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Digestive Diseases Center

Making the Case for Liver Cancer (HCC) Screening

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Objectives

- To understand the incidence of HCC
- To understand the risk factors associated with HCC
- To understand the evidence behind why we should do surveillance for HCC

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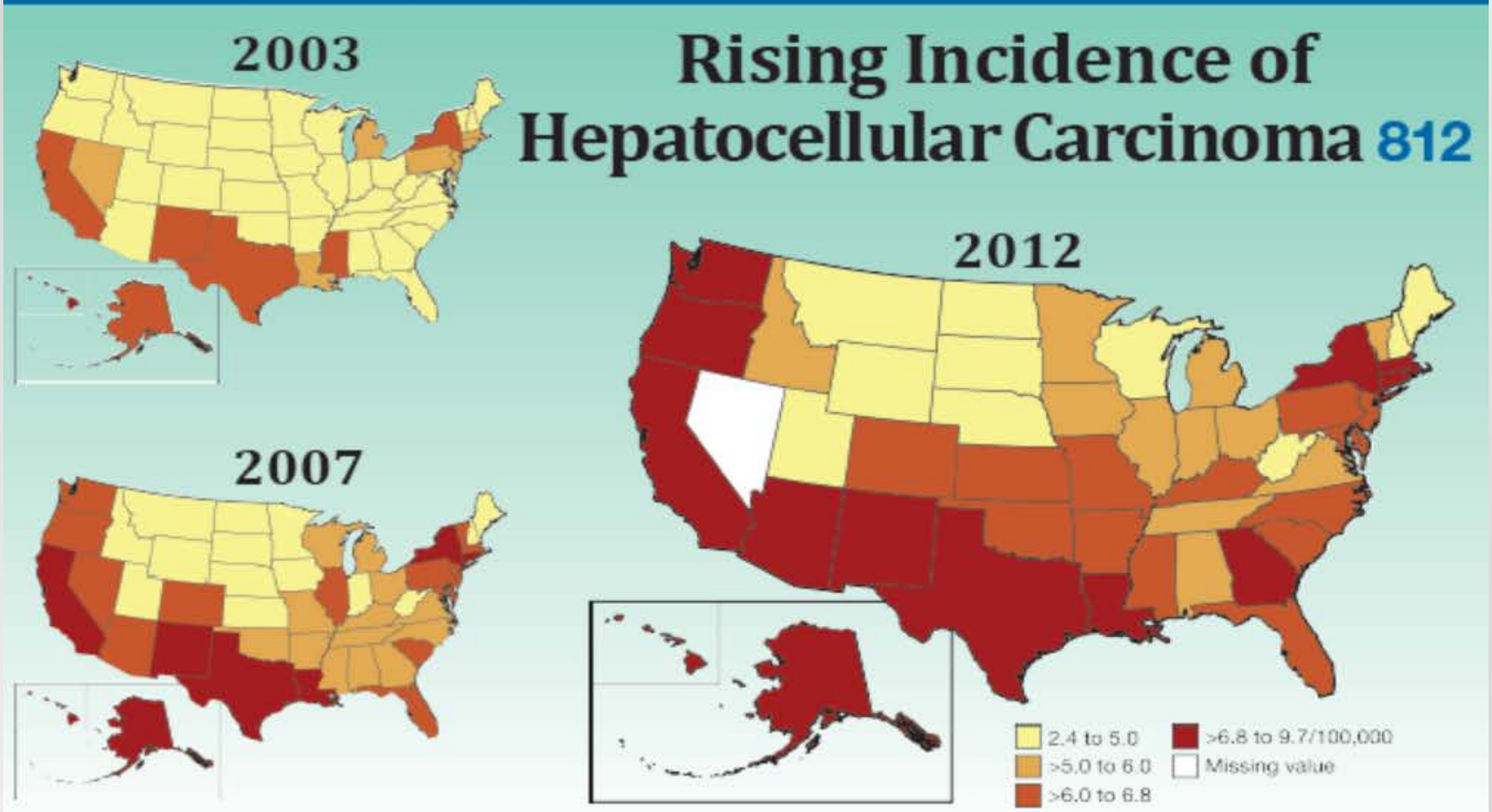

Rising Incidence of Hepatocellular Carcinoma 812

Burden of HCC

- Hepatocellular carcinoma (HCC) accounts for 85-90% of primary liver cancers
    - 5 year mortality is 18%
- **Fourth** leading cause of cancer mortality worldwide
    - Median survival following diagnosis is 6-20 months
    - Projected to surpass breast and CRC to become 3rd leading cause of cancer-related death in US by 2030

1. Parkin DM et al. Int J Cancer 1999;80:827-41. 2. World Health Organization .3. Sangiovanni A et al. Hepatology. 2006;43(6):1303-10. 4. El-Serag HB et al. N Engl J Med 1999;340:745-50 .

