

Clinical Scenario

- 42-year-old man with chronic hepatitis B infection came to ER due to abdominal pain for two weeks
- CT showed multiple hepatomas in liver, the largest one spanning around 15 cm
- Not able for surgical treatment
- Patient died within 2 months of diagnosis

Clinical Scenario

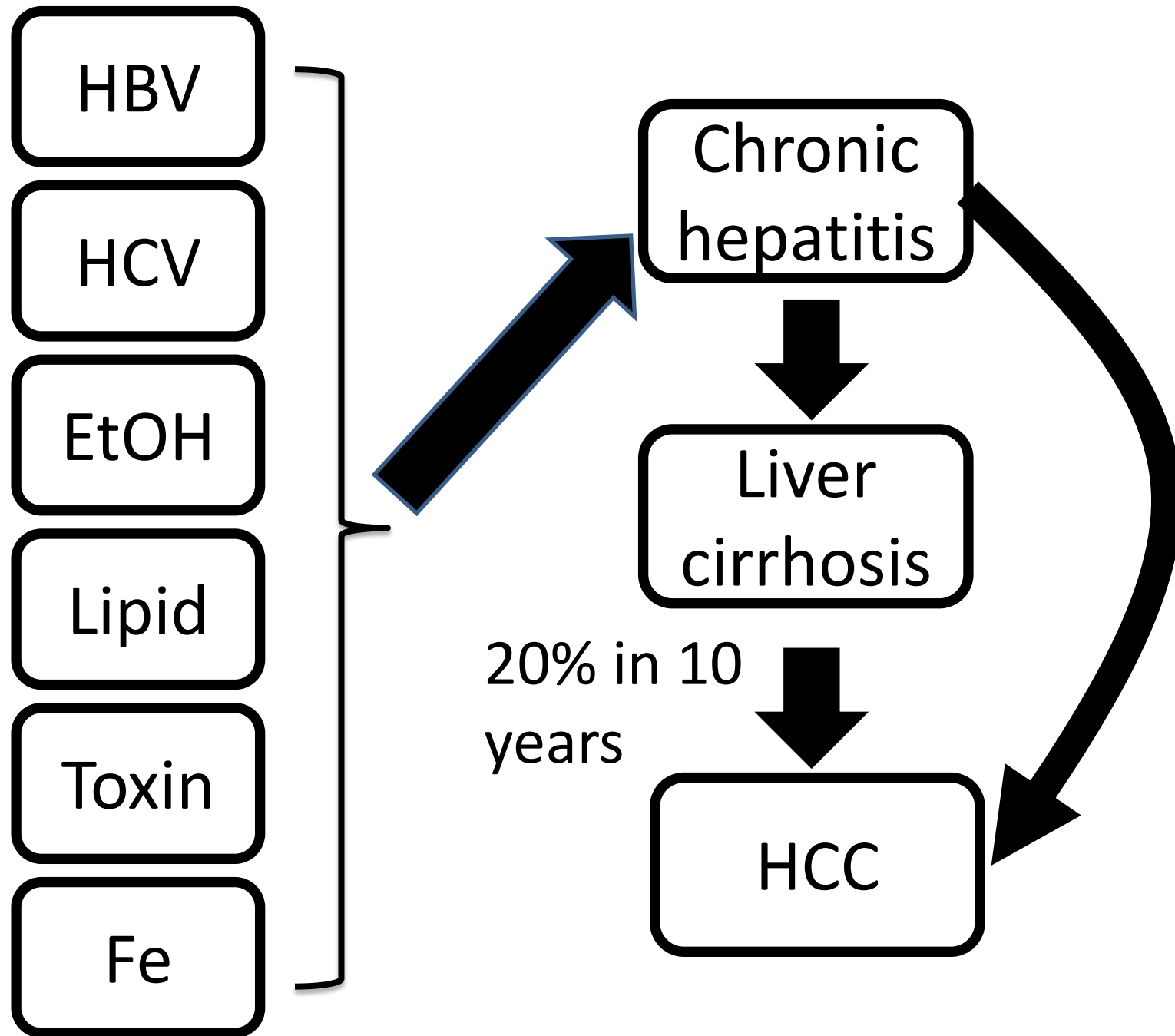
- 56-year-old man with chronic hepatitis B
- Last abdominal echo was three years ago and no abnormal tumor was seen at then
- Came to OPD because of fatigue, poor appetite and jaundice recently
- CT showed a huge hepatoma (20cm) with portal vein thrombosis
- Patients died 6 months after diagnosis

