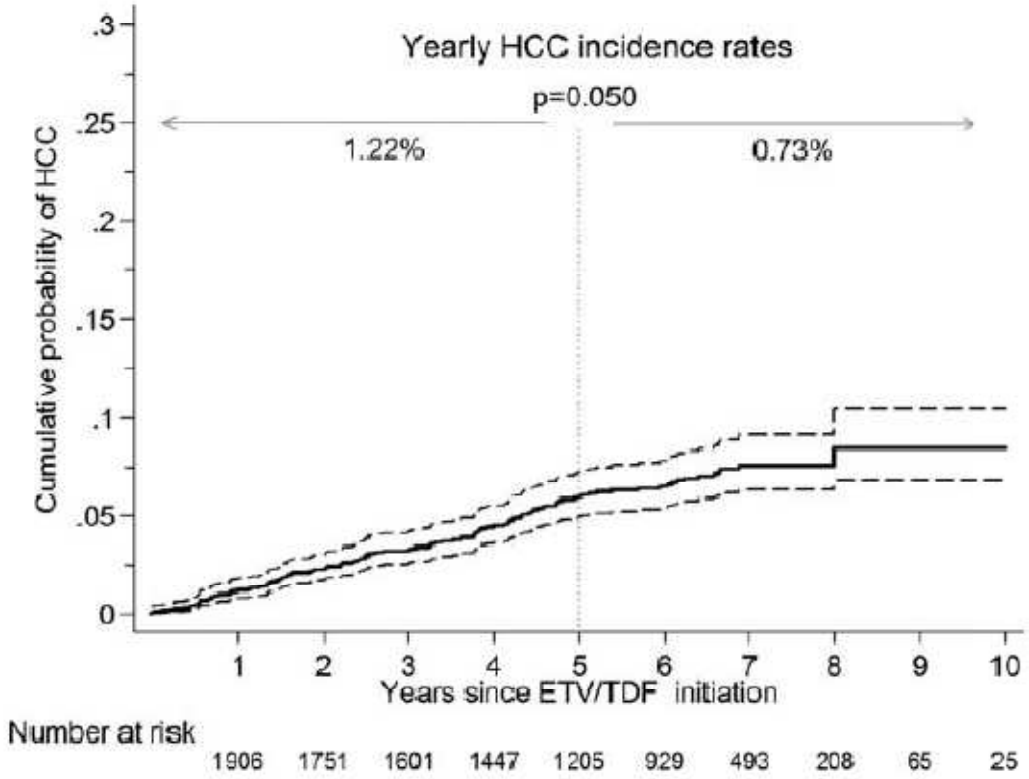
p < 0.01

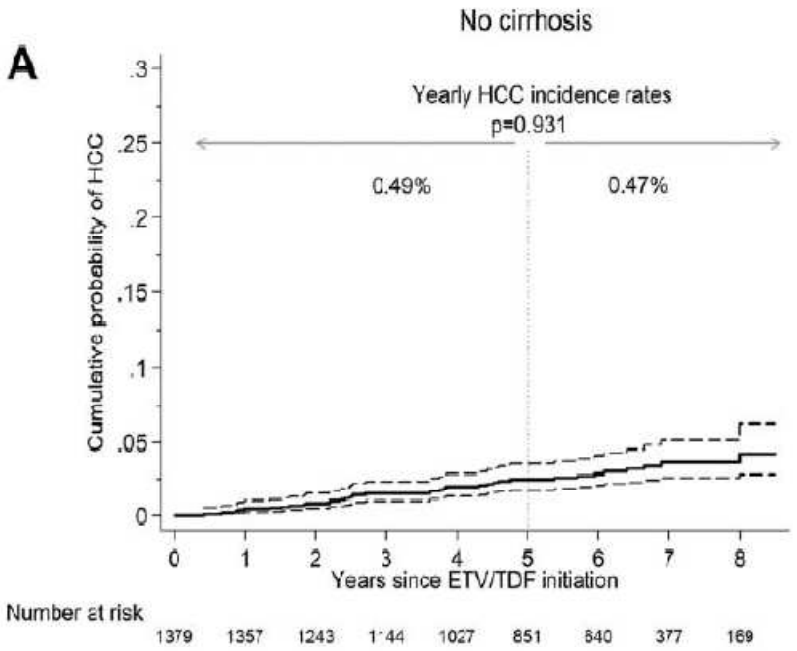
Bo-Heng Zhang et al., J Cancer Res Clin Onco, 2004.

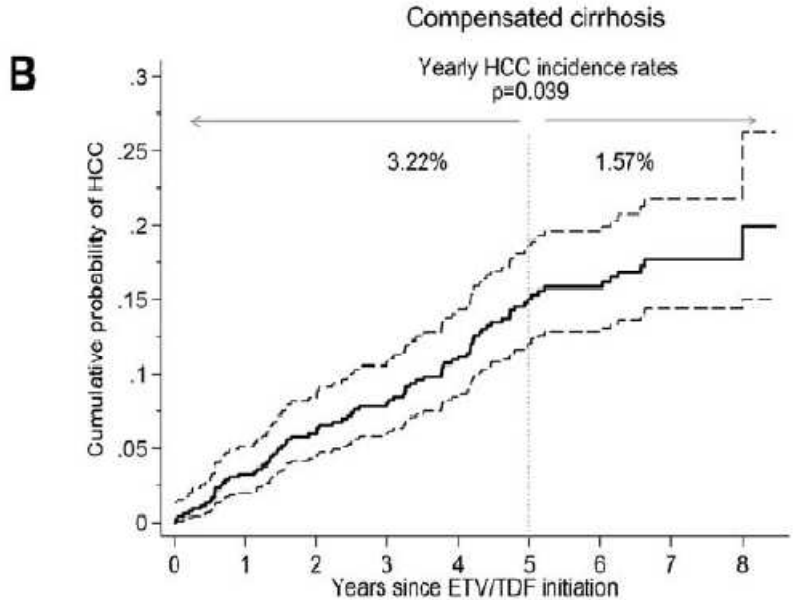
HEPATOLOGY

HEPATOLOGY, VOL. 66, NO. 5, 2017

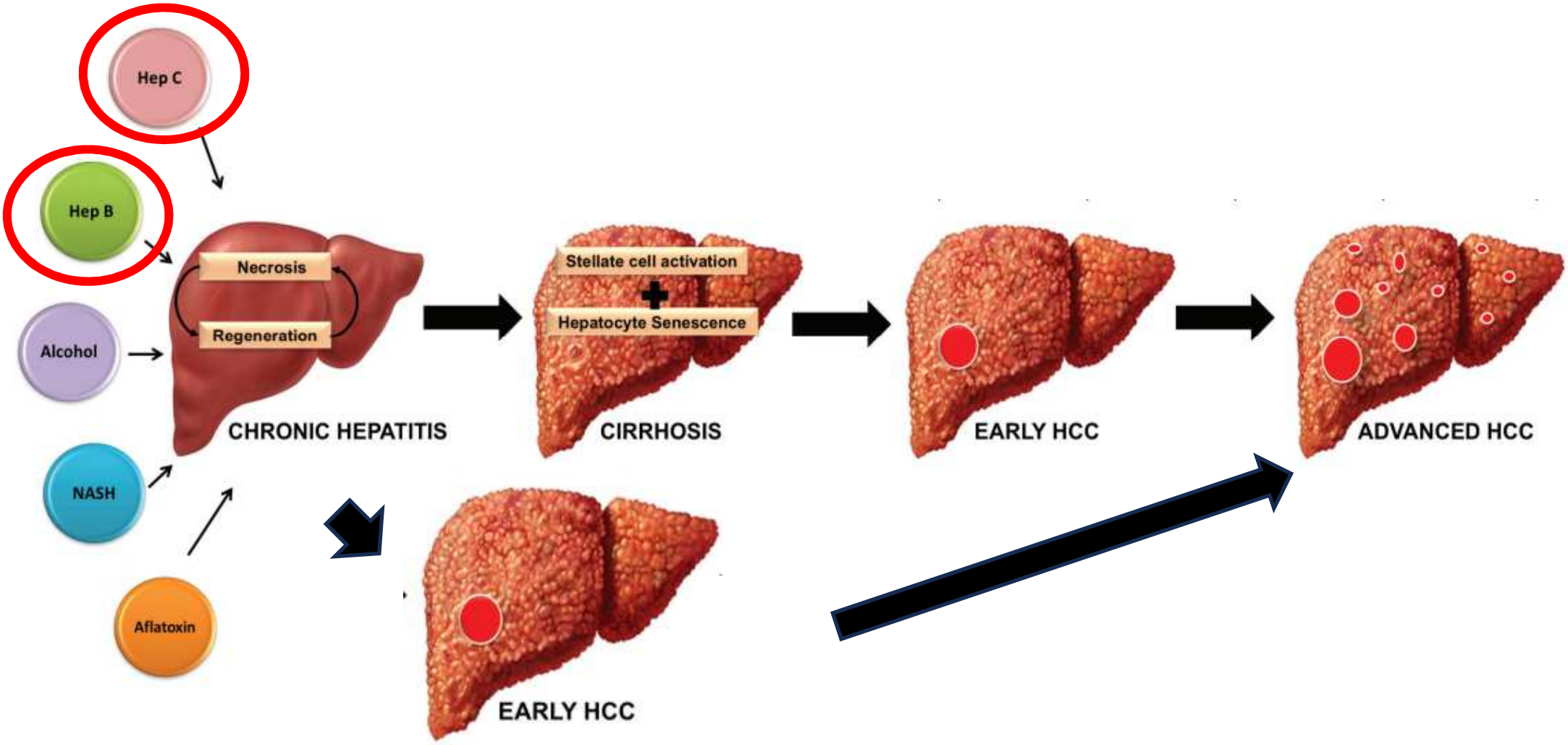
The Risk of Hepatocellular Carcinoma Decreases After the First 5 Years of Entecavir or Tenofovir in Caucasians With Chronic Hepatitis B