HCC: 5 year survival is dismal

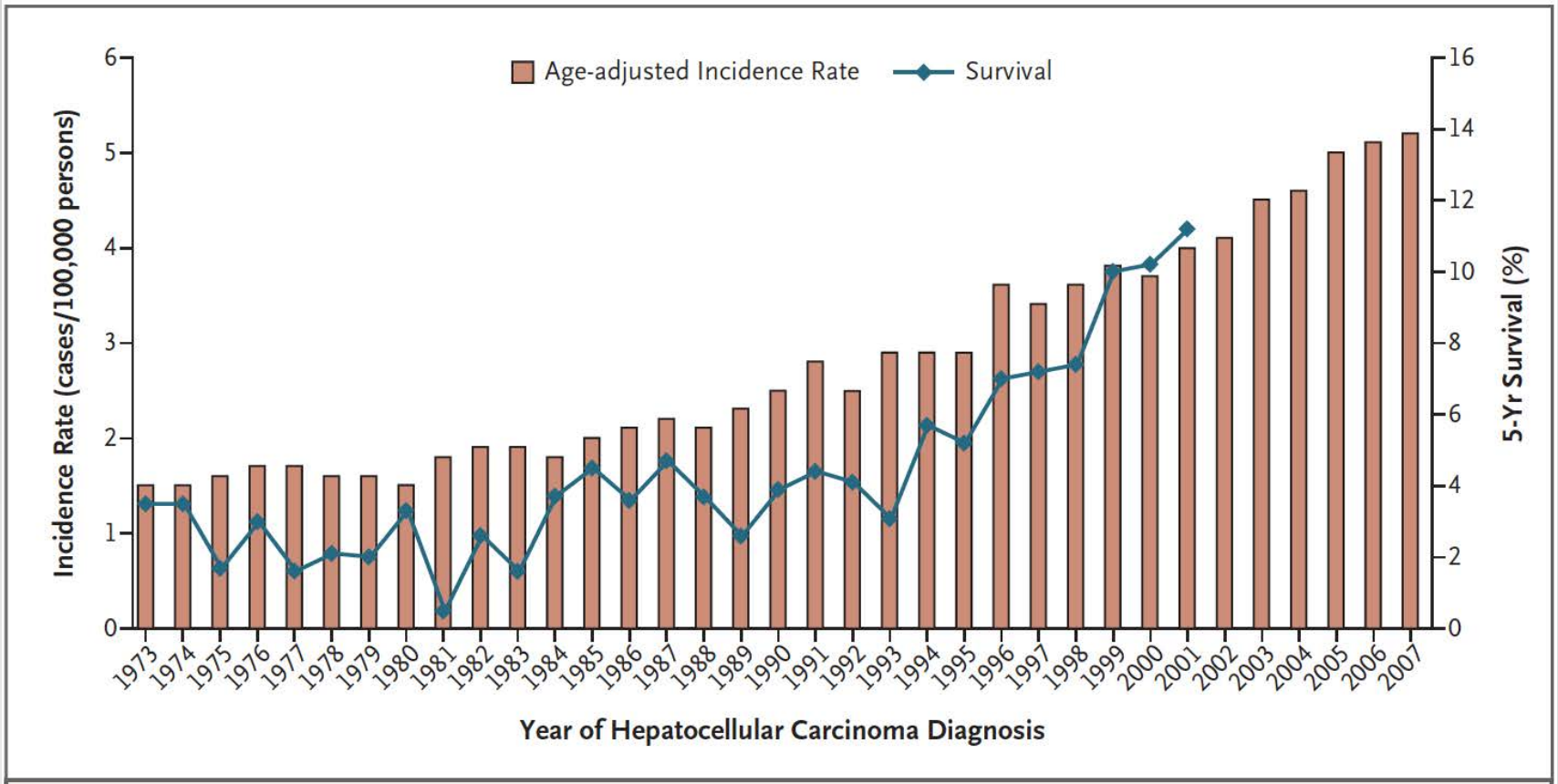

Figure 2. Age-Adjusted Incidence and 5-Year Survival Rates for Patients with Hepatocellular Carcinoma in the United States, 1973–2007.

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El Serag HB. NEJM 2011; 365:1118-1127

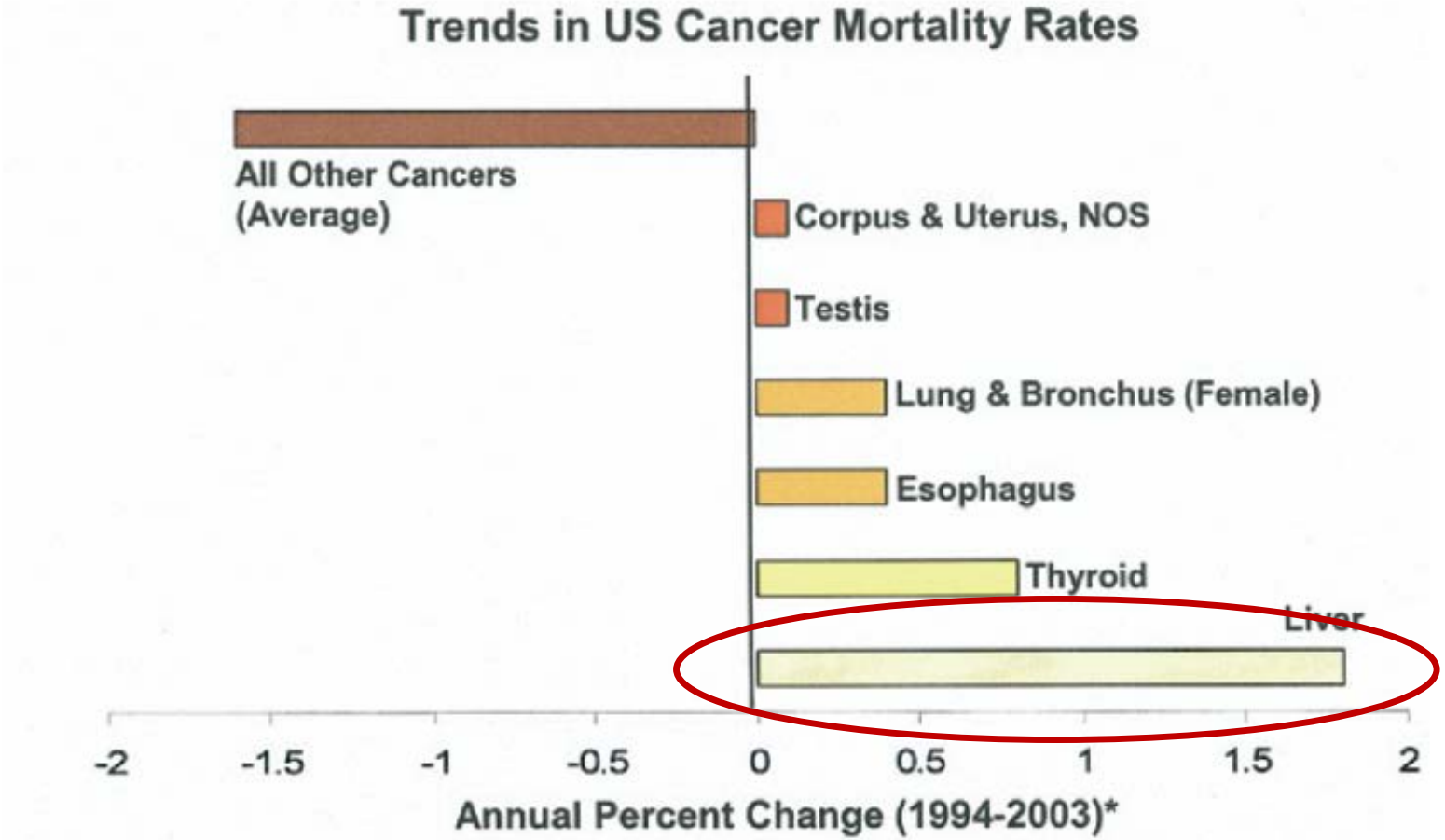
Why is incidence of HCC increasing?

- Growing numbers of patients with HCV cirrhosis
- Aging of patients who acquired HCV in the 60s
  - HCV cirrhosis is the most common risk factor
    - 2-8% per year
    - HCC is the most common cause of death in HCV cirrhosis

1. Parkin DM et al. Int J Cancer 1999;80:827-41. 2. World Health Organization .3. Sangiovanni A et al. Hepatology. 2006;43(6):1303-10. 4. El-Serag HB et al. N Engl J Med 1999;340:745-50 .

Why is incidence of HCC increasing?

- Improved overall survival of patients with cirrhosis
- Increased obesity and diabetes rates
- HCC projected to continue to increase up to 2040



National Cancer Institute Website: http://seer.cancer.gov/csr/1975_2003/sections.html

Global incidence of HCC: Hepatocellular carcinoma is 4th leading cause of cancer-related death worldwide