Clinical Scenario

- 65-year-old woman, with hepatitis history, but does not know whether it's B or C
- Regular having some blood test at local medical clinical for “liver function testing”
- Referred to OPD due to hepatoma noticed in echo
- Multiple metastatic tumors in lung and bone
- Died 8 months after diagnosis

Questions

- Is HCC so hard to treat
 - Yes
- Can HCC ever be cured
 - Yes
- How to improve cure rate?
 - Prevention, surveillance, and early detection



Prevention of HCC - HBV

- Vaccination
 - Since 1985, new-born children in Taiwan would all get HBV vaccination
 - The incidence of HCC decreased 69% when comparing those who received vaccine with those who did not receive vaccination

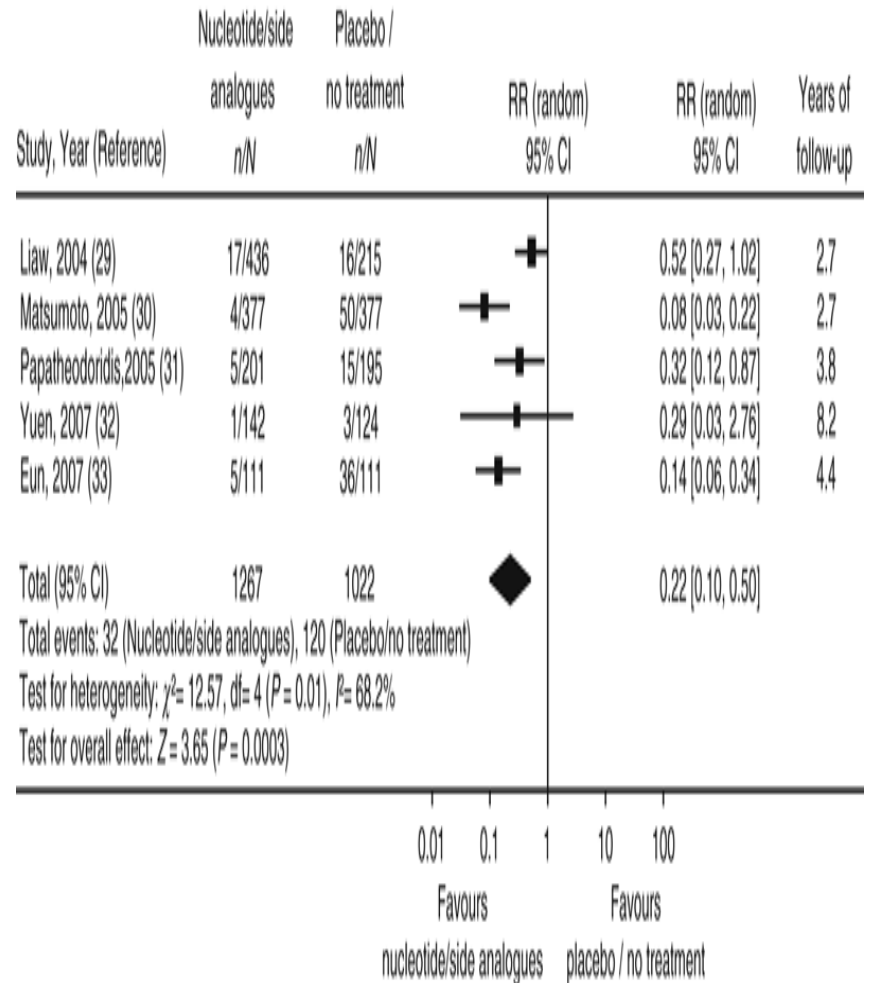
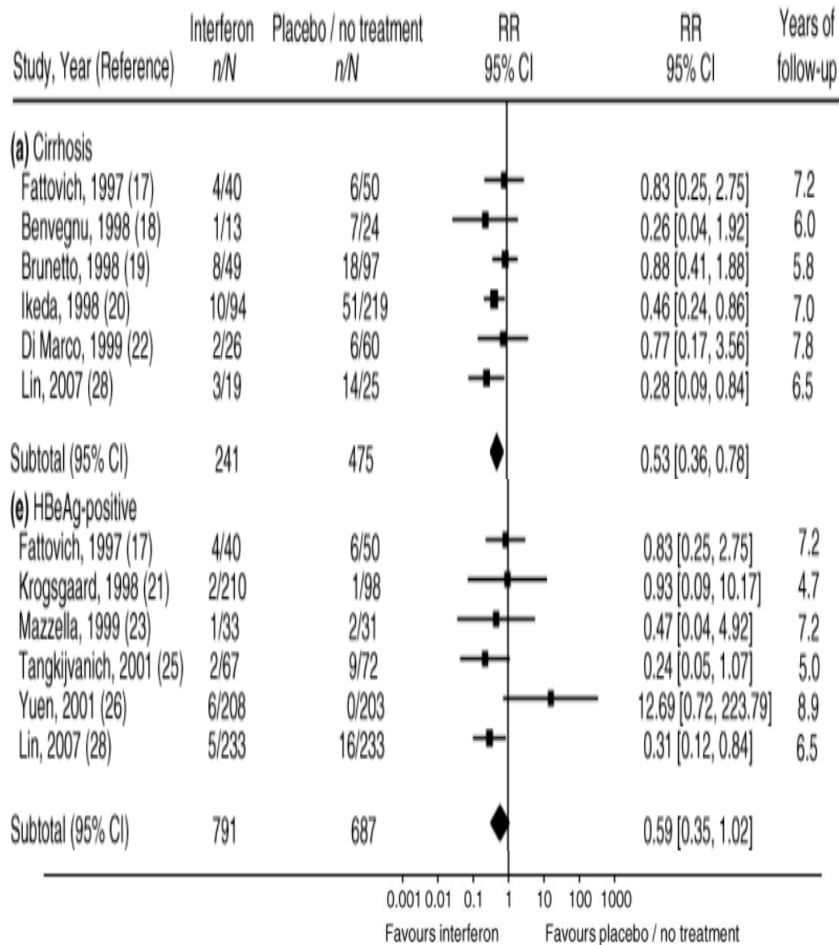
Prevention of HCC- HBV

