Hepatitis C and Liver Cancer: What's the Link – Identify, Treat and Prevent

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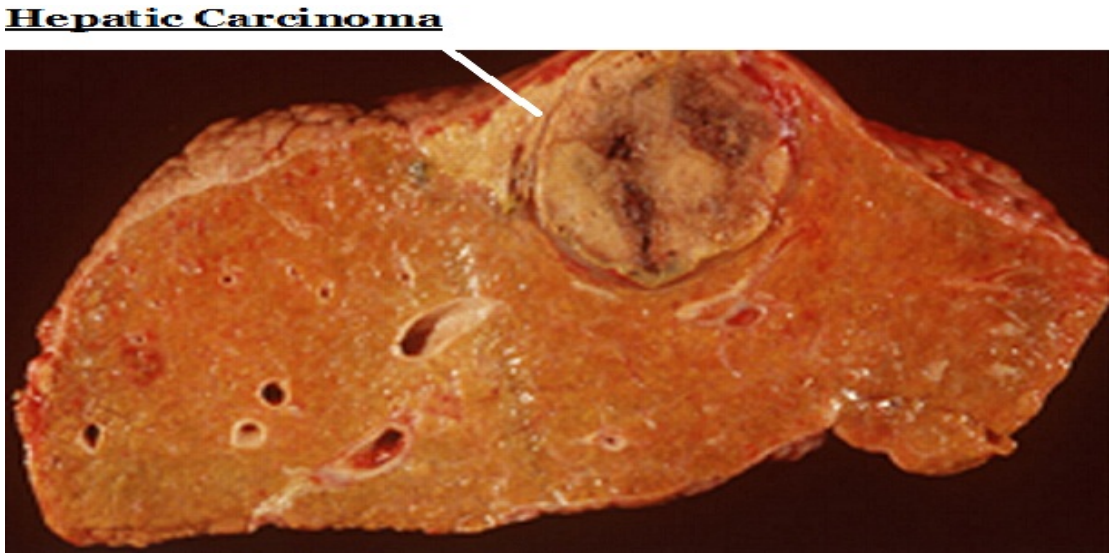
Hepatocellular Carcinoma

Hepatocellular Carcinoma (HCC)

A **primary malignancy** of the liver that most always occurs in persons with **underlying liver disease**



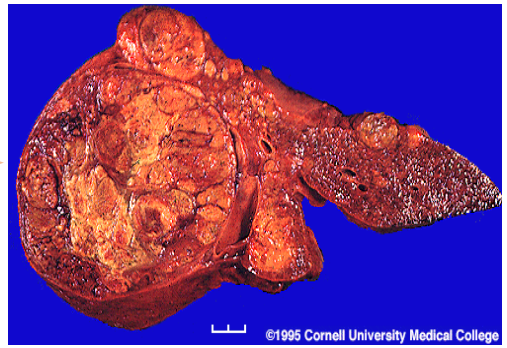
Malignant Transformation – Multistep Process

Normal liver

Chronic Injury or Inflammation

Liver cirrhosis

Epigenetic alterations
Genetic alterations
Dysplastic nodules[1]

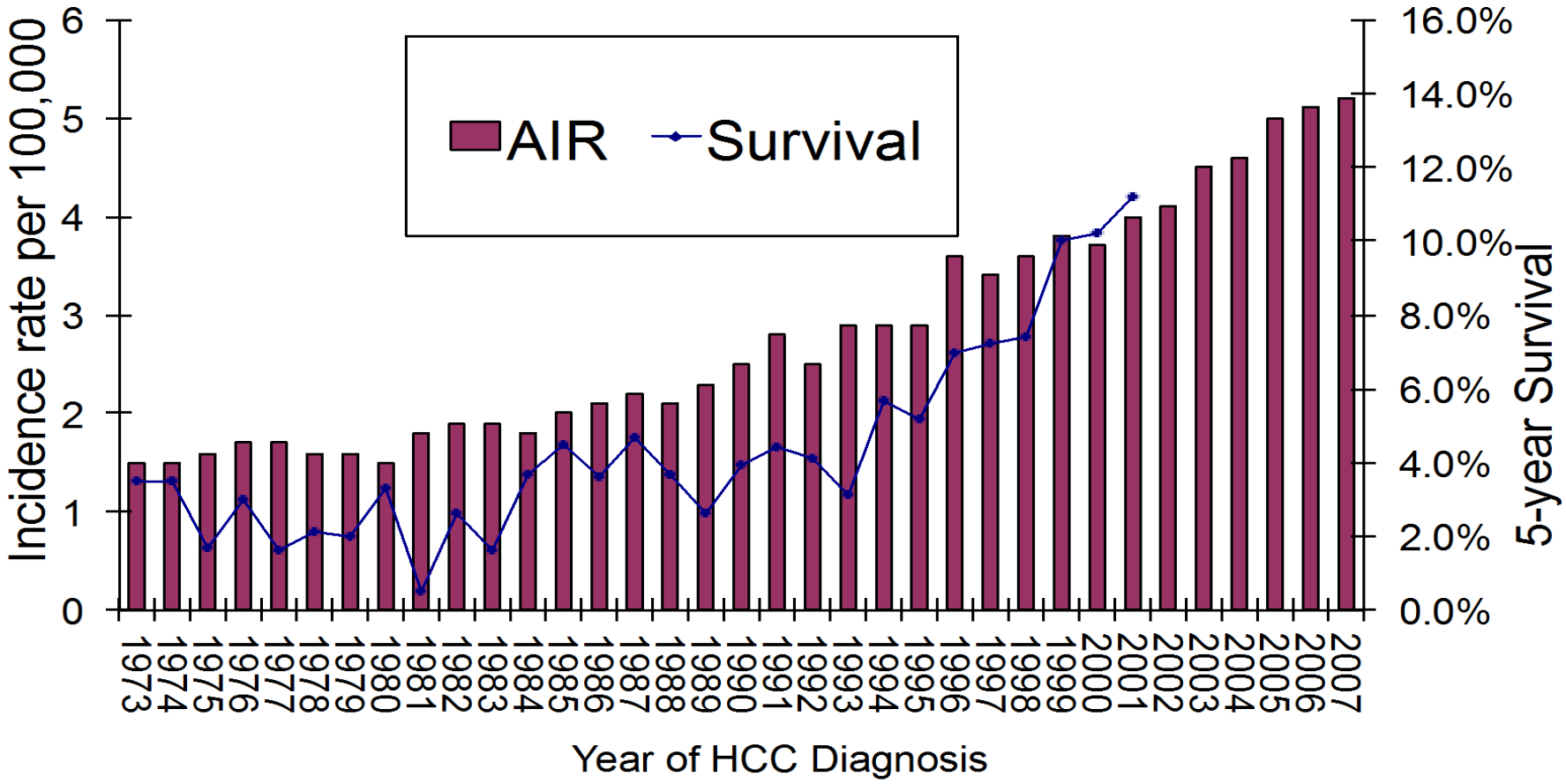


Tornillo L, et al. Lab Invest. 2002
Verslype C, et al. AASLD 2007.

HCC – Is it Important?

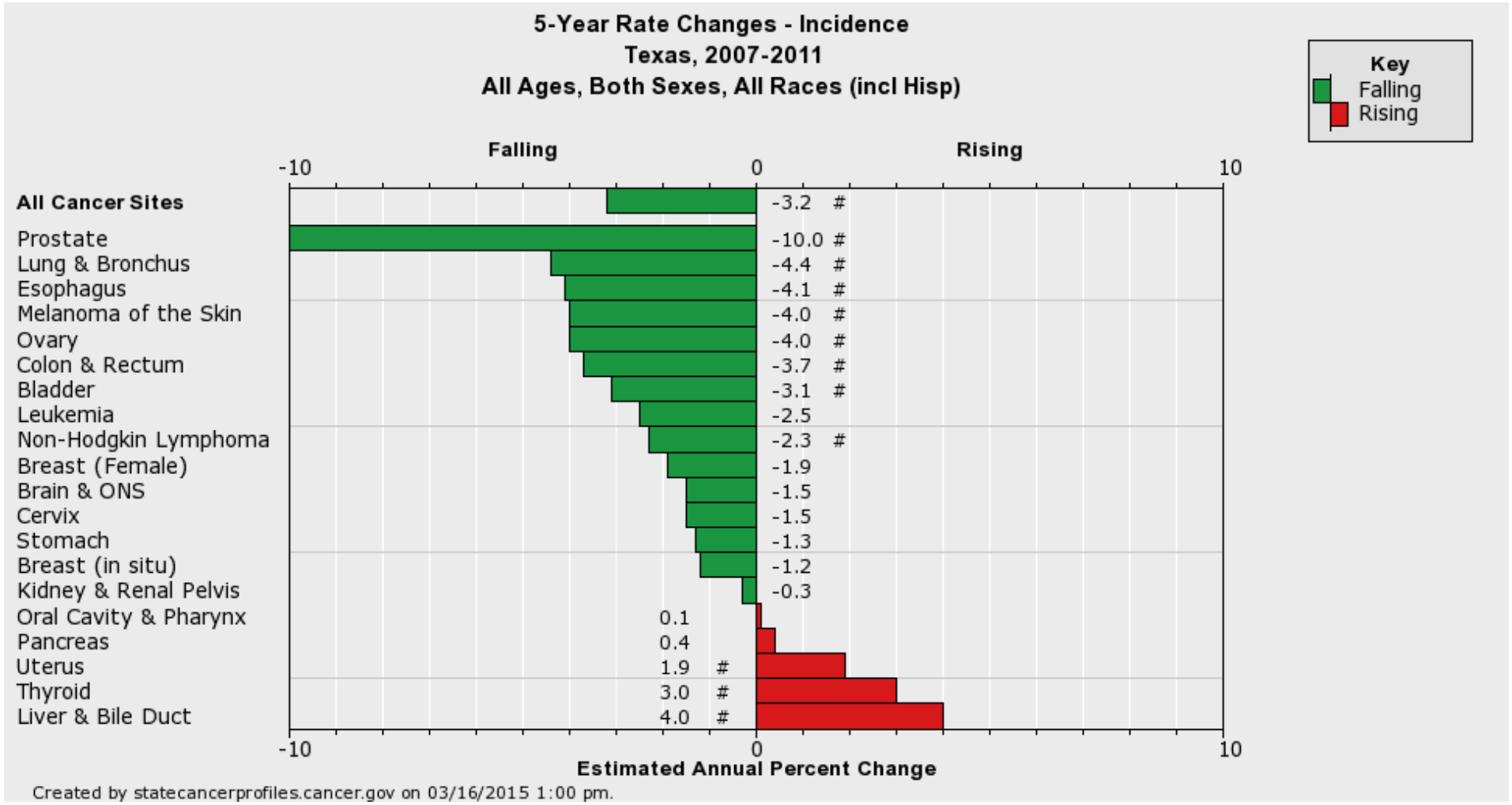
- 5th most common type cancer
  - Approx. 750,000 cases per year worldwide
- 3rd most common cause of cancer mortality
  - > 600,000 deaths annually
- Distribution worldwide follows HBV & HCV infection
  - 84% of infections are in developing countries
  - Subsaharan Africa, Middle East and SE Asia are areas of endemic infection
  - HCC is the leading cause of cancer death in Asia & Middle East
- Incidence is increasing in the U.S.
  - Incidence has tripled in the last three decades – 36,000 cases expected this year
- Alarming increase in parts of Texas

