NEEDED : IMPROVED METHODS FOR EARLY DETECTION OF LIVER CANCER

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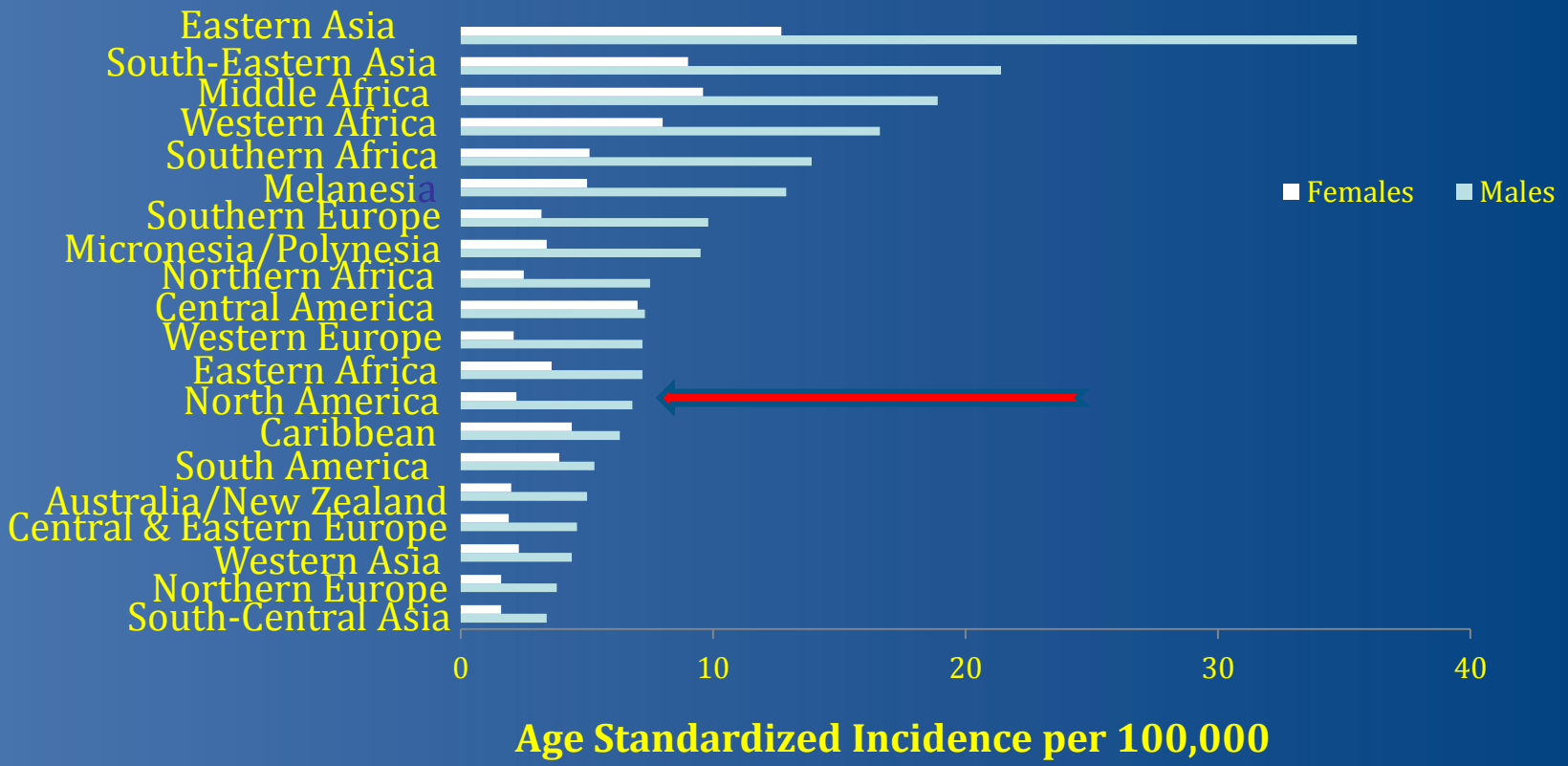
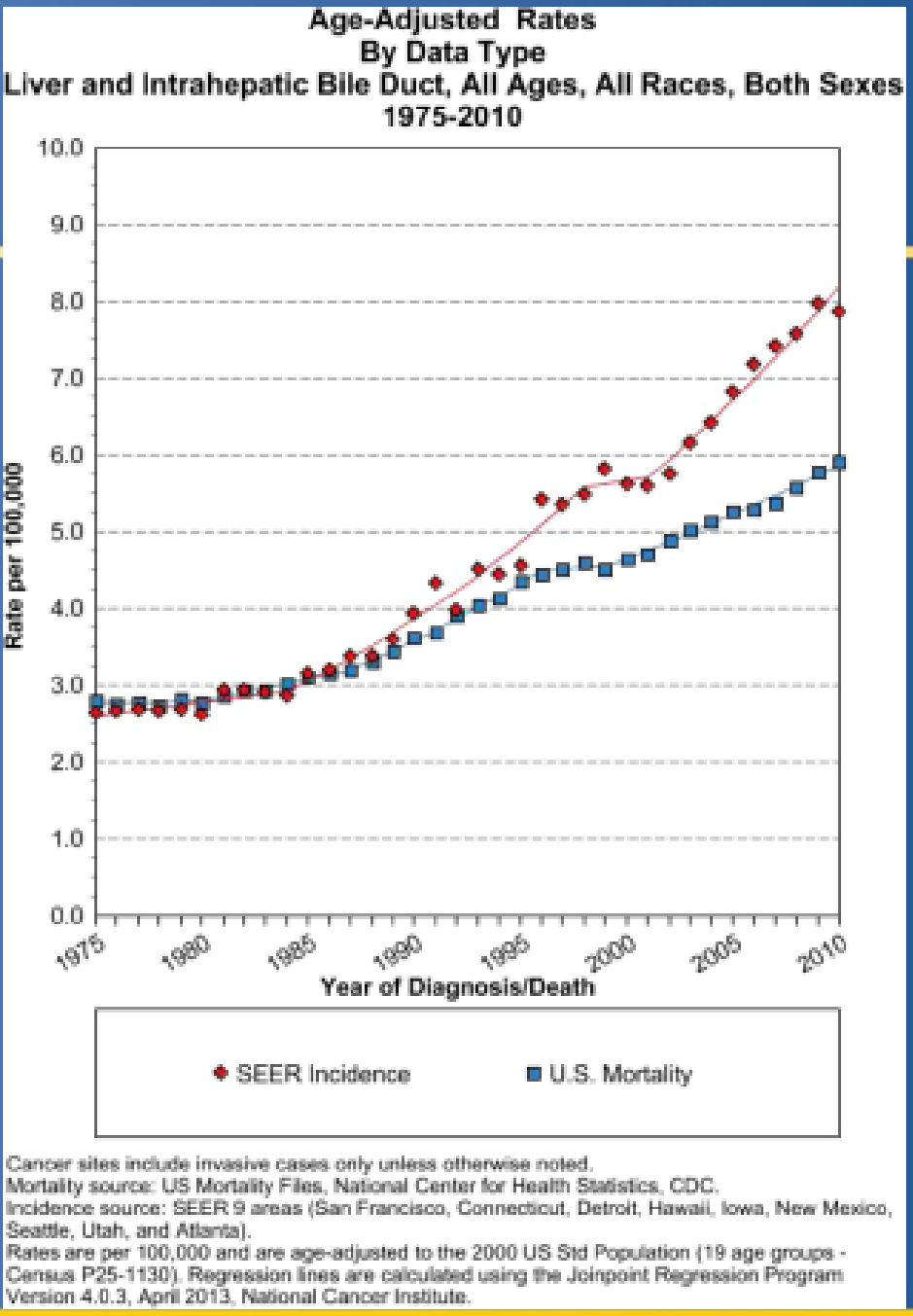
DISCLOSURES