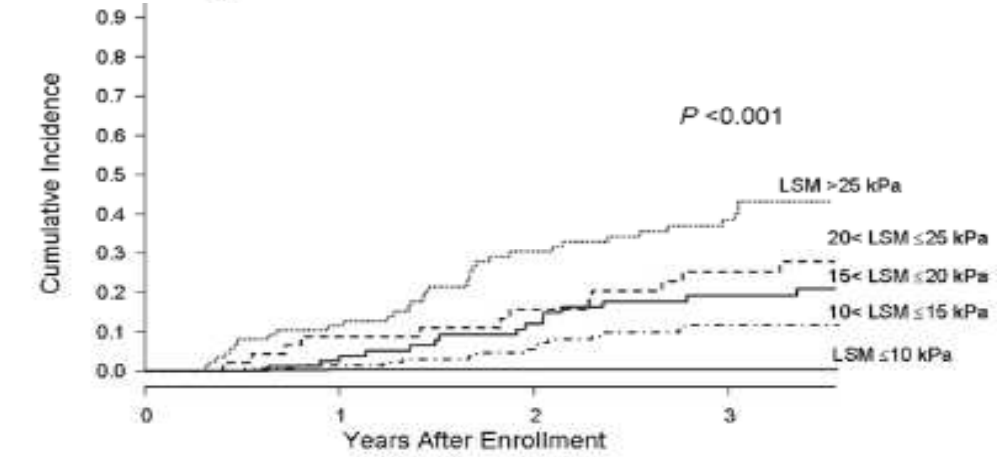
WHY?



Dhanasekaran R et al, F1000Research, 2016.

VIRUS EPATITE C

Currently, HCC surveillance is not recommend in patients with chronic hepatitis C without cirrhosis[7]. Eradication of HCV with sustained viral response (SVR) has been shown to decrease the risk for HCC. Morgan



No. at risk				
≤10 kPa	511	501	476	427
10.1-15 kPa	142	130	111	94
15.1-20 kPa	79	76	63	51
20.1-25 kPa	47	41	36	29
>25 kPa	87	75	54	41

Fig. 1. Cumulative incidence of HCC development stratified based on LSM (N = 866). LSM, liver stiffness measurement.

Masuzaki R, et al., Hepatology 2009

Table 2. Event rate per 100 person-years.

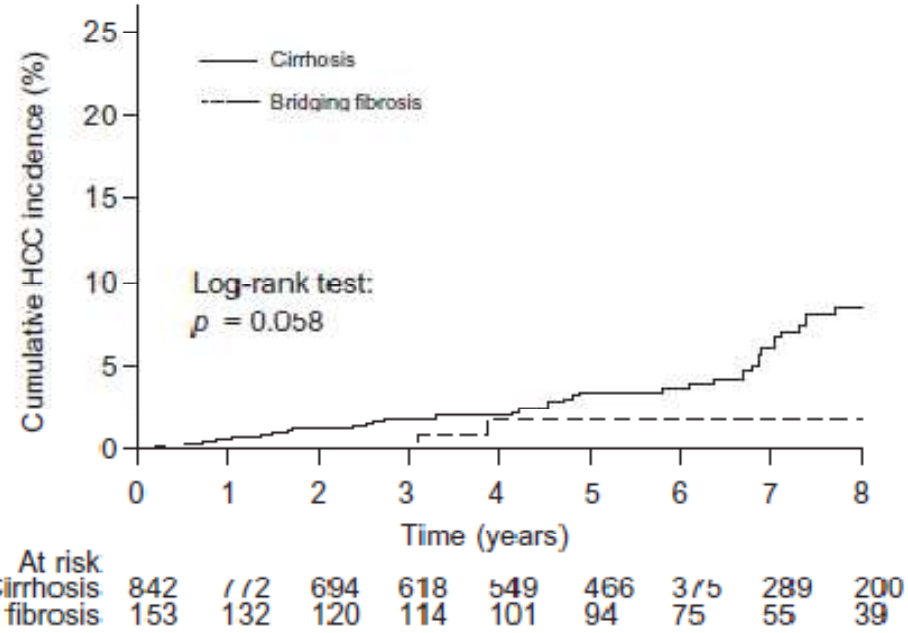
	Events No.	Observation period, person-years	Rate/100 person-years (95% CI)
Hepatocellular carcinoma	51	5671	0.90 (0.67–1.18)
Liver failure	26	5664	0.46 (0.30–0.67)
All-cause mortality	56	5750	0.97 (0.74–1.26)
Clinical disease progression	101	5592	1.80 (1.47–2.20)

CI; confidence interval.

