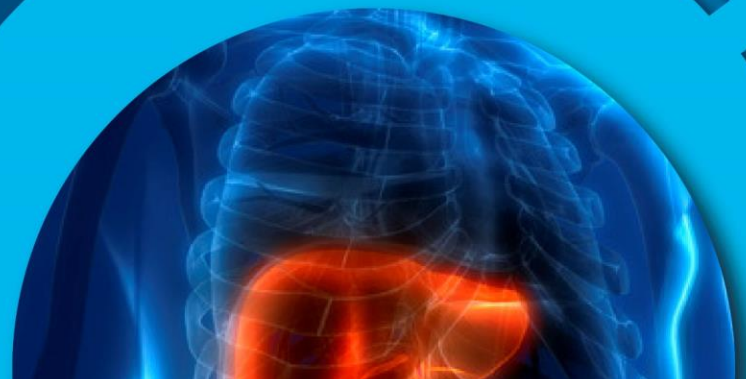

Patient Journey

Approccio personalizzato al paziente e esperienze a confronto: Epatocarcinoma e Colangiocarcinoma

01 Febbraio 2024

VERONA

CROWNE PLAZA
Via Belgio, 16

EPATOCARCINOMA

I numeri in Italia, fattori di rischio, prevenzione, diagnosi e terapia: il ruolo del Gastroenterologo

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AIGOM
ASSOCIAZIONE ITALIANA
GRUPPI ONCOLOGICI MULTIDISCIPLINARI

Disclosures

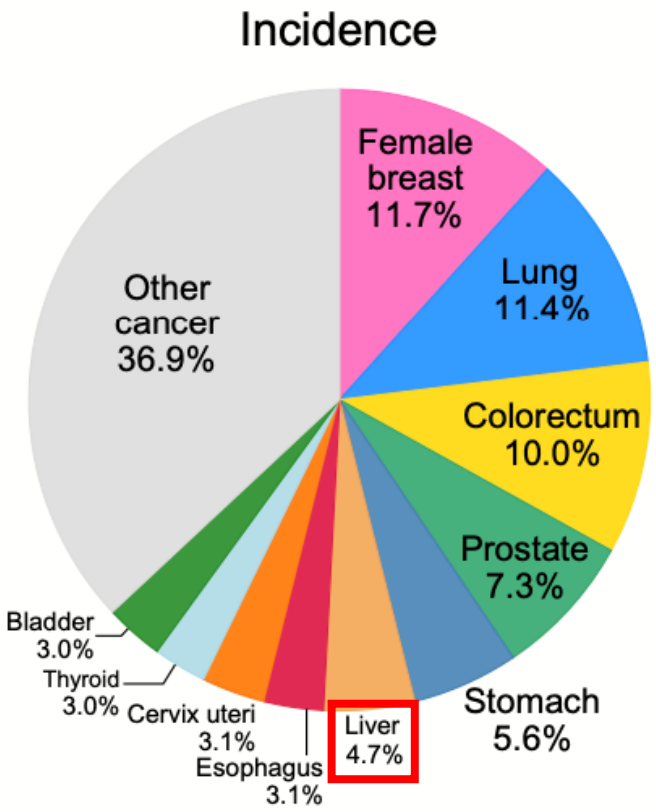
No conflict of interest

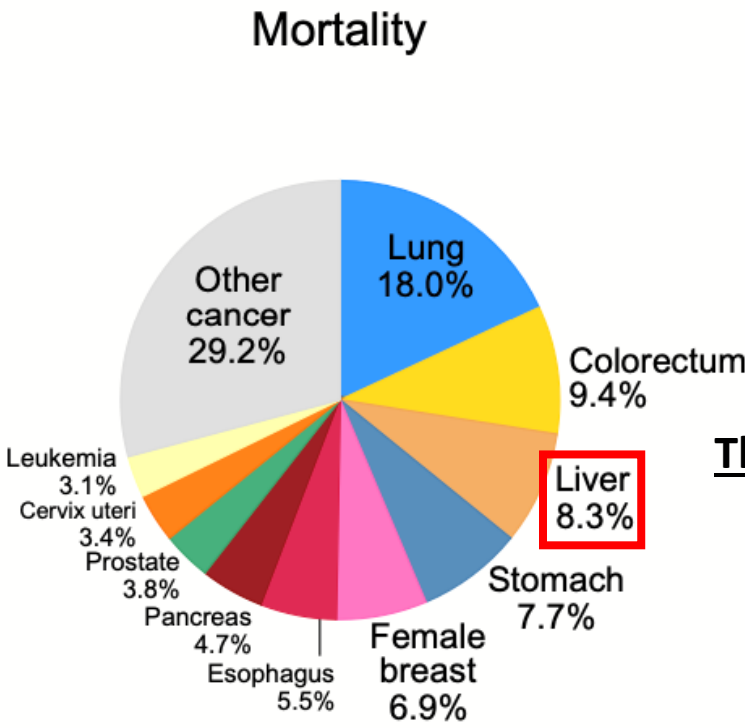
Agenda

- Epidemiology of hepatocellular carcinoma
- Temporal trends and risk factors
- Primary prevention and surveillance
- Diagnosis of HCC: the need for liver biopsy
- Treatment: multiparametric and multidisciplinary assessment

Global incidence and mortality – 2020 estimates

Sixth most commonly diagnosed cancer





Third most common cause of cancer-related death

Sung H, et al. CA Cancer J Clin. 2021;71(3):209-249. doi: 10.3322/caac.21660.

Global incidence and mortality – 2020 estimates

Table 1. Estimated number of primary liver cancer cases and deaths, and age-standardised incidence and mortality rates per 100,000 persons in 2020, by world region and HDI.

	Population		Incidence				Mortality			
	Total (thousands)	Percentage of world total (%)	Number of cases	Percentage of world total (%)	ASR	M:F	Number of deaths	Percentage of world total (%)	ASR	M:F
Eastern Africa	445,406	5.7	12,300	1.4	5.0	1.6	11,500	1.4	4.8	1.6
Middle Africa	179,595	2.3	6,100	0.7	6.1	2.3	5,700	0.7	5.9	2.3
Northern Africa	246,233	3.2	31,900	3.5	15.2	1.9	30,400	3.7	14.5	1.9
Southern Africa	67,504	0.9	2,600	0.3	4.6	2.2	2,400	0.3	4.3	2.3
Western Africa	401,861	5.2	17,600	1.9	8.4	2.0	16,900	2.0	8.2	2.0
Caribbean	43,532	0.6	3,400	0.4	5.5	1.6	3,200	0.4	5.0	1.6
Central America	179,670	2.3	11,800	1.3	6.3	1.2	11,200	1.4	5.9	1.2
South America	430,760	5.5	24,300	2.7	4.3	1.6	23,200	2.8	4.1	1.6
Northern America	368,870	4.7	46,600	5.1	6.8	2.7	34,800	4.2	4.7	2.4
Eastern Asia	1,678,090	21.5	491,700	54.3	17.8	3.0	449,500	54.1	16.1	3.1
China	1,447,470	18.6	410,000	45.3	18.2	3.1	391,200	47.1	17.2	3.0
South-Eastern Asia	668,620	8.6	99,300	11.0	13.7	3.0	95,700	11.5	13.2	3.0
South-Central Asia	2,014,709	25.8	54,700	6.0	3.0	2.0	52,800	6.4	2.8	2.0
India	1,380,004	17.7	34,700	3.8	2.6	2.3	33,800	4.1	2.5	2.3
Western Asia	278,429	3.6	11,300	1.3	4.7	1.9	10,900	1.3	4.5	1.9
Central-Eastern Europe	293,013	3.8	24,800	2.7	4.3	2.6	23,000	2.8	3.9	2.6
Northern Europe	106,261	1.4	11,900	1.3	5.0	2.1	10,500	1.3	3.9	2.1
Southern Europe	153,423	2.0	24,800	2.7	6.7	3.3	21,200	2.6	5.1	3.2
Western Europe	196,146	2.5	26,100	2.9	5.4	3.3	23,700	2.8	4.5	3.1
Australia/ New Zealand	30,322	0.4	3,300	0.4	6.1	3.3	2,500	0.3	4.1	2.7
Melanesia, Micronesia & Polynesia	12,356	0.2	1,100	0.1	11.3	1.7	1,000	0.1	11.2	1.7
Low HDI	990,175	12.7	33,100	3.7	6.2	1.8	31,600	3.8	6.0	1.8
Medium HDI	2,327,556	29.9	100,000	11.0	4.7	2.3	95,900	11.5	4.5	2.3
High HDI	2,909,468	37.3	548,900	60.6	14.0	2.8	524,300	63.2	13.3	2.8
Very high HDI	1,564,286	20.1	223,300	24.7	7.9	2.8	178,100	21.5	5.1	2.8
World	7,794,799	100.0	905,700	100.0	9.5	2.7	830,200	100.0	8.7	2.7

ASR, age-standardised rate per 100,000; HDI, Human Development Index; M:F, male:female ASR ratio.

Rumgay H, et al. J Hepatol. 2022;77(6):1598-1606. doi: 10.1016/j.jhep.2022.08.021.

Incidence of liver cancer in Italy - 2020

Sede	Maschi	Femmine	Totale
	N. (%)	N. (%)	N. (%)
Vie Aero Digestive Superiori -VADS*	7.276 (3,7)	2.580 (1,4)	9.856 (2,6)
Esofago	1.710 (0,9)	684 (0,4)	2.394 (0,6)
Stomaco	8.458 (4,3)	6.098 (3,4)	14.556 (3,9)
Colon-Retto	23.420 (12,0)	20.282 (11,2)	43.702 (11,6)
Fegato	8.978 (4,6)	4.034 (2,2)	13.012 (3,5)
Pancreas	6.847 (3,5)	7.416 (4,1)	14.263 (3,8)
Colecisti e vie biliari	2400 (1,2)	3.000 (1,7)	5.400 (1,4)
Polmone	27.554 (14,1)	13.328 (7,3)	40.882 (10,9)
Melanomi	8.147 (4,2)	6.716 (3,7)	14.863 (4,0)
Mesotelioma	1.523 (0,8)	463 (0,3)	1.986 (0,5)
Totale	**194.754 ******	**181.857**	**376.611**

TABELLA 6. Numero di nuovi casi di tumore (e percentuali sul totale) stimati per il 2020 in base al sesso e per le sedi più frequenti[§]. Sono esclusi i carcinomi della cute non melanomi

AIRTUM, https://www.registri-tumori.it/cms/pubblicazioni/i-numeri-del-cancro-italia-2020