- Prevent transmission of HBV
 - Screening for blood donations
 - Passive HBV immunization for patients exposed to HBV (eg: needle stick)

Prevention of HCC - HBV

- Active treatment for HBV carriers
- Early treatment decreases the risk of developing HCC for HBV carriers
 - HBeAg (+)
 - HBV with liver cirrhosis
- Interferon
- Nucleotide analogue

Both Antiviral Treatments Are Good



Prevention of HCC - HCV

- Prevent HCV infection and cirrhosis
- HCV is more prevalent in Yun-Lin county than another other parts of Taiwan
- Poor health-related procedure and equipment hygiene
- Drug abusers, needle users

Prevention of HCC - HCV

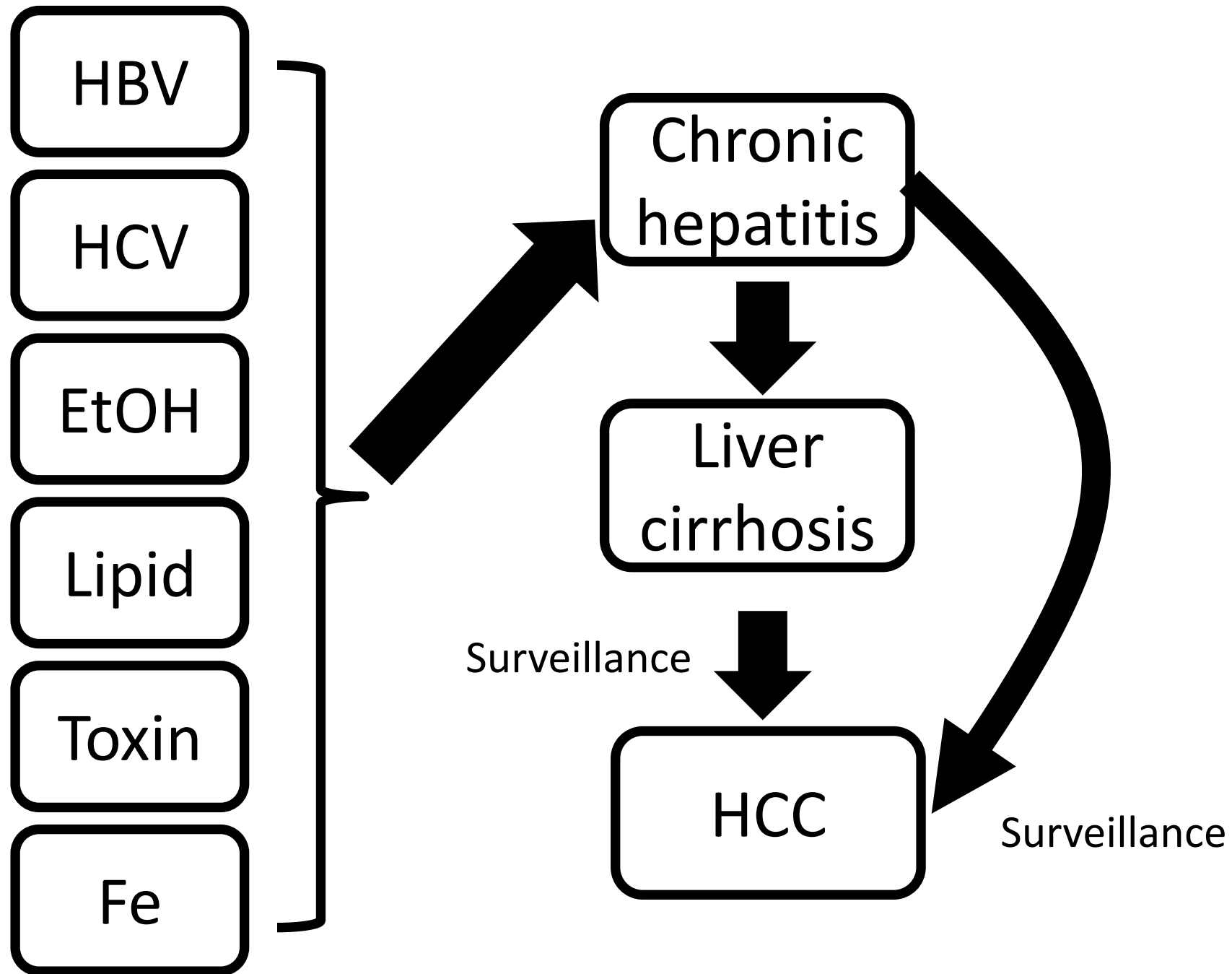
- Screening for high risk population
- Close follow-up of HCV activity and early treatment of HCV when possible