The Incidence and 5-Year Survival of HCC in US



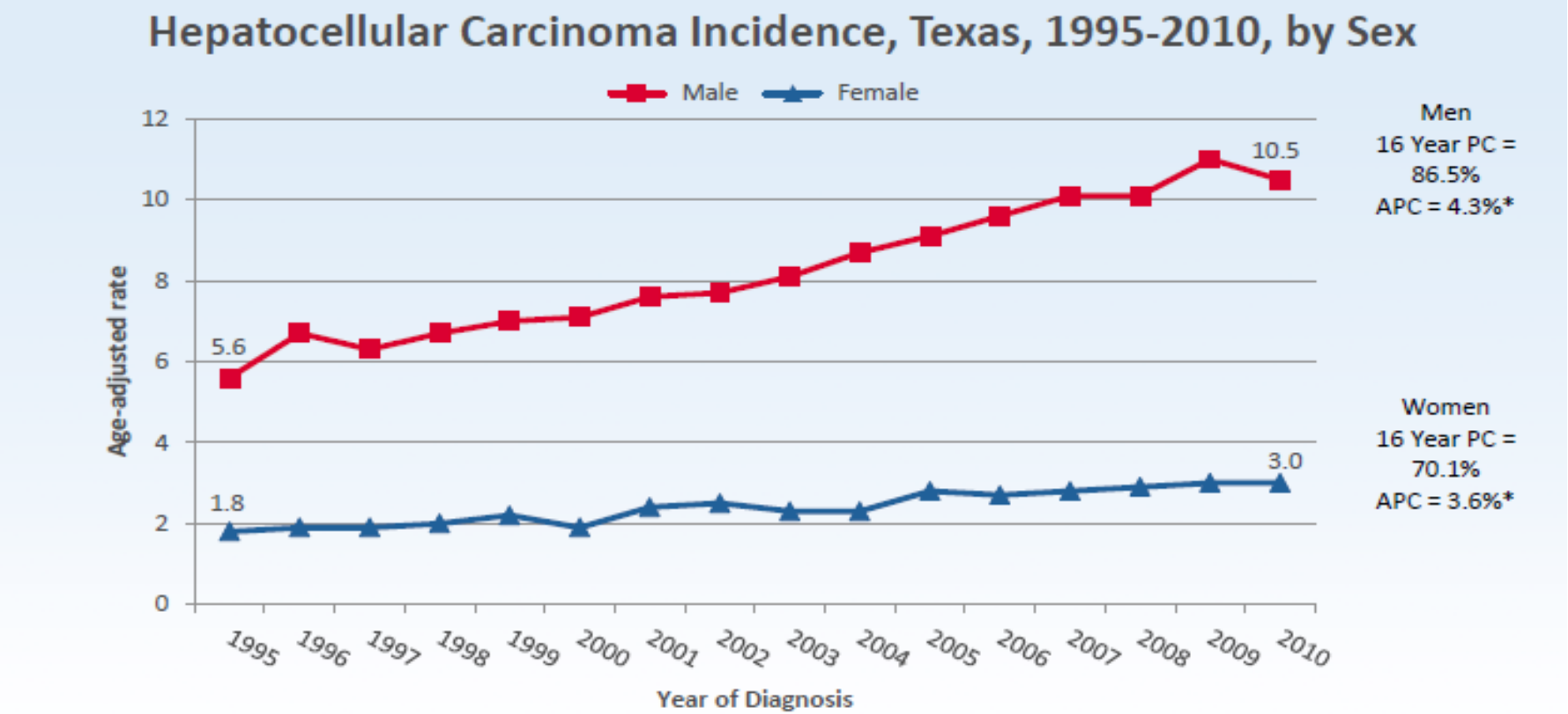
El-Serag HB. N Engl J Med 2011

HCC is increasing in Texas in the last 5 yrs.



http://statecancerprofiles.cancer.gov/

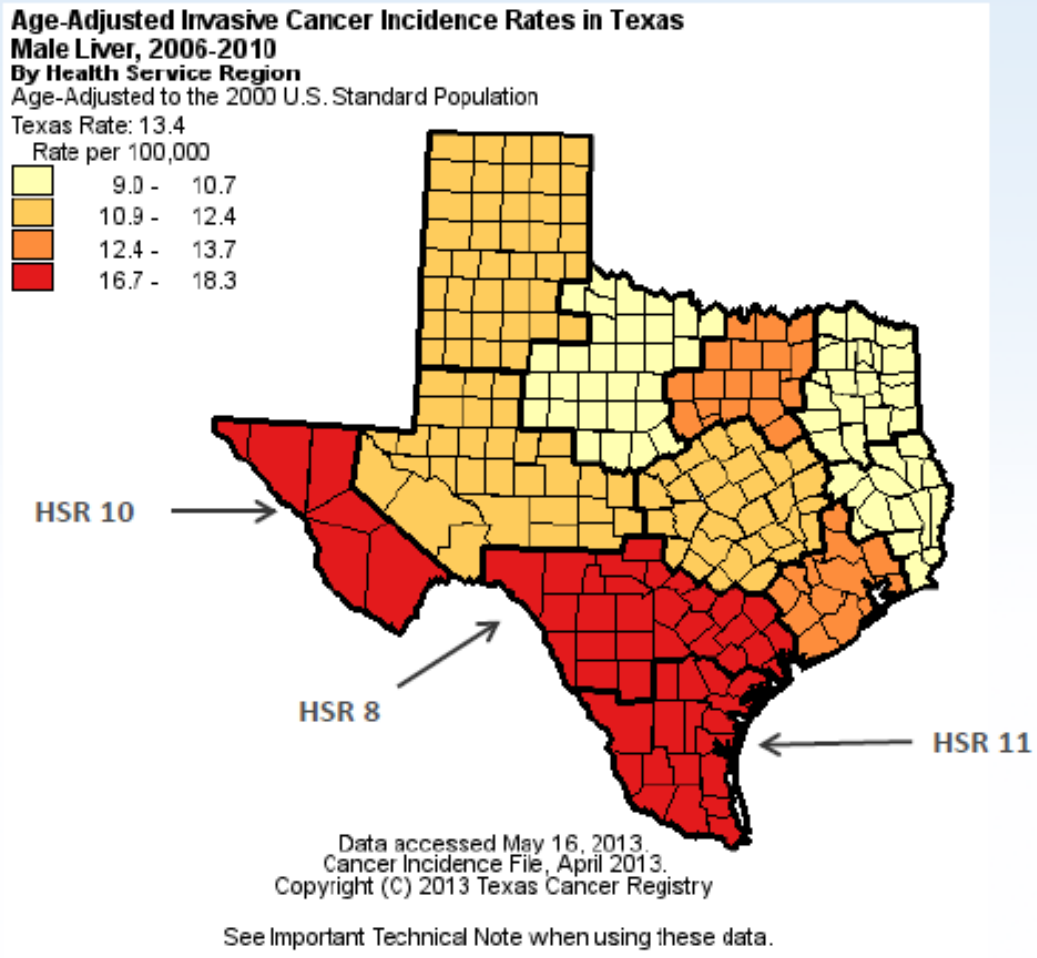
Texas HCC Incidence Doubled in the Past 15 yrs



Rates are per 100,000 and age-adjusted to the 2000 US Standard Population (19 age groups - Census P25-1130) standard.
Percent changes were calculated using 1 year for each end point; APCs were calculated using weighted least squares method.

Data Source: Texas Department of State Health Services, Cancer Epidemiology and Surveillance Branch, Texas Cancer Registry, Incidence – Texas, 1995-2010, Cut-off 11/30/12, SEER*Prep 2.5.2.