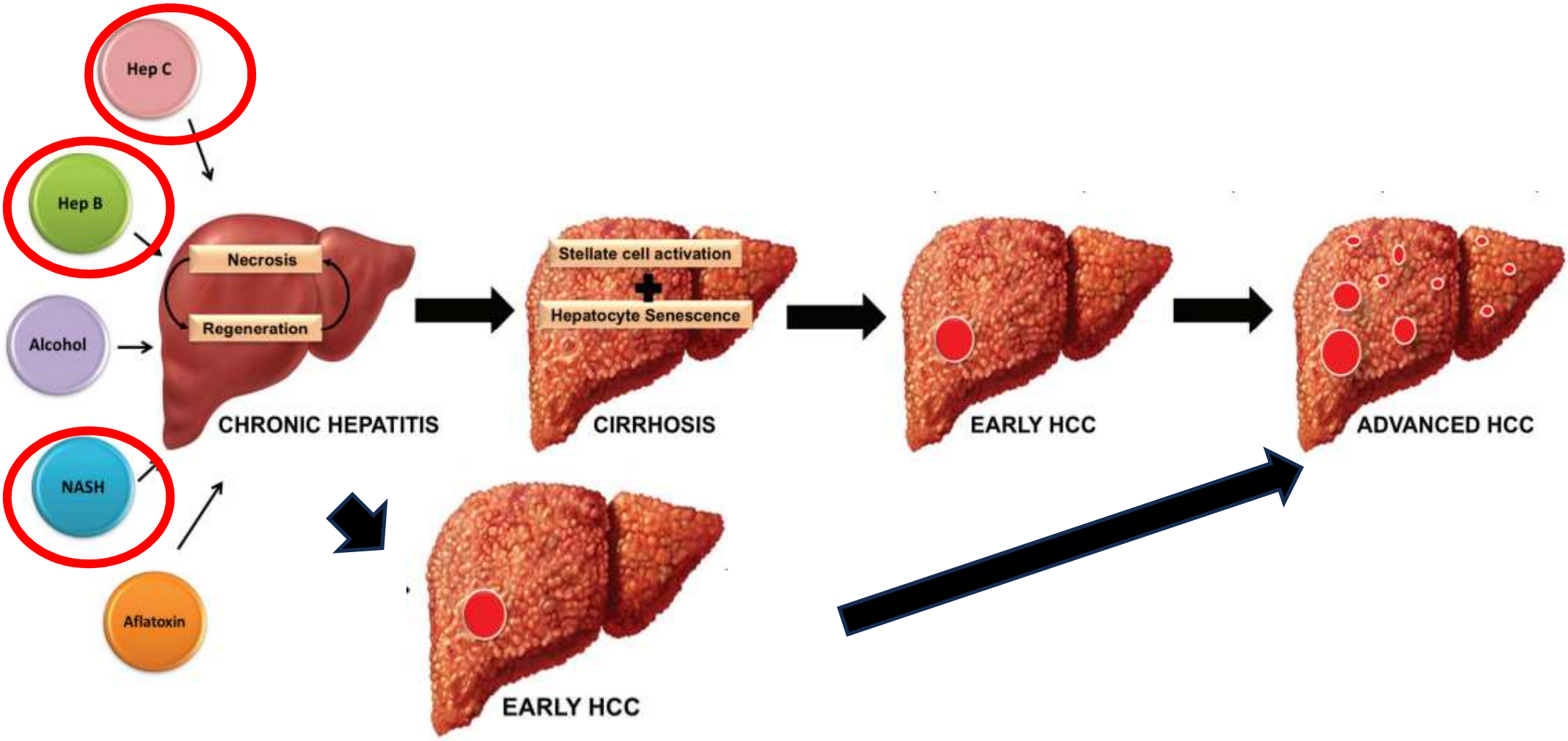
rch Article

EASL | JOURNAL OF HEPATOLOGY

Risk of cirrhosis-related complications in patients with advanced fibrosis following hepatitis C virus eradication



WHY?



Dhanasekaran R et al, *F1000Research,* 2016.

MAFLD

Research Article
Genetic and Metabolic Diseases

JOURNAL
OF HEPATOLOGY

Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016–2030

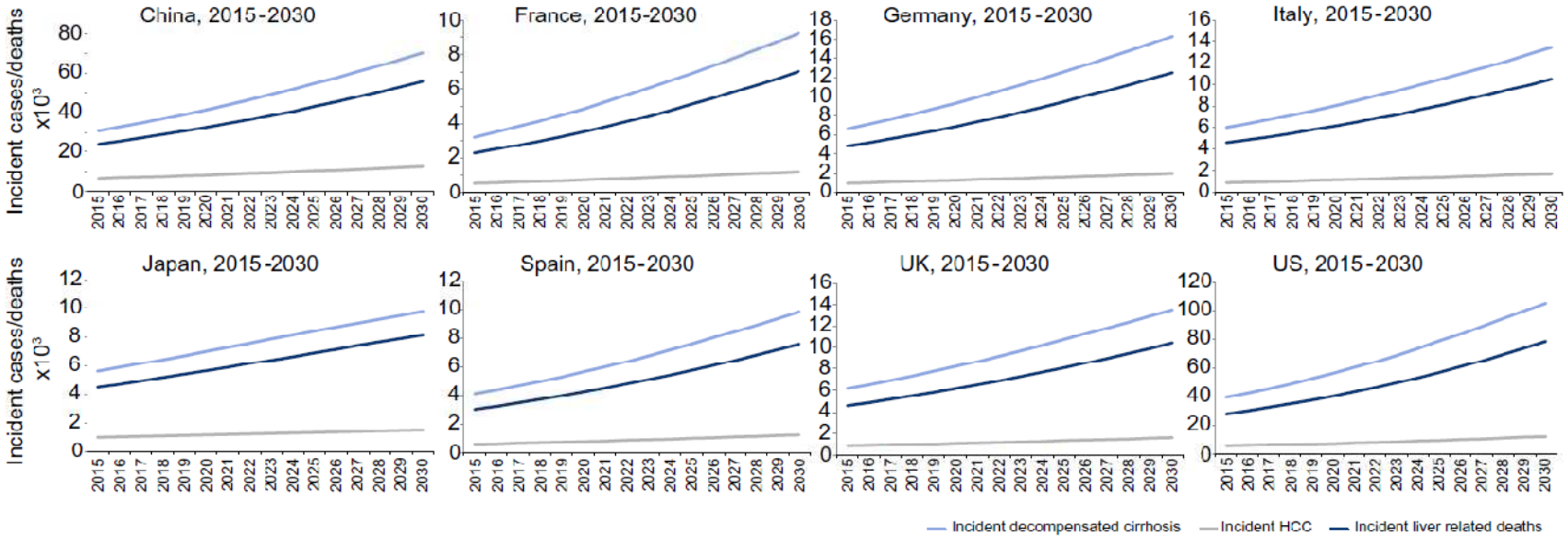
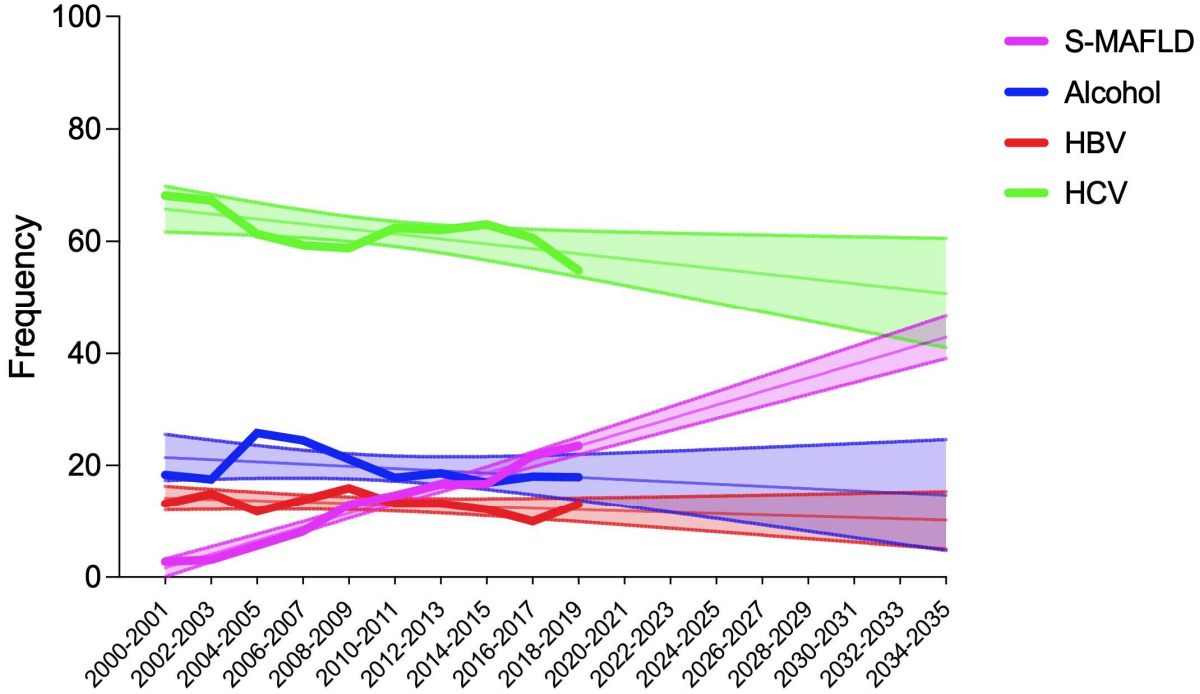


Fig. 3. Incident decompensated cirrhosis, HCC and liver-related deaths among prevalent NAFLD population – 2015–2030. HCC, hepatocellular carcinoma; NAFLD, non-alcoholic fatty liver disease.

TREND EPIDEMIOLOGICO MAFLD periodo 2000-2019

- La proporzione di pazienti MAFLD è aumentata nel periodo in studio;
- L'HCV correlata si è ridotta nel periodo in studio;
- L'eziologia alcolica e HBV correlata si sono mantenute costanti;
- La MAFLD ha già superato l'eziologia alcolica e HBV correlata.



	2000-2001	2002-2003	2004-2005	2006-2007	2008-2009	2010-2011	2012-2013	2014-2015	2016-2017	2018-2019	-
Alcol	42	61	86	92	118	138	167	160	134	134	-
HBV	30	52	39	52	89	102	118	114	74	97	-
HCV	156	234	204	223	328	484	558	595	452	411	-
MAFLD	2	6	13	24	62	100	137	145	165	174	-

MAFLD

Hindawi Publishing Corporation
BioMed Research International
Volume 2014, Article ID 106247, 6 pages
http://dx.doi.org/10.1155/2014/106247

Hindawi

Review Article

Nonalcoholic Fatty Liver Disease and Hepatocellular Carcinoma

Luciana Kikuchi, Cláudia P. Oliveira, and Flair J. Carrilho

TABLE 1: Case reports of HCC associated with NAFLD [7].