Incidence and mortality of liver cancer in Italy

FEGATO	
Incidenza	Nel 2023, sono state stimate circa 12.200 nuove diagnosi (rapporto U:D 2:1)
Mortalità	Nel 2022, sono state stimate 9.600 morti (6.300 negli uomini e 3.300 nelle donne). Le stime per il 2023 non sono disponibili
Sopravvivenza netta a 5 anni dalla diagnosi	22% negli uomini e 22% nelle donne
Probabilità di vivere ulteriori 4 anni condizionata ad aver superato il primo anno dopo la diagnosi	40% negli uomini e 39% nelle donne
Prevalenza	Sono 33.800 le persone viventi in Italia dopo una diagnosi di tumore del fegato (uomini = 25.300; donne = 8.500)

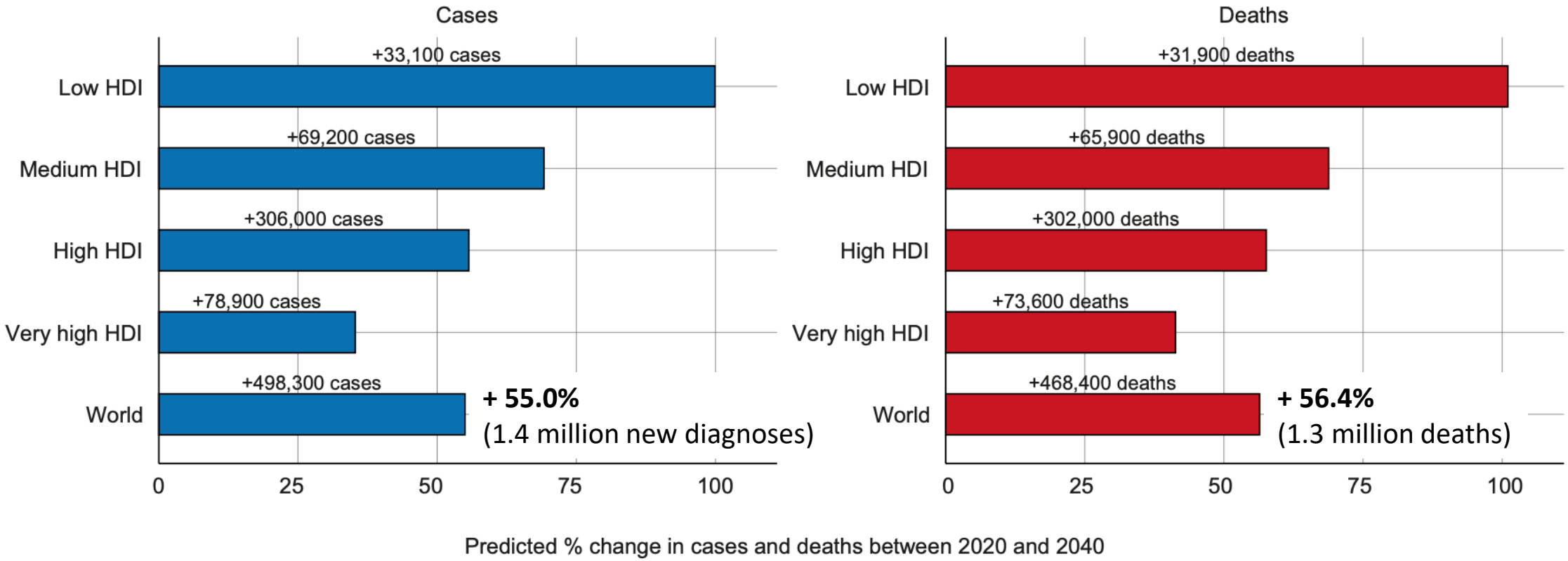
AIRTUM, https://www.registri-tumori.it/cms/pubblicazioni/i-numeri-del-cancro-italia-2023

Agenda

- Epidemiology of hepatocellular carcinoma
- Temporal trends and risk factors
- Primary prevention and surveillance
- Diagnosis of HCC: the need for liver biopsy
- Treatment: multiparametric and multidisciplinary assessment

Predicted increase of cases and deaths from liver cancer

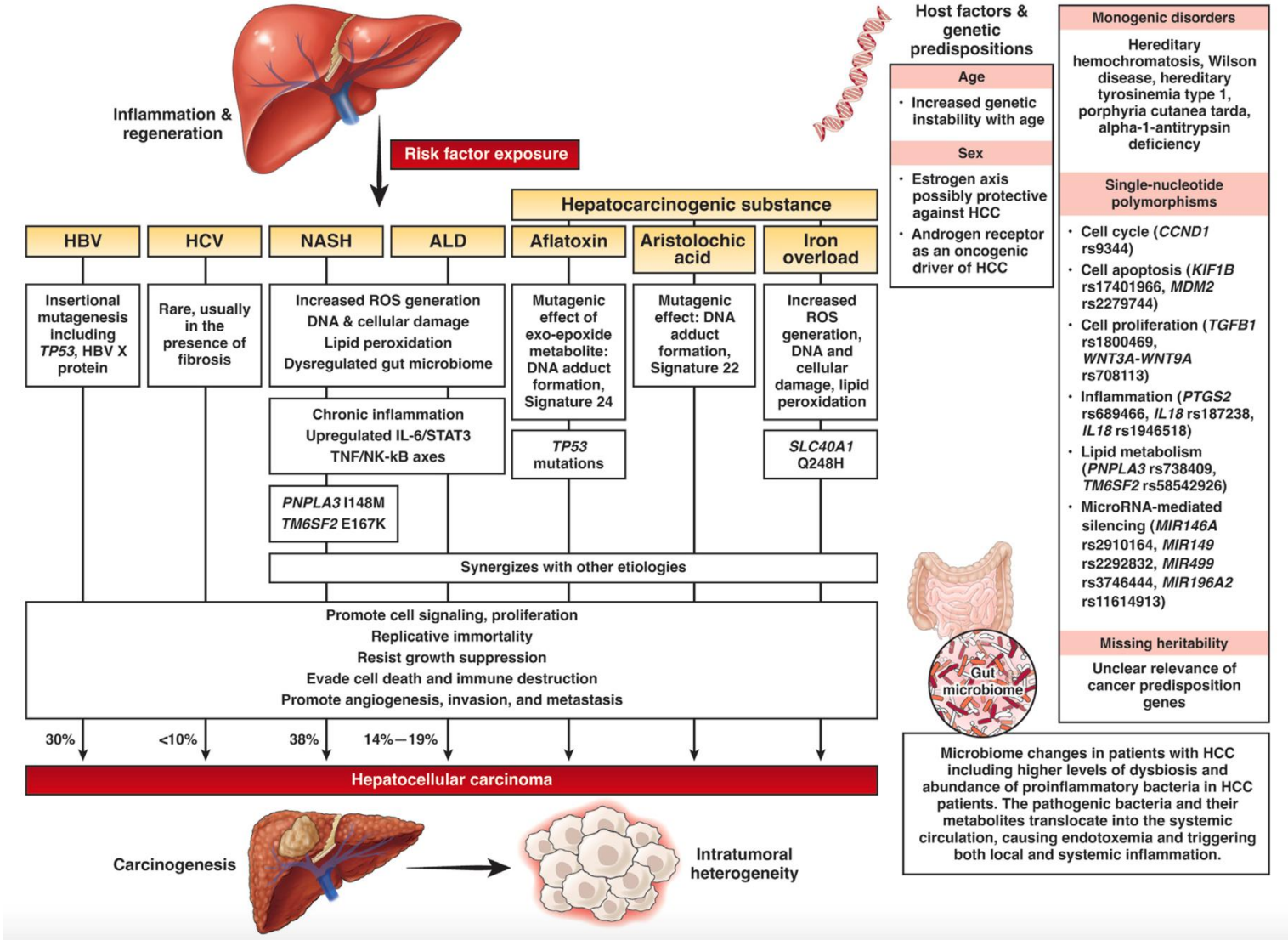
2020 → 2040



Rumgay H, et al. J Hepatol. 2022;77(6):1598-1606. doi: 10.1016/j.jhep.2022.08.021.

HCC risk factors

- HBV and HCV infections
- Excessive alcohol consumption
- Metabolic syndrome, T2DM, obesity
- NAFLD/NASH
- Tobacco smoking
- Aflatoxin



(1) Toh MR, et al. Gastroenterology. 2023 Apr;164(5):766-782. doi: 10.1053/j.gastro.2023.01.033. **(2)** McGlynn KA, et al. Hepatology. 2021 Jan;73 Suppl 1(Suppl 1):4-13. doi: 10.1002/hep.31288.

HCC risk factors – HBV and HCV

Table 1. Number of liver cancer cases in 2012 and fraction attributable to HBV and HCV by regions and development status

	Total number of cases[1]	HBV			HCV		
		Attributable cases[1]	AF	95% CI	Attributable cases[1]	AF	95% CI
By region							
Northern Europe	6,400	510	8	(2–20)	1,800	28	(10–55)
Rest of Europe	57,000	11,000	20	(15–26)	23,000	40	(32–49)
Northern America	33,000	2,400	7	(2–17)	19,000	59	(37–79)
Latin America	30,000	6,800	22	(13–35)	13,000	44	(29–59)
Eastern Asia	540,000	370,000	69	(63–74)	58,000	11	(9–14)
Western-Central Asia	48,000	22,000	46	(35–57)	14,000	28	(19–39)
Northern Africa	20,000	1,800	9	(4–16)	16,000	79	(69–86)
Sub-Saharan Africa	39,000	19,000	50	(39–60)	8,100	21	(13–32)
Australia and New Zealand	28,000	1,000	51	(43–58)	410	21	(16–27)
By development status							
More developed	190,000	44,000	23	(20–27)	82,000	44	(38–49)
Less developed	580,000	390,000	67	(61–72)	71,000	12	(10–15)
Total	770,000	430,000	56	(52–60)	150,000	20	(18–22)

Abbreviations: AF, attributable fraction; CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus.
[1]Estimated numbers of cases are rounded to two significant figures.