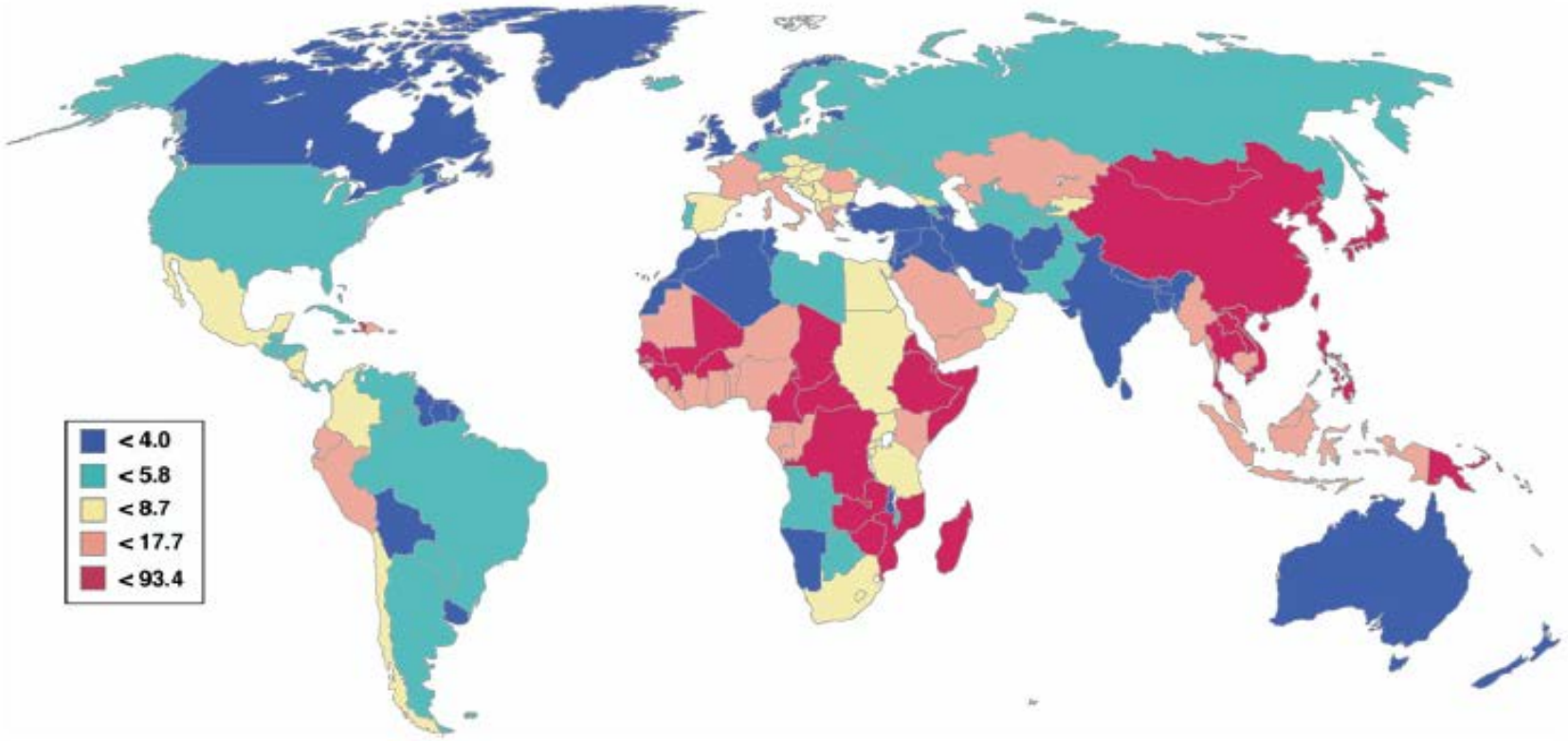


Figure 1. Regional variations in the mortality rates of HCC categorized by age-adjusted mortality rates. The rates are reported per 100,000 persons.