Case number	Age (years)	Sex	Comorbidity	Interval between liver disease and HCC (years)	Number/size (cm) HCC	Liver histology	Treatment	Survival
1	52	F	DM	4	Mult/—	Cirrhosis	Resection	Dead
2	62	M	DM, Ob	4	1/3	Cirrhosis	PEI	Dead
3	72	F	DM	10	3/1.4	Cirrhosis	NR	NR
4	67	F	DM	0	1/2.6	Fibrosis	Resection	NR
5	66	F	DM	2.5	1/1.5	Cirrhosis	Resection	Recurrence
6	68	F	NR	2	1/2	Cirrhosis	TAE	Alive
7	69	F	DM, Ob	0.5	1/2.5	Cirrhosis	TAI	Recurrence
8	72	M	Ob	0	1/3	Cirrhosis	TAE, PEI	Recurrence
9	63	M	DLP, Ob	0	1/2	Cirrhosis	Resection	Alive
10	56	M	DM	0	Mult/6	Cirrhosis	TAE	Dead
11	76	M	DM, Ob	10	1/1.9	Cirrhosis	RFA	Alive
12	74	M	DM, Ob	0	1/4	Fibrosis	Resection	NR
13	64	M	DM, Ob	0	1/—	Steatosis	TAE, resection	Alive
14	67	F	Res. Ins	2	2/1.5	Cirrhosis	TAE	Dead
15	64	M	Ob, DLP	0	Mult/13	Fibrosis	NR	Dead
16	70	M	DM, Ob	0	1/4.5	Cirrhosis	TAE, resection	NR

M: male, F: female, DM: diabetes mellitus, Ob: obese, DLP: dyslipidemia, Mult: multinodular, PEI: percutaneous ethanol injection, TAE: transarterial embolization, TAI: transarterial chemotherapy infusion, RFA: radiofrequency ablation, and NR: not reported.

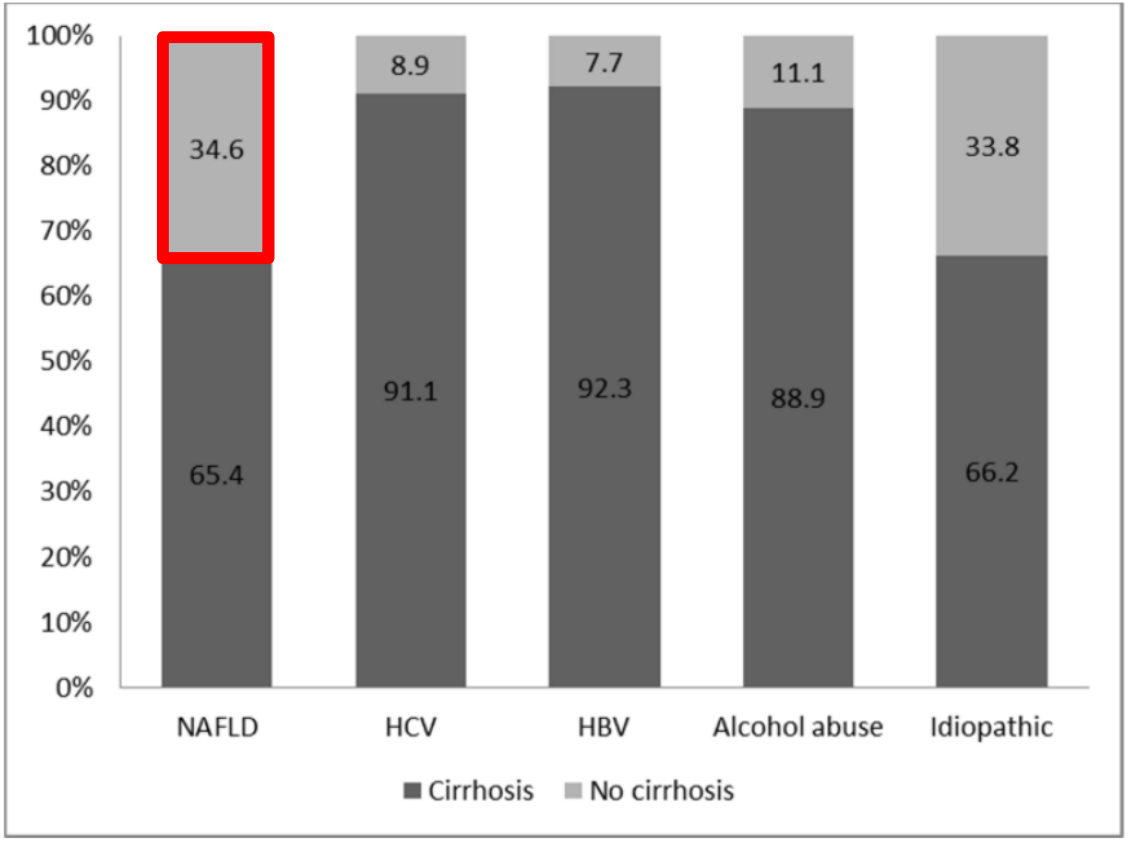
MAFLD

HHS Public Access
Author manuscript
Clin Gastroenterol Hepatol. Author manuscript; available in PMC 2017 January 01.

Published in final edited form as:
Clin Gastroenterol Hepatol. 2016 January ; 14(1): 124–131.e1. doi:10.1016/j.cgh.2015.07.019.

Hepatocellular Carcinoma in the Absence of Cirrhosis in US Veterans is Associated with Non-Alcoholic Fatty Liver Disease

Sahil Mittal, MD, MS[1,3], Hashem B. El-Serag, MD, MPH[1,2,3], Yvonne H. Sada, MD[1], Fasiha Kanwal, MD, MS[1,2,3], Zhigang Duan, MD, MS[1], Sarah Temple, BA[1], Sarah B. May, MS[1], Jennifer R. Kramer, PhD, MPH[1], Peter A. Richardson, PhD[1], and Jessica A. Davila, PhD[1]



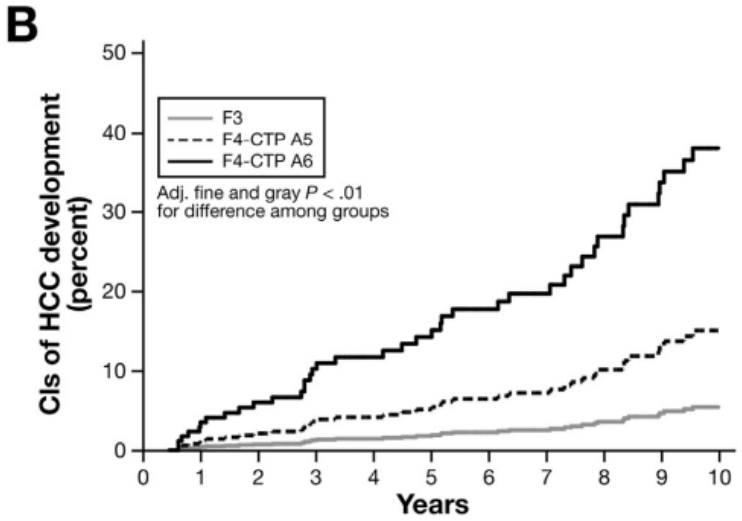
Conclusions—Approximately 13% of patients with HCC in the VA system do not appear to have cirrhosis. NAFLD and metabolic syndrome are the main risk factors HCC in the absence of cirrhosis.

