Banner 11th Liver Disease Symposium
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HCC surveillance strategies

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Hepatocellular carcinoma in the US

27,000 deaths in 2016

5th cancer related death in men in the US

8th cancer related death in women in the US

American Cancer Society 2016

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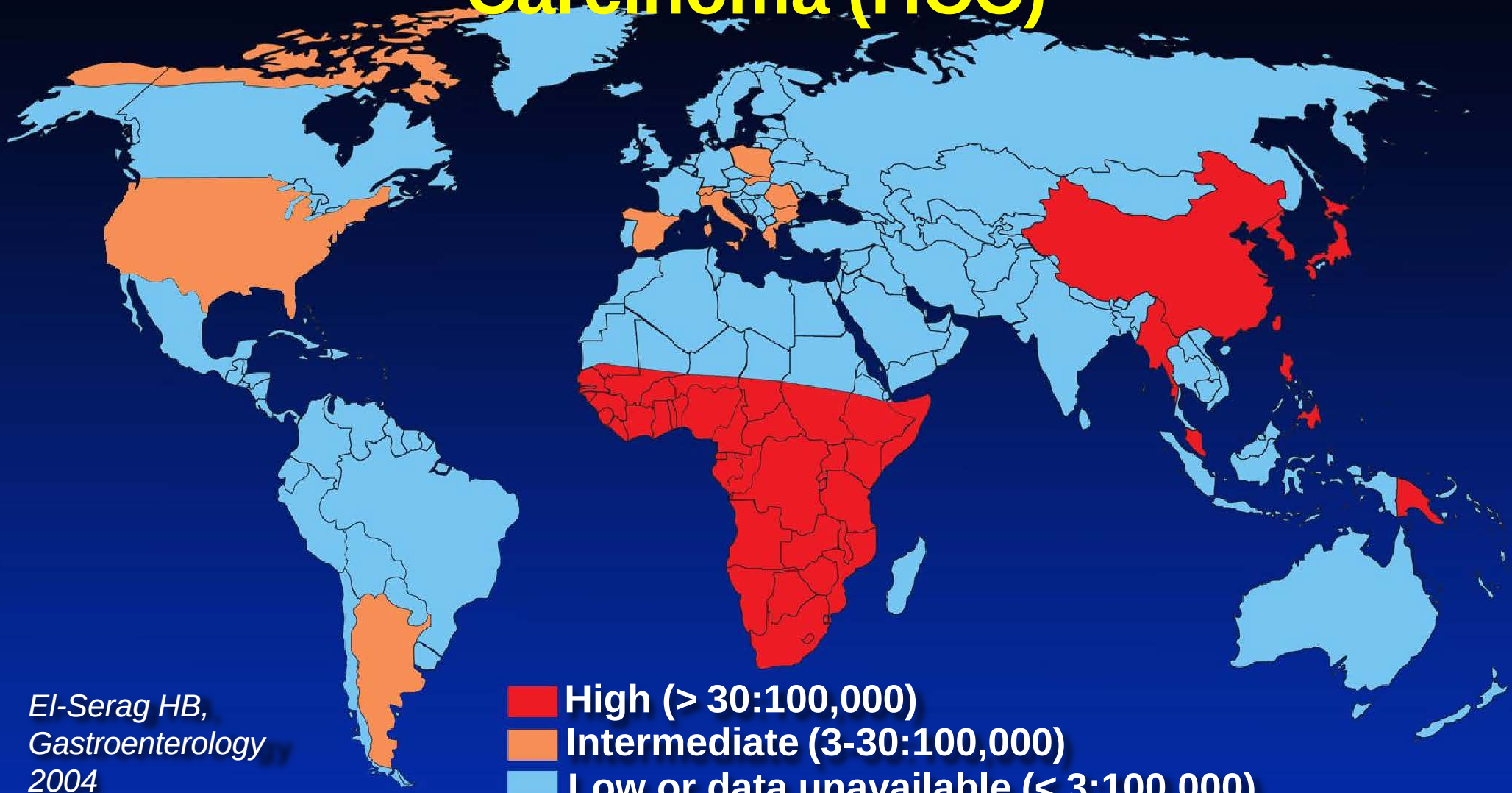
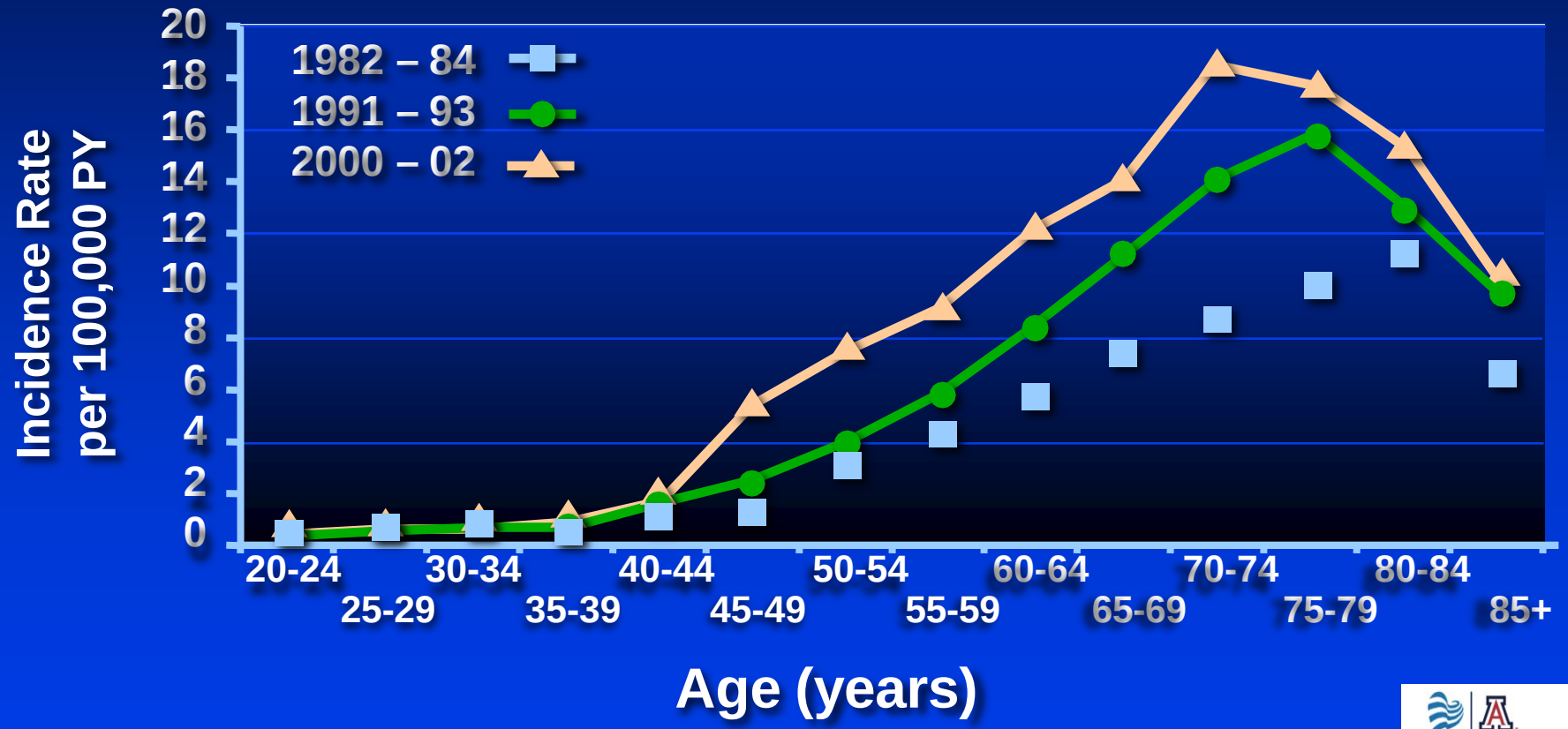
Worldwide Incidence of Hepatocellular Carcinoma (HCC)