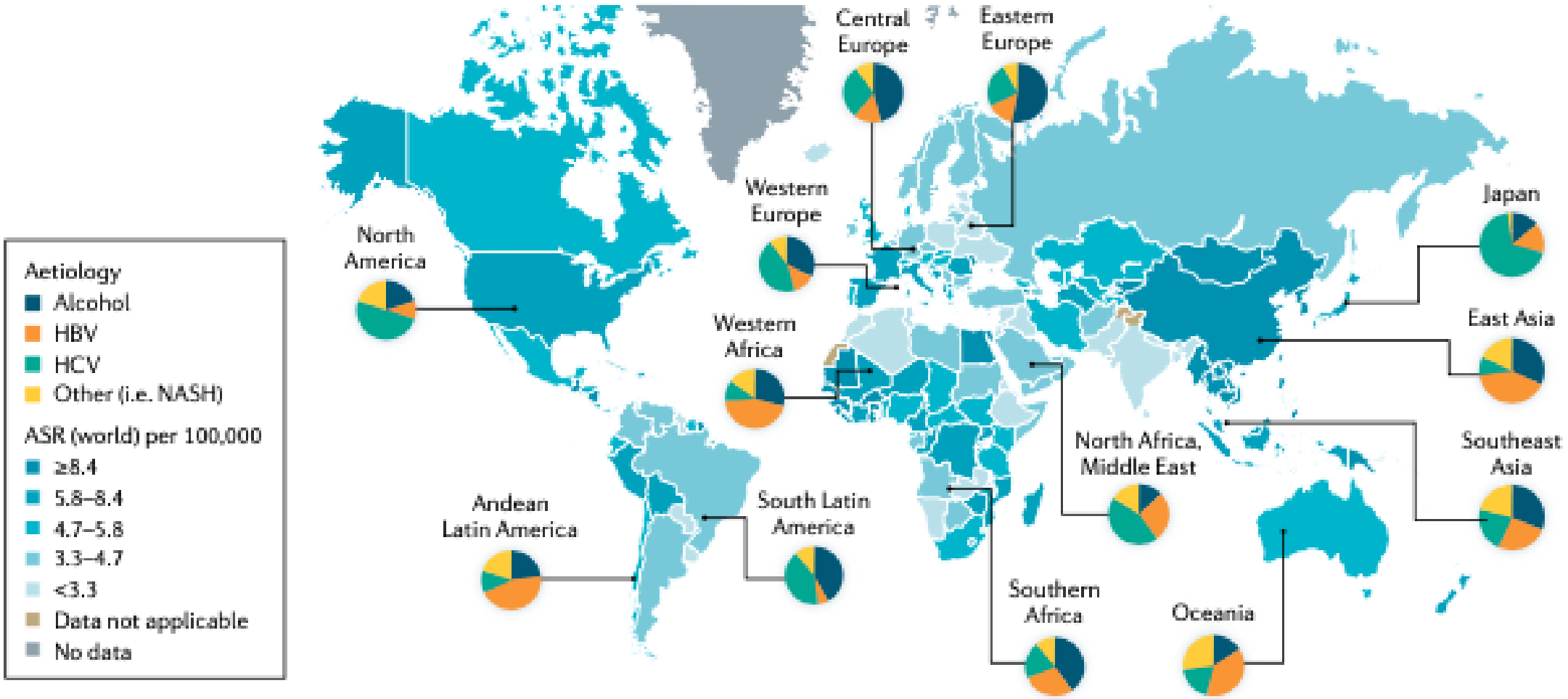
Maucort-Boulch D, et al. Int J Cancer. 2018 Jun 15;142(12):2471-2477. doi: 10.1002/ijc.31280.

HCC risk factors – alcohol

	Males			Females			Total		
	Alcohol-attributable cases	Population attributable fraction	Age-standardised incidence rate per 100 000 males	Alcohol-attributable cases	Population attributable fraction	Age-standardised incidence rate per 100 000 females	Alcohol-attributable cases	Population attributable fraction	Age-standardised incidence rate per 100 000 people
Lip and oral cavity cancer (C00–C06)	66 700 (40 000–105 300)	25·9% (15·6–40·9)	1·6 (0·9–2·5)	8200 (4600–14 300)	7·3% (4·1–12·7)	0·2 (0·1–0·3)	74 900 (44 600–119 600)	20·2% (12·1–32·3)	0·9 (0·5–1·4)
Pharyngeal cancer (C09–C10, C12–C13)	37 000 (15 200–63 400)	25·3% (10·4–43·4)	1·8 (0·7–3·1)	2500 (940–4400)	7·4% (2·8–13·4)	0·1 (0·0–0·2)	39 400 (16 100–67 800)	22·0% (9·0–37·8)	0·5 (0·4–1·6)
Oesophageal cancer (C15)*	163 100 (94 200–231 000)	39·2% (22·7–55·6)	3·9 (2·2–5·5)	26 600 (16 700–43 700)	14·3% (9·0–23·5)	0·6 (0·4–0·9)	189 700 (110 900–274 600)	31·6% (18·4–45·7)	2·1 (1·3–3·1)
Colon cancer (C18)	76 900 (57 700–95 400)	13·0% (9·7–16·1)	1·8 (1·3–2·2)	14 600 (10 600–19 100)	2·7% (1·9–3·5)	0·3 (0·2–0·4)	91 500 (68 300–114 500)	8·1% (6·0–10·1)	1·0 (0·7–1·2)
Rectal cancer (C19–C20)	57 300 (42 700–71 800)	13·0% (9·7–16·3)	1·4 (1·0–1·7)	7800 (5800–10 300)	2·7% (2·0–3·6)	0·2 (0·1–0·2)	65 100 (48 500–82 000)	9·0% (6·7–11·3)	0·7 (0·5–0·9)
Liver cancer (C22)†	141 300 (39 600–255 000)	22·7% (6·4–40·9)	3·3 (0·9–6·0)	13 400 (4100–26 400)	5·0% (1·5–9·8)	0·3 (0·1–0·5)	154 700 (43 700–281 500)	17·3% (4·9–31·6)	1·7 (0·5–3·2)
Laryngeal cancer (C32)	26 400 (15 100–41 600)	16·6% (9·5–26·1)	0·6 (0·4–1·0)	1200 (620–1700)	4·7% (2·5–7·0)	0·0 (0·0–0·0)	27 600 (15 700–43 300)	15·0% (8·6–23·6)	0·3 (0·2–0·5)
Breast cancer (C50)	..	..	..	98 300 (68 200–130 500)	4·4% (3·0–5·8)	2·2 (1·3–3·2)	98 300 (68 200–130 500)	4·4% (3·0–5·8)	1·1 (0·7–1·6)
All sites excluding non-melanoma skin cancer (C00–C97 excluding C44)	568 700 (422 500–731 100)	6·1% (4·6–7·9)	13·4 (10·0–17·4)	172 600 (135 900–220 100)	2·0% (1·6–2·5)	3·7 (2·7–5·0)	741 300 (558 500–951 200)	4·1% (3·1–5·3)	8·4 (6·2–10·9)

Rumgay H, et al. Lancet Oncol. 2021;22(8):1071-1080. doi: 10.1016/S1470-2045(21)00279-5.

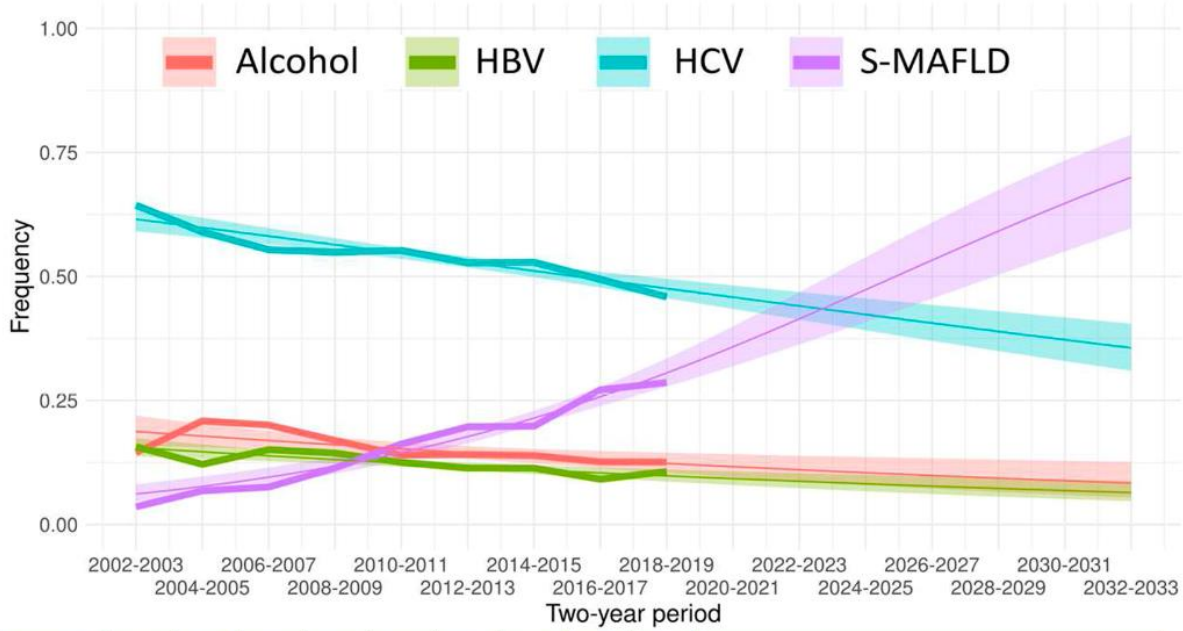
HCC risk factors



Llovet JM et al., Nat Rev Dis Prim, 2021;7:6

HCC risk factors – temporal trends in Italy

The major risk factors appear to be in transition, with the prevalence of HBV and HCV declining and excess body weight and diabetes increasing in many regions.



S-MAFLD	28	28	35	76	146	208	230	261	169	---
Alcohol	102	86	93	113	125	150	159	124	73	---
HBV	104	50	70	96	113	120	130	86	62	---
HCV	450	243	257	366	496	557	608	469	268	---

Vitale A, et al. Gut. 2023;72(1):141-152. doi: 10.1136/gutjnl-2021-324915.