Prevention of HCC - Cirrhosis

- Alcohol
- Non-alcoholic steatohepatitis (NASH)
- Metal
 - Fe (hemochromatosis)
 - Copper (Wilson's disease)
- Toxin - Aflatoxin
- Autoimmune
 - Primary biliary cirrhosis
 - Primary sclerosing cholangitis

Prevention of HCC – Control DM

- Taiwan's Data
- DM correlated with HCC
 - HR 1.73 (95% CI 1.47 – 2.03)
- Some drugs related to decreased risk of HCC
 - Metformin HR 0.49 (95% CI 0.37 -0.66)
 - Thiazolidinediones HR 0.56 (95% CI 0.37 -0.84)



Cost-effectiveness of Surveillance

Population group	Incidence of HCC
Surveillance recommended	
Asian male hepatitis B carriers over age 40	0.4-0.6 percent per year
Asian female hepatitis B carriers over age 50	0.3-0.6 percent per year
Hepatitis B carrier with family history of HCC	Incidence higher than without family history
African/North American blacks with hepatitis B	HCC occurs at a younger age
Cirrhotic hepatitis B carriers	3-8 percent per year
Hepatitis C cirrhosis	3-5 percent per year
Stage 4 primary biliary cirrhosis	3-5 percent per year
Genetic hemochromatosis and cirrhosis	Unknown, but probably >1.5 percent per year
Alpha 1-antitrypsin deficiency and cirrhosis	Unknown, but probably >1.5 percent per year
Other cirrhosis	Unknown

Incidence of HCC in HBV Carriers

- Caucasian
 - 0.2%
- Asian
 - 0.4% -0.6%
 - Start to exceed 0.2% since age of 40 in men
- African
 - HCC at an earlier age