South Texas – Highest Incidence of HCC

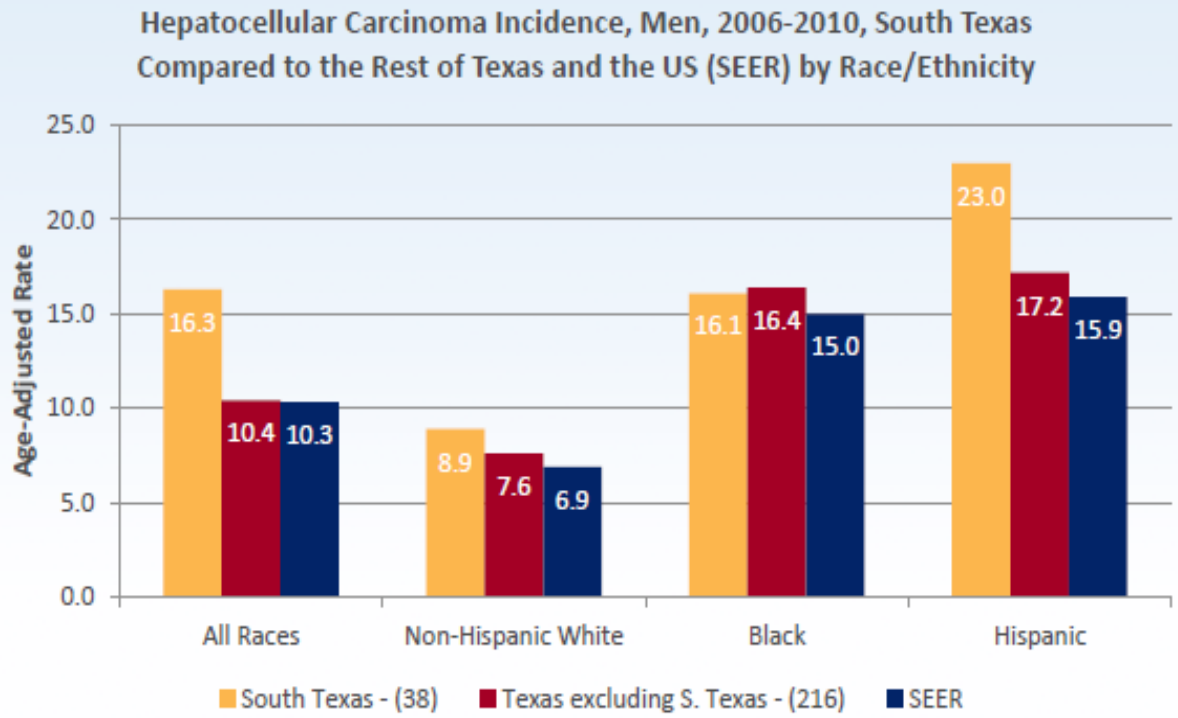


Age-adjusted Rate
per 100,00 population

US	7.7
Texas	9.1
South Texas	16.3

Comparison of Hepatocellular Carcinoma in Men in the South Texas Region

- Hispanics in the 38 South Texas Counties have a significantly higher incidence rate of HCC than Hispanics in the remainder of Texas (216 counties) and Hispanics in the US (SEER)
- Non-Hispanic whites in South Texas have a significantly higher rate than non-Hispanic whites in the US (SEER)



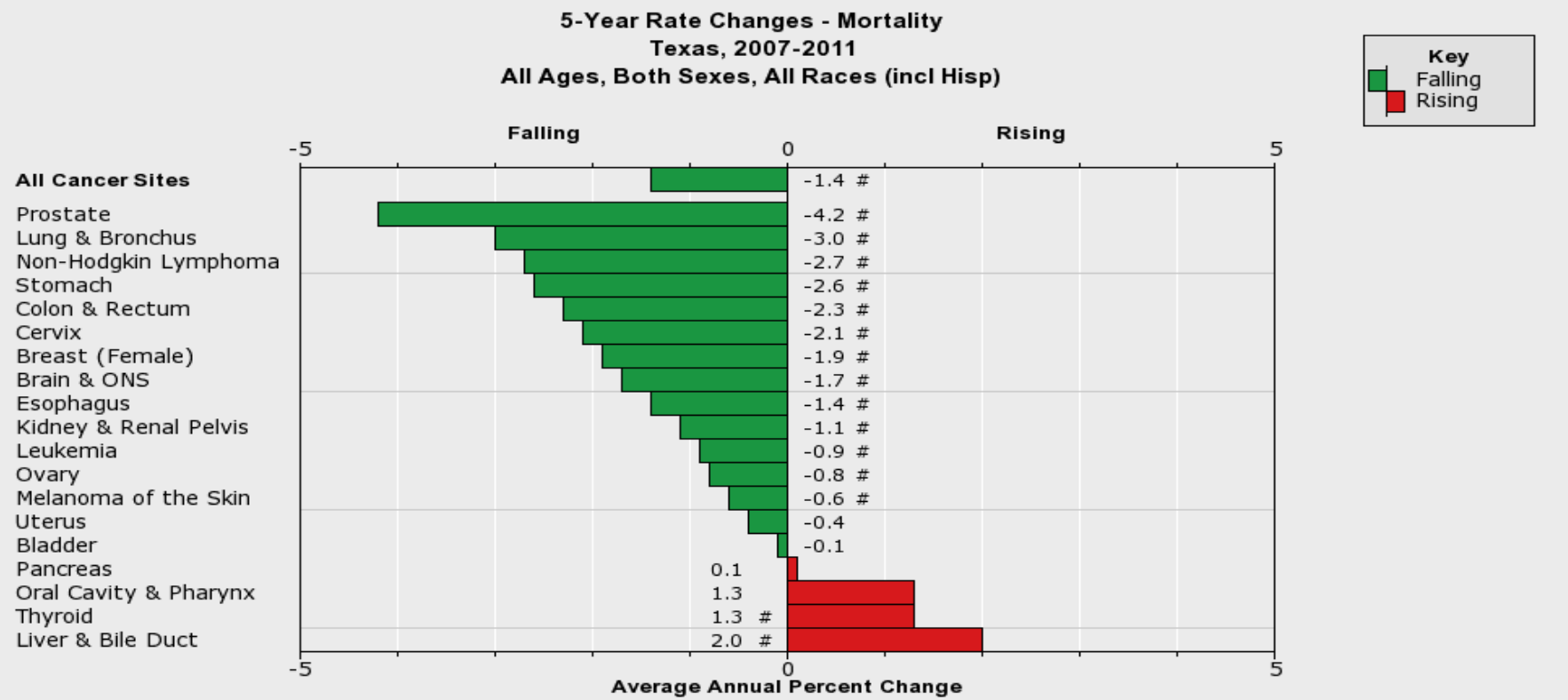
Rates are per 100,000 and age-adjusted to the 2000 US Standard Population (19 age groups - Census P25-1130) standard.

HCC in the US: Effect of Immigration

	1999-2001	1989-1991	1979-1981
Hispanic Native	**13**	8.2	5.8
Hispanic Immigrant	**6.9**	4.8	4.8
Asian Native	6.7	4.9	6.1
Asian Immigrant	18.3	17.9	13.8

El-Serag et al, Arch Intern Med 2007

HCC Mortality is Increasing in Texas in Past 5-yrs Compared to Other Cancers



Created by statecancerprofiles.cancer.gov on 03/16/2015 1:12 pm.

Source: Death data provided by the National Vital Statistics System public use data file. Death rates calculated by the National Cancer Institute using SEER*Stat . Death rates (deaths per 100,000 population per year) are age-adjusted to the 2000 US standard population (19 age groups: <1, 1-4, 5-9, ... , 80-84, 85+). Population counts for denominators are based on Census populations as modified by NCI. The 1969-2012 US Population Data File is used with mortality data.
Please note that the data comes from different sources. Due to different years of data availablility, most of the trends are AAPCs based on APCs but some are EAPCs calculated in SEER*Stat. Please refer to the source for each graph for additional information.

- The annual percent change is significantly different from zero (p<0.05).