- I have no commercial relationships which are relevant to this presentation

Global Variation In Primary Liver Cancer Incidence



Adapted from Jemal A, et al. Ca Cancer J Clin. 2011;61:69-90.



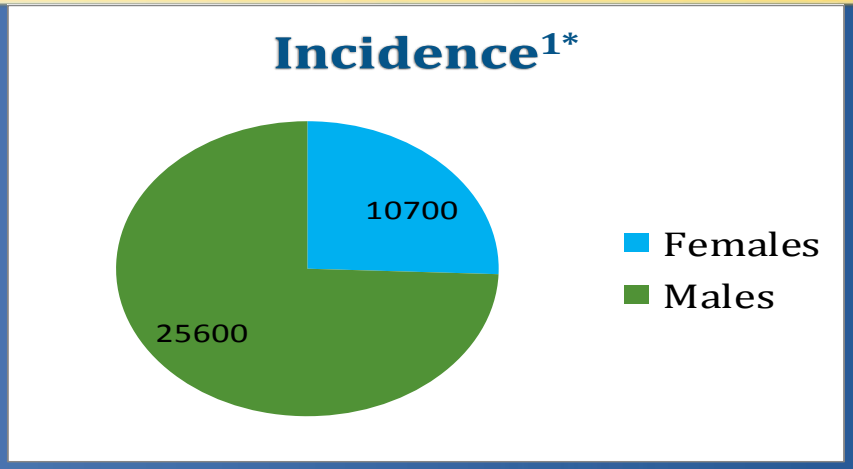
JOHNS HOPKINS MEDICINE

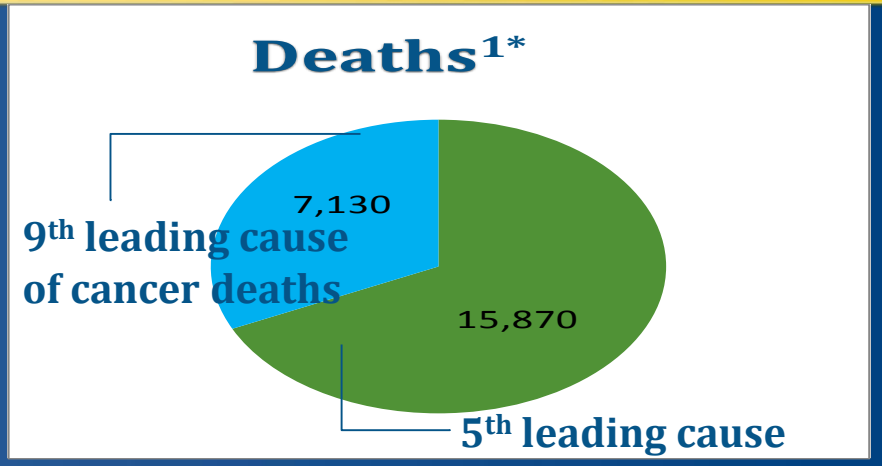
INCREASING LIVER CANCER INCIDENCE IN THE US

Surveillance, Epidemiology, and End Result (SEER 9)

El Serag, HB. Hepatology;;2014;60: 1767-1775.

BURDEN OF LIVER CANCER IN THE US





- Median age at diagnosis
  - 64 years[2]
- Highest mean annual % change in incidence rate in persons 50-59 years[2]
- Increasing incidence of HCC likely caused by[3]
  - Aging of persons who acquired HCV during 1960s
  - Improved survival of cirrhotic patients
  - Increasing obesity and diabetes rates

1. American Cancer Society: Cancer Facts & Figures 2015. Atlanta, GA. 2. Centers for Disease Control and Prevention. *Morbidity and Mortality Weekly Report*. 2010;59:517-20. 3. McGlynn KA, et al. *Cancer Epidemiol Biomarkers Prev*. 2006;15:1198-1203.

*Estimated; includes intrahepatic bile duct cancers.

PRIMARY LIVER TUMORS

- Hepatocellular carcinoma (HCC) : 75 – 90%
- Cholangiocarcinoma : 8- 25%
- Sarcoma : fibrosarcoma/liposarcoma/ angiosarcoma
- Hepatic hemangioendothelioma
- Lymphoma/ teratoma

