
Hepatitis C Choices in Care

Hepatitis C and Liver Cancer

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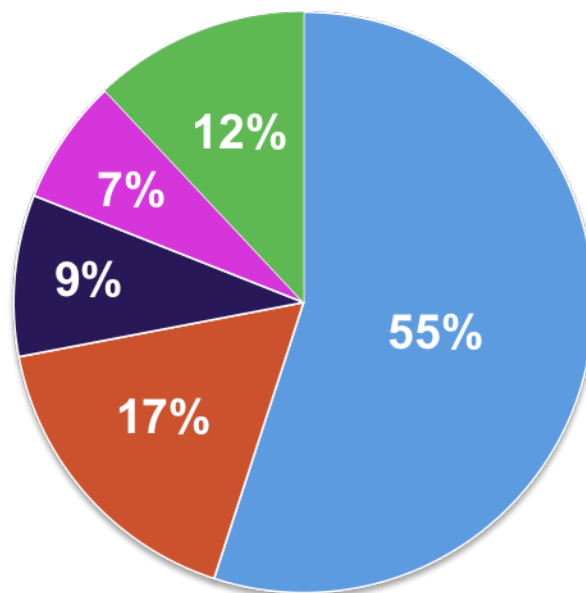


HCC: Epidemiology

- HCC is the most common primary liver malignancy
- Worldwide incidence >600,000 cases per year
 - Liver cancer is the most rapidly increasing cancer in the U.S.
 - 19,160 new cases and 16,780 deaths in 2007
- More common in men than women (4:1)
- For resection, rate of recurrence can be as high as 50% at 2 years
 - Only 12% are eligible for resection or for transplant
 - 80%-90% of HCC cases occur in cirrhotic livers

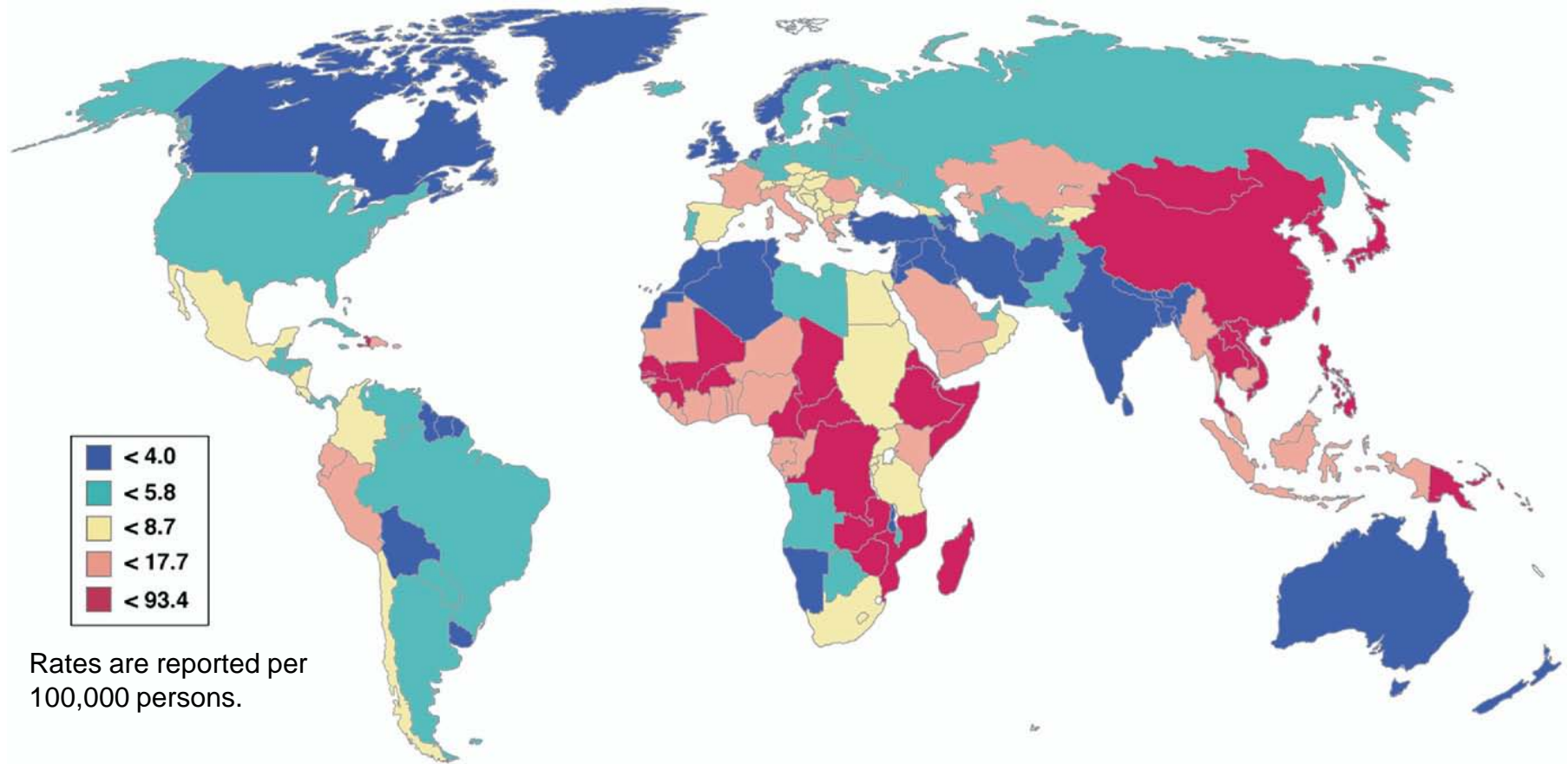
Presumed Etiology of HCC in the U.S.