El-Serag HB, Gastroenterology 2004

Temporal Trends in The Age Distribution of Hepatocellular Carcinoma



El-Serag HB, Mason A, N Engl J Med 1999

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Why is HCC Incidence Rising?

- Rising incidence of cirrhosis
  - HCV (main reason in the USA)
  - HBV (main reason across the globe)
  - NAFLD (more recently)
- Improved survival of patients with cirrhosis

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Risk factors associated with HCC

- HBV (54% worldwide)
- HCV (31% worldwide)
- ETOH
- Aflatoxin
- Hemochromatosis
- Obesity and DM II
- Co-factors
  - Smoking
  - HIV

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J of Hepatol 2012; 56:908-43
Ann Hepatol 2010; 9:120

Risk factors associated with HCC

- HBV
  - With or without cirrhosis
    - Treatment decreases but does not eliminate the HCC risk
    - Spontaneous seroconversion decreases but does not eliminate the HCC risk
- HCV
  - Treatment decreases but does not eliminate the HCC risk

Clin Gastroenterol Hepatol 2010; 56:908
Ann Intern Med 2013; 158:329
Aliment Pharmacol Ther 2016;43:1253

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Risk of developing HCC

- 1/3 of all cirrhotics will have HCC
  - 1 to 8 % a year
    - 3 to 5% / year in HCV patients
    - 3 to 8%/ year in HBV patients
- Higher risk in:
  - Male
  - Older
  - More advanced liver disease

J of Hepatol 2012; 56:908-43 EASL Guidelines

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Incidence of HCC in cirrhosis

Population group	Annual incidence (percent per year) for which surveillance is considered to be cost-effective	Incidence of HCC
Surveillance recommended		
Asian male hepatitis B carriers over age 40	0.2	0.4-0.6% per year
Asian female hepatitis B carriers over age 50	0.2	0.3-0.6% per year
Hepatitis B carrier with family history of HCC	0.2	Incidence higher than without family history
African/North American blacks with hepatitis B	0.2	HCC occurs at a younger age
Cirrhotic hepatitis B carriers	0.2-1.5	3-8% per year
Hepatitis C cirrhosis	1.5	3-5% per year
Stage 4 primary biliary cholangitis	1.5	3-5% per year
Genetic hemachromatosis and cirrhosis	1.5	Unknown, but probably >1.5% per year
Alpha-1 antitrypsin deficiency and cirrhosis	1.5	Unknown, but probably >1.5% per year
Other cirrhosis	1.5	Unknown
Surveillance benefit uncertain		
Hepatitis B carriers younger than 40 (males) or 50 (females)	0.2	<0.2% per year
Hepatitis C and stage 3 fibrosis	1.5	<1.5% per year
Non-cirrhotic NAFLD	1.5	<1.5% per year

HCC: hepatocellular carcinoma; NAFLD: nonalcoholic fatty liver disease.

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Bruix J, Sherman M, Hepatology 2010. AASLD Guidelines

Why do surveillance for HCC?

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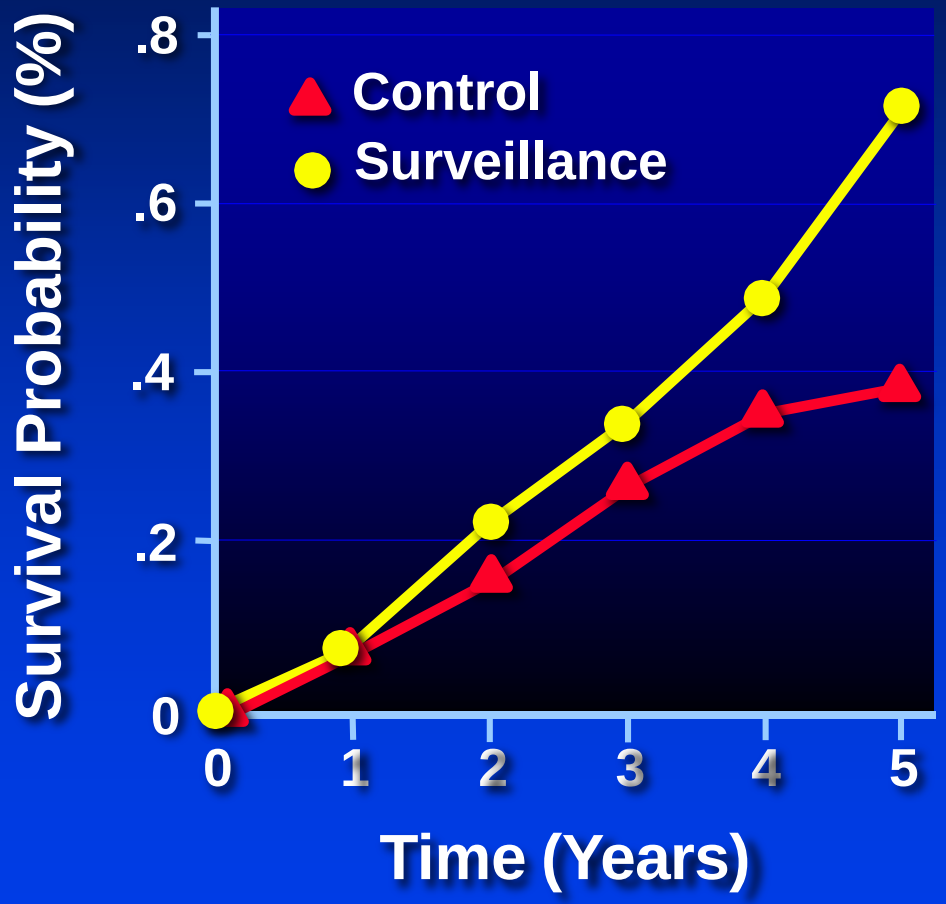
Surveillance for HCC reduces mortality