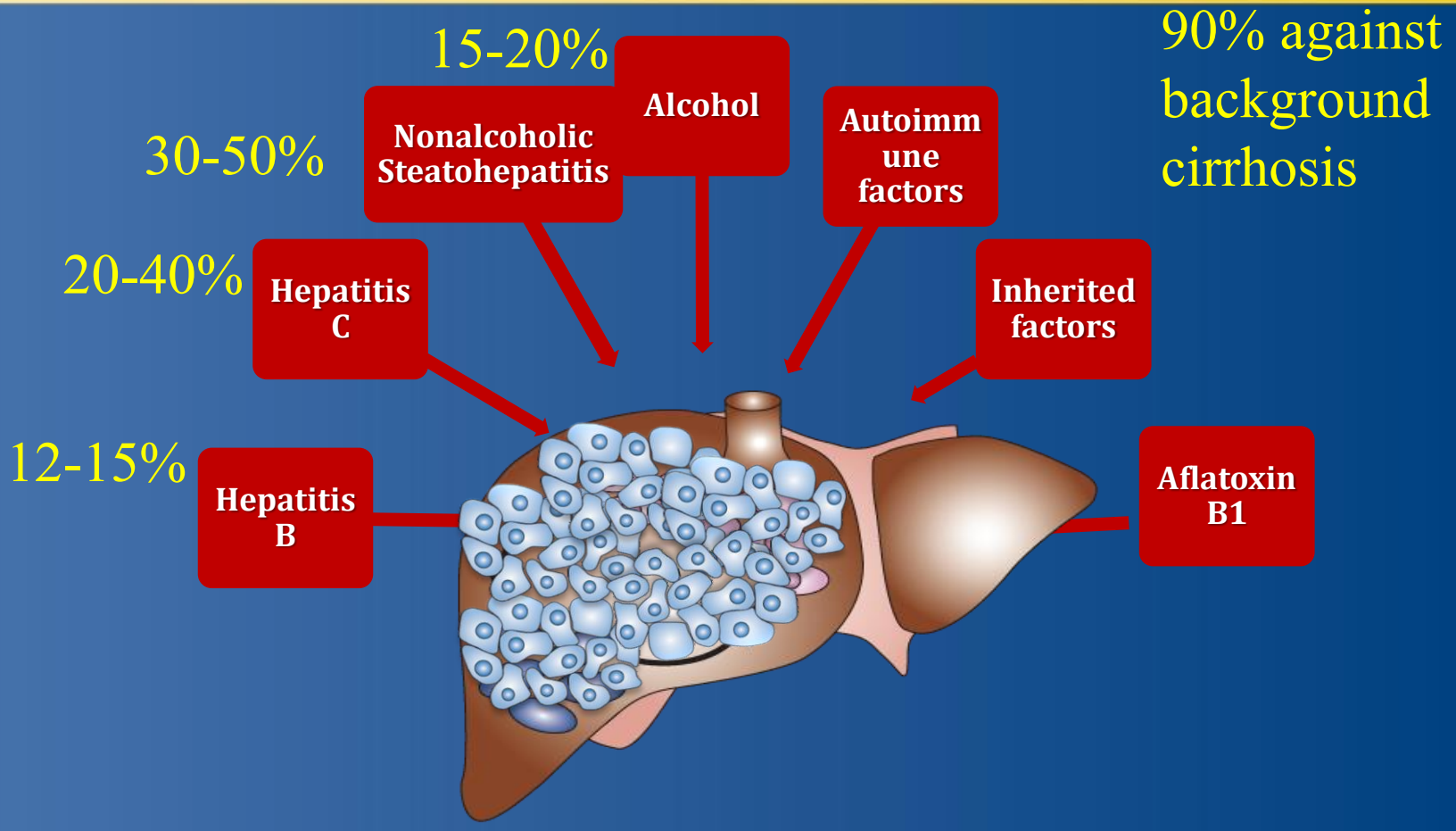
SURVEILLANCE KEY TO EARLY CANCER DETECTION
WHO Criteria for cancer screening

JOHNS HOPKINS MEDICINE

- **Identifiable target population**[1]
- Screening must be effective [1,2]
  - Detects cancers earlier than if detected by symptom development
  - Earlier treatment results in improved outcome
- Test must be acceptable to the target population and to health care professionals [1]
- Screening test should be affordable [1]

1. Collier J, et al. *Hepatology*. 1998;27:273-78. 2. National Cancer Institute. Cancer Screening Overview (PDQ®). Available at: http://www.cancer.gov/cancertopics/pdq/screening/overview/HealthProfessional/AllPages. Accessed August 22, 2012.