Hepatitis C is the Predominant Cause



- HCV
- HBV
- Alcohol
- Cryptogenic
- Other

Regional Variations in the Mortality Rates of HCC Categorized by Age-Adjusted Mortality Rates



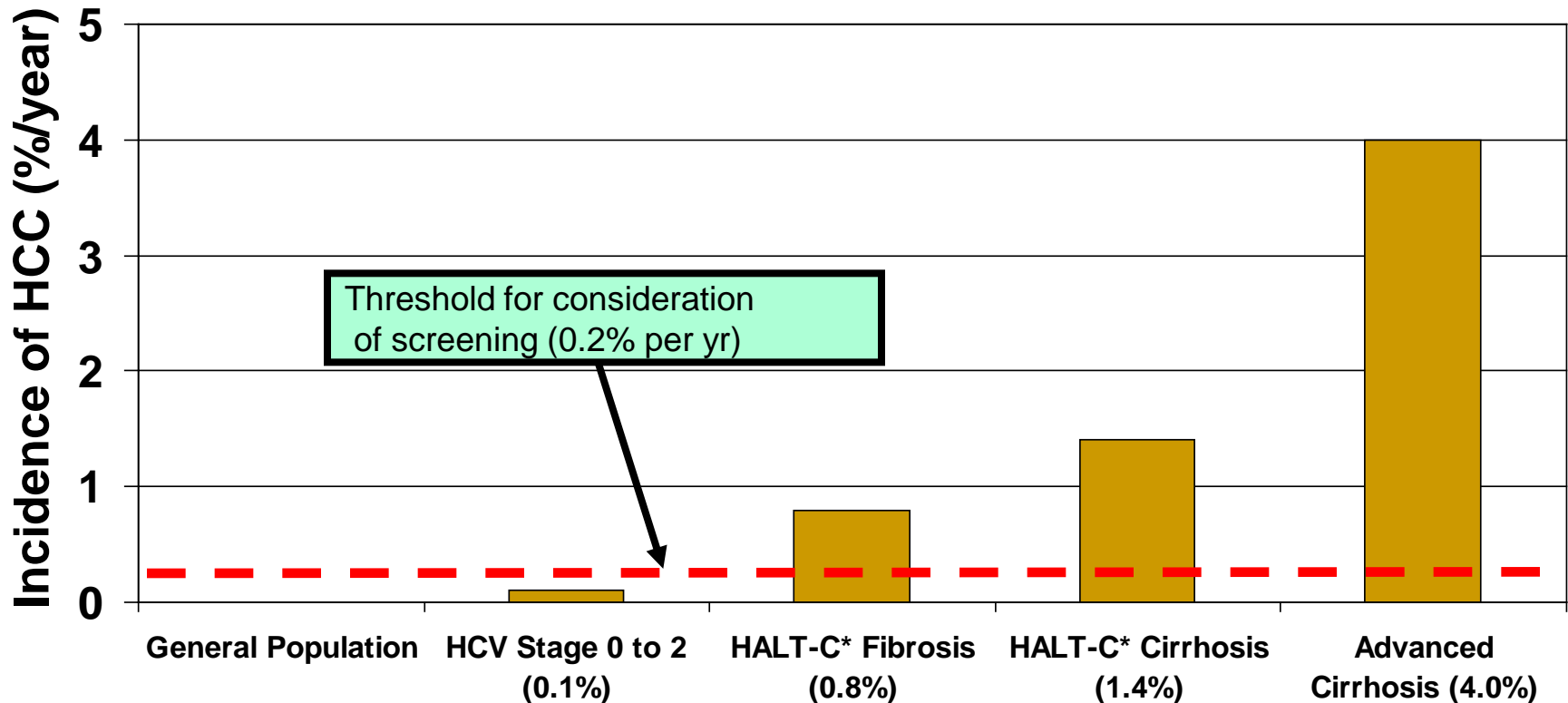
Risk Factors for HCC

- Cirrhosis or advanced fibrosis
- Males > females and older age
- Co-morbidities—HBV, HIV, and alcohol use
- African American race
- HCV patients with diabetes or insulin resistance
- Smoking (possible risk factor)

HALT-C Multivariate Model

	<u>P Value</u>
Platelet Count	0.001
Age	0.01
Alkaline phosphatase	0.01
Esophageal Varices	0.02
Black race	0.04
History of smoking	0.07