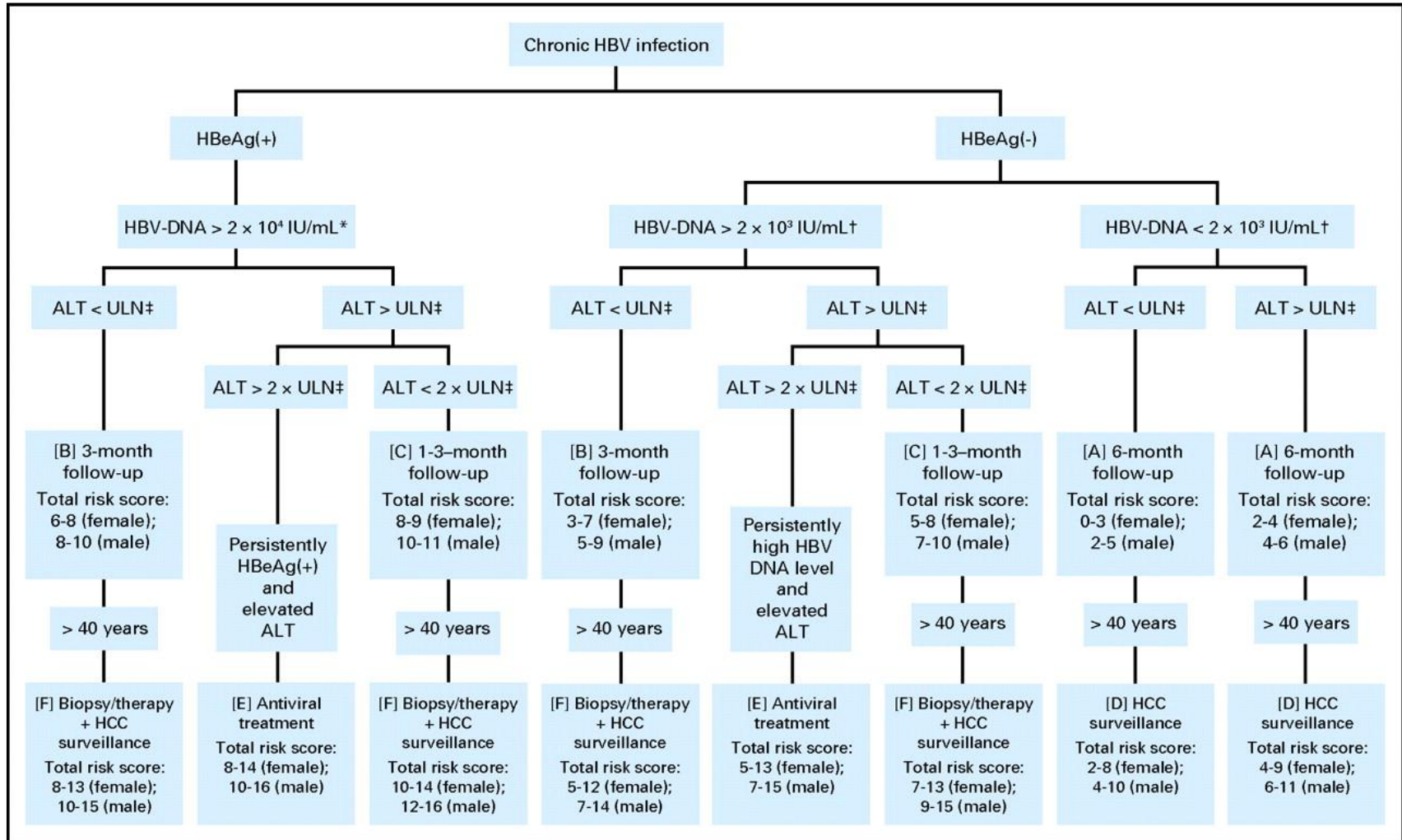
Risk of HCC with A Family History

- A Taiwan study
- The risk of HCC increases for patients with HBV with a family history
- For men, if one relative with HCC
 - Relative risk 2.09 (95% CI 1.21 – 3.62)
- For men, If two or more relatives diagnosed with HCC
 - Relative risk 5.55 (95% CI 2.02 – 15.26)

Surveillance for HBV Carriers

- Asian men over the age of 40 years
- Asian women over the age of 50 years
- Patients with HBV and cirrhosis
- Africans and North American blacks
- Patients with a family history of HCC
- For HBV carrier who have treated with anti-viral therapy

HCC Risk Nomogram for HBV Pts



Surveillance for Cirrhosis Patients

- HBV
 - Even virus are cleared
- HCV
- Alcohol
- NASH
- Autoimmune
- Heavy meta metabolism

Improved Survival for Patients Dx HCC Within Surveillance (Cirrhotic pts, Asia)