El-Serag H, Rudolph KL. Gastro 2007; 132:2557-2576

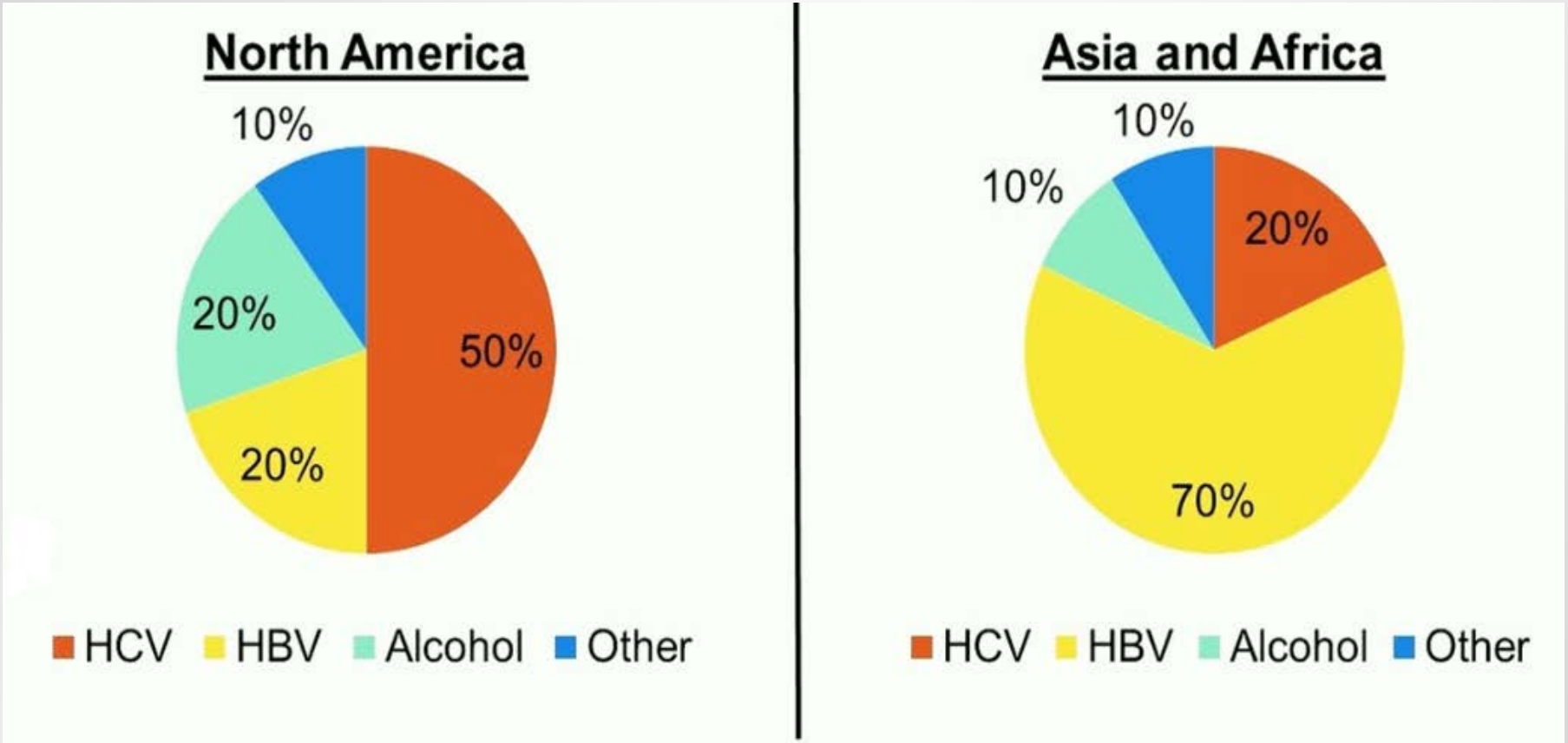
Risk factors for HCC

- **HBV**
- **HCV**
- **Alcohol**

- Nonalcoholic fatty liver disease
- Diabetes

- Environmental toxins (aflatoxin)
- Cirrhosis of any etiology

Etiology of HCC around the world



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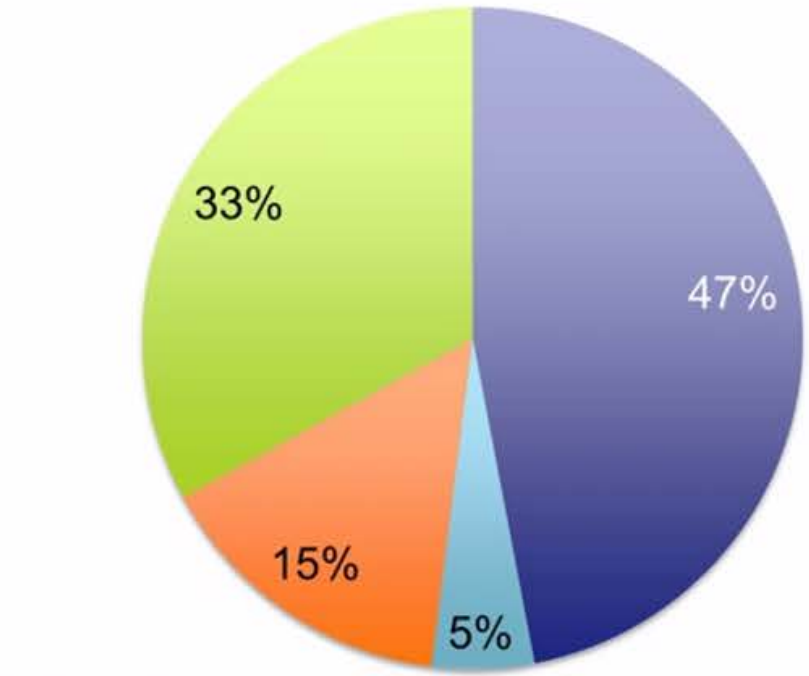
Forner A et al. Lancet 2012; 379 (9822): 1245-55

HBV and HCC

- HBV is globally the most frequent underlying risk factor
- Highest in Asia (except Japan) and Africa

- Chronic HBV carriers have a 5 to 15 fold increased risk
- Up to 10-30% of HCC occurs in HBV patients ***WITHOUT*** cirrhosis

HCV is the dominant risk factor



HCV
Both
HBV
Neither

(N=691)

- HBV most frequent in Asians
- HCV most frequent in whites and blacks

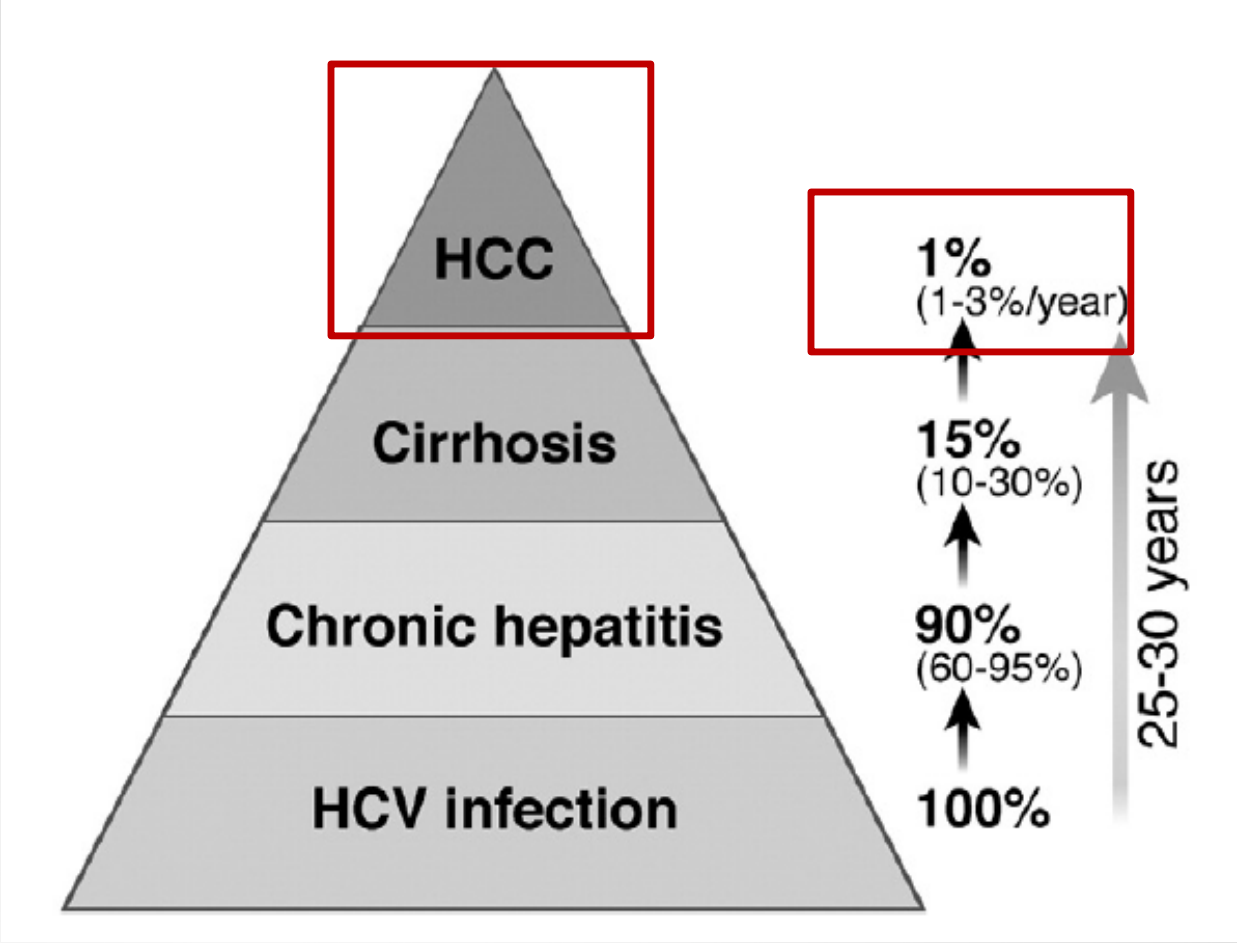
Elserag H, Gastro 2017

HCV and HCC

- HCV infected large numbers of adults in N. America, S and Central Europe in the 60s and 70s due to IVDA
- Infected national blood supplies until screening test developed in 1990