MAFLD

Gastroenterology 2018;■:1–15

Fibrosis Severity as a Determinant of Cause-Specific Mortality in Patients With Advanced Nonalcoholic Fatty Liver Disease

Eduardo Vilar-Gomez,[1,2,*] **Luis Calzadilla-Bertot**,[3,*] Vincent Wai-Sun Wong,[4] Marlen Castellanos,[5] Rocio Aller-de la Fuente,[6] Mayada Metwally,[7] Mohammed Eslam,[7] Licet Gonzalez-Fabian,[8] María Alvarez-Quiñones Sanz,[9] Antonio Felix Conde-Martin,[10] Bastiaan De Boer,[11] Duncan McLeod,[12] Anthony Wing Hung Chan,[13] Naga Chalasani,[1] Jacob George,[7] Leon A. Adams,[3,§] and Manuel Romero-Gomez[2,§]



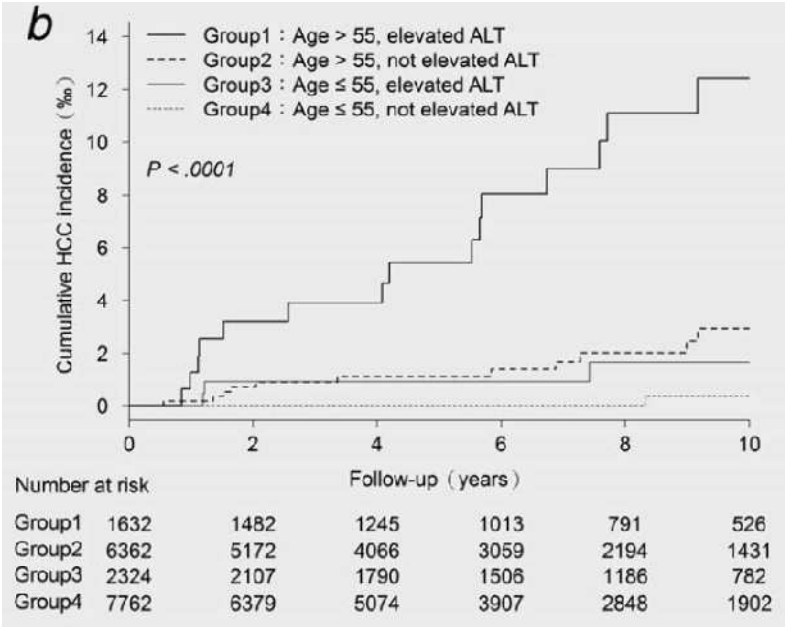
NEW FINDINGS

Patients with NAFLD cirrhosis have predominantly liver-related events whereas those with bridging fibrosis have predominantly non-hepatic cancers and vascular events.

IJC
International Journal of Cancer

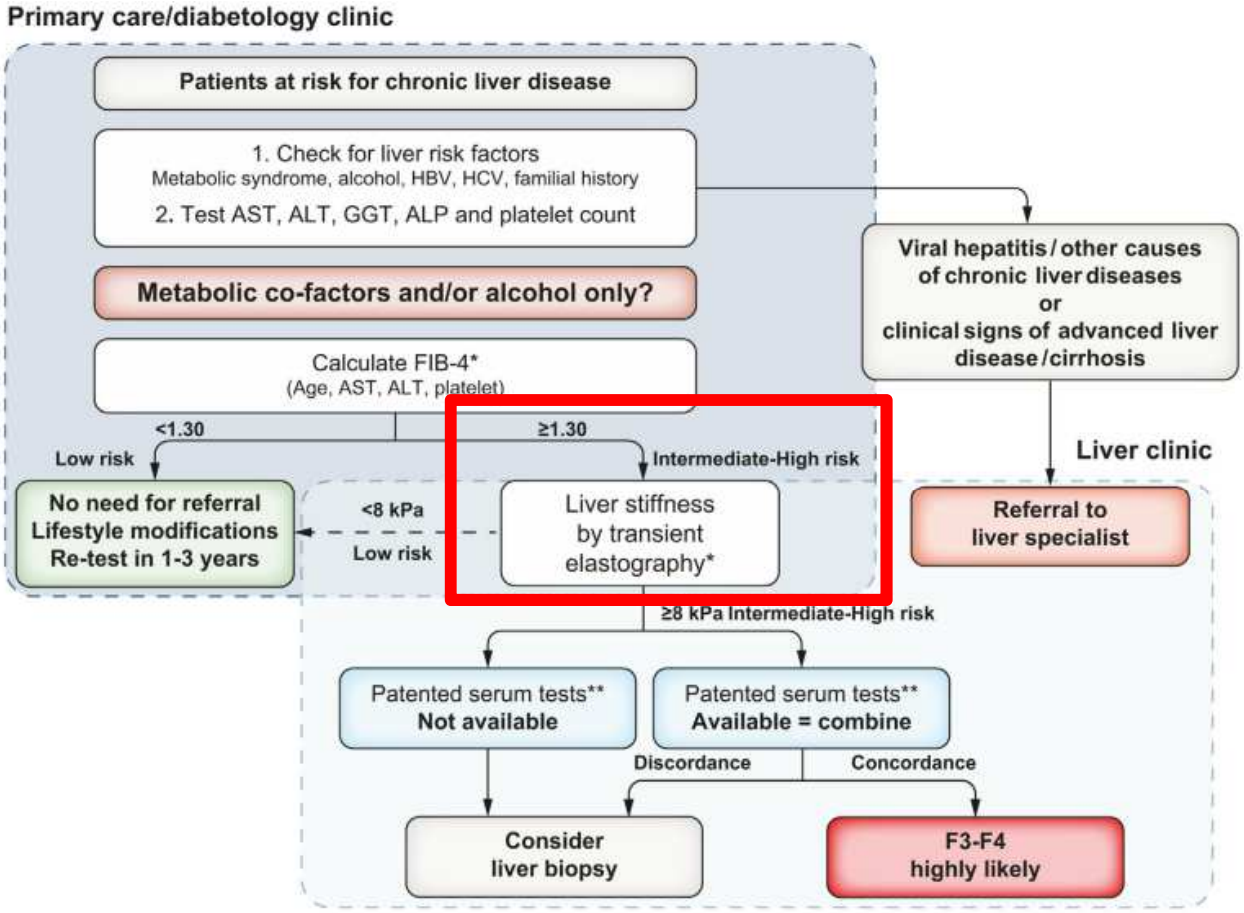
The occurrence of hepatocellular carcinoma in different risk stratifications of clinically noncirrhotic nonalcoholic fatty liver disease

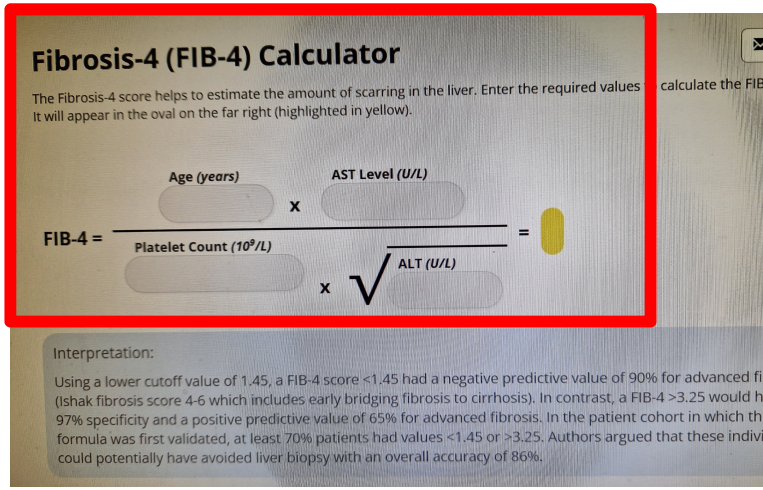
Teng-Yu Lee[1,2], Jaw-Ching Wu[3,4], Shi-Hang Yu[1], Jaw-Town Lin[5,6,7], Ming-Shiang Wu[8] and Chun-Ying Wu[1,9,10,11]



HCC risk is significantly increased in older patients
With elevated serum ALT

MAFLD





EASL CPG: non-invasive liver tests for evaluation of liver disease severity and prognosis. Frontline Gastroenterol. 2022.

PERFORMANCE SCORE DI FIBROSI

- Il BARD si conferma efficiente nei pazienti non cirrotici;
- Il FIB-4 si evidenzia molto efficiente, risultando più efficiente del BARD in maniera significativa;
- Il NFS e l'APRI si confermano non efficienti;

	Low-risk	High-risk	P
NAFLD fibrosis score	88 (45.1)	107 (54.9)	<0.0001
FIB-4	50 (25.8)	144 (74.2)	
NAFLD fibrosis score	88 (45.1)	107 (54.9)	<0.0001
APRI	135 (66.2)	69 (33.8)	
NAFLD fibrosis score	88 (45.1)	107 (54.9)	0.12
BARD	72 (36.9)	123 (63.1)	
FIB-4	50 (25.8)	144 (74.2)	<0.0001
APRI	135 (66.2)	69 (33.8)	
FIB-4	50 (25.8)	144 (74.2)	0.02
BARD	72 (36.9)	123 (63.1)	
APRI	135 (66.2)	69 (33.8)	<0.0001
BARD	72 (36.9)	123 (63.1)	

NAFLD

Analisi di Cox di confronto dell'efficacia tra i vari score di fibrosi.
Nella Tabella sono mostrate le percentuali di riga e non di colonna.