Agenda

- Epidemiology of hepatocellular carcinoma
- Temporal trends and risk factors
- Primary prevention and surveillance
- Diagnosis of HCC: the need for liver biopsy
- Treatment: multiparametric and multidisciplinary assessment

Primary prevention – HBV

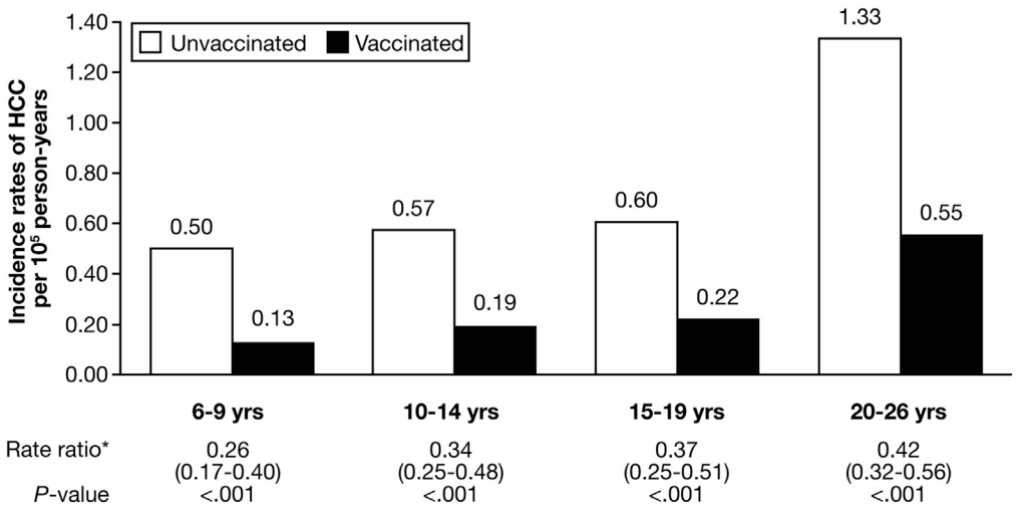


Table 3. Comparison of the Relative Risks for Developing Hepatocellular Carcinoma in 6- to 26-Year-Olds Unvaccinated and Differently Vaccinated Birth Cohorts

Variable group	No. of HCCs	Person-years	Incidence rate (per 10^5 person-years)	RR	95% CI	*P* value
Cohort						
Unvaccinated[a]	1,343	145,810,471	0.92	1.00	Referent	
Vaccinated	166	73,804,848	0.23	0.24	0.21–0.29	<.001
Vaccinated birth cohort (July to June)						
1984–1986[a]	59	14,388,916	0.41	0.45	0.34–0.57	<.001
1986–1992[a]	76	31,513,457	0.24	0.26	0.21–0.33	<.001
1992–2005[a]	31	27,902,475	0.11	0.12	0.08–0.17	<.001
					Trend test	.001
Vaccinated birth cohort (July to June)						
1984–1986[b]	59	14,388,916	0.41	1.00	Referent	
1986–1992[b]	76	31,513,457	0.24	0.59	0.42–0.83	.002
1992–2005[b]	31	27,902,475	0.11	0.27	0.17–0.42	<.001
					Trend test	<.001
Vaccinated birth cohort (July to June)						
1986–1992[c]	76	31,513,457	0.24	1.00	Referent	
1992–2005[c]	31	27,902,475	0.11	0.46	0.30–0.70	<.001

[a]Comparison of the RR of HCC between unvaccinated birth cohort (RR = 1) vs birth cohorts of 1984–1986, 1986–1992, or 1992–2005, respectively.
[b]Comparison of the RR of HCC between birth cohorts of 1984–1986 (RR = 1) vs birth cohorts of 1986–1992 or 1992–2005, respectively.
[c]Comparison of the RR of HCC between birth cohorts of 1986–1992 (RR = 1) vs birth cohorts of 1992–2005.

Chang MH et al., Gastroenterology, 2016;151(3):472-480.e1. doi: 10.1053/j.gastro.2016.05.048.

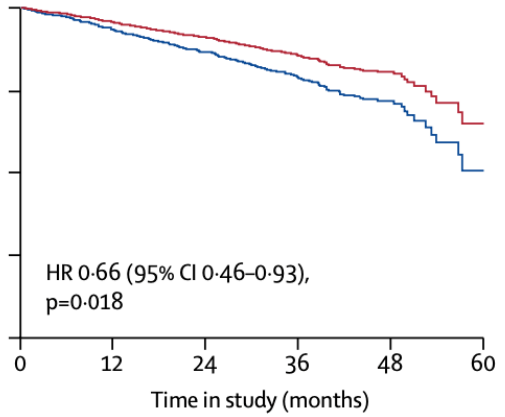
Primary prevention – HCV

	Received direct-acting antivirals (exposed)		Did not receive direct-acting antivirals (not exposed)		Exposed vs not exposed	
	n per person-years	Incidence per 100 person-years (95% CI)	n per person-years	Incidence per 100 person-years (95% CI)	Univariable HR (95% CI)	Multivariable adjusted HR (95% CI)
All patients (n=9895)						
All-cause mortality	129/13 626	0·95 (0·79–1·12)	89/12 709	0·70 (0·56–0·86)	1·14 (0·85–1·52)	0·48 (0·33–0·70)
Liver-related	48/13 626	0·35 (0·26–0·47)	25/12 709	0·20 (0·13–0·29)	1·46 (0·89–2·39)	0·39 (0·21–0·71)
Non-liver-related	61/13 626	0·45 (0·34–0·58)	53/12 709	0·42 (0·31–0·55)	0·92 (0·62–1·37)	0·60 (0·36–1·00)
Hepatocellular carcinoma	187/13 375	1·40 (1·20–1·61)	71/12 660	0·56 (0·44–0·71)	2·77 (2·07–3·71)	0·66 (0·46–0·93)
Decompensated cirrhosis	74/13 520	0·55 (0·43–0·69)	32/12 698	0·25 (0·17–0·36)	3·83 (2·29–6·42)	1·14 (0·57–2·27)
Patients with cirrhosis (n=3045)						
All-cause mortality	94/6320	1·49 (1·20–1·82)	41/1578	2·60 (1·86–3·52)	0·35 (0·23–0·53)	0·34 (0·22–0·55)
Liver-related	42/6320	0·66 (0·48–0·90)	19/1578	1·20 (0·72–1·88)	0·32 (0·17–0·59)	0·28 (0·15–0·54)
Non-liver-related	36/6320	0·57 (0·40–0·79)	15/1578	0·95 (0·53–1·57)	0·36 (0·18–0·71)	0·40 (0·19–0·83)
Hepatocellular carcinoma	166/6104	2·72 (2·32–3·17)	57/1539	3·70 (2·80–4·80)	0·63 (0·44–0·90)	0·57 (0·40–0·81)
Decompensated cirrhosis	67/6223	1·08 (0·83–1·37)	28/1567	1·79 (1·19–2·58)	0·67 (0·40–1·11)	0·95 (0·48–1·89)
Patients without cirrhosis (n=5978) or with an unknown fibrosis score (n=872)						
All-cause mortality	35/7307	0·48 (0·33–0·67)	48/11 131	0·43 (0·32–0·57)	0·94 (0·58–1·50)	0·74 (0·43–1·28)
Liver-related	6/7307	0·08 (0·03–0·18)	6/11 131	0·05 (0·02–0·12)	1·33 (0·46–3·84)	ND
Non-liver-related	25/7307	0·34 (0·22–0·51)	38/11 131	0·34 (0·24–0·47)	0·89 (0·51–1·56)	0·75 (0·42–1·35)
Hepatocellular carcinoma	21/7271	0·29 (0·18–0·44)	14/11 120	0·13 (0·07–0·21)	2·49 (1·18–5·27)	1·02 (0·40–2·61)
Decompensated cirrhosis	7/7297	0·10 (0·04–0·20)	4/11 131	0·04 (0·01–0·09)	3·59 (0·66–19·5)	ND

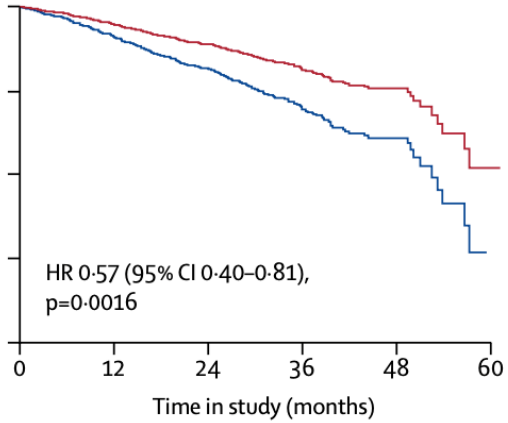
HR=hazard ratio. ND=not done because of insufficient number of events.

Table 2: **Incidence of and risk for death, hepatocellular carcinoma, and decompensated cirrhosis, according to exposure to direct-acting antiviral treatment during follow-up**

All patients



Cirrhotic patients



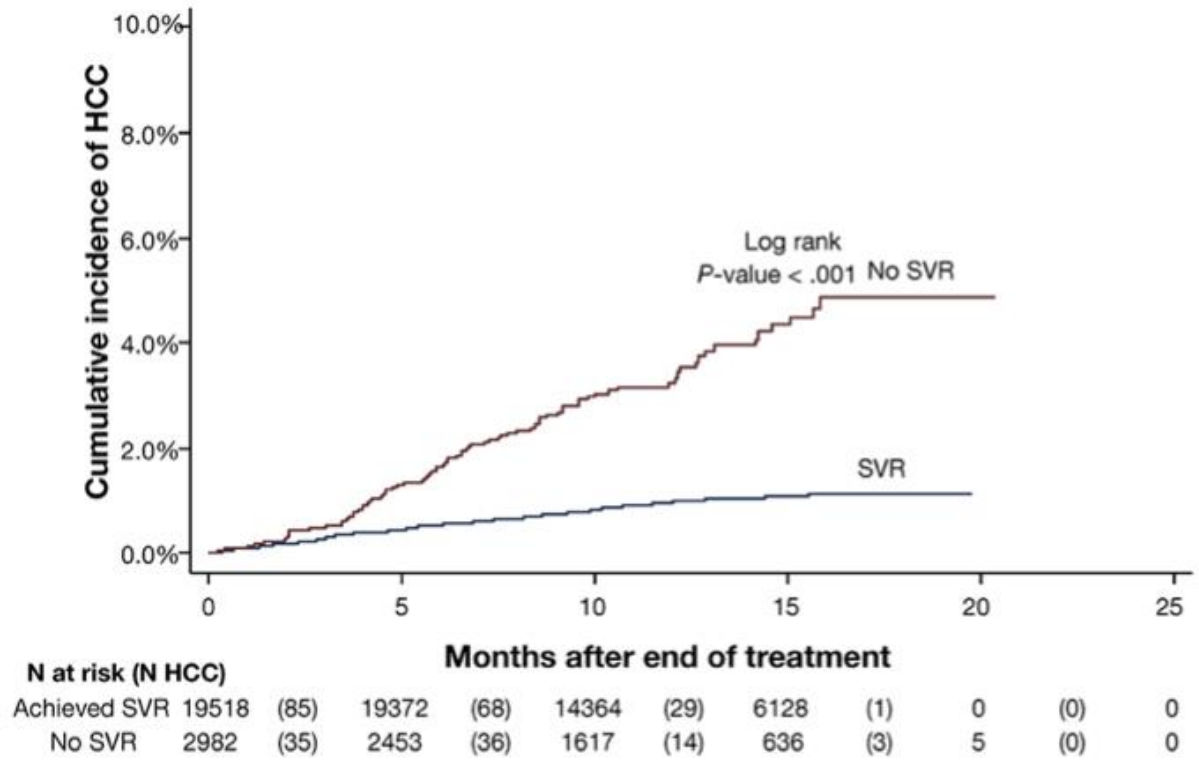
Carrat F, et al. Lancet. 2019;393(10179):1453-1464. doi: 10.1016/S0140-6736(18)32111-1.