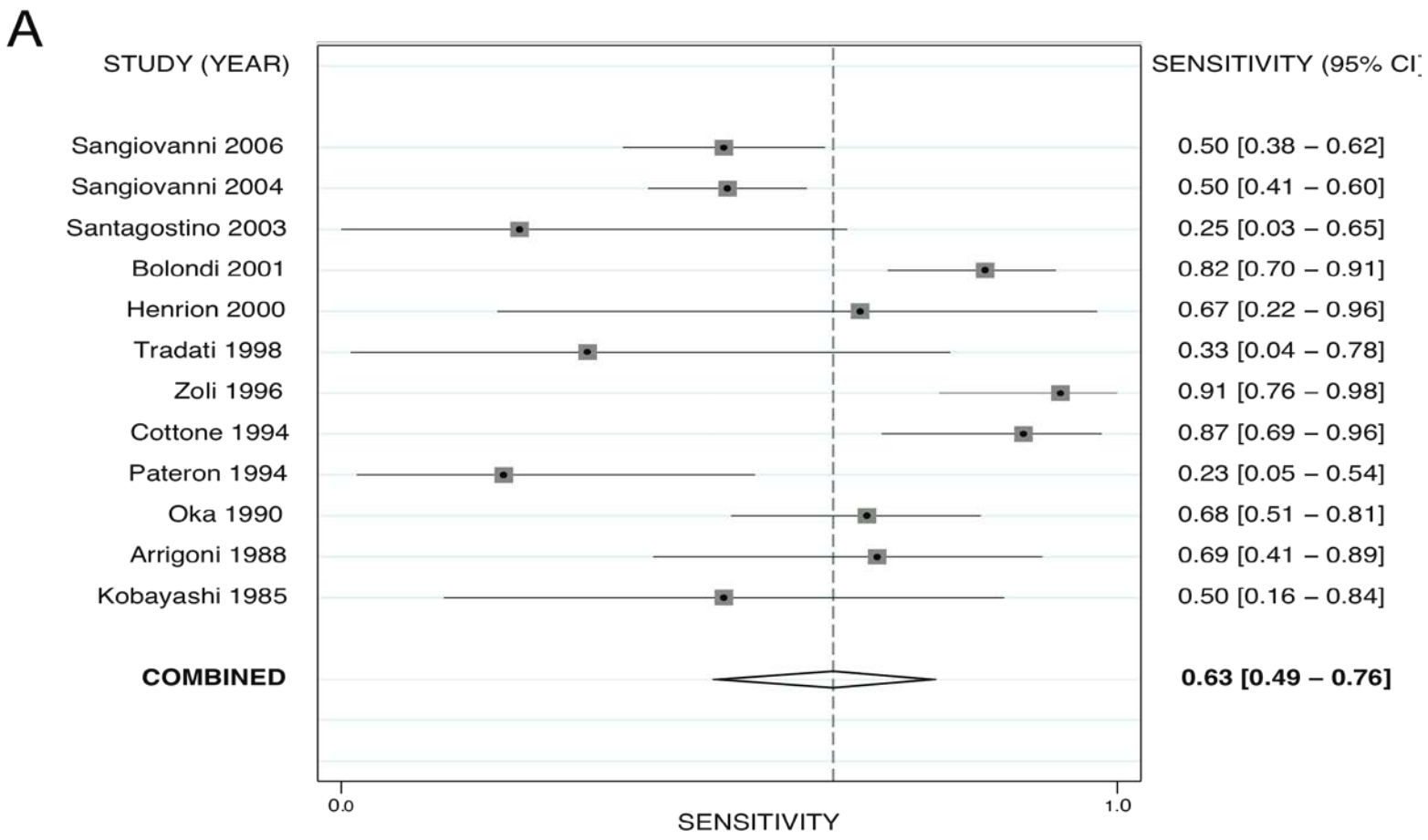
http://statecancerprofiles.cancer.gov/

Most HCC patients are diagnosed at late stages

Tumor Stage	1998–2008	1992–1993	1997–1999	2003-2004	1-year Survival
Localized	42%	28%	33%	44%	67%
Regional	28%	22%	28%	29%	39%
Distant	18%	22%	19%	17%	15%

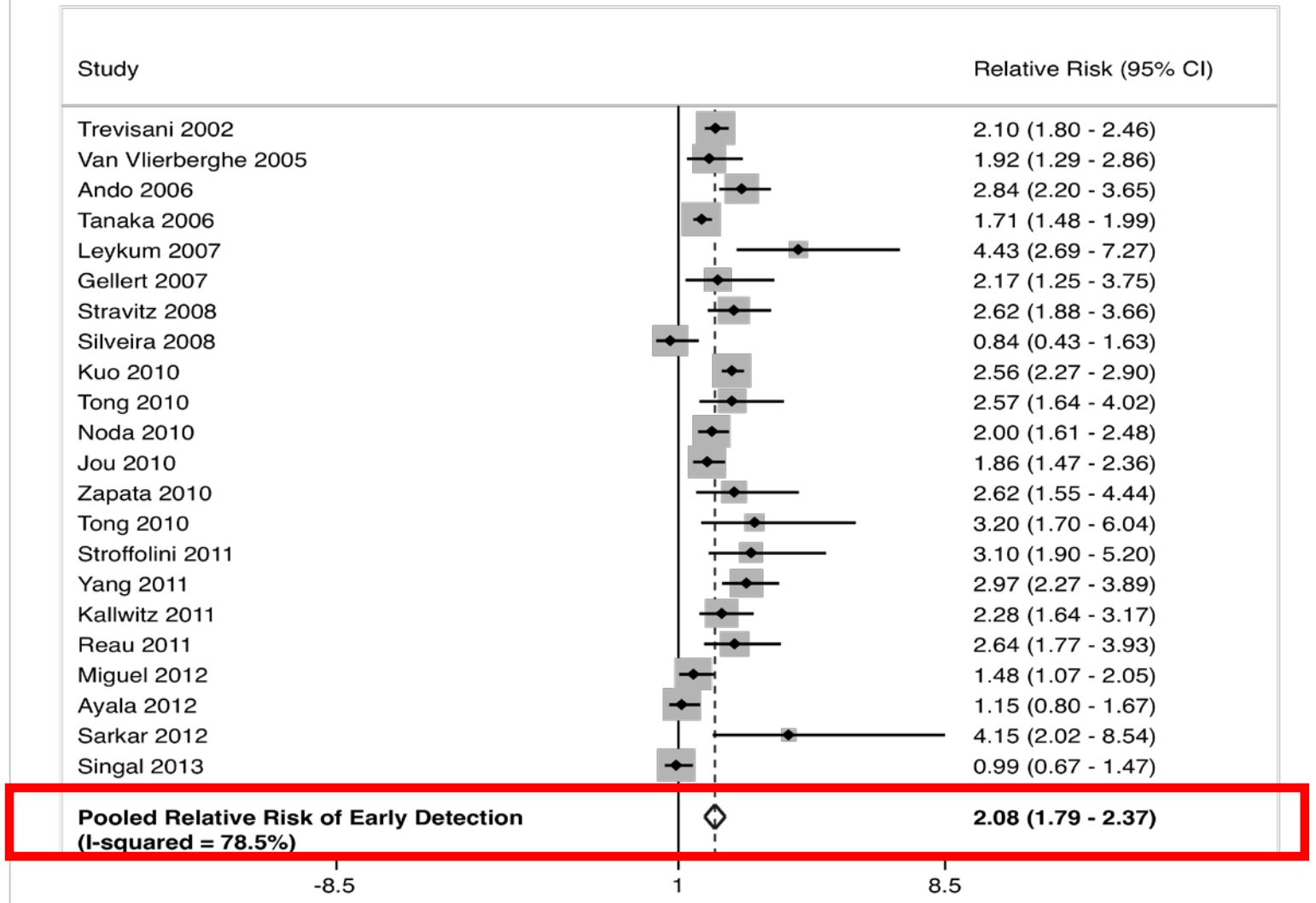
Altekruse et al, Hepatology 2012
Altekruse et al. J Clin Oncol 2009