PERFORMANCE SCORE DI FIBROSI

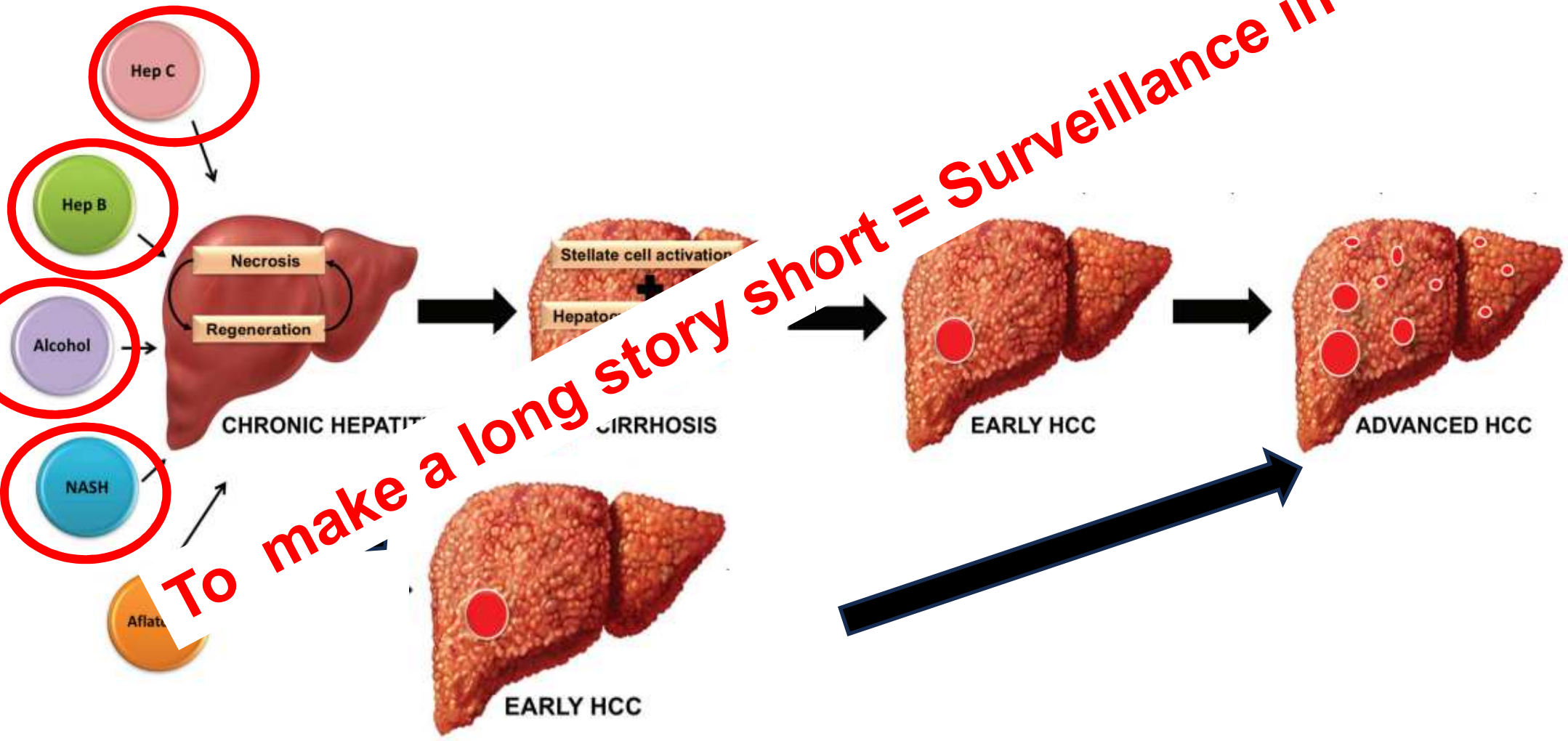
- Il BARD e il FIB-4 risultano efficienti;
- Non c'è differenza significativa di efficienza tra il BARD e il FIB-4;
- Il NAFLD fibrosis score e l'APRI non risultano efficienti.

	Low-risk	High-risk	P
NAFLD fibrosis score	41 (52.6)	37 (47.4)	0.001
FIB-4	27 (27.8)	70 (72.2)	
NAFLD fibrosis score	41 (52.6)	37 (47.4)	0.03
APRI	73 (68.2)	34 (31.8)	
NAFLD fibrosis score	41 (52.6)	37 (47.4)	0.004
BARD	35 (31)	78 (69)	
FIB-4	27 (27.8)	70 (72.2)	<0.0001
APRI	73 (68.2)	34 (31.8)	
FIB-4	27 (27.8)	70 (72.2)	0.65
BARD	35 (31)	78 (69)	
APRI	73 (67.6)	34 (30.4)	<0.0001
BARD	35 (31)	78 (69)	

MAFLD

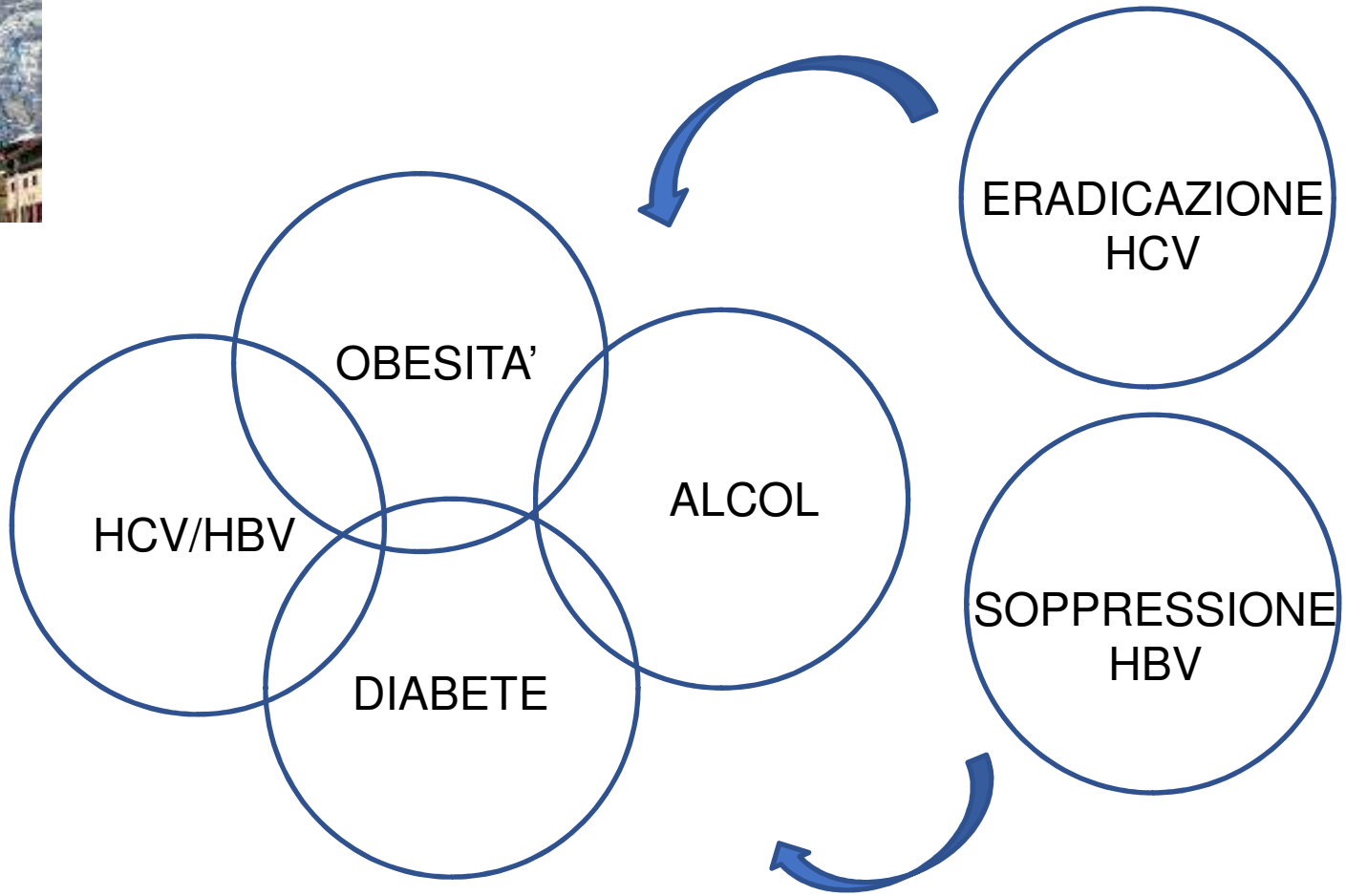
Analisi di Cox di confronto dell'efficacia tra i vari score di fibrosi.
Nella Tabella sono mostrate le percentuali di riga e non di colonna.