Incidence of HCC is Related to Stage of Fibrosis

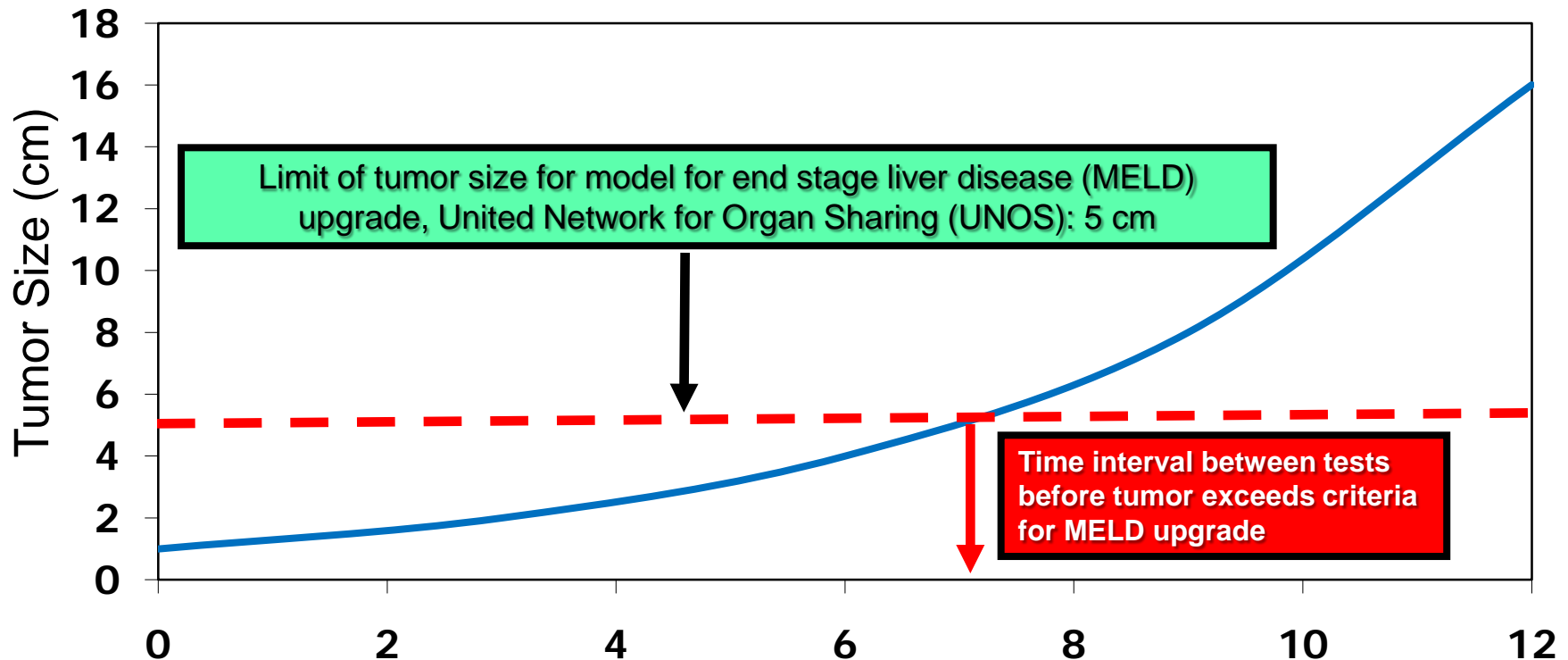


* HALT-C : Hepatitis C Antiviral Long-term Treatment against Cirrhosis

Screening Tests in HCC

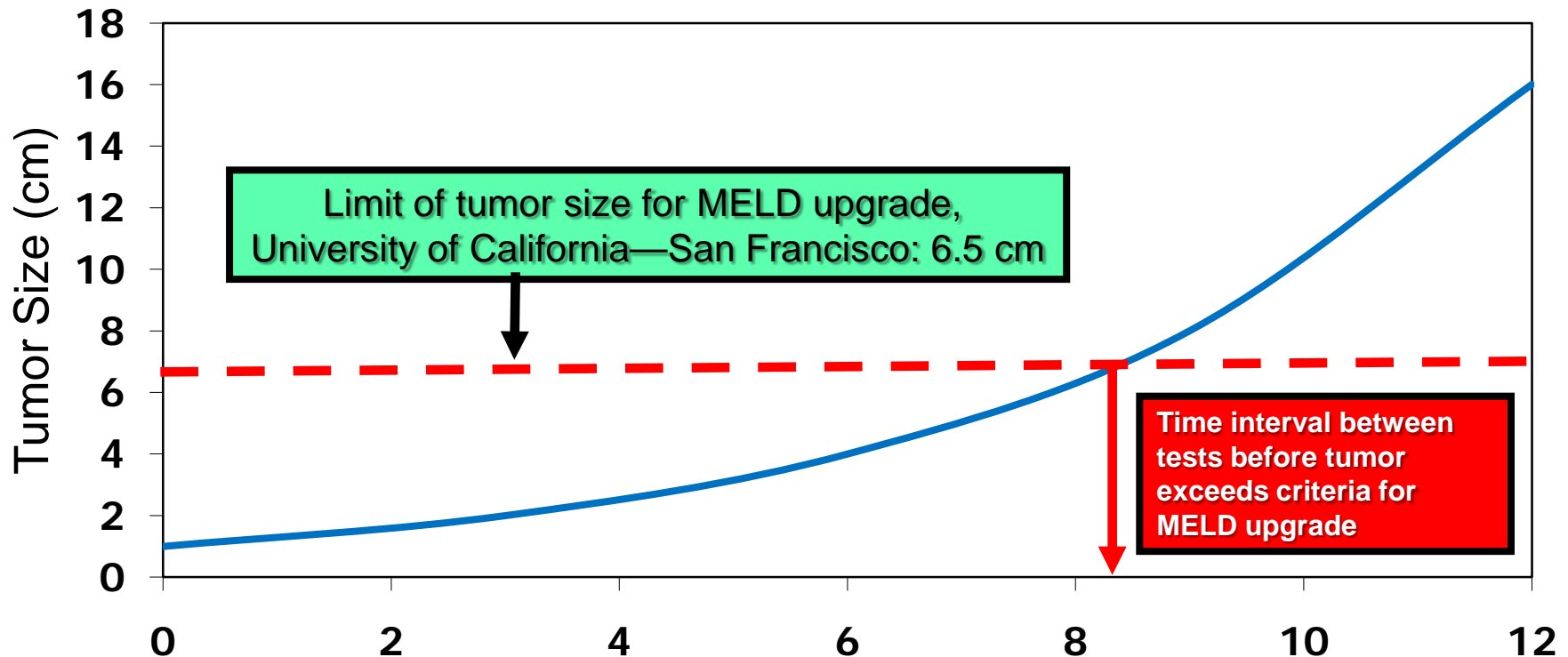
- Screening improves detection of HCC (most of the data are from ultrasonography)
- Radiology is most reliable screening tool
- Value of AFP (or DCP, or AFP-L3) unproven
- Screening may improve clinical outcome

Growth Rate of HCC and Frequency of Screening Test



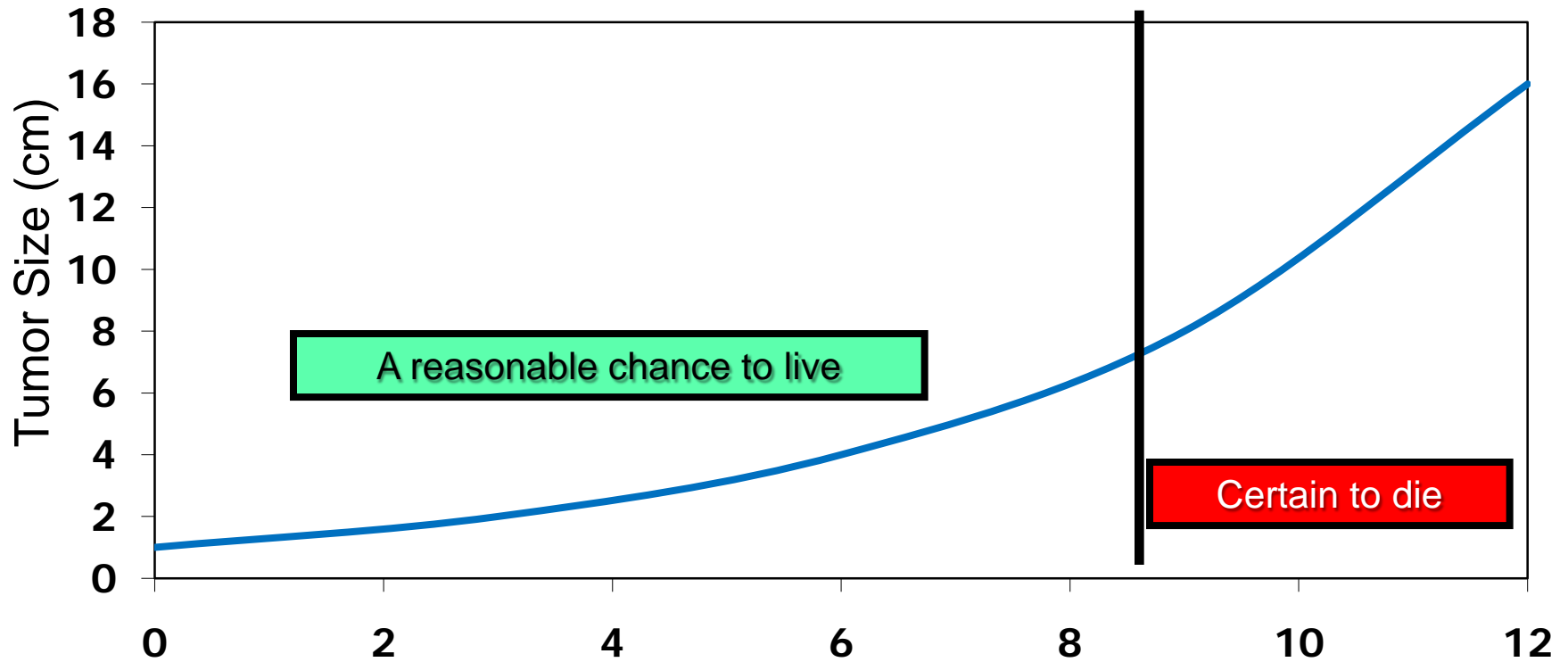
Months After First Test Missed a 1-cm HCC,
Assuming Tumor Doubling Every 3 Months