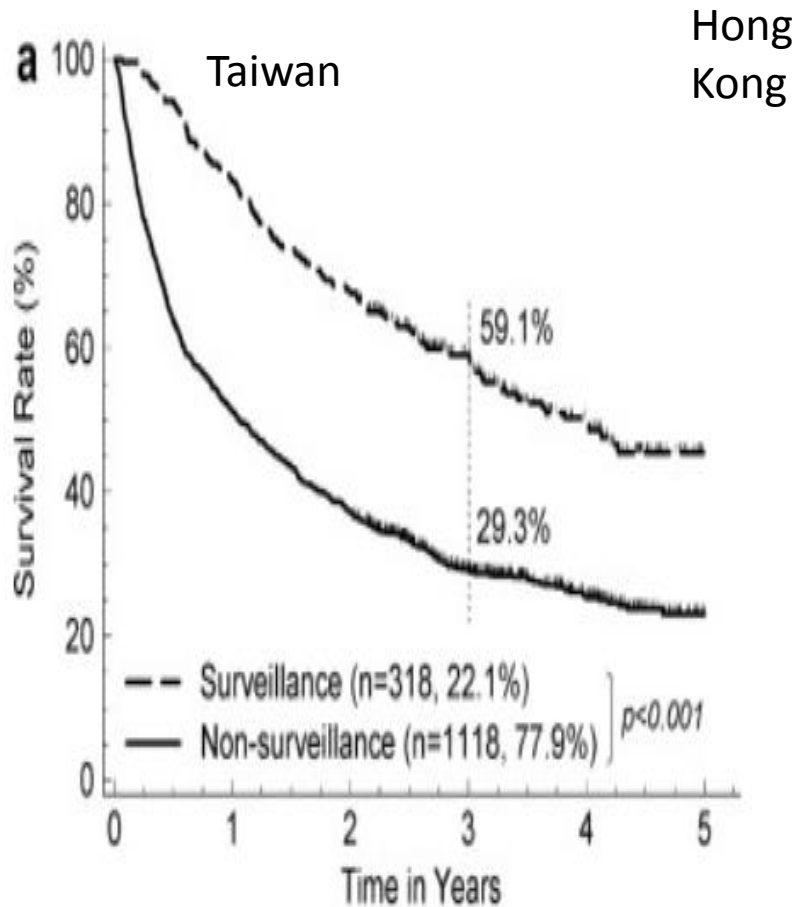


TABLE 3. The Median Survival of Different Subsets of 306 Patients With HCC

	Group 1	Group 2	P
Number of patients	142	164	
Median survival (mo)			
All patients	22	5	<.0001
Child's A patients	>47	19	.0001
Child's B patients	12	3	.0072
Child's C patients	2	2	NS
Patients with surgical resection	32	*	.04
Patients with TACE	26	11	.0003

TABLE 2. The Characteristics of 306 Patients With HCC

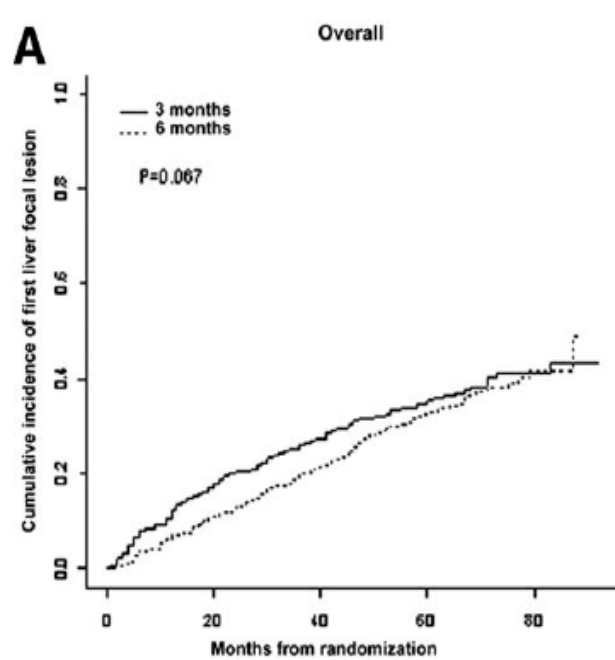
	Group 1	Group 2	P
Number of patients	142	164	
Median tumor size (range)	3.5 cm (0.5-15)	8.1 cm (1.3-25)	<.0001
Tumor size <3 cm (%)	40.1	4.9	<.0001
Tumor size <5 cm (%)	61.3	11.6	<.0001
Bilobar involvement (%)	15.5	33.5	.0005
Multifocal HCC (%)	32.4	50	.0027
Diffuse HCC (%)	0.7	8.5	.0037
Portal vein infiltration (%)	9.2	38.4	<.0001
Neovascularization (%)	79.5	88.5	NS
Metastasis (%)	2.8	15.9	.0003
Median AFP levels in ng/mL (range)	111 (1-261,500)	824.5 (1-1,720,600)	.0001