WHY? 4

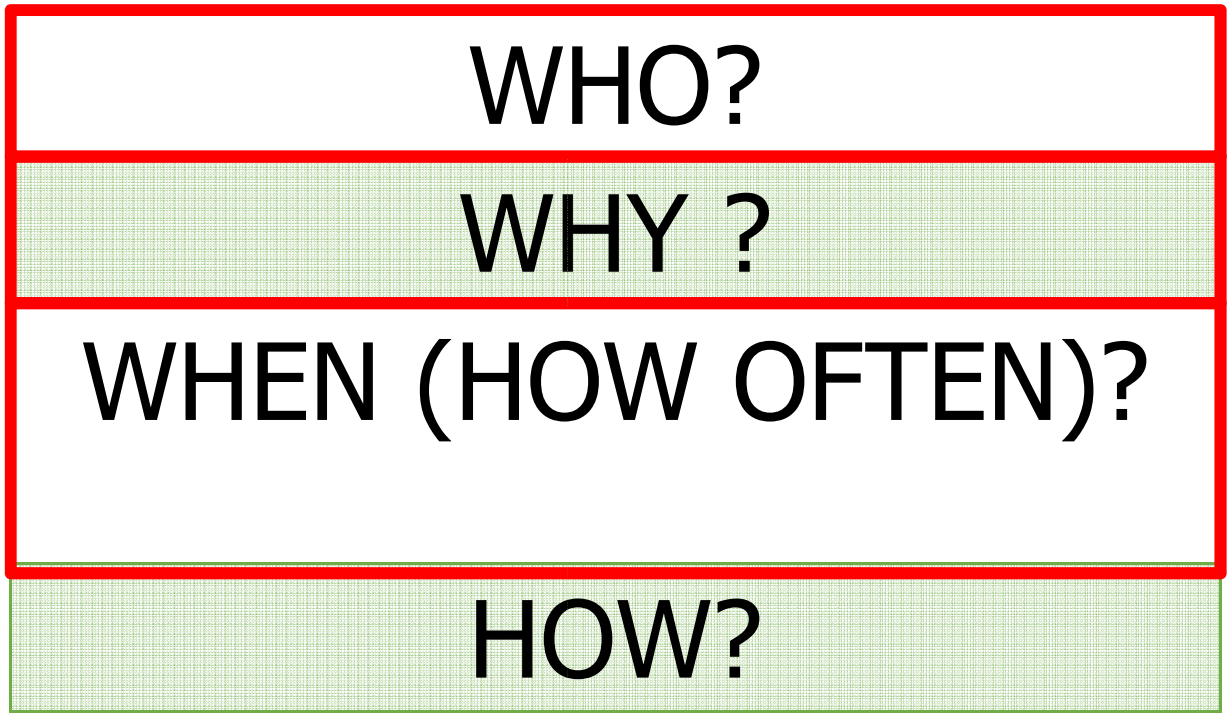


Dhanasekaran R et al, *F1000Research,* 2016.

Scenari complessi



SORVEGLIANZA 3



WHEN (HOW OFTEN)?

Interval should be dictated by rate of tumour growth and tumour incidence in target population

6-month interval is reasonable and cost-effective

→ **3 months**: no clinical benefit

→ **12 months**: fewer early stage diagnoses and shorter survival

Forner A, et al. Lancet 2018;391:1301–1314; EASL CPG HCC. J Hepatol 2018.

Digestive and Liver Disease 54 (2022) 927–936

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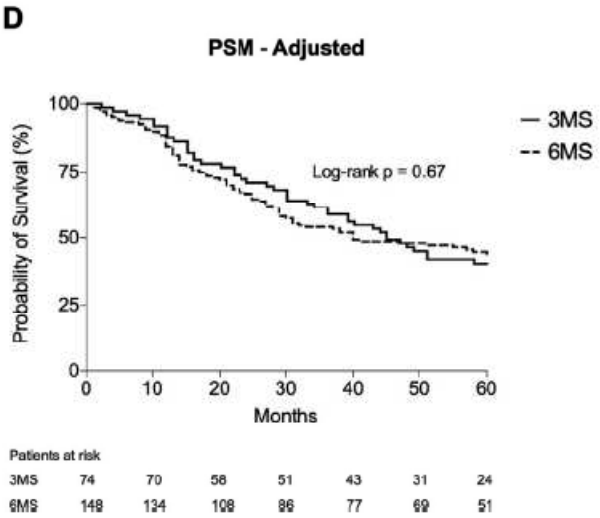
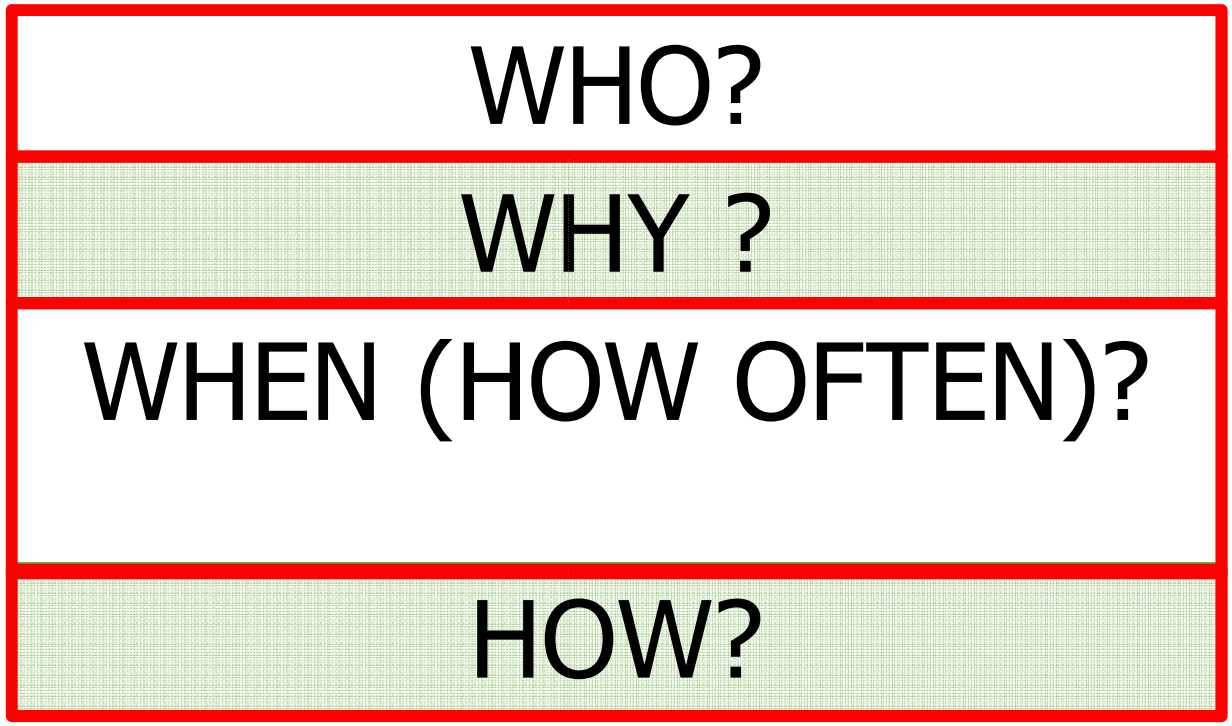
cology

rveillance for hepatocellular carcinoma with a 3-months interval in xtremely high-risk" patients does not further improve survival



SORVEGLIANZA 4



HOW?

- Benefit of surveillance has not been established in all risk groups
- US remains the method of choice
  - Serological tests are not currently cost-effective

Recommendations	Level of evidence	Grade of recommendation
Role of **surveillance for patients with NAFLD** without ci…	Low	
Surveillance should be performed by **experienced**… …**h-risk populations** using **abdominal US every 6 months**	Moderate	Strong
Tumour **biomarkers** for accurate earl… …**cking***	Low	-

E il colangiocarcinoma?

Forner A, et al. Lancet 2018;391:1301–1314; EASL CPG HCC. J Hepatol 2018.