- HCC risk increased 17-fold in HCV+ patients compared to controls

Progression of HCV



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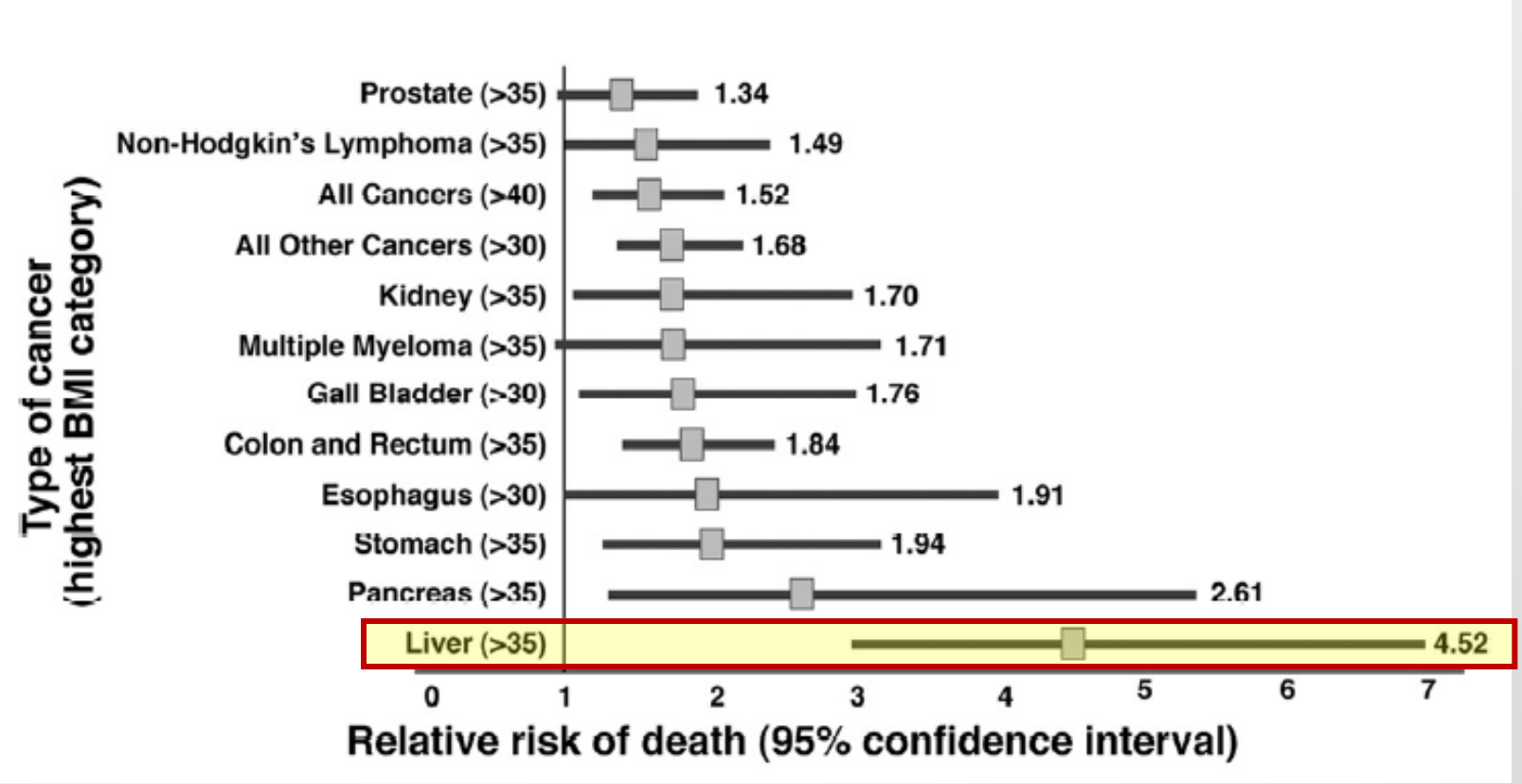
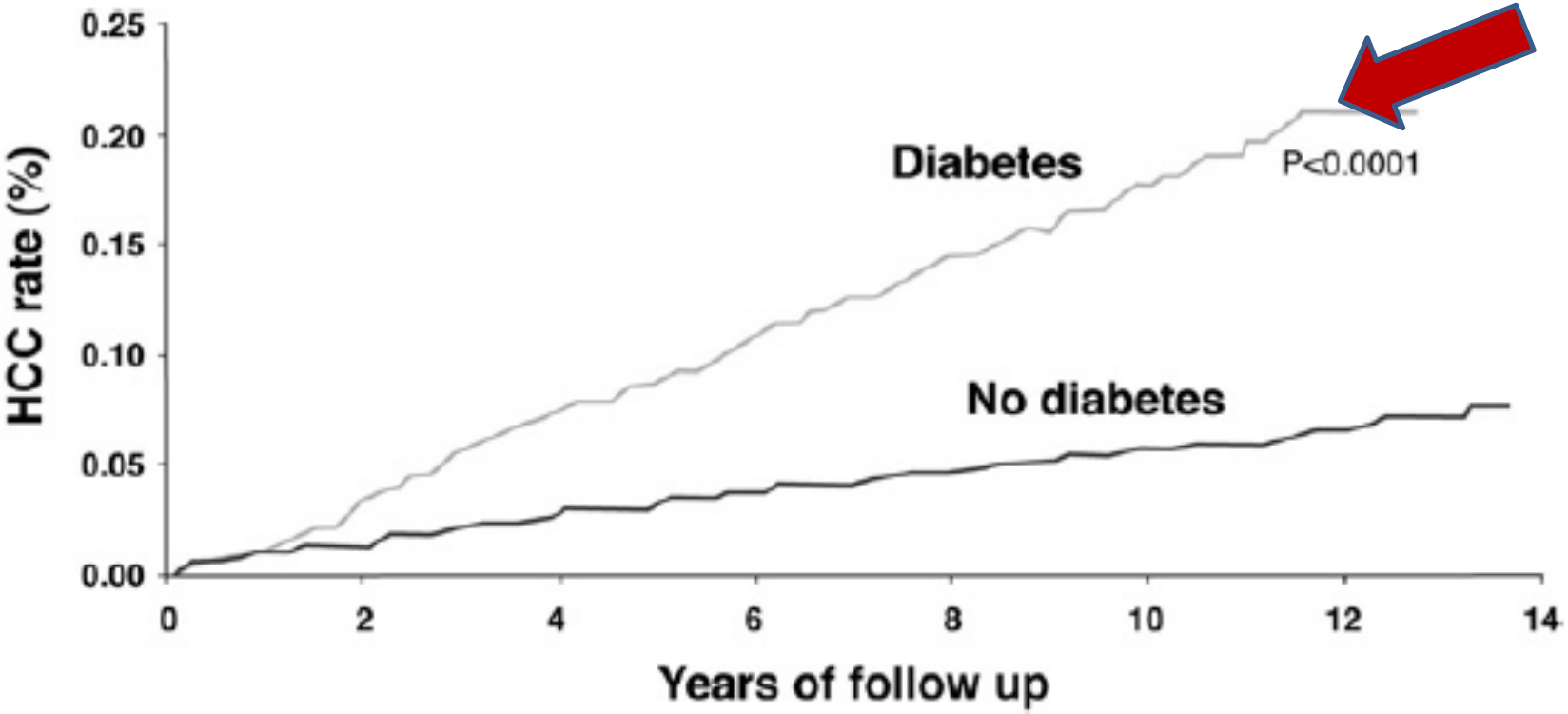
Hassan MM et al. J Clin Gastroenterol 2002;35:266-269
El-Serag H, Rudolph KL. Gastro 2007; 132:2557-2576