Ultrasound can be efficacious for early HCC detection



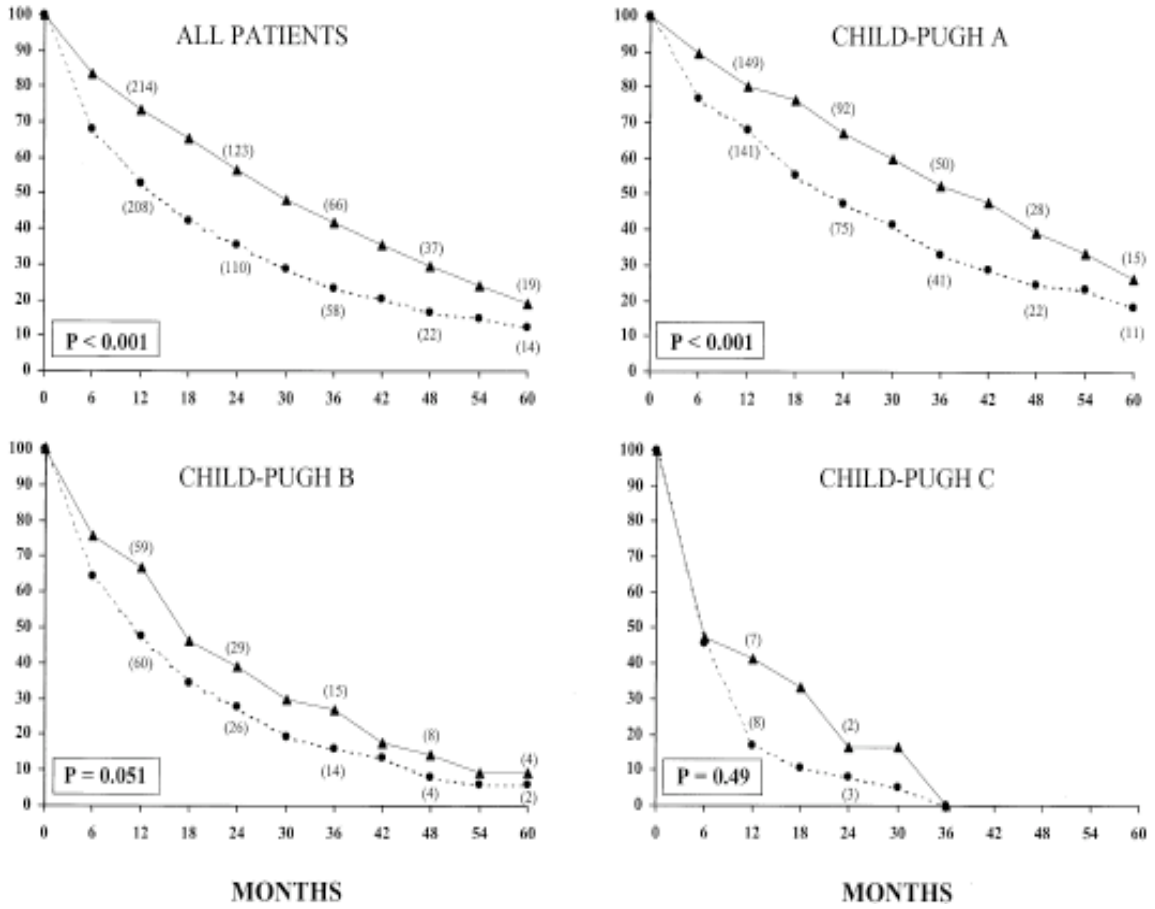
Singal et al. Aliment Pharm Ther 2009

Surveillance associated with early HCC detection in patients with cirrhosis



Singal et al PLOS Medicine 2014

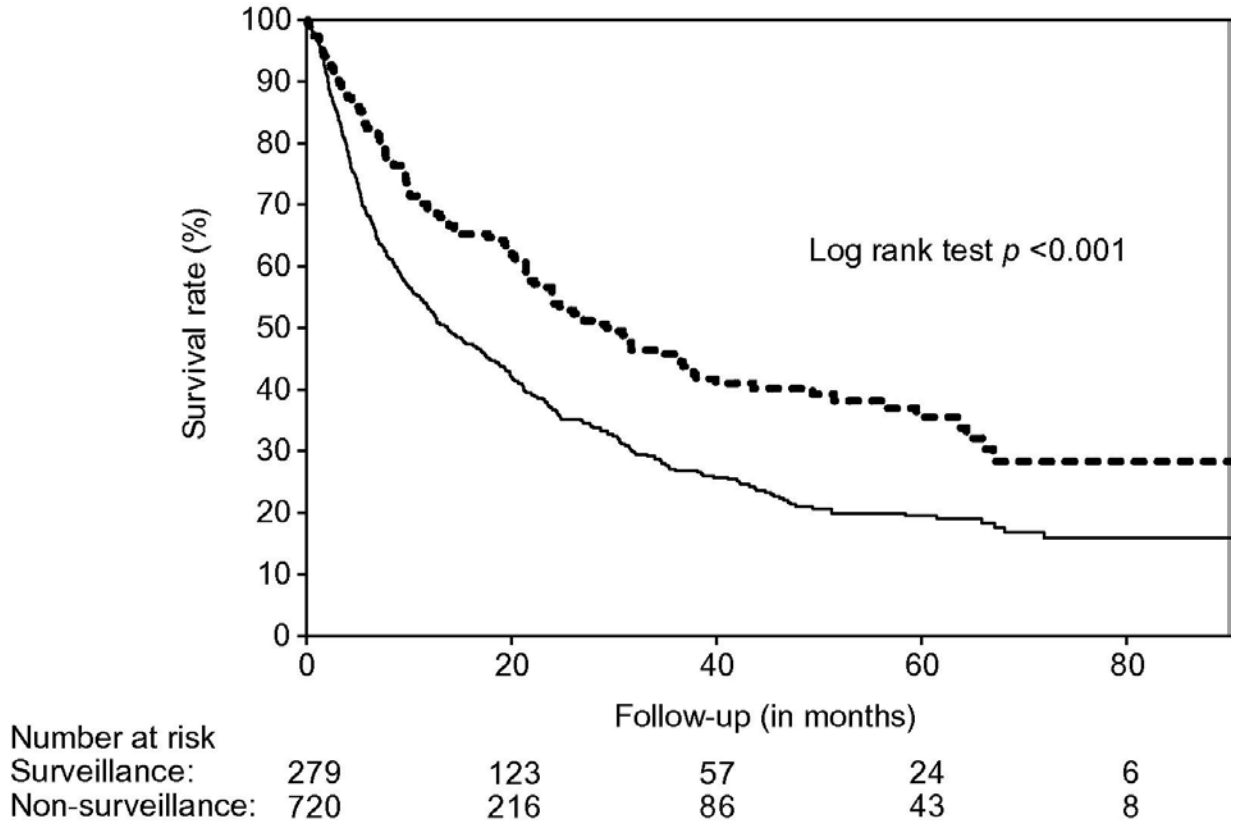
Surveillance associated with survival benefit in patients with cirrhosis



N=370 surveillance HCC
vs. 450 incidental HCC

Trevisani et al Am J Gastro 2002

Surveillance associated with survival benefit in patients with cirrhosis



Surveillance (n=295)
vs. other (n=779)

Tumor size
2.7 vs. 6.0 cm

Early stage HCC
61% vs. 21%

Curative treatment
57% vs. 32%

Van Meer et al J Hepatology 2015

Surveillance is cost-effective in patients with cirrhosis

Study	Cohort	Cost-effective Surveillance Strategy	ICER
Lin 2004	Child A cirrhosis	US and AFP q6 months	$28703
Thompson 2007	Child A cirrhosis	AFP triage q6 months	£30,400
Andersson 2008	Child A cirrhosis	US q6 months	$30,700

Why Is Liver Cancer Increasing?

- Liver cancer is increasing because ***cirrhosis*** is increasing
- Cirrhosis is increasing because
  - There are a lot of baby boomers
  - They have a high prevalence of hepatitis C
  - They are getting older
  - They are getting fatter

HCC Risk Factors

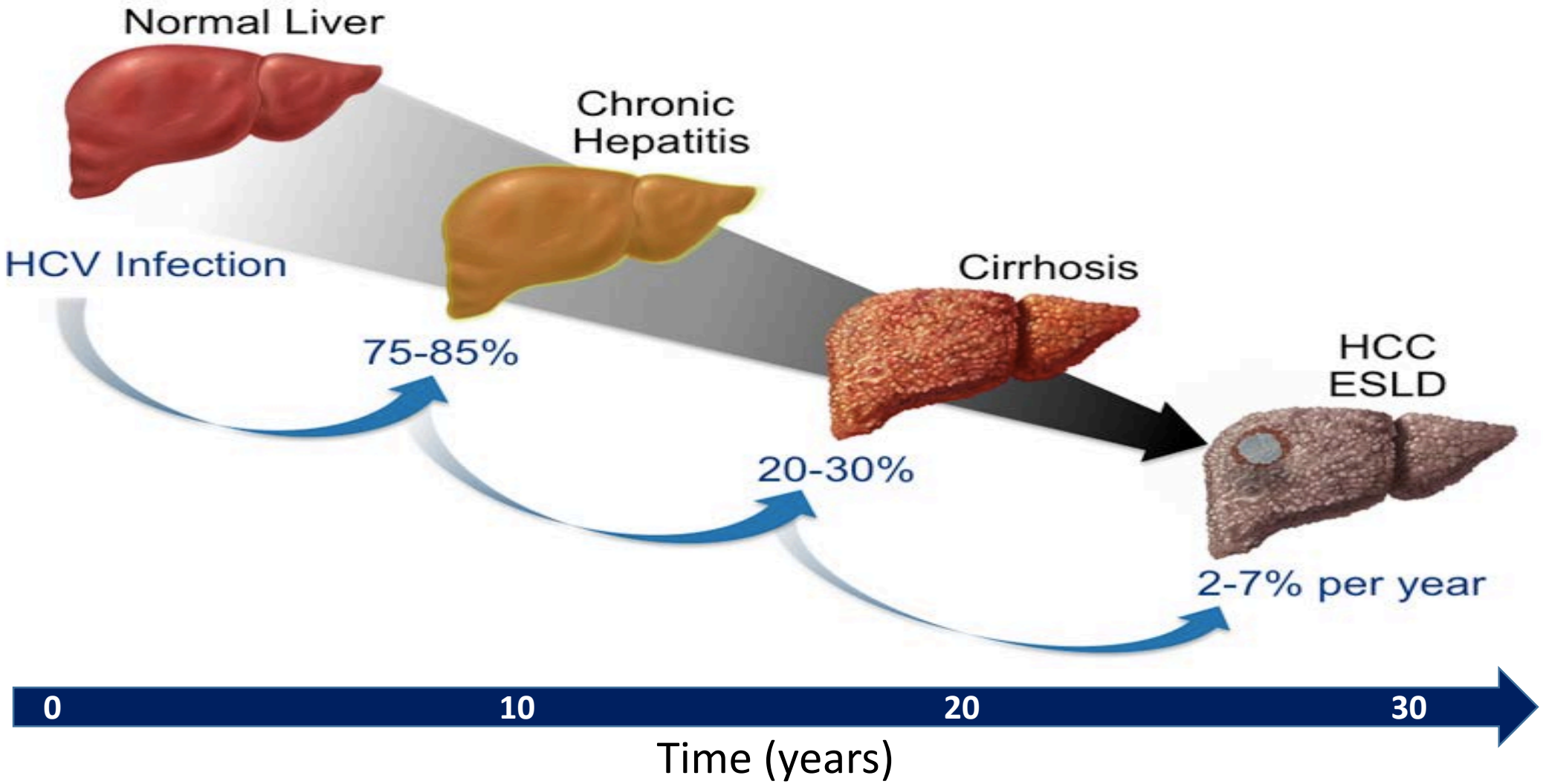
	Prevalence in general population	Risk estimate of HCC	Current prevalence in HCC cases	Population attributable fraction
HBV	0.5-1%	20-25	10-15%	5-10%
HCV	1-2%	20-25	**30-60%**	20-25%
Alcoholic liver disease	10-15%	2-3	20-30%	20-30%
Metabolic syndrome	30-40%	1.5-2.5	**20-50%**	30-40%