Primary prevention – HCV

Table 2. Association Between SVR and Incident HCC in Patients Treated With DAA Agents

SVR	PY of follow-up	HCC N	Incidence rate (per 100 PY, 95% CI)	Adjusted hazard ratio[a] (95% CI)	*P* value
No	2547.34	88	3.45 (2.73–4.18)	1	
Yes	20,415.3	183	0.90 (0.77–1.03)	0.28[b] (0.22–0.36)	<.0001

CI, confidence interval; DAA, direct acting antiviral; HCC, hepatocellular cancer; HCV, hepatitis C virus; PY, person-years; SVR, sustained virological response.
[a]Multivariable model adjusted for age, gender, race, cirrhosis diagnosis, HCV genotype, diabetes, HIV, alcohol use, drug use, Deyo index, and number of outpatient visits in the year prior to DAA treatment (full model is presented in Supplementary Appendix Table 1).
[b]The magnitude and direction of SVR did not change in the multivariable model that used FIB-4 in lieu of cirrhosis diagnosis.



SVR protective effect according to cirrhosis status:
- Cirrhotics: aHR=0.32 (95% CI 0.23-0.44)
- Non cirrhotics: aHR=0.18 (95% CI 0.11-0.30)

Kanwal F, et al. Gastroenterology, 2017;153(4):996-1005.e1. doi: 10.1053/j.gastro.2017.06.012.

Surveillance efficacy

RCT on surveillance in HBV-infected persons [1,2]

ORIGINAL PAPER

Bo-Heng Zhang · Bing-Hui Yang · Zhao-You Tang

Randomized controlled trial of screening for hepatocellular carcinoma

	Screening group (86)	Control group (67)
Stage[a]		
Stage I	52(60.5%)	0(0%)
Stage II	12(13.9%)	25(37.3%)
Stage III	22(25.6%)	42(62.7%)
Small HCC	39(45.3%)	0
Treatment		
Resection	40(46.5%)	5(7.5%)
TACE/PEI	28(32.6%)	28(41.8%)
Conservative treatment	18(20.9%)	34(50.7%)
Survival (%)[b]		
1-year	65.9	31.2
2-year	59.9	7.2
3-year	52.6	7.2
4-year	52.6	0
5-year	46.4	0

[a] $\chi^2 = 61.41$, $p < 0.01$
[b] Log-rank $\chi^2 = 35.50$, $p < 0.01$

	Screening group	Control group
Person-years in the study	38,444	41,077
HCC occurrence		
No. of cases	86	67
Total incidence(per 100,000)	223.7	163.1
Rate ratio (95% CI)	1.37(0.99, 1.89)	
Deaths from HCC		
No. of death	32	54
Total mortality(per 100,000)	83.2	131.5
Rate ratio (95% CI)	0.63(0.41, 0.98)	

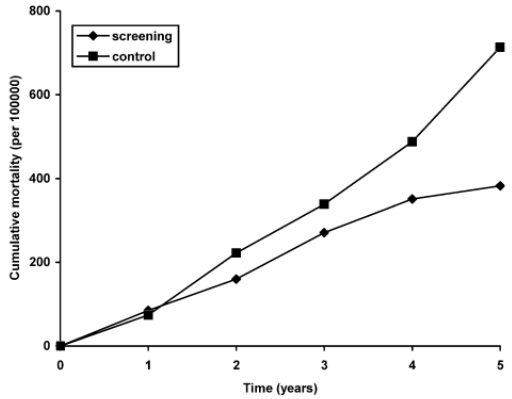
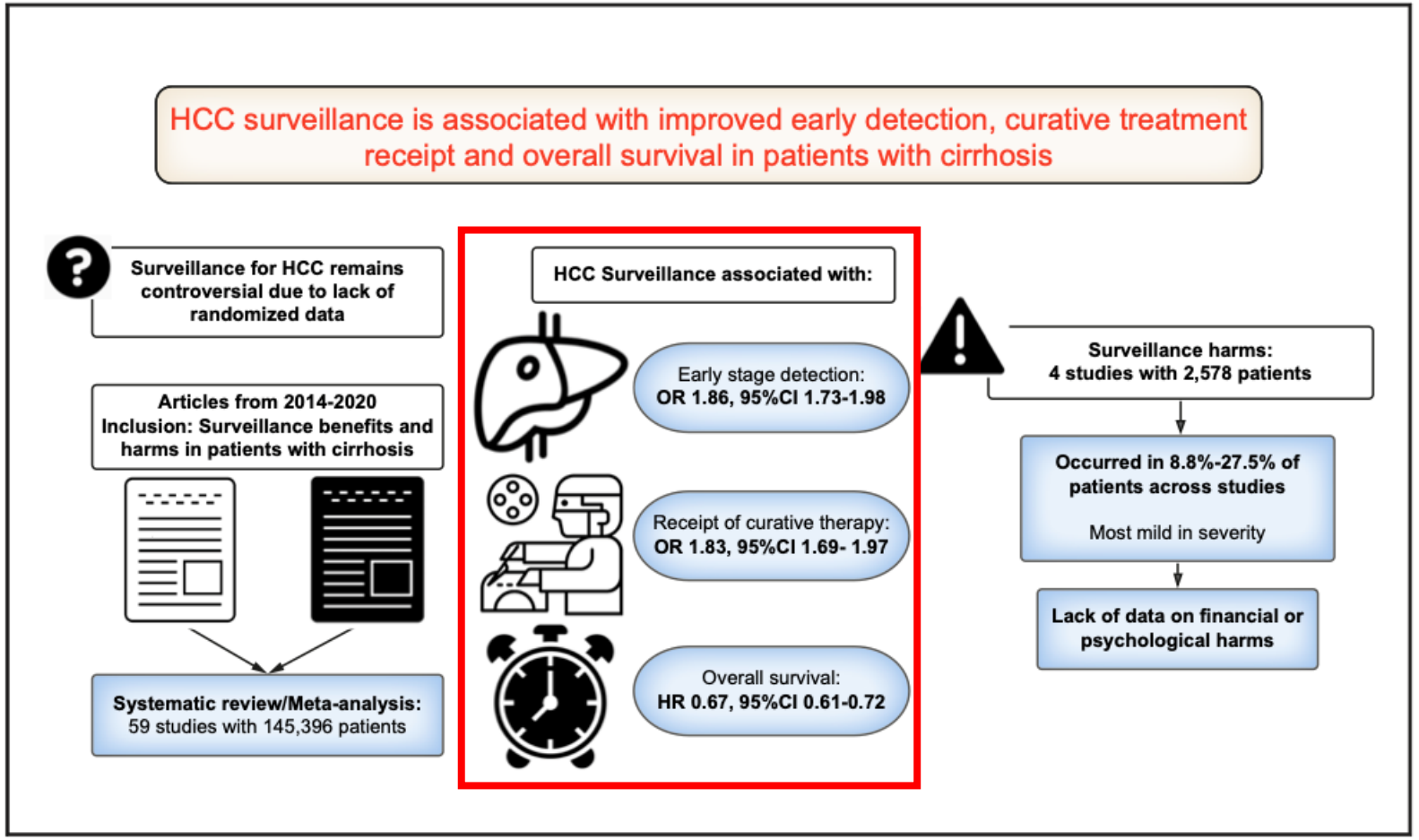


Fig. 5 Cumulative survival in different stages HCC patients

Reduction in HCC-related mortality of **37%** in the surveillance arm (increased applicability of resection)

(1) Yang B et al., J Cancer Res Clin Oncol, 1997;123:357-60. **(2)** Zhang BH et al., J Cancer Res Clin Oncol, 2004; 130:417-22

Surveillance efficacy



Singal AG et al., J Hepatol. 2022;77(1):128-139. doi: 10.1016/j.jhep.2022.01.023.

Surveillance interval

The ideal interval of surveillance should be dictated by:

1. Rate of tumor growth up to the limit of its detectability (**tumor volume doubling time**) –> **<u>6 months in HCC</u>** [1]
2. Tumor incidence in the target population

In Surv6 vs. Surv12 increased detection of early HCC and better prognosis

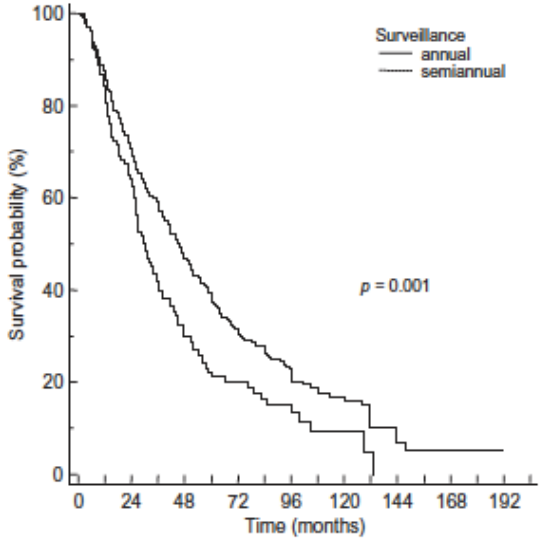
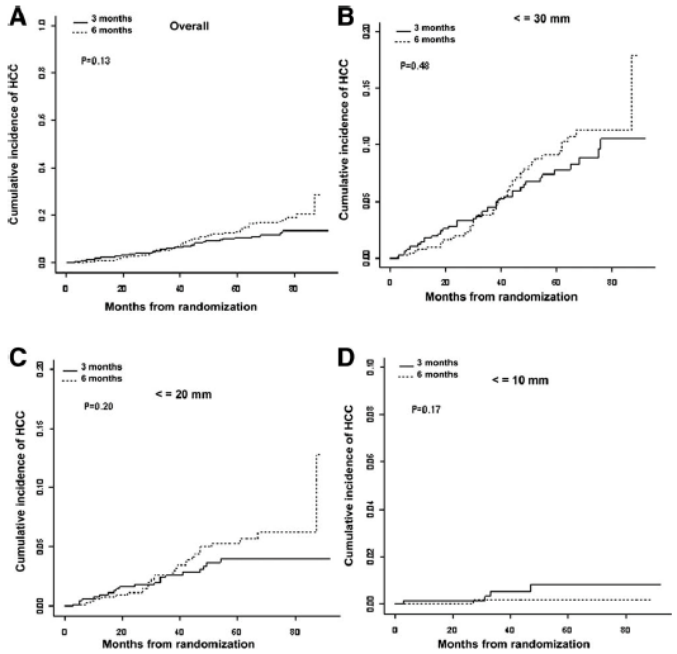


Fig. 1. Observed survival of patients under semiannual or annual surveillance. The semiannual surveillance significantly increased the survival with respect to yearly program.