HCC, BMI and mortality



El-Serag H et al. Gastro. 2004;126:460-468

HCC and diabetes



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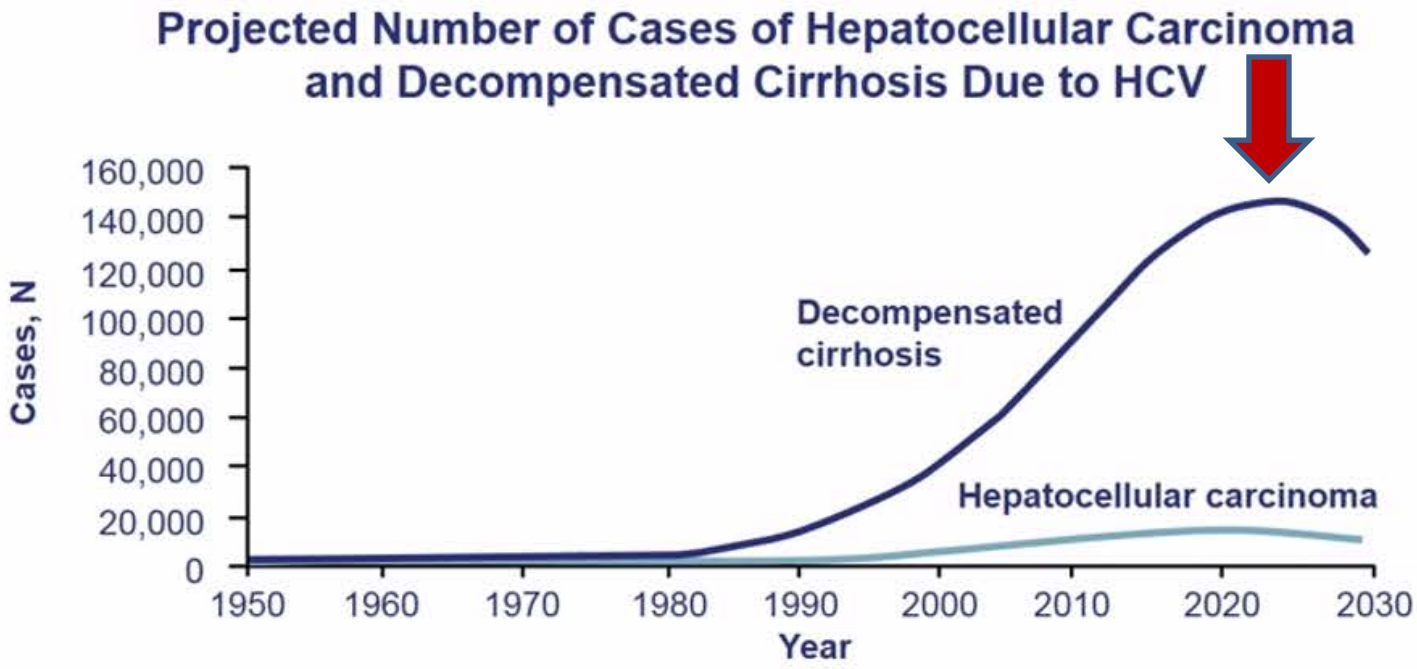
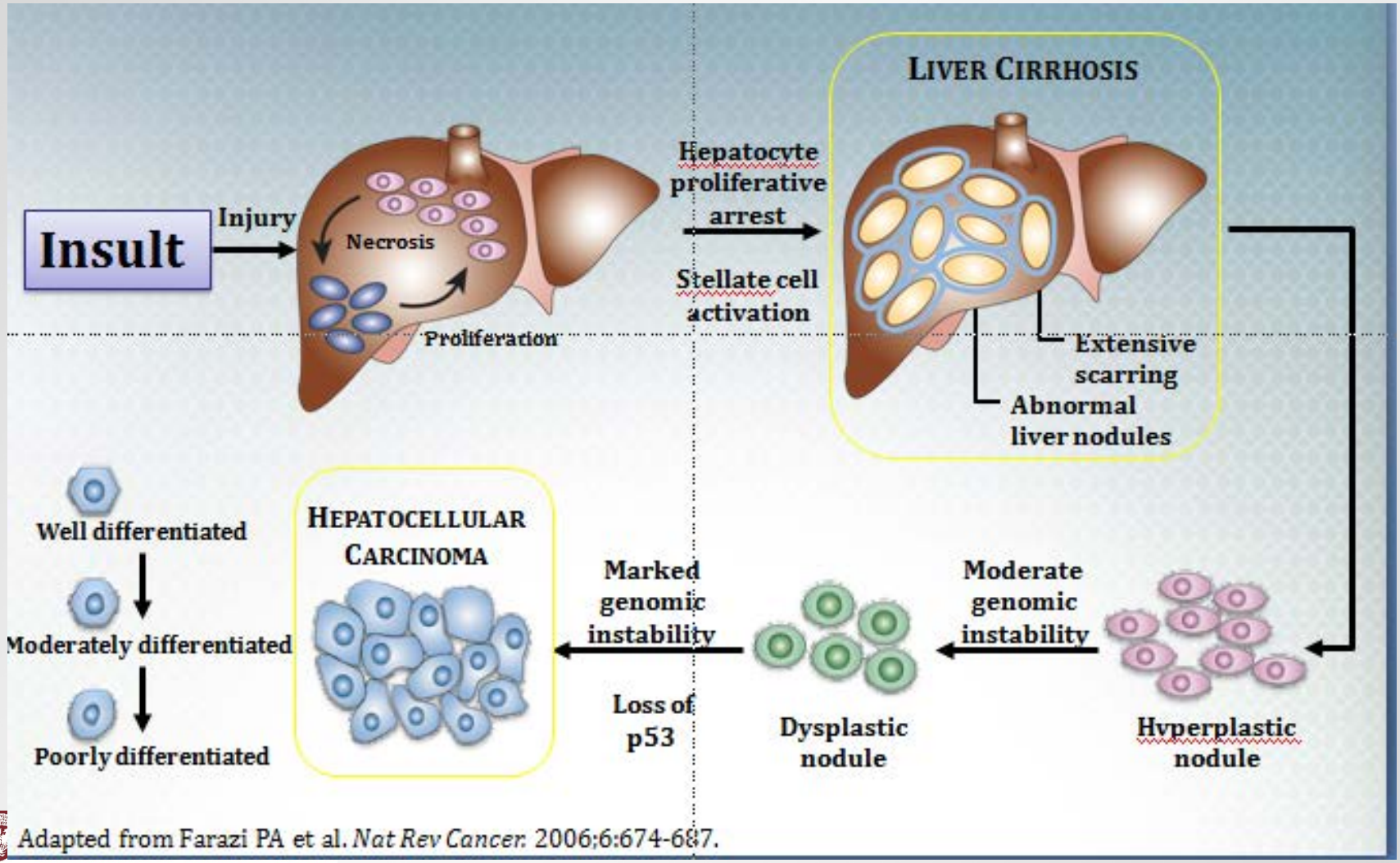
El-Serag H et al. Gastro. 2004;126:460-468

Decompensation from HCV cirrhosis has not peaked yet!



Davis GL, *Gastroenterology*. 2010;138:513-521.

Pathogenesis of HCC



Adapted from Farazi PA et al. *Nat Rev Cancer.* 2006;6:674-687.

Is there proof for HCC surveillance?

Criteria for cancer screening

- Screening must be effective
  - Must detect cancer earlier than if cancer were detected due to symptoms
  - Treatment initiated due to screening results in better outcome
- Test must be acceptable to the target population and to health care professionals
- Identifiable target population
- Screening test should be affordable

1. Adapted from Wilson JMG et al,. Principles and Practice of Screening for Disease. Geneva: World Health Organization; 1968.

Is there proof for surveillance of HCC?