Surveillance Methods

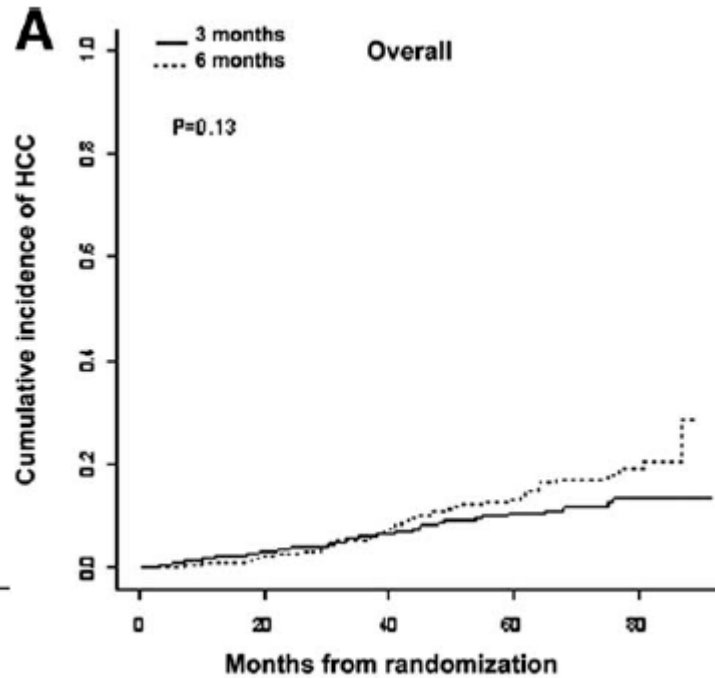
- Ultrasonography
- Alpha-fetoprotein (AFP)
- Intensive screening
 - Lipiodol Computed tomography (LICT)

Abdominal US

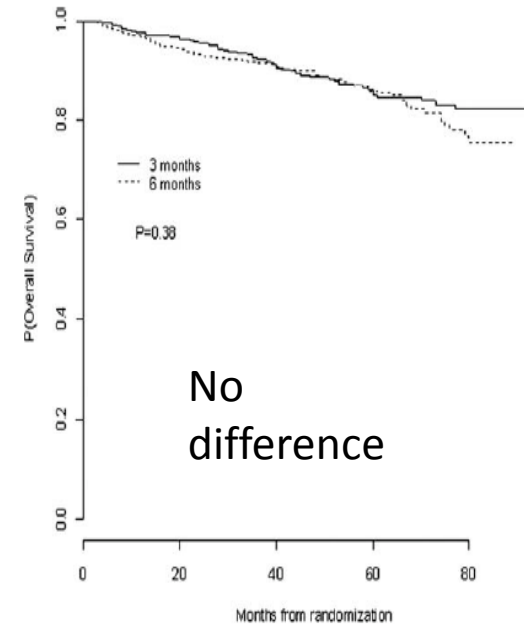
- 6 months standard (3 month not better)