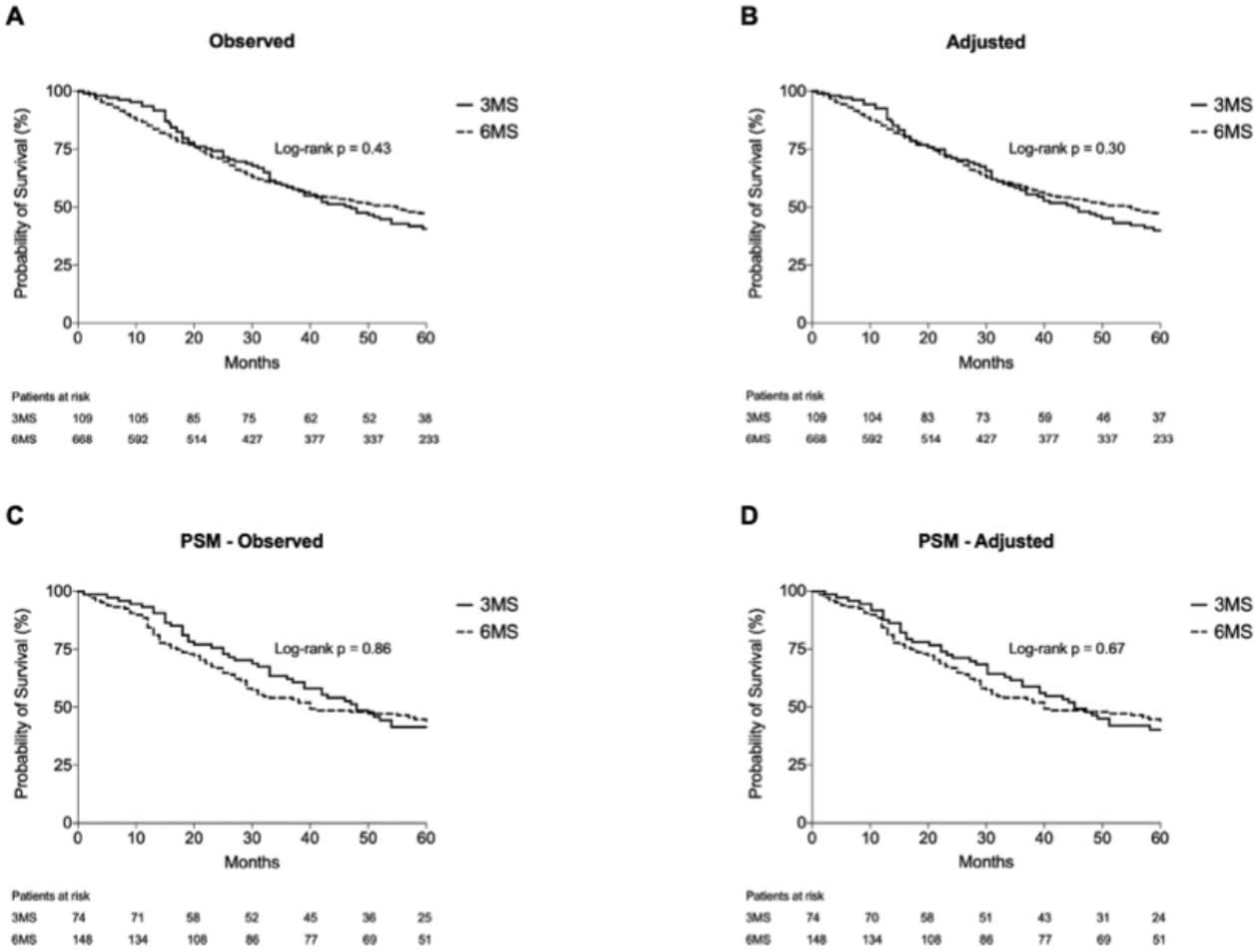


No differences in survival between Surv3 and Surv6

(1) Nathani P et al., Gut. 2021;70(2):401-407. doi: 10.1136/gutjnl-2020-321040. **(2)** Santi V et al., J Hepatol. 2010;53(2):291-7. doi: 10.1016/j.jhep.2010.03.010. **(3)** Trinchet JC et al., Hepatology. 2011;54(6):1987-97. doi: 10.1002/hep.24545.

Surveillance interval

Surv3 vs. Surv6 in viral cirrhotics



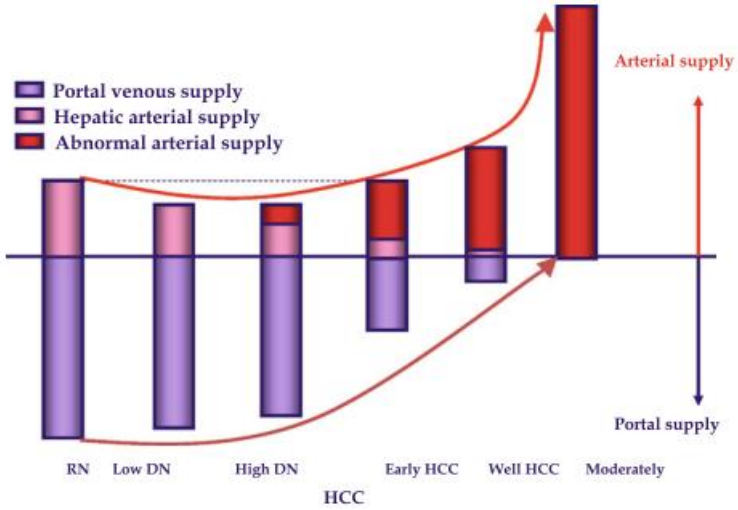
Pelizzaro F, et al. Dig Liver Dis. 2022;54(7):927-936. doi: 10.1016/j.dld.2021.08.025.

Agenda

- Epidemiology of hepatocellular carcinoma
- Temporal trends and risk factors
- Primary prevention and surveillance
- Diagnosis of HCC: the need for liver biopsy
- Treatment: multiparametric and multidisciplinary assessment

Diagnosis of hepatocellular carcinoma

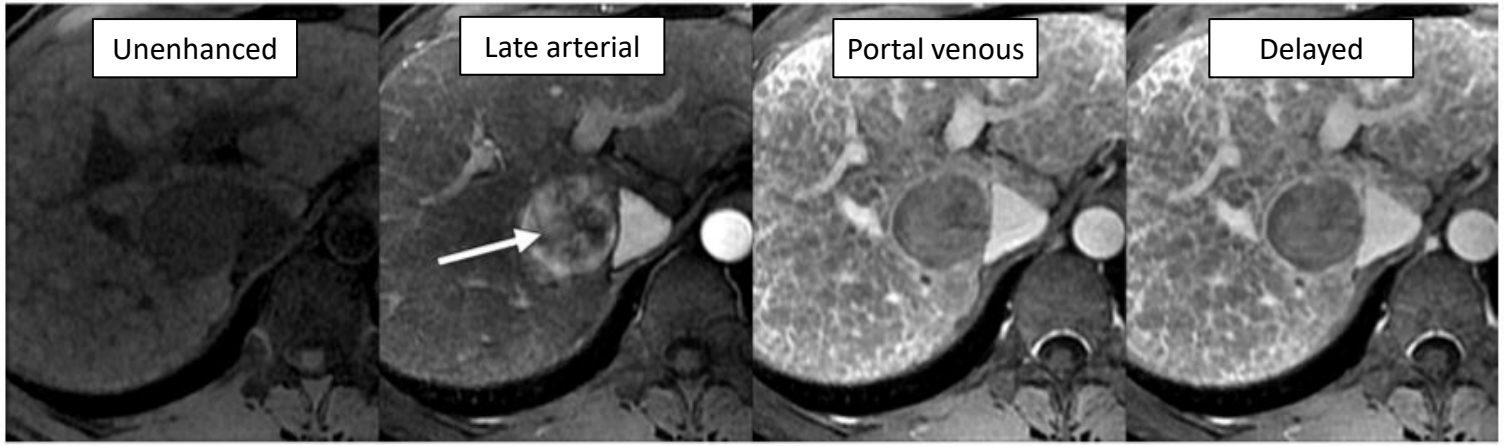
1. Peculiar vascular derangement occurring during hepatic carcinogenesis [1]
2. High pre-test probability of HCC in the setting of cirrhosis [2-5]



<u>Typical hallmark</u>:

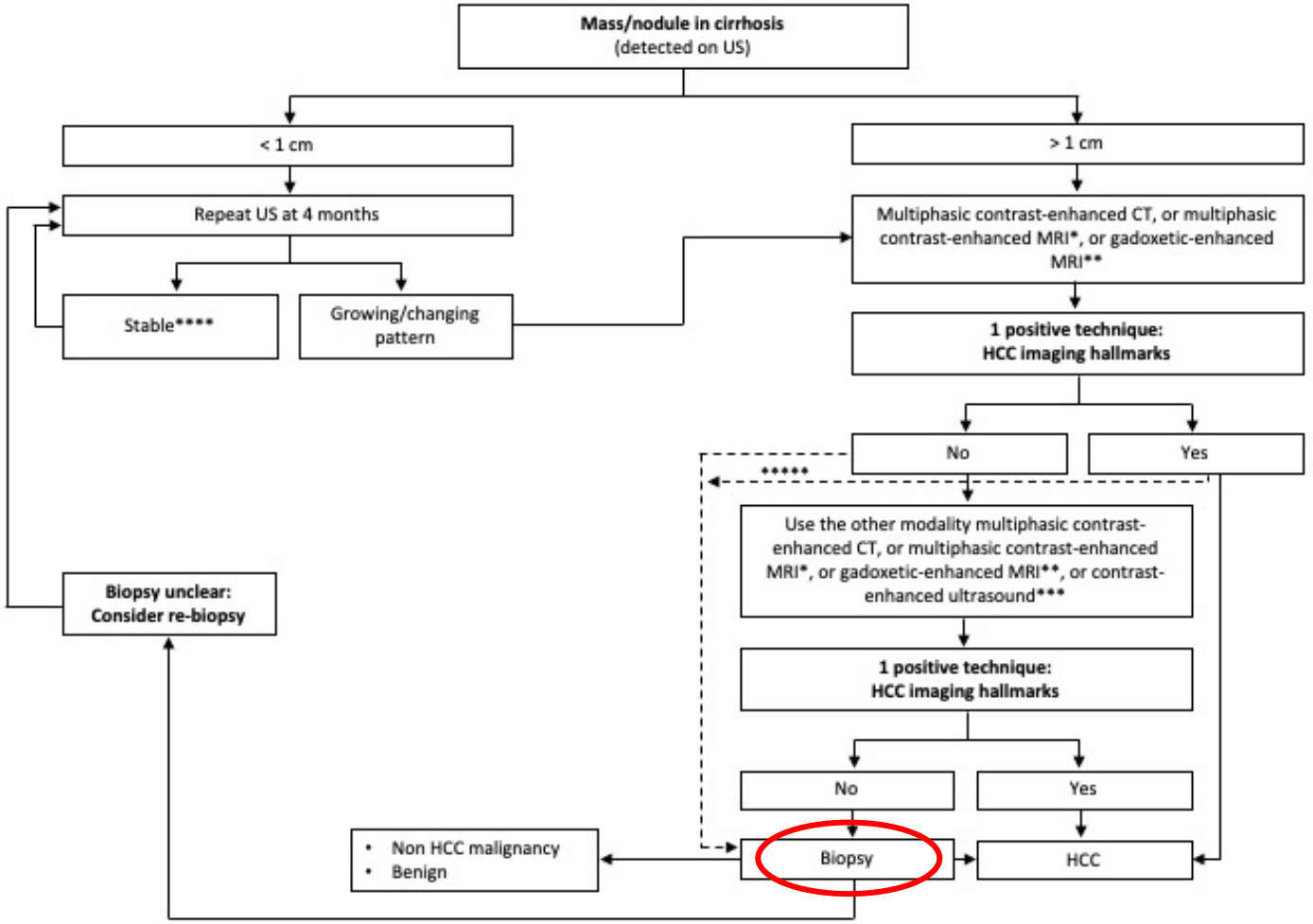
a) Hypervascularity in late arterial phase (**arterial phase hyperenhancement, APHE**)

b) **Washout** on portal venous and/or delayed phases



(1) Matusi O et al., Abdom Imaging, 2011:36:264-72. **(2)** Burrel M et al., Hepatology, 2003;38:1034-42. **(3)** Forner A et al., Hepatology, 2008;47:97-104. **(4)** Bolondi L et al., Gut, 2001;48:251-9. **(5)** Sangiovanni A et al., Gut, 2010;59:638-44