- RCT showed screening decreases mortality in HBV carriers:
  - Effective in a RCT of 18,816 Chinese patients with HBV
  - AFP + US Q 6 months vs no surveillance
  - 37% ↓ in HCC- related mortality; despite < 60% adherence to surveillance

Zhang BH et al. J Cancer Res Clin Oncol 2004;130:417-422

Screening for HCC

- Survival benefit with early screening
  - Dismal prognosis after onset of symptoms (0-10% 5 yr survival)
  - Dismal prognosis in patients with large liver cancer
    - Median survival is 6-9 months
- Smaller lesions may be **cured** (resection, transplantation)
  - Currently only 25% are eligible for resection or liver transplantation on presentation
  - HCC patients receive priority in liver transplant allocation
- Five year survival rates **>70% with OLT for *early* HCC**

1. Bruix J et al. AASLD Guidelines July 2010.
2. Zhang BH et al. J Cancer Res Clin Oncol 2004;130:417-422
3. Vauthey JN,. J Clin Oncol. 2002;20(6):1527

AASLD PRACTICE GUIDELINE

Management of Hepatocellular Carcinoma: An Update

- Surveillance recommended for at-risk groups
  - Specific hepatitis B carriers
    - Asian males ≥ age 40
    - Asian females ≥ age 50
    - Africans > age 20
  - All cirrhotics
- US preferred at 6 month intervals

Bruix J, Sherman M. *Hepatology.* 2010

HCC surveillance is recommended by several professional society guidelines

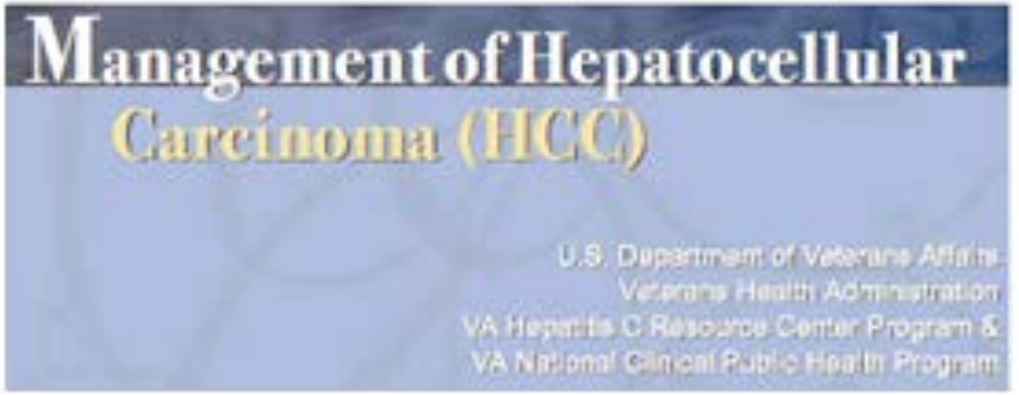
AASLD PRACTICE GUIDELINE

Management of Hepatocellular Carcinoma: An Update

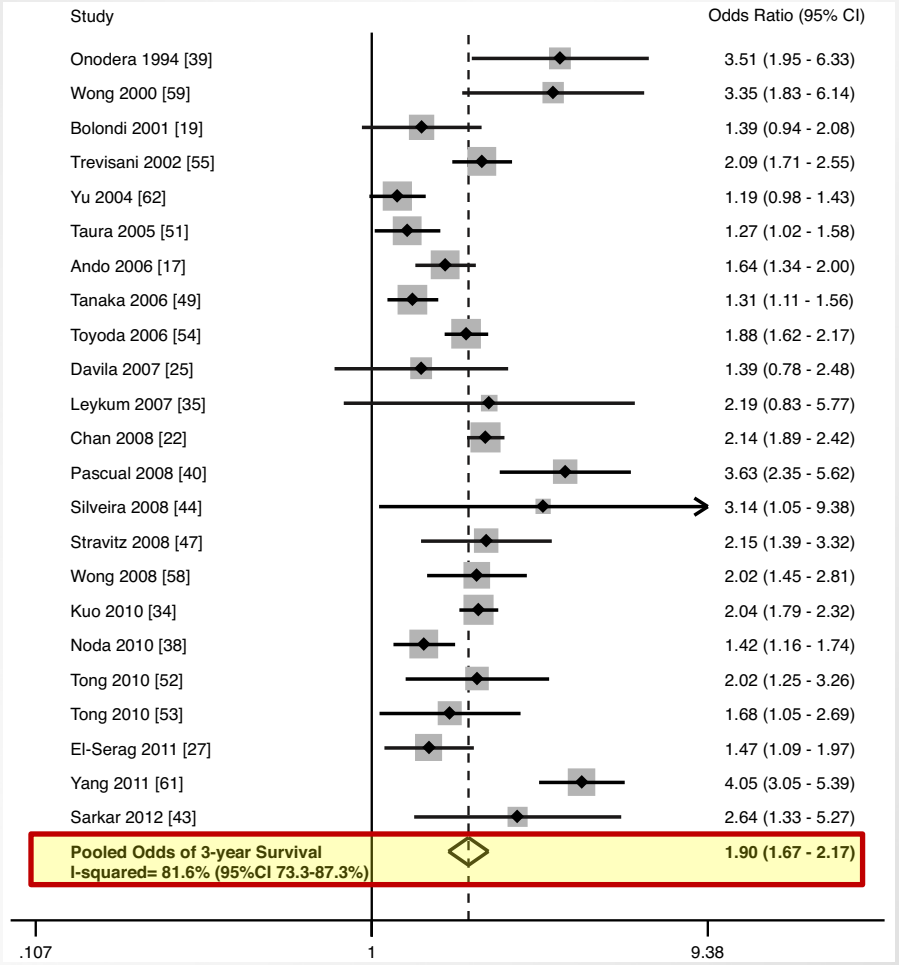
EASL–EORTC Clinical Practice Guidelines: Management of hepatocellular carcinoma

Asian Pacific Association for the Study of the Liver consensus recommendations on hepatocellular carcinoma