Time to first nodule



HCC incidence



Overall survival

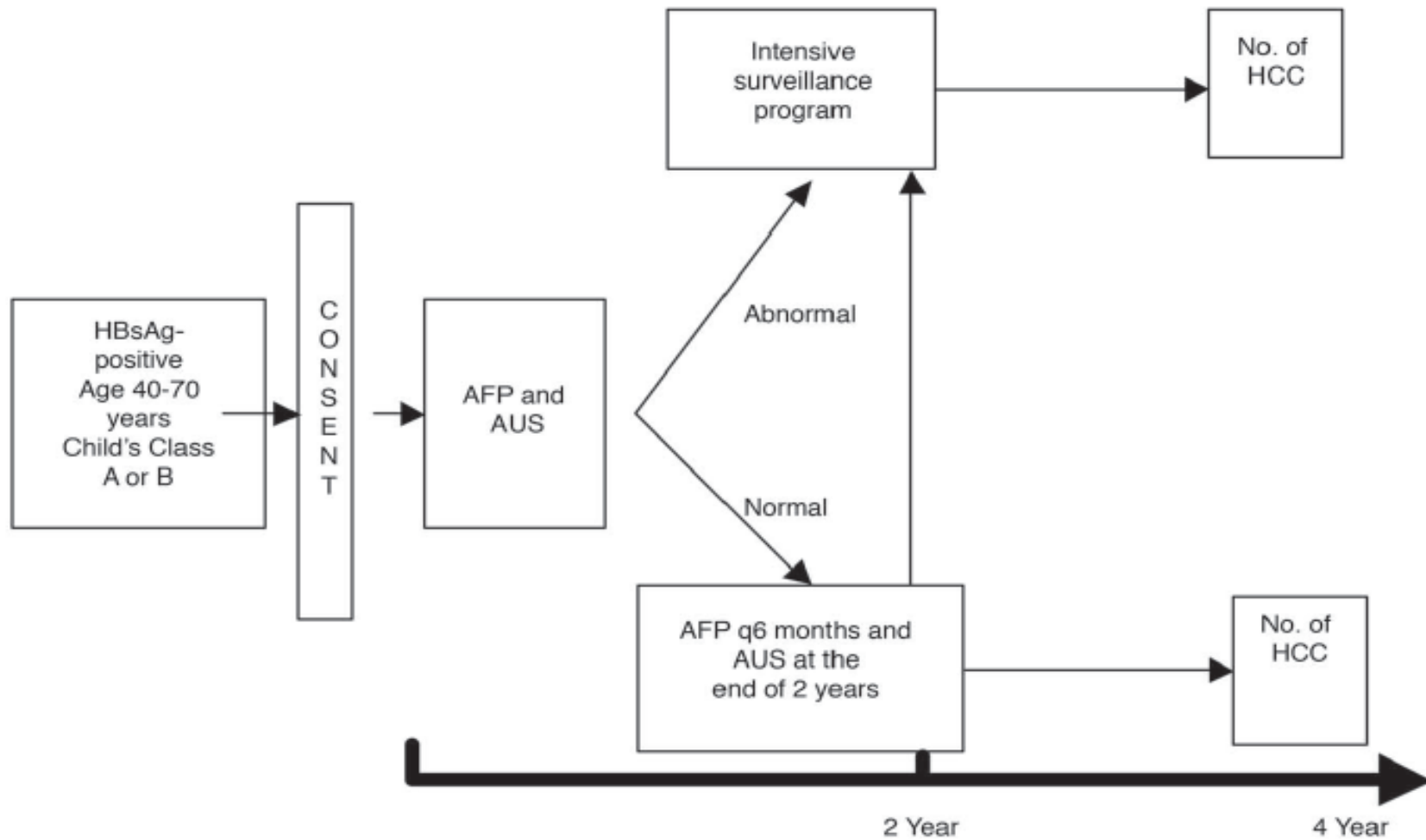
Abdominal US + AFP

Table 2 Detection rate, false positive rate, positive predictive value of screening tests and their 95% confidence intervals

	<i>Detection rate (%)</i>	<i>False positive rate (%)</i>	<i>Positive predictive value (%)</i>
AFP and/or US positive	92 (80 to 97)	7.5 (7.1 to 7.9)	3.0 (2.2 to 3.8)
AFP alone positive	69 (54 to 80)	5.0 (4.7 to 5.3)	3.3 (2.2 to 4.4)
US alone positive	84 (73 to 93)	2.9 (2.7 to 3.1)	6.6 (4.7 to 8.5)

AFP = α fetoprotein; US = ultrasonography.

Intensive Screening With CT



No Improvement in Earlier Diagnosis

Table 1. Patients' Characteristics and Liver Functions at Enrollment

	Group A (n = 78)		Group B (n = 93)		Group C (n = 847)		Total (n = 1,018)	
	No.	%	No.	%	No.	%	No.	%
Male/female ratio	62:16		72:21		554:293		688:330	
Age, years								
Mean	51.5		48.6		47.5		48.7	
Range	40-67		40-69		40-69		40-69	
Bilirubin > 34 μ mol/L	4	5.0	4	4.3	15	1.8	23	2.3
ALT > 90 U/L	30	38.5	24	25.8	104	12.3	158	15.5
Albumin \leq 35 g/L	38	48.7	27	18.3	87	7.3	152	10.8
INR > 1.7	1	1.3	1	1.1	6	0.7	8	0.8
Ascites	5	6.4	2	2.1	12	1.4	19	1.8
Encephalopathy	0	0	0	0	1	0.1	1	0.1
Ultrasonographic evidence of cirrhosis	60	76.9	61	65.6	262	30.9	383	37.6
Child's class B cirrhosis	7	8.9	7	7.5	28	3.3	42	4.1

Surveillance for HBV Carriers

- Asian men over the age of 40 years
- Asian women over the age of 50 years
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Recommended method

- Abdominal ultrasonography with or without alpha-fetal protein (AFS) every 6 months
- CT screening is not recommended

Evaluation of Nodules on US

- Nodules smaller than 1cm are usually not HCC, but such lesions should be monitored at shorter intervals (eg 3 months), until proven stable or disappear
- Nodules larger than 1 cm should be evaluated by CT (triphasic) or MRI, if still not typical , may consider biopsy
- A negative biopsy doesn't excluded HCC. Keep monitoring every 3 to 6 months is suggested

Take Home Message

- Prevention from HCC related risk factors is important
- Surveillance is suggested in HBV infected patients (selected criteria) and all patients who have liver cirrhosis
- Abdominal ultrasound with or without AFP is every 6 months is currently recommended surveillance method