A Randomized Controlled Trial



Zhang BH et al, J Cancer Res Clin Oncol 2004

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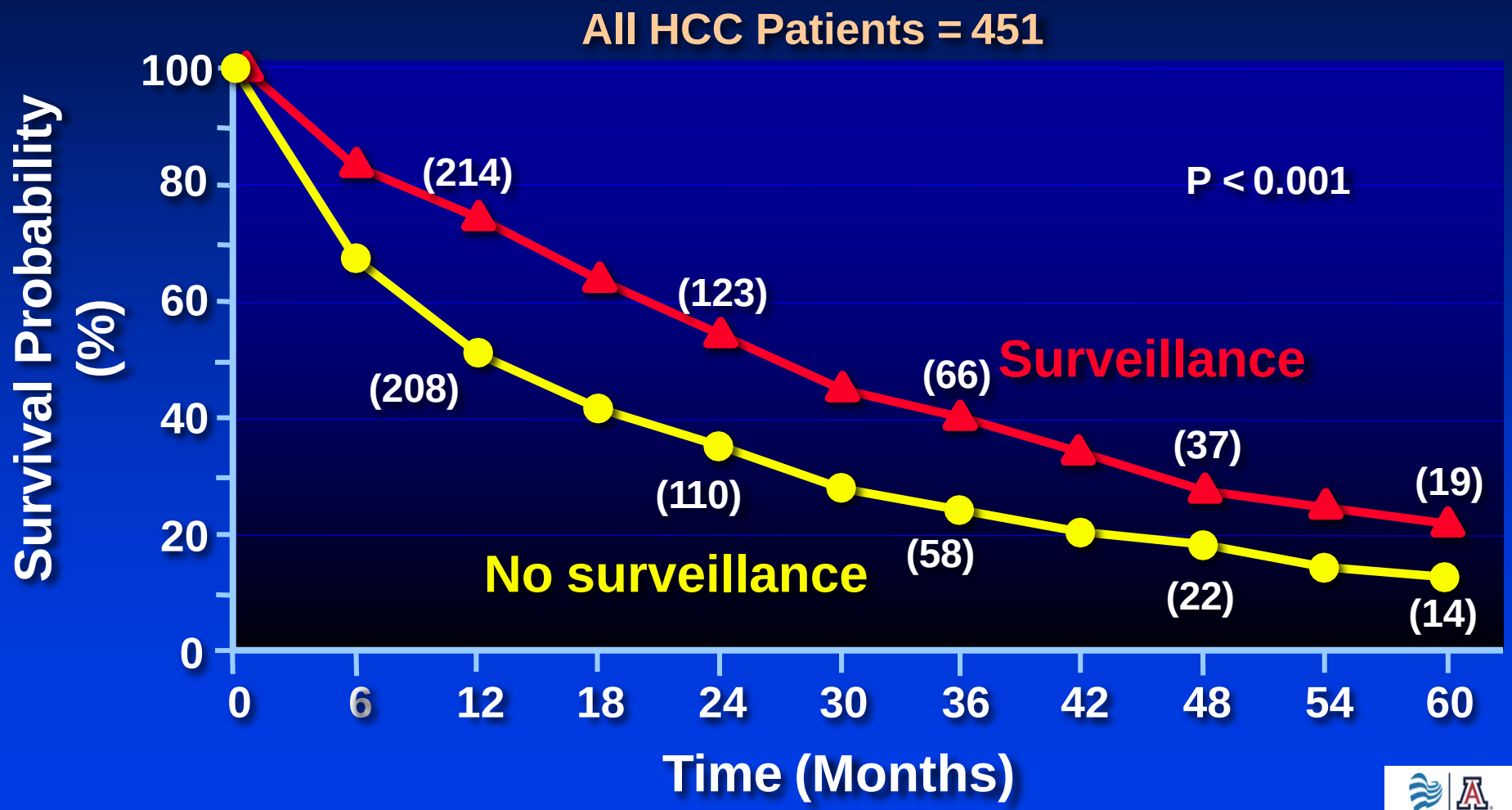
Surveillance for HCC prolongs survival