NCCN National Comprehensive Cancer Network®



HCC surveillance associated with improved survival in patients with cirrhosis



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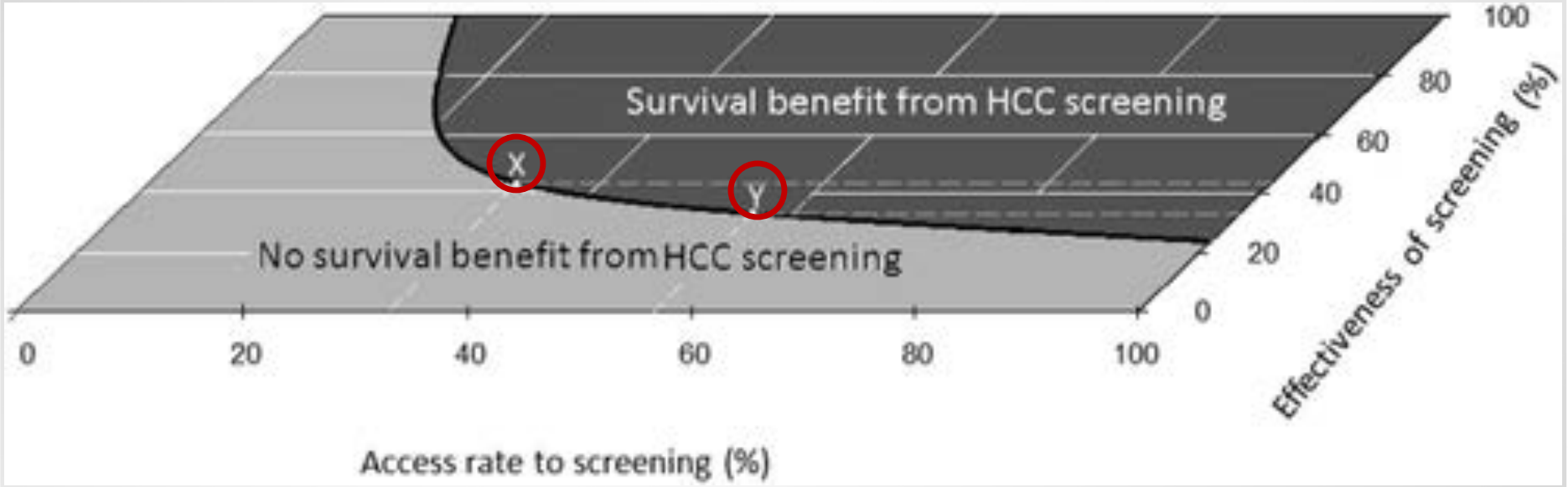
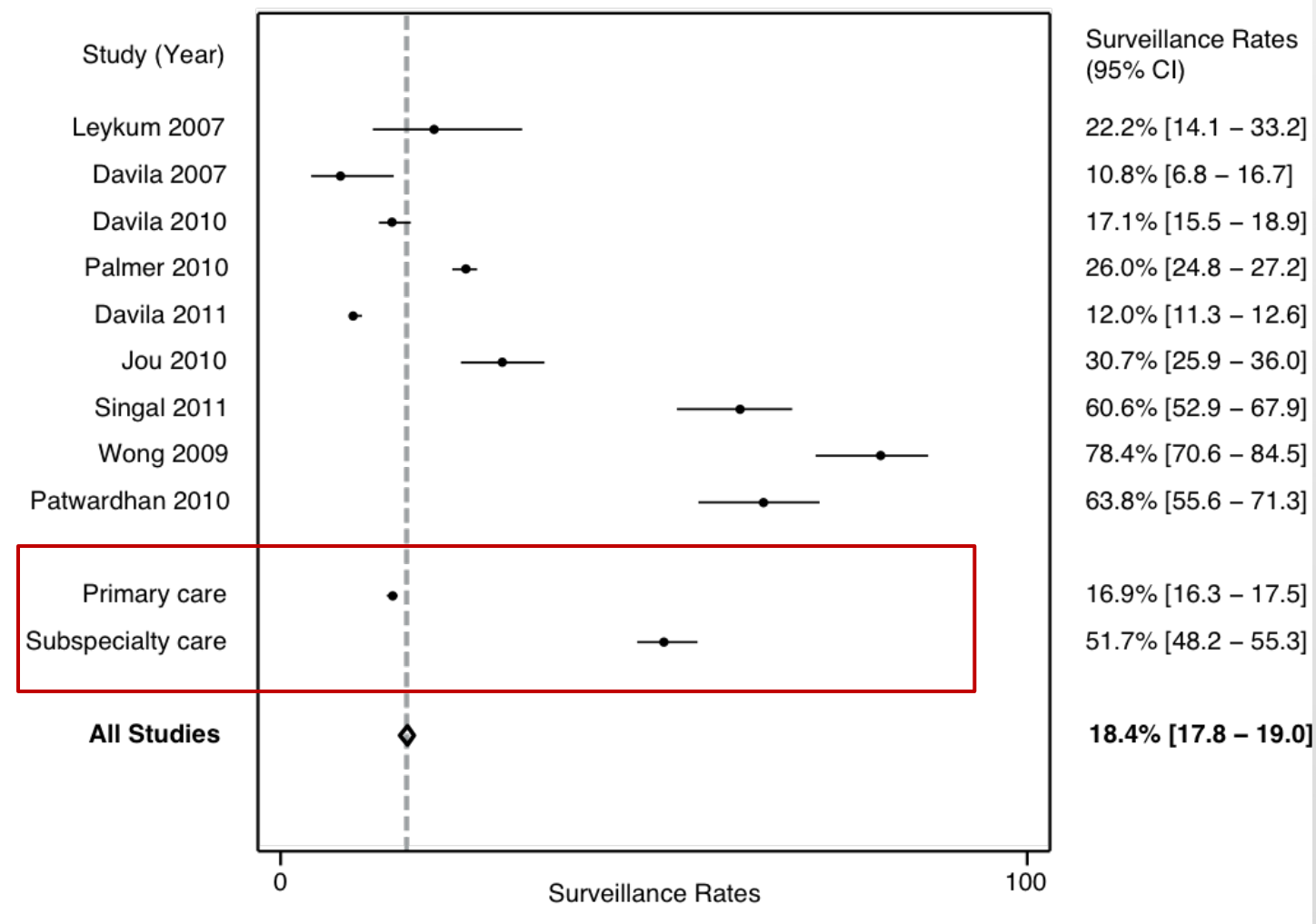
Singal et al PLOS Medicine 2014

Hepatocellular carcinoma screening in patients with compensated hepatitis C virus (HCV)-related cirrhosis aware of their HCV status improves survival: A modeling approach



Mourad et al Hepatology 2014

HCC surveillance is underused, especially by non-subspecialists



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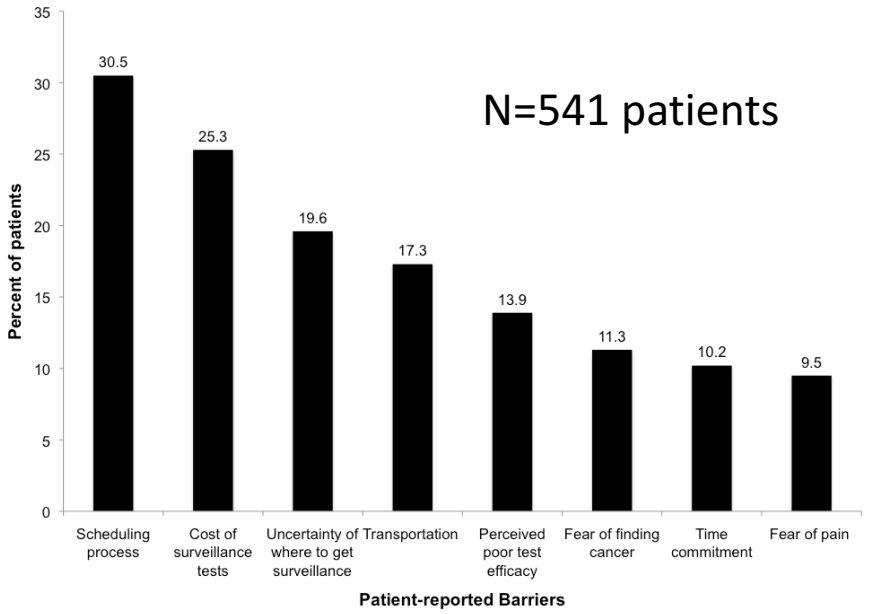
Singal et al, J Gen Intern Med 2012

Provider-reported barriers	Safety-net health system (n=77)	Tertiary care system (n=100)
Lack of knowledge about guidelines	68.2%	79.1%
Competing interests in clinic	51.6%	37.4%
Lack of time in clinic	40.5%	52.8%
Difficulty recognizing at-risk patients	35.4%	30.0%
Ultrasound capacity	23.0%	10.1%
Responsibility of subspecialists > PCP	5.3%	29.4%



Farvardin et al. Hepatology 2017

Dalton Fitzgerald et al. Clin Gastro Hep 2015
Simmons et al Clin Gastro Hep 2018

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Conclusions

- Increasing incidence of hepatocellular carcinoma (HCC)
- Risk factors for HCC vary by geographic region
- Survival benefit with early screening and continued surveillance
- Compliance with existing guidelines needed with endorsement from major cancer societies
- Education is key!!

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Give thanks. Give life.