Hepatitis C

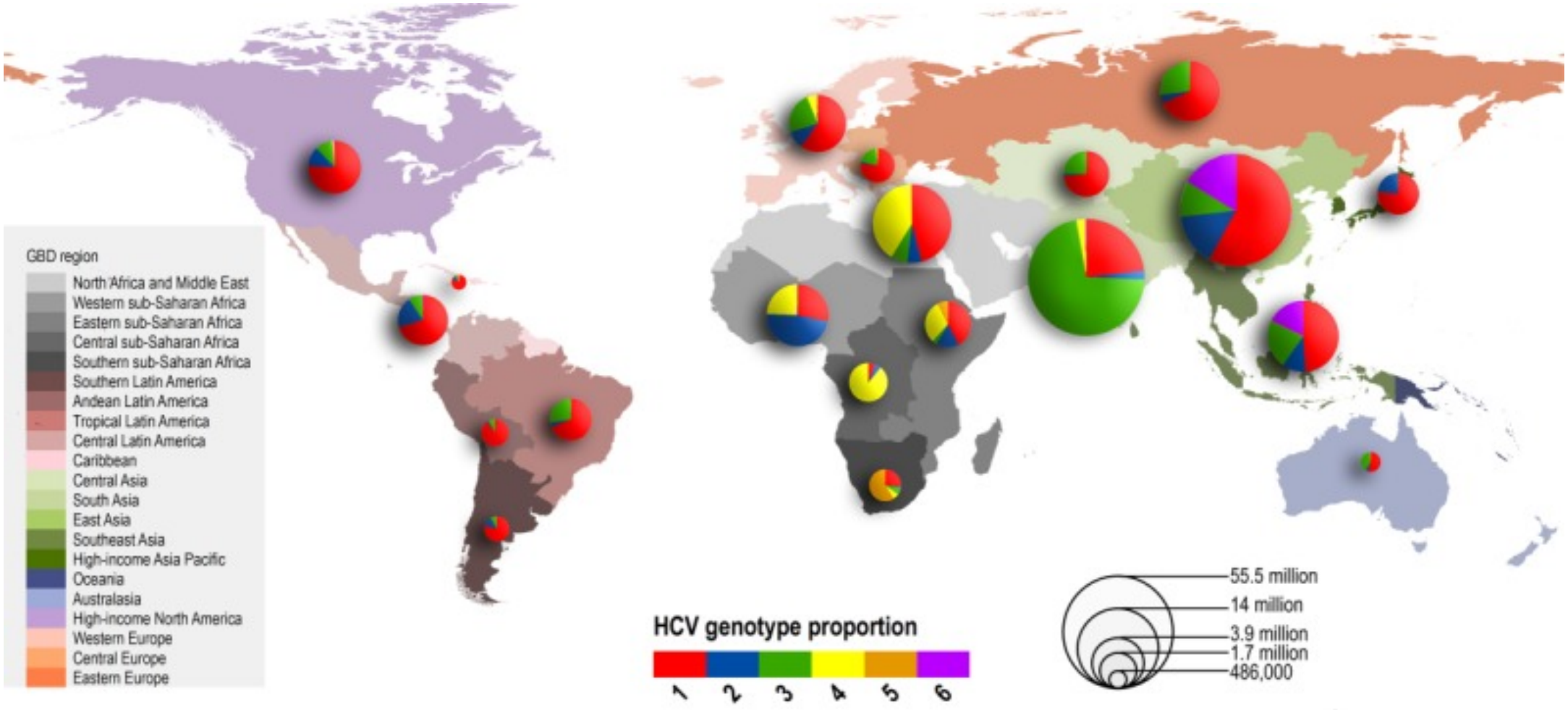
HCV Epidemiology 101: Worldwide burden of disease is increasing

- WHO estimates 130 – 170 million people, (3% of world's population) HCV infected and at risk of cirrhosis / HCC
- There are 3 – 4 million new infection / yr.
- HCV is responsible for 50 - 75% of all HCC and 50 – 60% of all liver transplants in the developed world
- HCV associated cirrhosis leads to liver failure and death in about 20 – 25% of cirrhotic patients

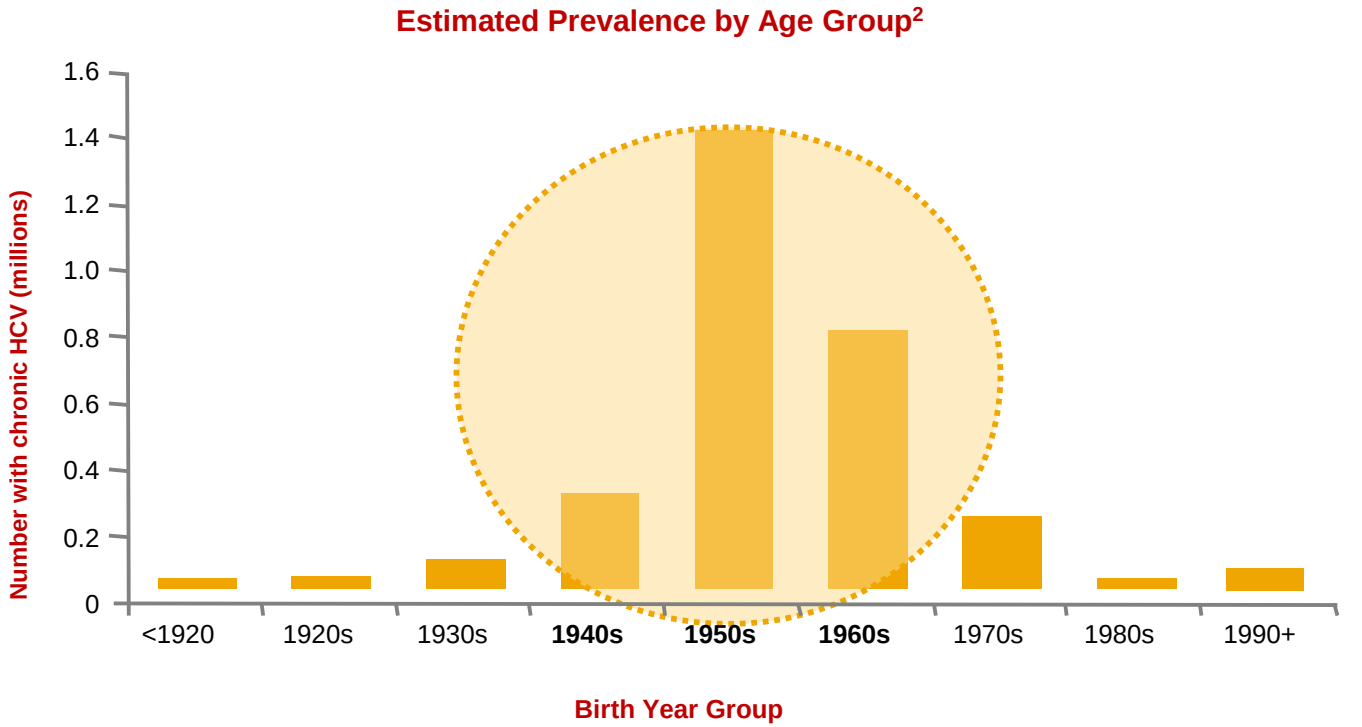
Natural History of Hepatitis C



World distribution of HCV per genotype



Baby Boomers (1945–1965) Account for 76.5% of HCV in the US



An estimated 35% of undiagnosed baby boomers with HCV currently have advanced fibrosis (F3-F4; bridging fibrosis to cirrhosis)[3]

Centers for Disease Control and Prevention. *MMWR*. 2012;61:1-32; Adapted from Pyenson B, et al. *Consequences of Hepatitis C Virus (HCV): Costs of a baby boomer Epidemic of Liver Disease*. New York, NY: Milliman, Inc; May 18, 2009. http://www.milliman.com/expertise/healthcare/publications/rr/consequences-hepatitis-c-virus-RR05-15-09.php Milliman report was commissioned by Vertex Pharmaceuticals; 3. McGarry LJ et al. *Hepatology.* 2012;55(5):1344-1355.

Who Should Be Tested for HCV

CDC Recommendations

Everyone born from 1945 through 1965 (one-time)

Persons who ever injected illegal drugs

Persons who received clotting factor concentrates produced before 1987

Chronic (long-term) hemodialysis

Persons with persistently abnormal ALT levels.