Diagnosis of hepatocellular carcinoma



Liver biopsy should be performed:

1. In patients **with liver cirrhosis**, when non-invasive diagnosis is unconclusive
2. In patients **without liver cirrhosis** (histological confirmation required)

Modified from: EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma, J Hepatol, 2018;69:182-236

Diagnosis - the role of liver biopsy

CONS

- Possibility to diagnose the tumor in cirrhotic patients with non-invasive criteria.
- Choice of treatment is independent form molecular and histological information
- Seeding and bleeding risk
- When compared to surgical specimen, low correspondence of tumor grading and microvascular invasion.

PROS

- Margin of error of non-invasive diagnosis (in particular for nodules ≤ 20 mm)
- Distinction between well-differentiated HCC and dysplastic nodule
- Distinction of HCC from iCCA and cHCC-CCA
- Prognostic information
  - Histotype and grade of differentiation
  - Presence of neurovascular and lymphatic involvement
  - Expression of phenotypic markers
- Guidance in treatment (not yet)

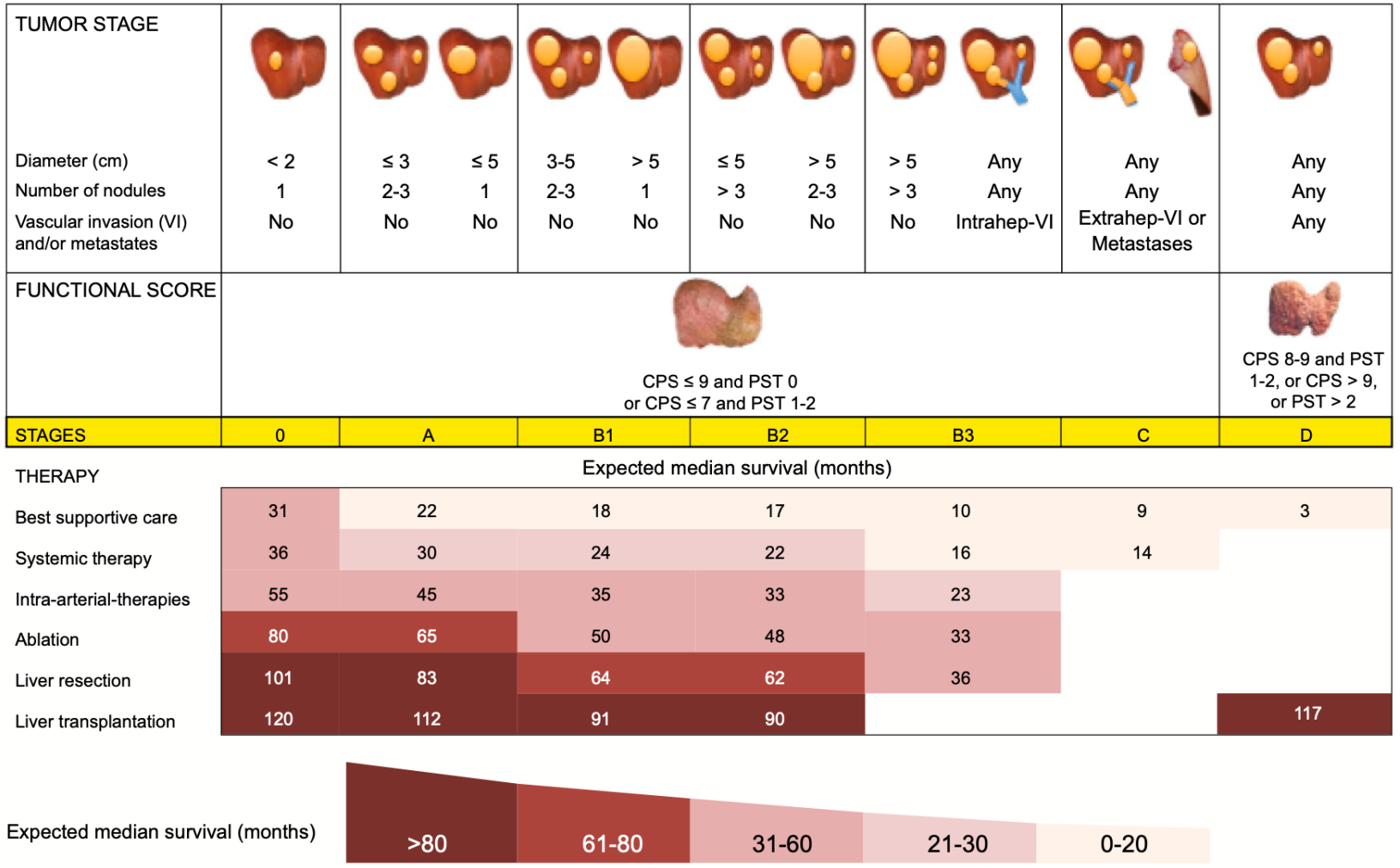
A liver biopsy might be performed not only in masses with atypical features but also in patients with imaging concerning for LIRADS 4 and 5 lesions, whenever feasible and safe.

(1) Jaffe A et al., Liver Int. 2022;42(12):2607-2619. doi: 10.1111/liv.15432. **(2)** Russo FP et al., Dig Liver Dis. 2018;50(7):640-646. doi: 10.1016/j.dld.2018.03.014.

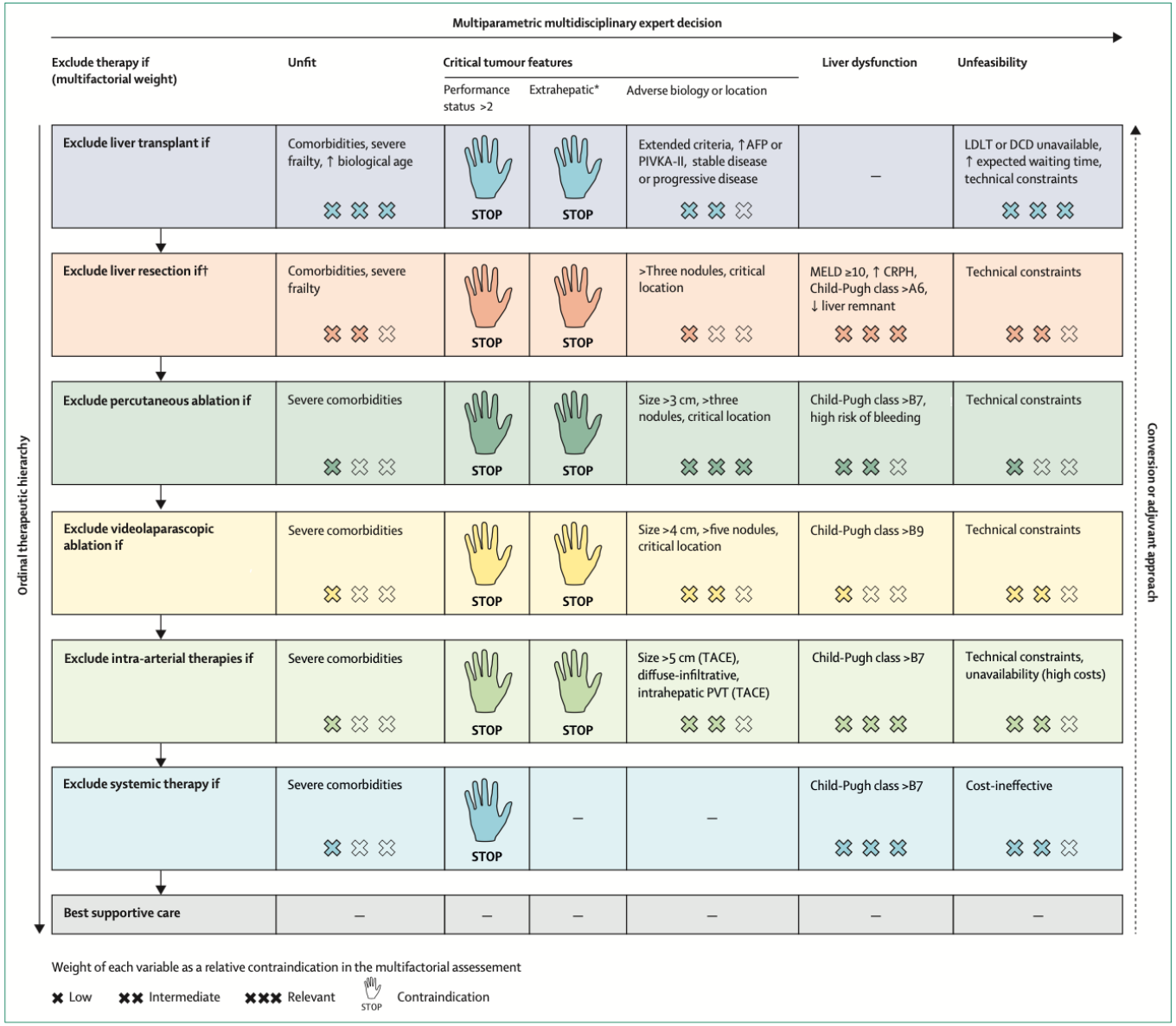
Agenda

- Epidemiology of hepatocellular carcinoma
- Temporal trends and risk factors
- Primary prevention and surveillance
- Diagnosis of HCC: the need for liver biopsy
- Treatment: multiparametric and multidisciplinary assessment

Therapeutic hierarchy



Vitale A et al., Hepatology, 2020;72(6):2206-2218. doi: 10.1002/hep.31187.