RISK FACTORS FOR HCC



Adapted from Farazi PA, et al. *Nat Rev Cancer.* 2006;6:674-87; Shariff MI, et al. *Exp Rev Gastroenterol Hepatol.* 2009;3(4):353-67.

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IS SURVEILLANCE FOR HCC EFFECTIVE ?

JOHNS HOPKINS MEDICINE

YES

- Uniformly fatal in advanced stages
- Excellent treatment options for those with early stage disease

American Cancer Society: Cancer Facts & Figures 2015. Atlanta, GA

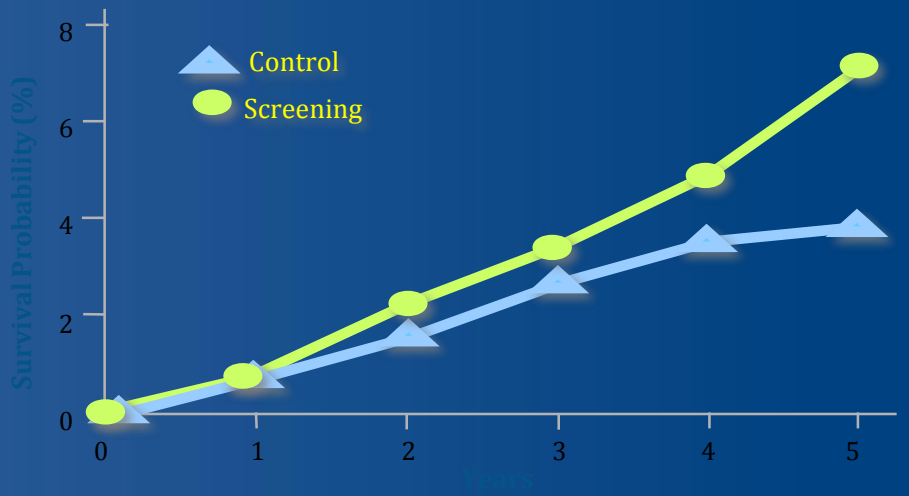
SURVEILLANCE FOR HCC IMPROVES SURVIVAL

JOHNS HOPKINS MEDICINE

Randomized, Controlled Trial in HBV or Chronic Hepatitis Patients in Shanghai, China

~ 64% of patients were HBsAg+

	Screened Group[a] (N = 9373)	Control Group[b] (N = 9443)
Person-years in study	38,444	41,077
HCC occurrence		
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		
Deaths	32	54
Total mortality (per 100,000)	83.2	131.5
Rate ratio (95% CI)	0.63 (0.41, 0.98)	



[a] Ultrasound and alpha-fetoprotein every 6 months.

[b] No screening/surveillance.

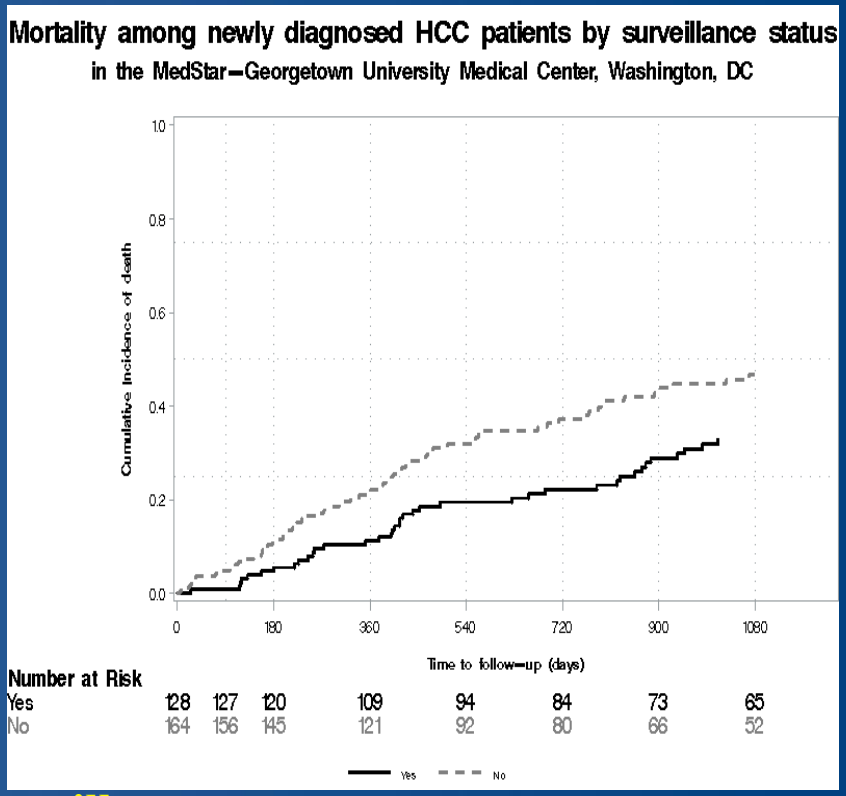
Zhang BH, et al. *J Cancer Res Clin Oncol*. 2004;130:417