Growth Rate of HCC and Frequency of Screening Test



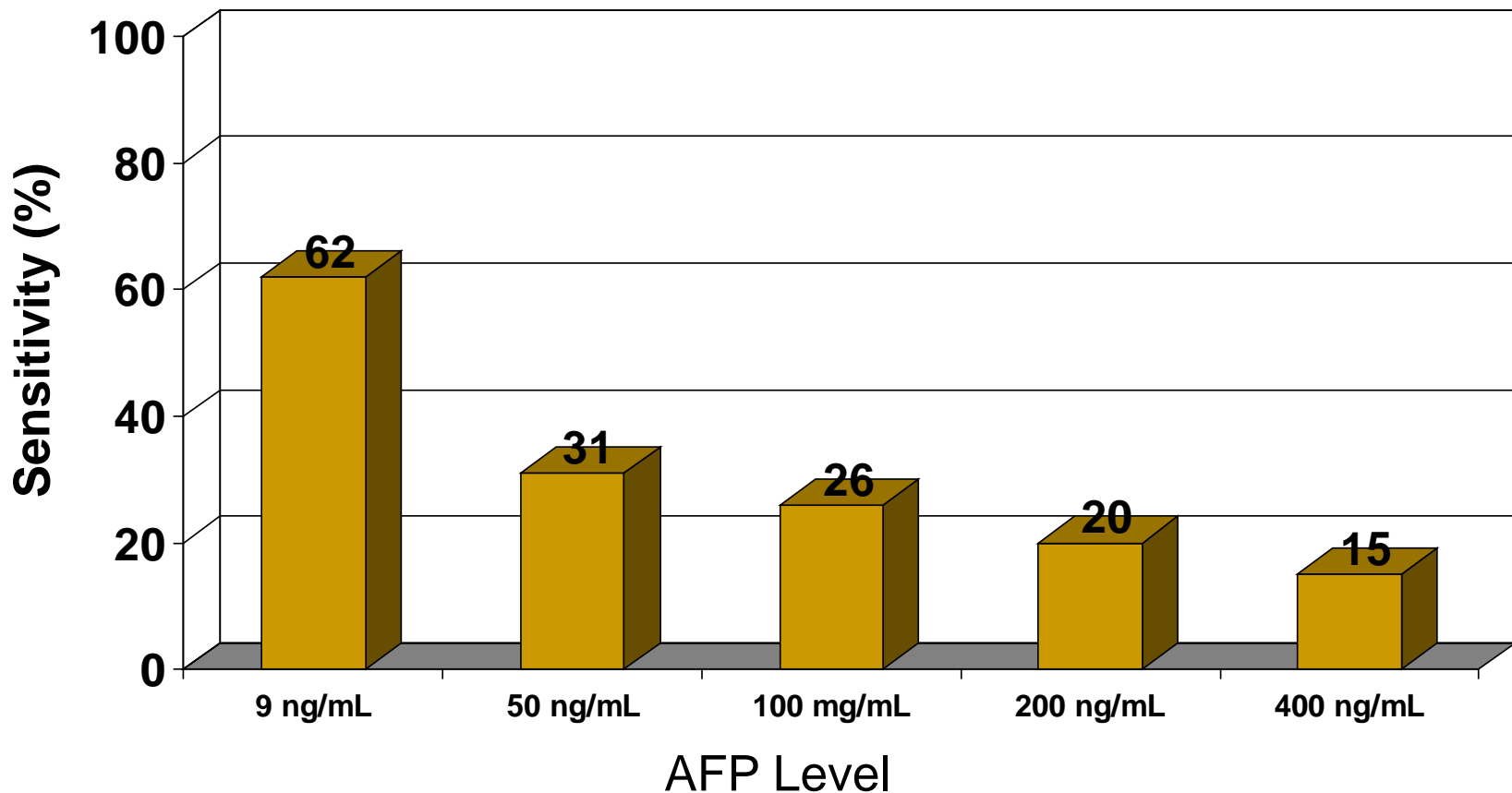
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From the Patient's Perspective



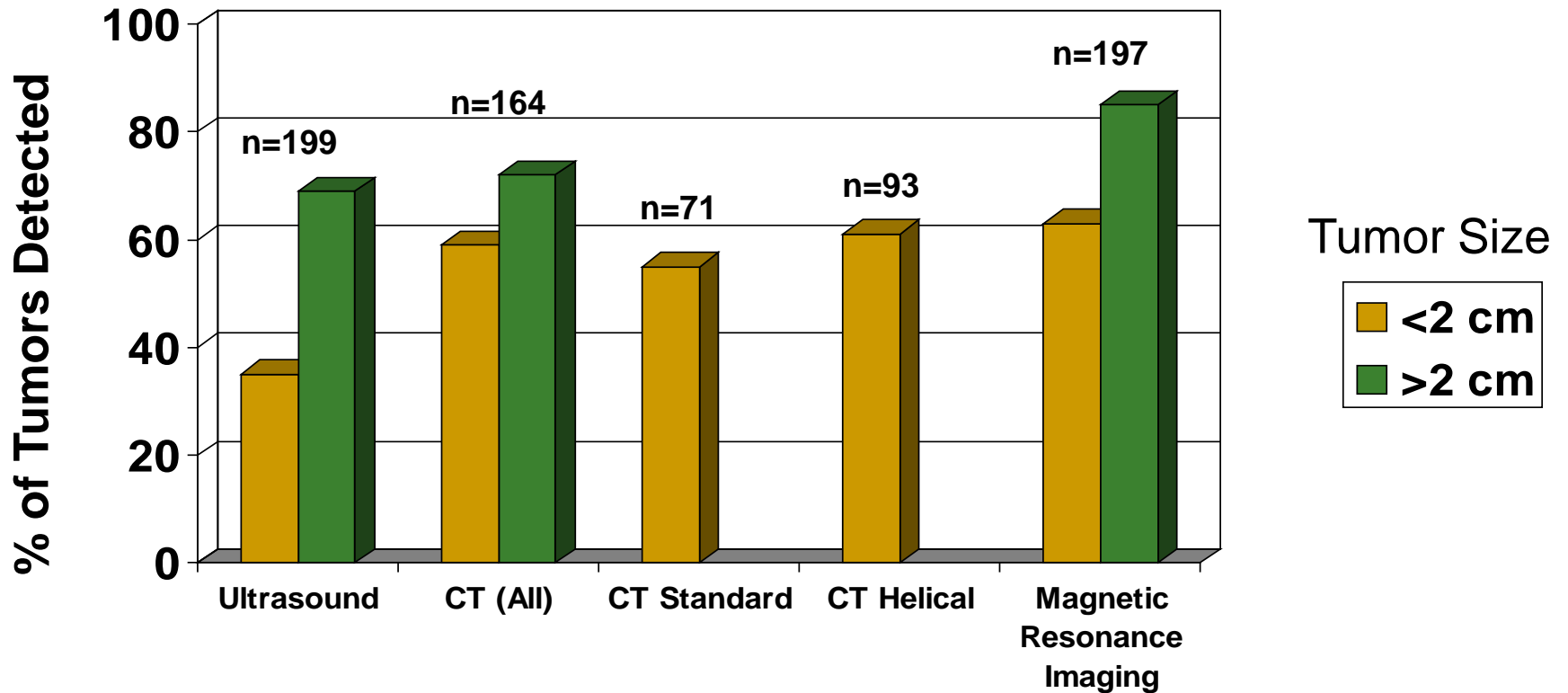
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AFP in Screening for HCC