Trevisani F et al, Am J Gastro 2002

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HCC surveillance

- Transplant and resection are potentially curative treatment
- Several options for treatment of the non transplant candidate are now available
- To decrease mortality and improve survival, early diagnosis is paramount

- **Early diagnosis = Surveillance**

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Surveillance for HCC

Characteristics of a good screening test:

- Cost effective
- Affordable
- Acceptable to the target population and health care professionals
- Standardized recall procedures must be available
- Acceptable level of accuracy

Cancer 2004

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Biochemical markers for HCC surveillance

- The AASLD did not include biomarkers on its guidelines
- Alpha- fetoprotein (AFP)
  - Low sensitivity
  - Combined with US may improve accuracy
- AFP L 3% (isomer of AFP)
  - Low accuracy alone or in combination with other biochemical markers
- Des-gamma carboxy prothrombin
  - Better accuracy for larger tumors with vascular invasion
- Micro RNA panels
  - Ongoing studies

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Gastroenterol Hepatol 2015; 11:38
Gastroenterol 2010;138;493
J Clin Oncol 2011;29:4781

Ultra sound for HCC Surveillance

- Sensitivity: 58 to 89%
- Specificity > 90%
- Pool of 19 studies 63% early stage
- Contrast enhanced U/S not better
- Operator dependent

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J of Hepatol 2012; 56:908-43 EASL Guidelines

What about CT and MRI

- No study has shown CT or MRI to be cost-effective for surveillance of HCC.
- CT has the associated risk of the radiation
- MRI has a much higher cost

J of Hepatol 2012; 56:908-43 EASL Guidelines

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U/S is the recommended test for HCC surveillance

- What is the recommended interval?
  - 6 and 12 months have shown similar results
  - 3 to 4 months superior to 6 months in Japan
  - Meta analysis of prospective studies
    - Sensitivity 70 % if done every 6 months
    - Sensitivity of 50% if done every 12 months