EFFICACY OF HCC SURVEILLANCE Observational Cohort (MGUH)

HCC surveillance status	HCC stage at diagnosis		
	Stage I	Stage II	Stage III and above
No surveillance	72 (44)	29 (18)	61 (38)
Surveillance*	83 (66)	33 (26)	10 (8)

HCC surveillance status	HCC treatment		
	No treatment	**Resection**	**Transplant**
No surveillance	117 (67)	17 (10)	40 (23)
Surveillance[a]	51 (39)	10 (8)	70 (53)

[a] Chi-square P <0.0001



HCC detected through surveillance

- Early stage (92vs 62%)
- Amenable to surgical therapy (61 vs 32%)
- Associated with higher survival

Nussbaum J. J Clin Gastro 2015 (March 5)

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May 1, 2015

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JOHNS HOPKINS MEDICINE

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HCC SURVEILLANCE
Guidelines for High-Risk Patients

SOCIETY /INSTITUTION	GUIDELINES
AASLD[1]	US every 6 months
EASL[2]	US every 6 months
APASL [3]	AFP+US every 6 months
NCCN [4]	AFP+US every 6-12 months
VA [5]	AFP+US every 6-12 months

1.Bruix J, Sherman. http://www.aasld.org/practiceguidelines/Documents/Bookmarked Practice Guidelines/HCCUpdate2010.pdf. Accessed 2.10.15

2.Bruix J et al. J Hepatology 2001;35:421-430 3. Omata M et al. Hepatol Int 2010;4:439-474.

4.Adapted from NCCN Practice Guidelines:http;//www.nccn.org/professionals/physician_gis/hepatobiliary pdf.Accessed 11/11/14

5. http://www.hepatitis.va.gov/pdf/2009HCC-guidelines.pdf. Accessed 2.10.15

Groups for whom HCC Surveillance is Recommended

Population Group	Incidence of HCC (%/yr)
Asian male: chronic hepatitis B, > age 40	0.4–0.6
Asian female: chronic hepatitis B, > age 50	0.3–0.6
Chronic hepatitis B with HCC family history	Incidence higher than without family history
African/North American Blacks with chronic Hep B	occurs at younger age
Hepatitis B cirrhosis	3–8
Hepatitis C cirrhosis	3–5
Other cirrhosis*	unknown

* Including stage 4 primary biliary cirrhosis, alpha-1 antitrypsin deficiency, genetic hemochromatosis, or other causes.

Bruix J, et al. *Hepatology*. 2011;53(3):1020-2.

HCC SURVEILLANCE
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COST EFFECTIVENESS OF HCC SURVEILLANCE

Benchmark :$50,000 / QALY

- Colorectal cancer: $19K – $44K [2]
- Breast Ca : $32K – 106K [3]
- HCC : $38k – $62K [1]

1. Thompson Coon J et al. Br J Ca 2008;;98(7) 1166-7
2. Lansdorp-Vogelaar I et al. Epidemiol Rev 2011;33:88-100
3. . Melnikow J et al. Value Health 2013 16(6):932-41