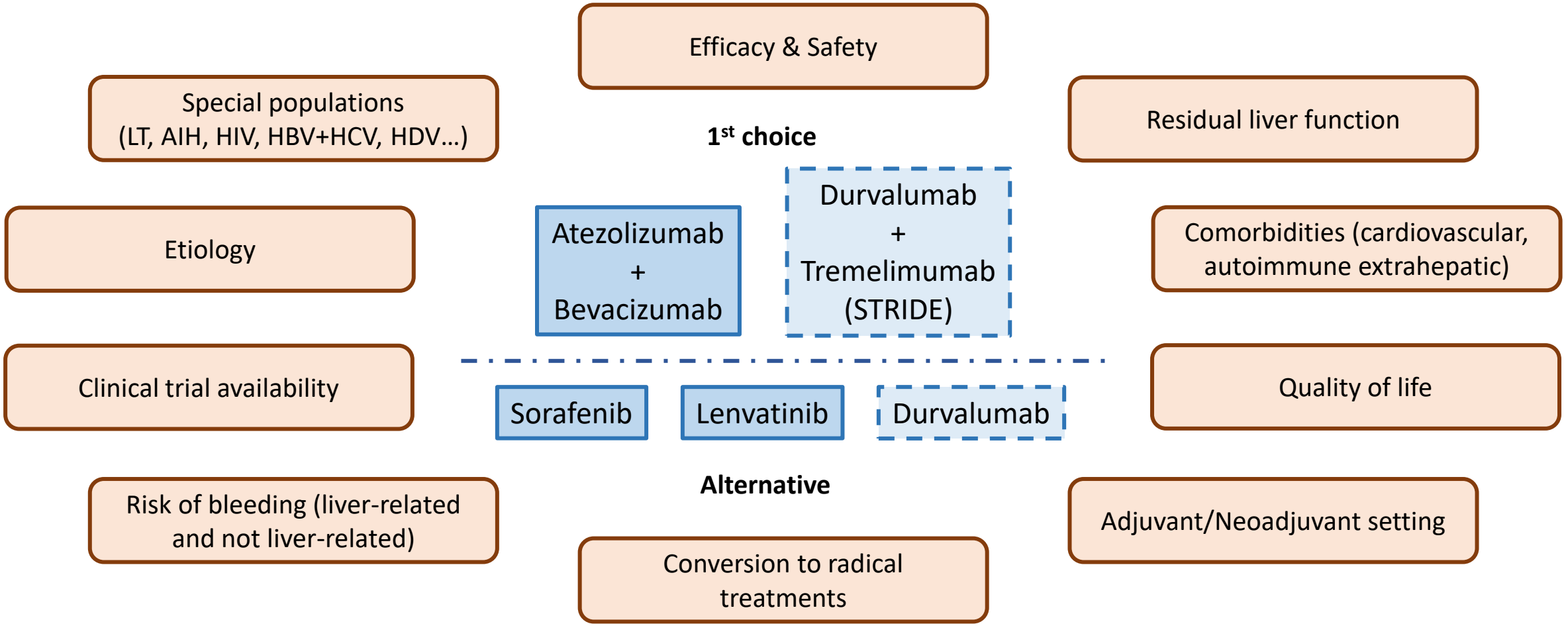
Multiparametric therapeutic hierarchy

<u>Multiparametric, multidisciplinary assessment</u>:

- Fitness (comorbidities, physical frailty)
- Critical tumor features
  - PS
  - Extrahepatic HCC
  - Aggressive biology (tumor burden, biomarkers, progression following locoregional therapies)
  - Location
- Liver disfunction (CPT, MELD, ALBI, indocyanine green test, liver stiffness, spleen stiffness, signs of CSPH)
- Unfeasibility (technical and logistic contraindications)

Vitale A ey al., Lancet Oncol. 2023;24(7):e312-e322. doi: 10.1016/S1470-2045(23)00186-9.

Systemic treatment options for uHCC



Conclusions

Managing patients with HCC and their co-existing liver disease is complex:

- ✓ Optimizing liver function;
- ✓ Evaluating and treating the underlying etiology of liver disease;
- ✓ Preventing further hepatotoxicity;
- ✓ Managing liver disease decompensation both before and after treatment;
- ✓ Assessing eligibility for liver transplantation;

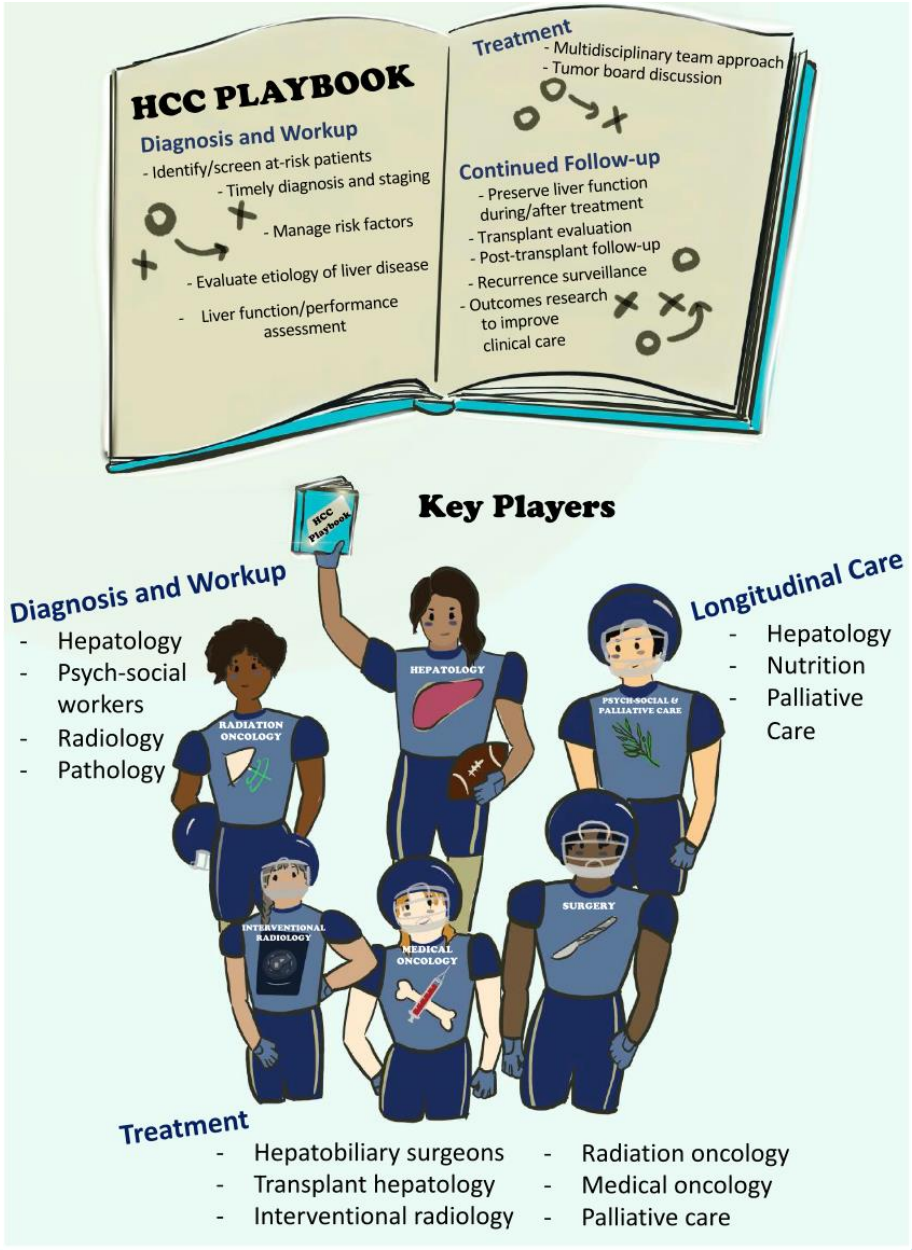
Critical tasks for achieving the best patient outcomes.

Jaffe A et al., Liver Int. 2022;42(12):2607-2619. doi: 10.1111/liv.15432.

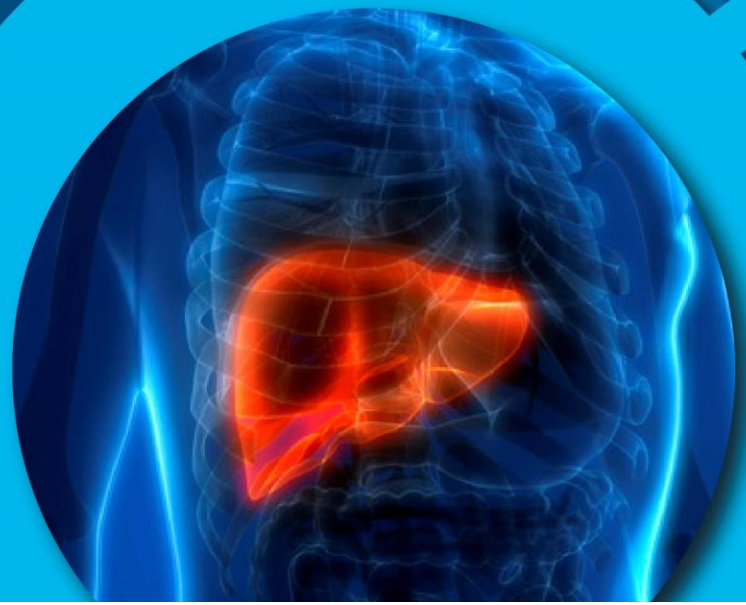
TABLE 1 Holistic approach to the patient with hepatocellular carcinoma

Preventative measures to promote "liver health" at all levels: "to inform is to cure"
Recognition of subjects with risk factors for liver disease and aggressive management
Assessment and management of social determinants of health and removal of barriers to care
Early treatment of liver disease to prevent chronicity
Preservation of liver function in patient with cirrhosis and chemoprevention of progression
Oncologic surveillance of patients at risk
Diagnosis of liver cancer and treatment strategy
Team-based multimodal treatment with personalization of care
Establishment of a treatment strategy going beyond the single episode
Management and treatment of comorbidities
Evaluation of potential candidacy for liver transplant
Post-treatment oncologic surveillance
Retreatment of recurrence as needed and feasible, again through a team-based approach
Identifying the transition time to palliative care and participation in palliative care delivery

Conclusions



Jaffe A et al., Liver Int. 2022;42(12):2607-2619. doi: 10.1111/liv.15432.



Patient Journey

Approccio personalizzato al paziente e esperienze a confronto: Epatocarcinoma e Colangiocarcinoma

01 Febbraio 2024

VERONA

CROWNE PLAZA

Via Belgio, 16

Thank you

AIGOM

ASSOCIAZIONE ITALIANA
GRUPPI ONCOLOGICI MULTIDISCIPLINARI