- U/S is to be performed every 6 months in those at risk for HCC

Bruix J, Sherman M, Hepatology 2010. AASLD Guidelines

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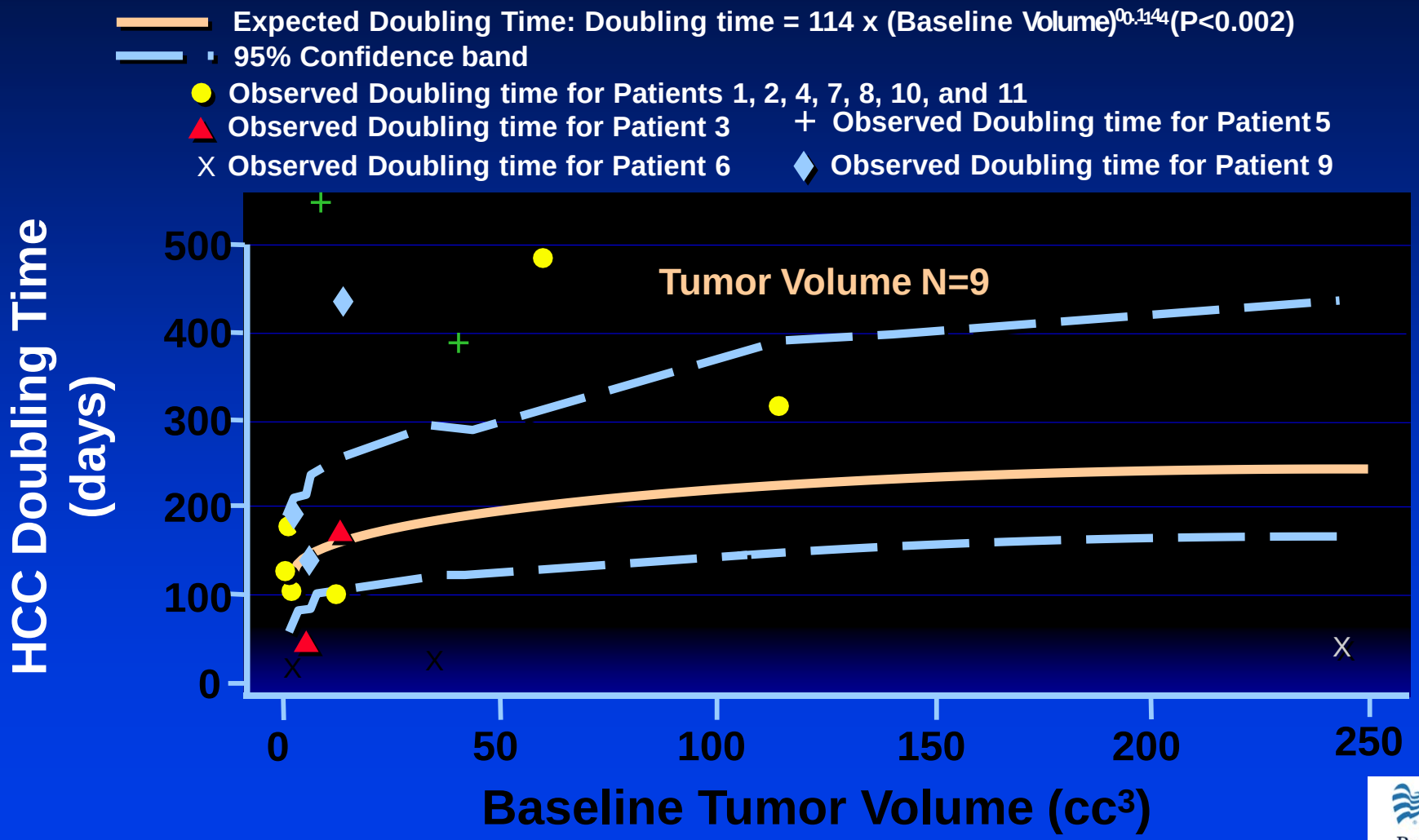
HCC Doubling Time
Rationale for Surveillance Every 6 Months



Taouli B et al, J Comput Assist Tomogr 2005

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HCC Surveillance

- **Exceptions:**
  - Patients with small nodules (less than 2 cm)
  - Patients listed for transplant

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J of Hepatol 2012; 56:908-43 EASL Guidelines

HCC surveillance recommendation

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Organization	Target population	Recommendation
AASLD	All cirrhotic patients Non-cirrhotic HBV with a family history of HCC Non-cirrhotic Africans and African Americans with HBV Non-cirrhotic Asian male with HBV and older than 40, non-cirrhotic Asian female with HBV and older than 50 years	US every 6 months
EASL	All cirrhotic patients Non-cirrhotic with HBV with active hepatitis or family history of HCC Non-cirrhotic patients with chronic HCV and advanced liver fibrosis (F3)	US every 6 months
APASL	Cirrhotic patients with HBV or HCV infection	US and AFP every 6 months
JSH	All cirrhotic patients Non-cirrhotic patients with chronic HBV Non-cirrhotic patients with chronic HCV infection	US end AFP/AFP L3%/DCP every 3 to 6 months

AASLD: American Association for the Study of Liver Diseases; AFP: alpha-fetoprotein; AFP-L3%: Lens culinaris agglutinin A-reactive fraction of AFP; APASL: Asian Pacific Association for the Study of the Liver; DCP: serum des-carboxy prothrombin; EASL: European Association for the Study of the Liver; HBV: hepatitis B virus; HCC: hepatocellular carcinoma; HCV:hepatitis C virus; JSH:Japan Society of Hepatology; US: ultrasonography.

Thank you!

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