NAFLD/MAFLD/MASLD (**Metabolic** dysfunction-**associated** steatotic **liver disease**)
- US less accurate = 1 year NMR (?)

arch Article
ic and Biliary Cancer

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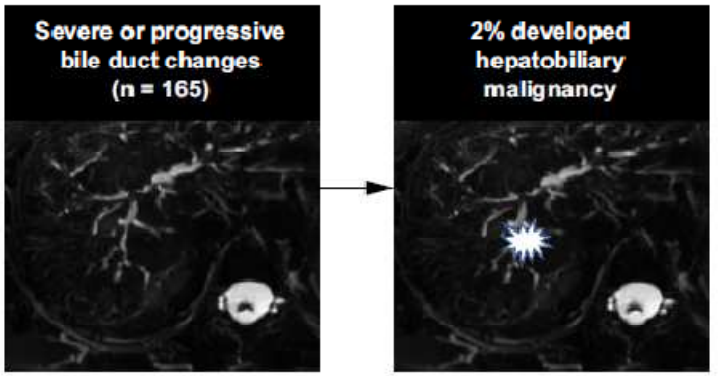
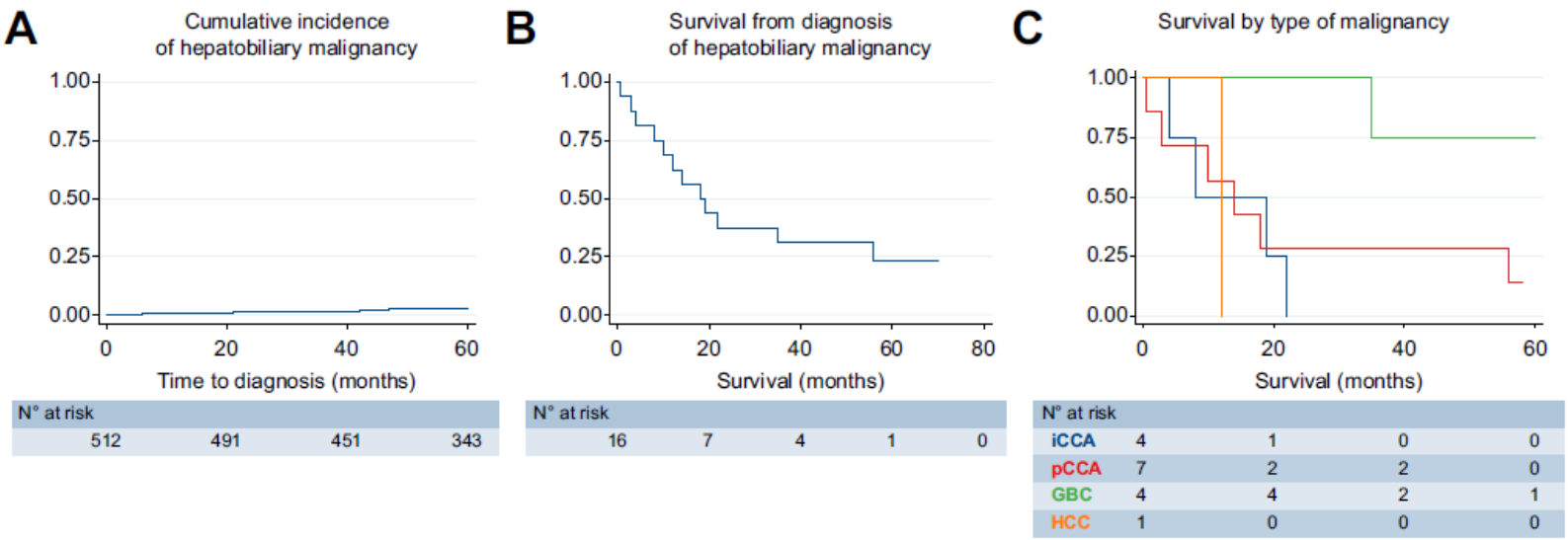
OF HEPATOLOGY

ospective surveillance for cholangiocarcinoma in unselected individuals with primary sclerosing cholangitis

ors

a Villard, Ingalill Friis-Liby, Fredrik Rorsman, ..., Therese Hagström, Emma Nilsson, Annika Bergquist





Conclusion: In an unselected cohort of patients with PSC, yearly CA19-9 and MRI/MRCP surveillance followed by ERCP was ineffective in detecting cancer early enough to support long-term survival. Given the low occurrence of CCA, studies on individualised strategies for follow-up and improved diagnostic methods for PSC-related CCA are warranted.

Clinics and Research in Hepatology and Gastroenterology 47 (2023) 102223

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Review

New epidemiologic trends in cholangiocarcinoma

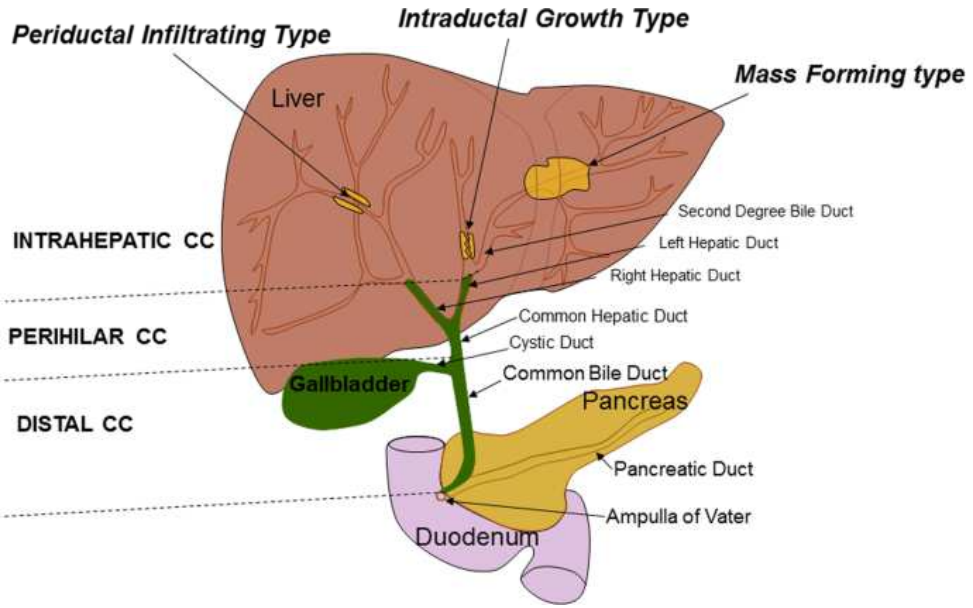

Table 2
Main risk factors for iCCA and eCCA.

Risk factor	OR	CCA type	Study type	Reference
Hepatobiliary flukes	27	CCA	Case-control	Honjo et al., Int J Cancer 2005 [11]
Hepatolithiasis	50	iCCA	Case-control	Lee et al., Am J Gastroenterol 2008
Choledocholithiasis	10.08/ 18.58	iCCA/ eCCA	Meta-analysis	Clements et al., J Hepatol 2020 [12, 44]
Choledochal cysts	26.71/ 34.94	iCCA/ eCCA	Meta-analysis	Clements et al., J Hepatol 2020 [44]
PSC	22/41	iCCA/ eCCA	Case-control	Petrick et al., PLoS One 2017 [39]
HCV/HBV infection	4.8/5.1	iCCA	Meta-analysis	Palmer and Patel, J Hepatol 2012
	3.38	iCCA	Meta-analysis	Li et al., World J Surg Oncol 2015
	4.28/ 4.57	iCCA	Meta-analysis	Clements et al., J Hepatol 2020 [31, 32,44]
Cirrhosis	22.9	iCCA	Meta-analysis	Palmer and Patel, J Hepatol 2012
	13.32/ 3.82	iCCA/ eCCA	Meta-analysis	Clements et al., J Hepatol 2020 [31, 44]
MAFLD	3.52/ 2.93	iCCA/ eCCA	Case-control	Petrick et al., PLoS One 2017
	2.09/ 2.05	iCCA/ eCCA	Meta-analysis	Wongjarupong et al., BMC Gastroenterol 2017
	2.19	iCCA	Meta-analysis	Corrao et al., Eur J Gastroenterol Hepatol 2021
Type 2 diabetes mellitus	1.73	iCCA	Meta-analysis	Clements et al., J Hepatol 2020 [39, 40,41,44]
Alcohol consumption	3.15/ 1.75	iCCA/ eCCA	Meta-analysis	Clements et al., J Hepatol 2020 [44]

TAKE HOME MESSAGES

❑**HCC**

- Ecografia addome superiore ogni 6 mesi nei:

a) Pazienti cirrotici;

b) Pazienti con infezione HBV relata;

c) Pazienti con FIB-4 >2.67 con

❑ **COLANGIOCARC** CA19-9 nella colangite sclerosante (?)
Intraepatico c

❑**AD** **CO**

nuale (RMN/TC) nelle donne;

b ezione negli uomini


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