Recipients of transfusions or organ transplants prior to 1992

Persons with recognized occupational exposures

Children born to HCV-positive women

HIV positive persons

USPSTF Grade B Recs*

Everyone born from 1945 through 1965 (one-time)

Past or present injection drug use

Sex with an IDU; other high-risk sex

Blood transfusion prior to 1992

Persons with hemophilia

Long-term hemodialysis

Born to an HCV-infected mother

Incarceration

Intranasal drug use

Receiving an unregulated tattoo

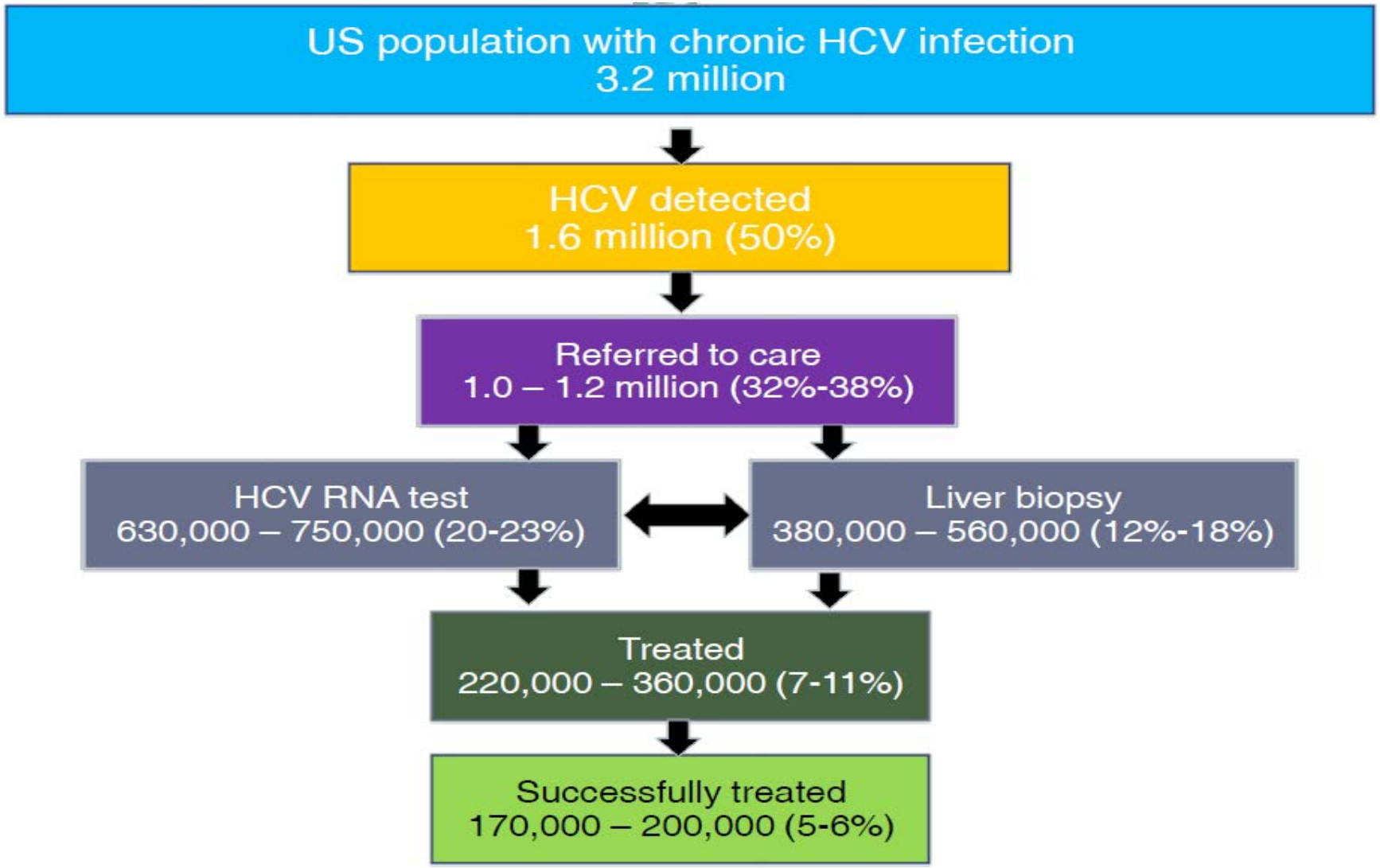
Occupational percutaneous exposure

Surgery before implementation of universal precautions

*Pertains to persons with normal liver enzymes; if elevated liver enzymes need HBV and HCV testing

Smith at al. Ann Intern Med 2012; 157:817-822. Moyer et al. Ann Intern Med epub 25 June 2013

Horrible job identifying patients and linking care



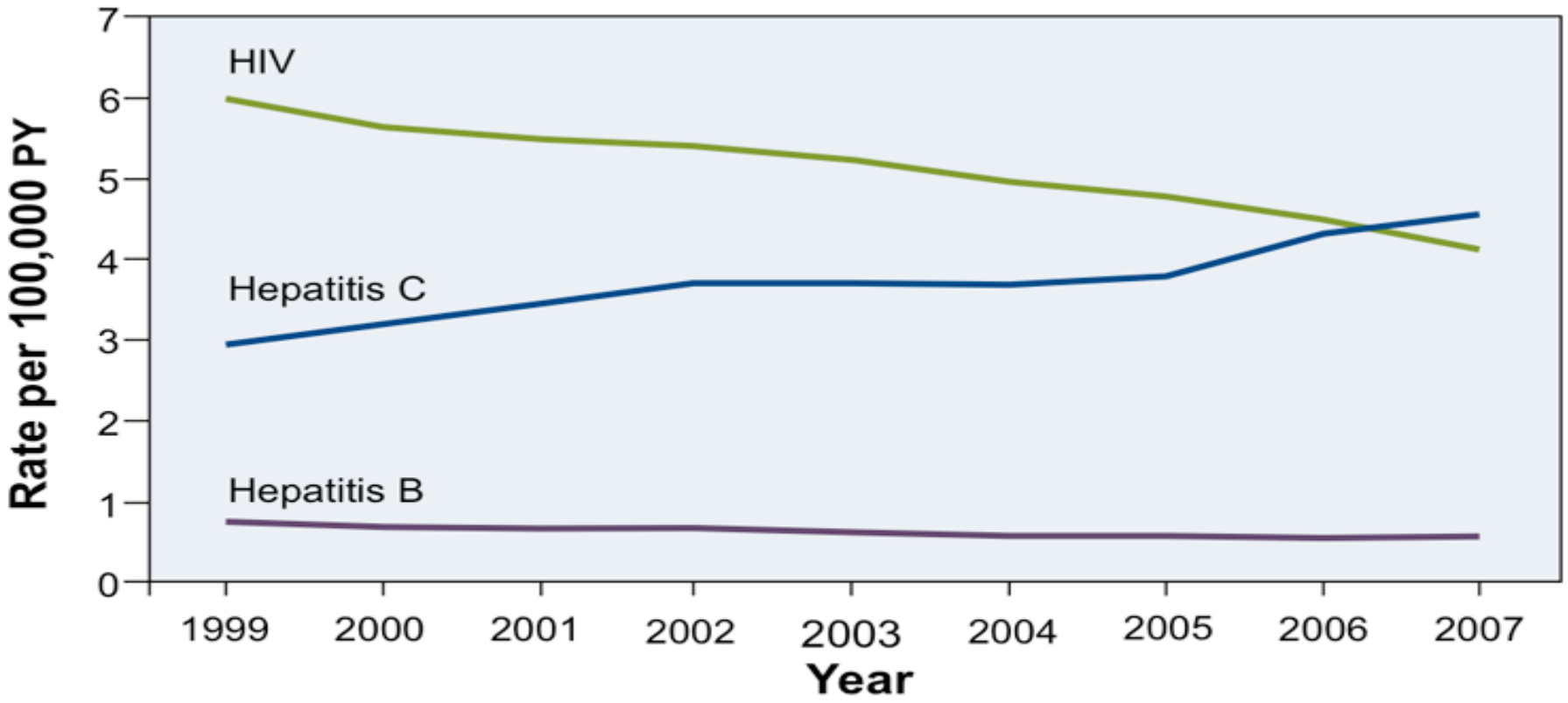
3 of 5 Patients With HCV Are Undiagnosed

SCREENING BARRIERS

- Lack of public awareness of risk factors
- Lack of routine risk assessment by many PCPs
- Patient reluctance to admit risk factors
  - *No risk factors identified in 69% of cases*
- Infected individuals often asymptomatic
- Liver panels/serologies currently triggered by ↑ALT