HCC SURVEILLANCE SHOULD BE STANDARD OF CARE

Efficacious, safe, targetable, affordable

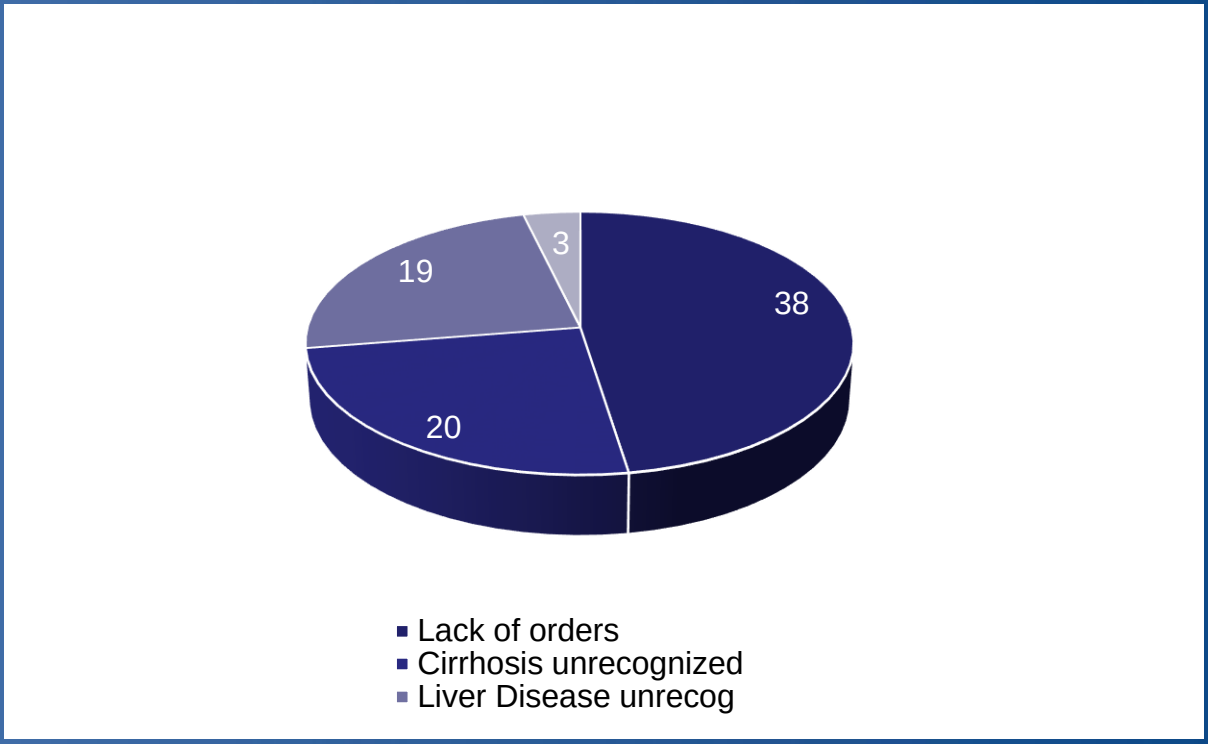
BUT GROSSLY UNDERUTILIZED

Documented surveillance rates

15 – 25%

Singal, AG *et al.*J Gen Intern Med, 27 (2012), 861–867

FAILURES IN SURVEILLANCE PROCESS



Singal AG, et al. Cancer Prev Res. 2012;5(9):1124-30.

Summary

- HCC incidence continues to increase[1,2]
- HCC is more often diagnosed at a late stage when patients cannot benefit from curative therapy[3]
- HCC treatment improves survival at all stages of disease, but is often suboptimal[4]
- HCC surveillance in at-risk populations improves likelihood of curative treatment and improves survival[5]

1. El-Serag HB. *N Engl J Med.* 2011;365:1118-27. 2. American Cancer Society: Cancer Facts and Figures 2011. Atlanta, GA. 3. Davila JA, et al. *Hepatology.* 2010;52:132-41. 4. Altekruse SF. *J Clin Oncol.* 2009;27:1485-91. 5. Zhang BH, et al. *J Cancer Res Clin Oncol*. 2004;130:417-22.

IMPROVED SURVEILLANCE WILL REQUIRE…

- Increased awareness of liver cancer
  - Only cancer whose incidence is rising
- Risk factor recognition
  - Cirrhosis/ hep C/ NASH
- Education regarding treatment availability
  - Liver cancer is curable

HCC:
The Elephant in the Room