HCC proven at explant, N=239 patients with HCC, 55% with HCV

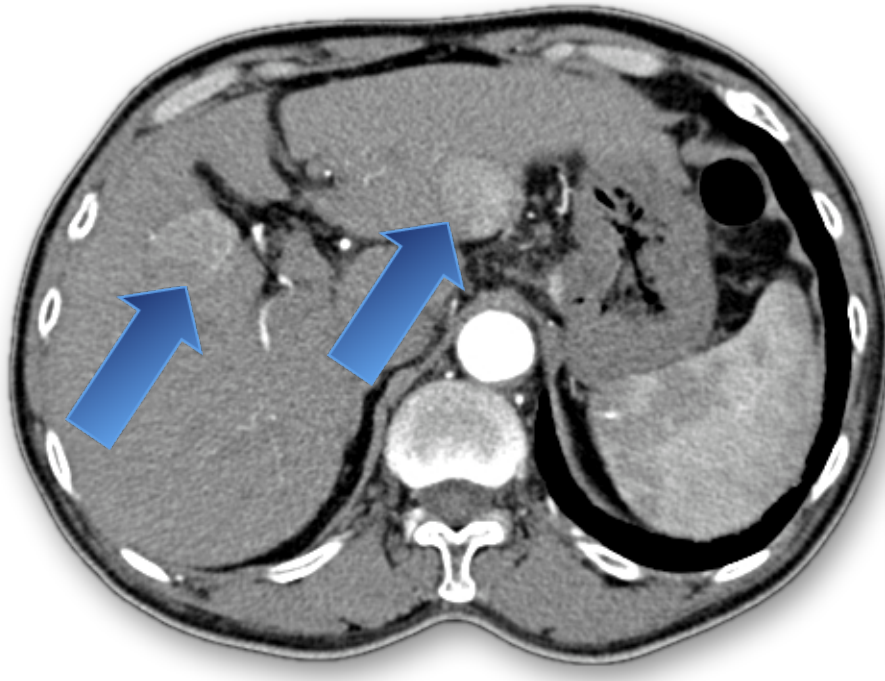
Pre-Transplant Ultrasound, Computed Tomography, Magnetic Resonance Imaging



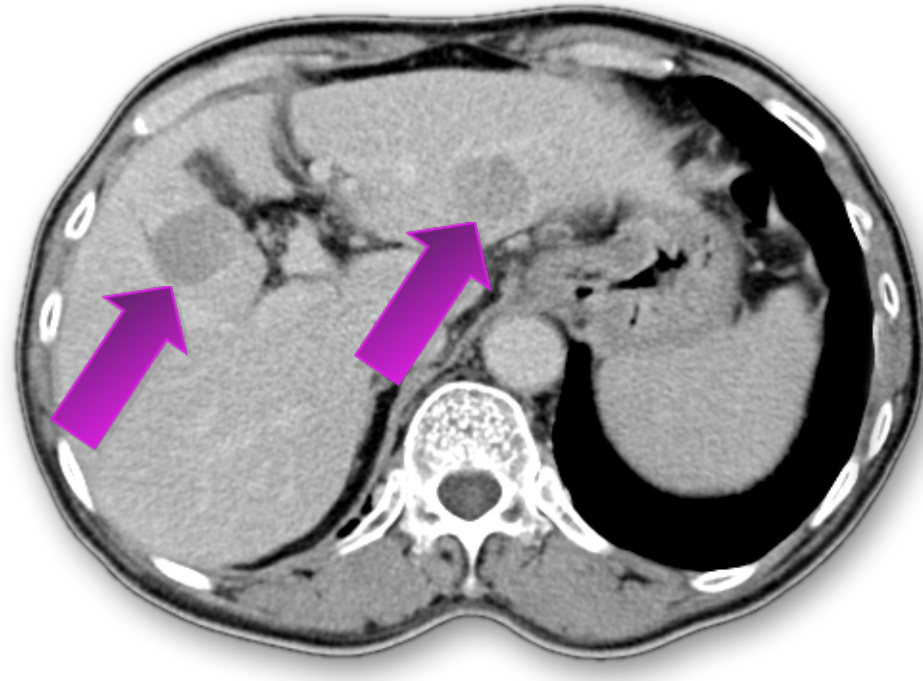
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CT SCAN of Multifocal HCC

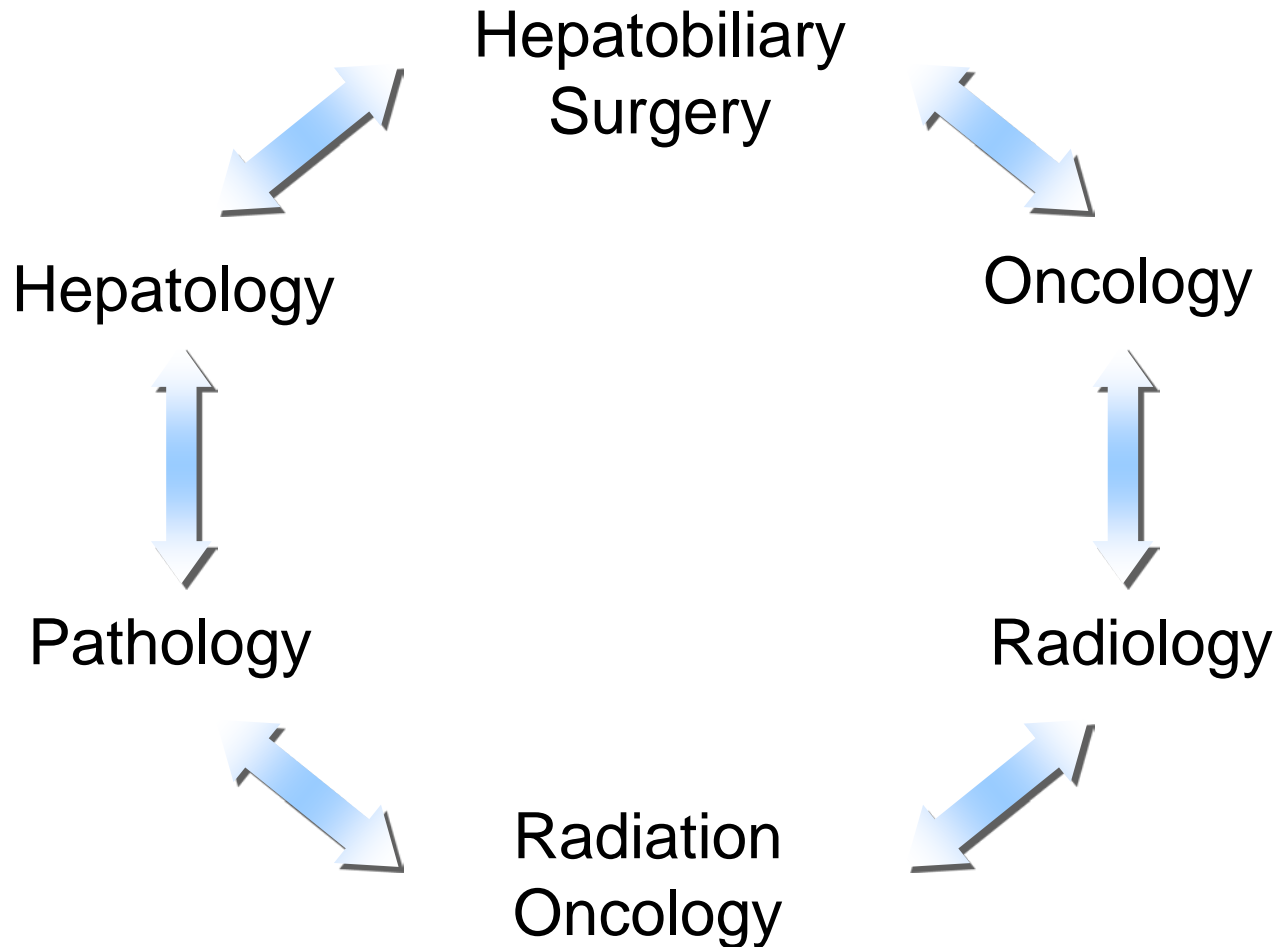
Arterial phase



Venous phase



Management of Hepatocellular Carcinoma Requires a Multidisciplinary Approach



Treatment Options for HCC

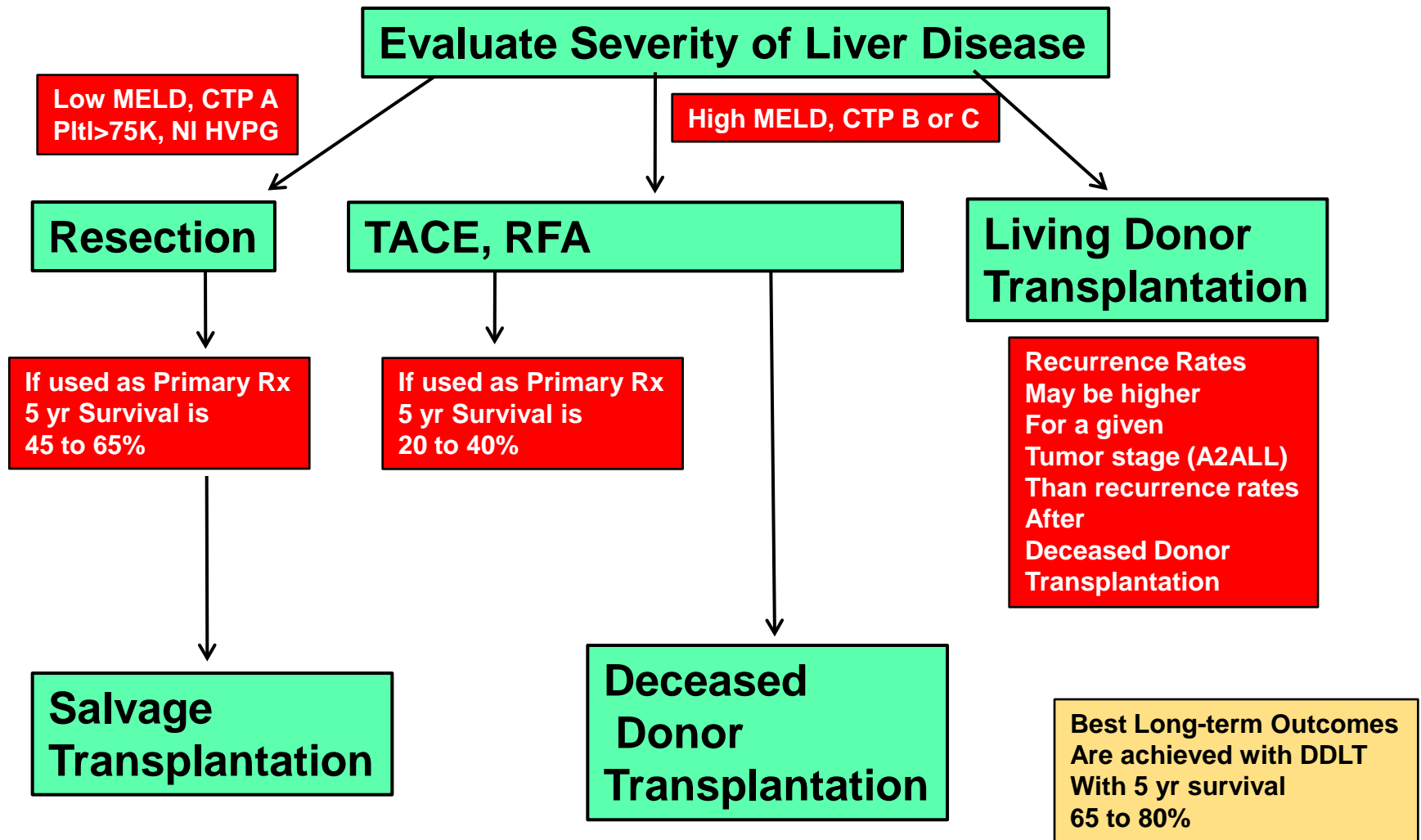
Local Therapies

- Transplantation
- Resection
- Ablation or embolization
 - Radiofrequency (RFA)
 - Chemoembolization (TACE)
 - TAFE (Bead embolization)
 - TARE – Radioembolization
 - ⁹⁰Y-microspheres

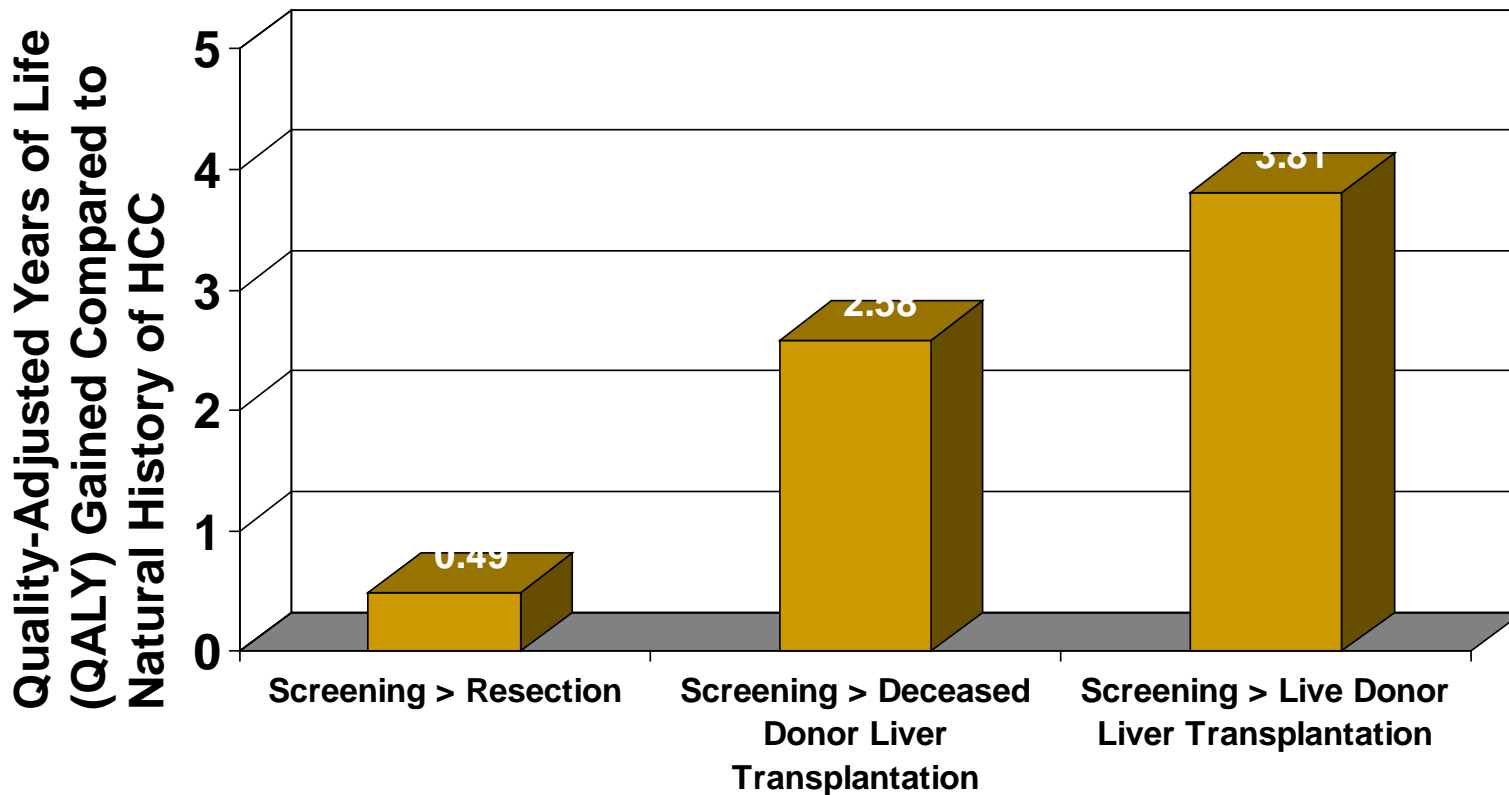
Systemic Therapies

- Sorafenib
- Clinical Trials

Selection of HCC Treatment Options



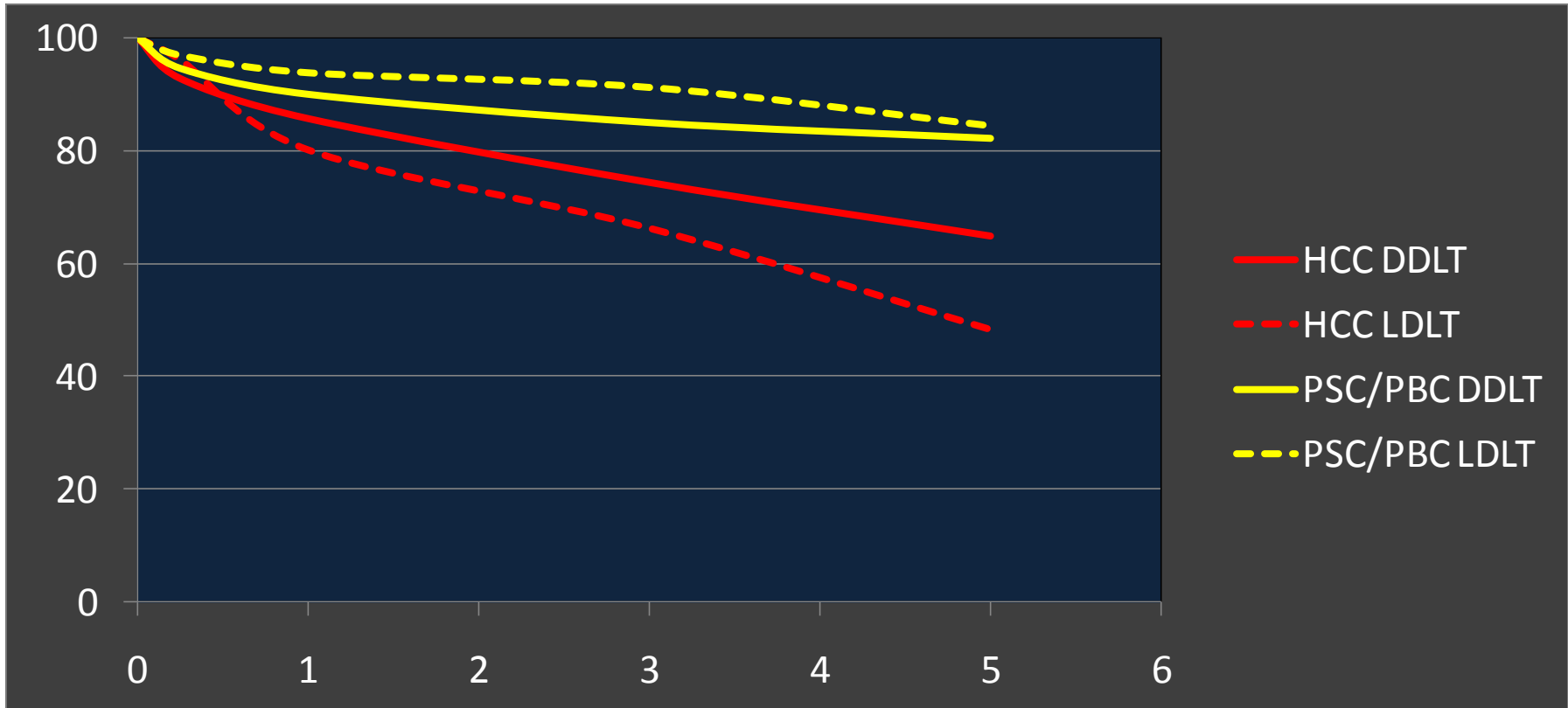
Impact of Surgical Treatments on Outcomes (QALY gained)



Outcomes achieved at less than \$51,000/QALY, sensitive mainly to outcomes and costs of HCC treatments.

Outcomes of Transplant for HCC

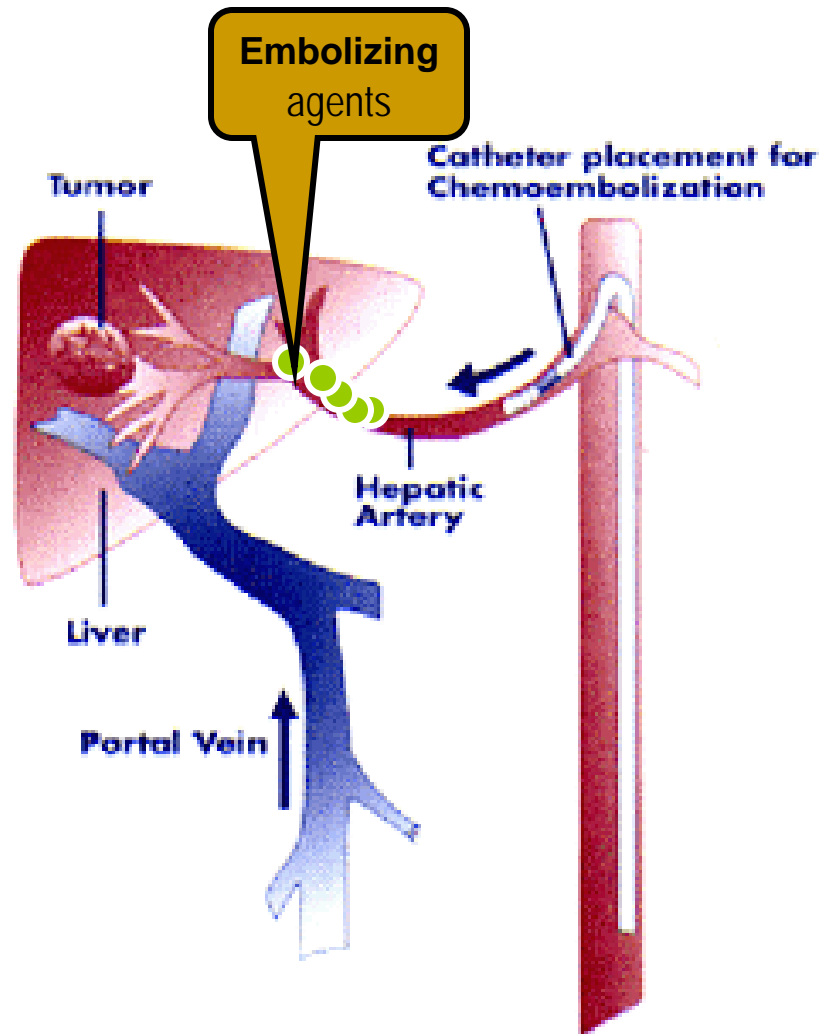
% Surviving



Years Post-Transplant

Transarterial Chemoembolization (TACE)

- Meta-analysis showed survival benefit in selected pts with TACE compared to control group
 - No benefit of embolization without chemotherapeutic agent
- No data on choice of chemo agent (doxorubicin, mitomycin, and cisplatin most common) or schedule for TACE
- Partial response 15 - 55%
- Complete necrosis 22 - 29%
- > 50% develop postembolization syndrome
- Contraindicated in Child C, portal vein thrombosis or hepatofugal flow



Sorafenib

- **Small molecule, orally administered**
- **Multi-kinase inhibitor**
- **Inhibits tumor-cell proliferation and tumor angiogenesis**
 - Inhibits molecular components of the Raf-MEK-ERK signaling pathway, thus inhibiting tumor growth
 - Inhibits the receptor tyrosine kinase activity of vascular endothelial growth factor receptors (VEGFRs) 1, 2, and 3 and platelet-derived growth factor receptor β (PDGFR- β), thus inhibiting neoangiogenesis

SHARP Study Conclusions

(Sorafenib HCC Assessment Randomized Protocol)

- Sorafenib prolongs both Overall Survival and Time to Progression in advanced HCC
- First systemic therapy to demonstrate a survival advantage
- Side Effect profile manageable
- FDA-approved for unresectable HCC

Concluding Remarks

- HCC is an increasing problem in the United States
- Patients at highest risk are those with cirrhosis or bridging fibrosis
- Screening leads to early detection and “likely” improves outcomes of HCC
- Transplantation (DDLT) yields best long-term survival, but availability is limited

For more information

Please talk with your hepatologist or specialist if you have more questions regarding liver cancer.