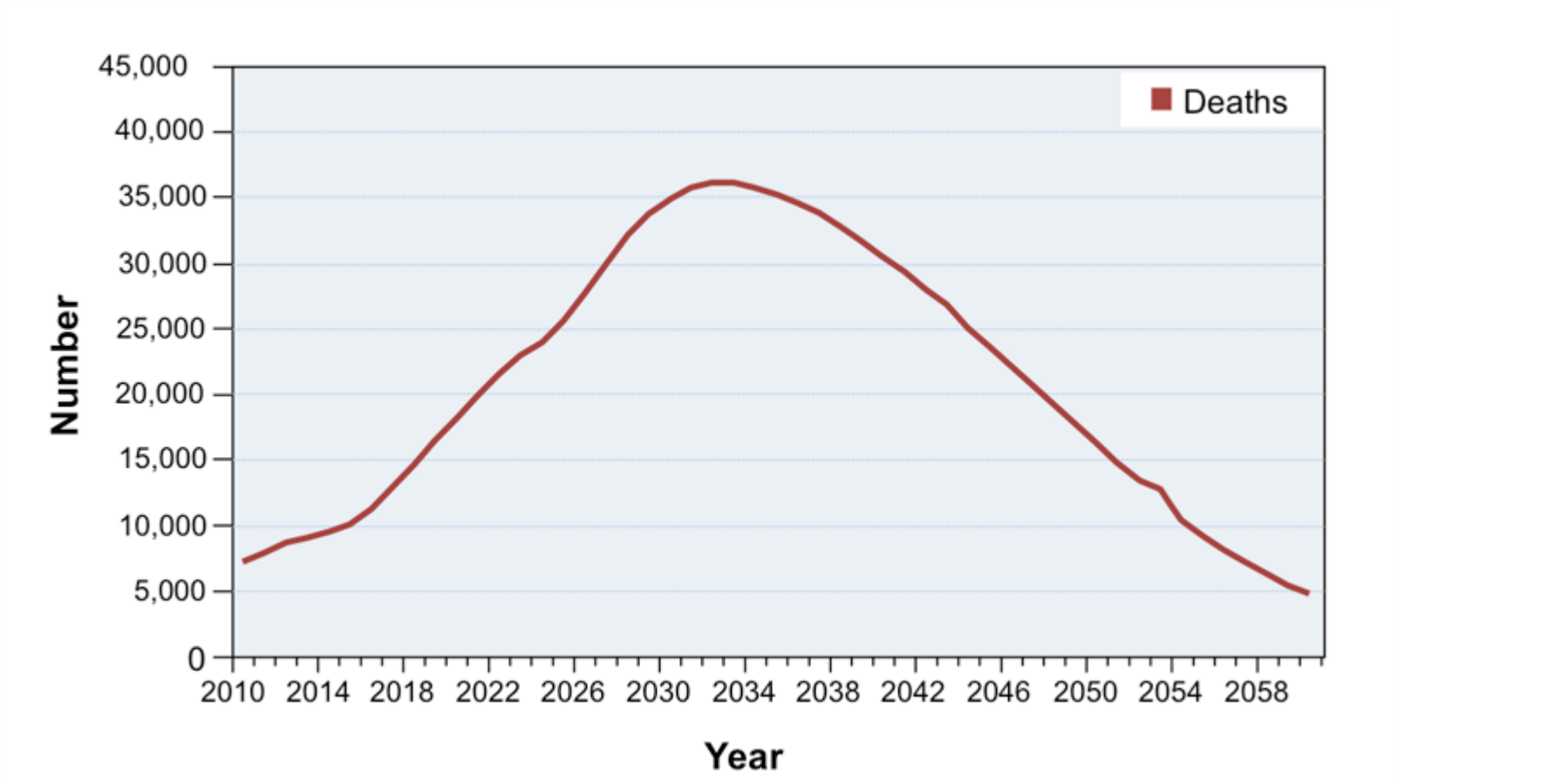
Shehab T, et al. *J Viral Hepat*. 2001;8:377-383.
Rawls R, et al. *J Clin Gastroenterol*. 2005;39:144-151.
American Liver Foundation. 2006. Available at: http://www.liverfoundation.org.

US Mortality Rates from HCV, HBV & HIV 1999 - 2007

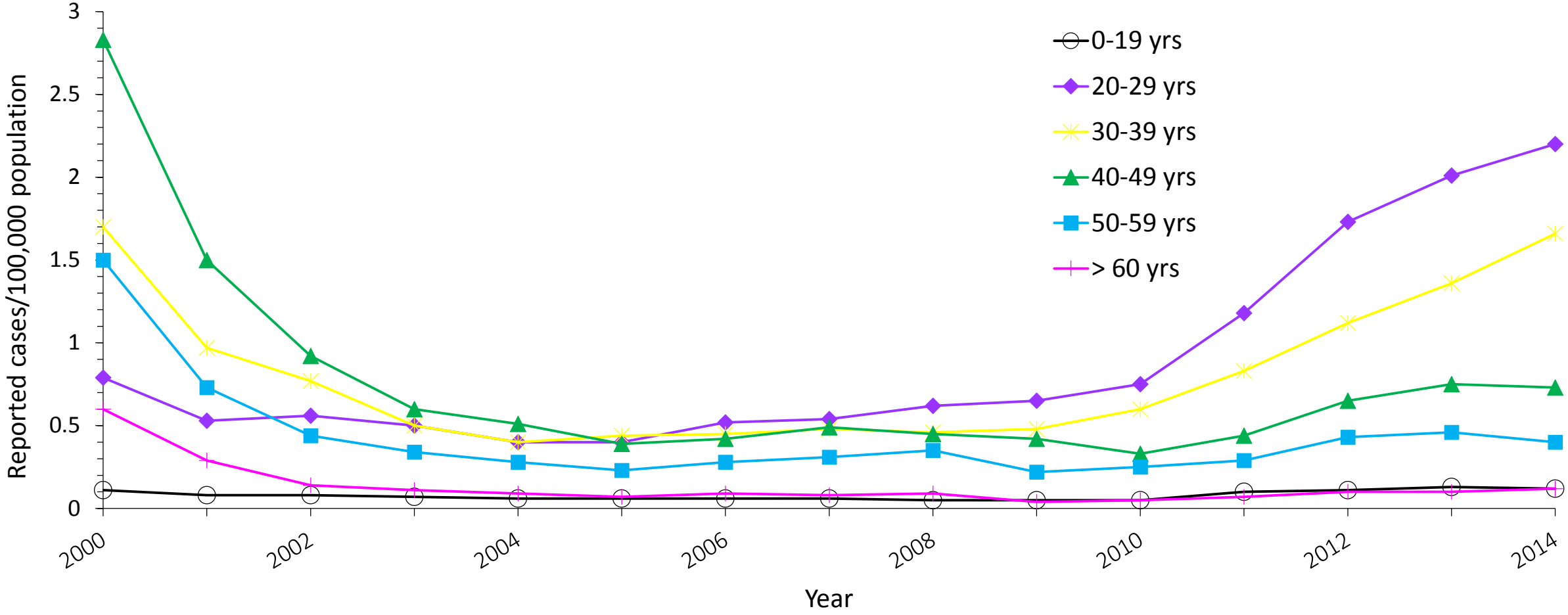


*Mortality Rates = HBV, HCV, HIV listed as cause of death
Because of decedent can have multiple causes of death, a record listing more than 1 type of infection was counted for each type of infection

Forecasted Annual Deaths Associated with HCV

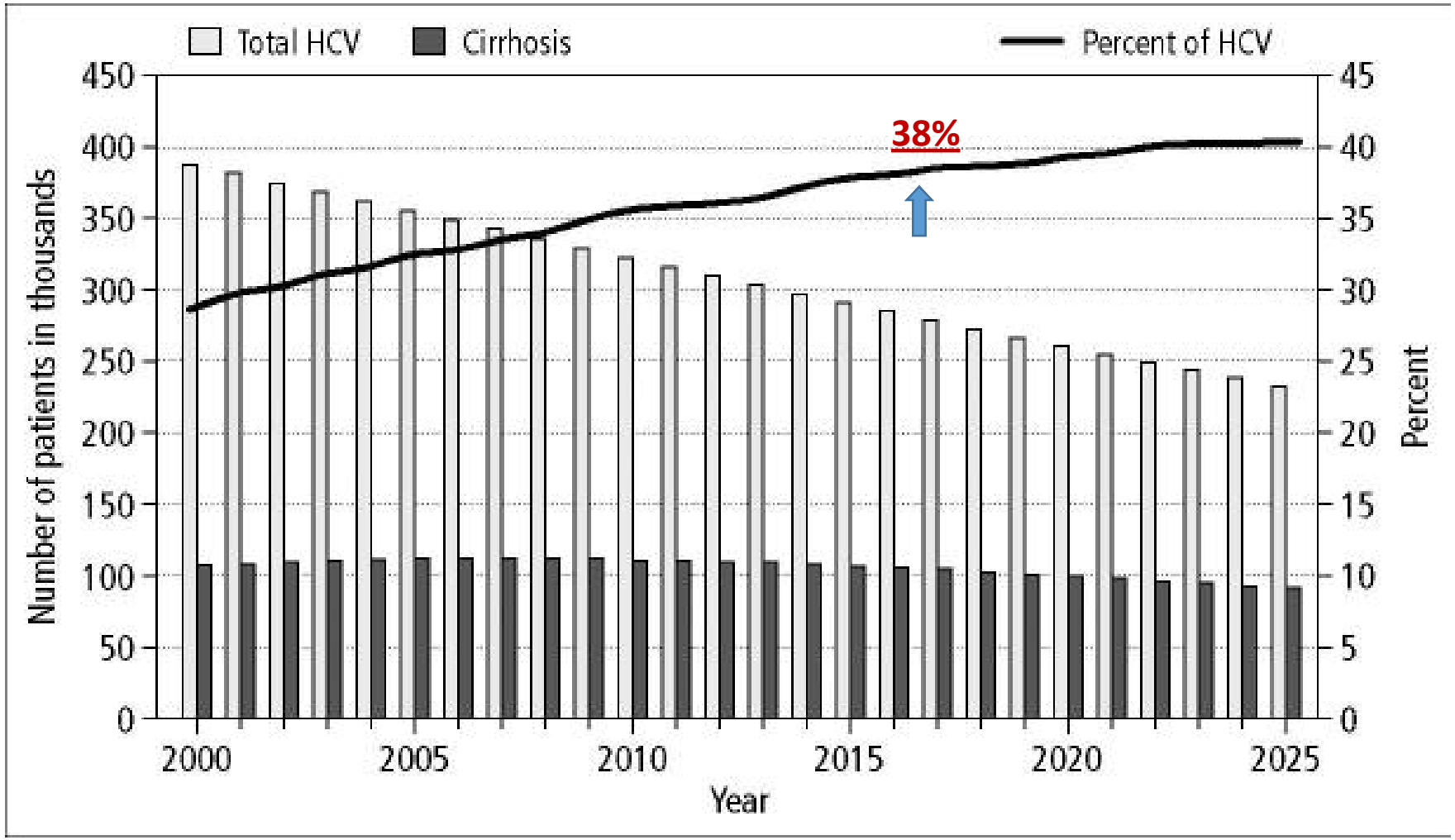


Incidence of Acute HCV by Age group



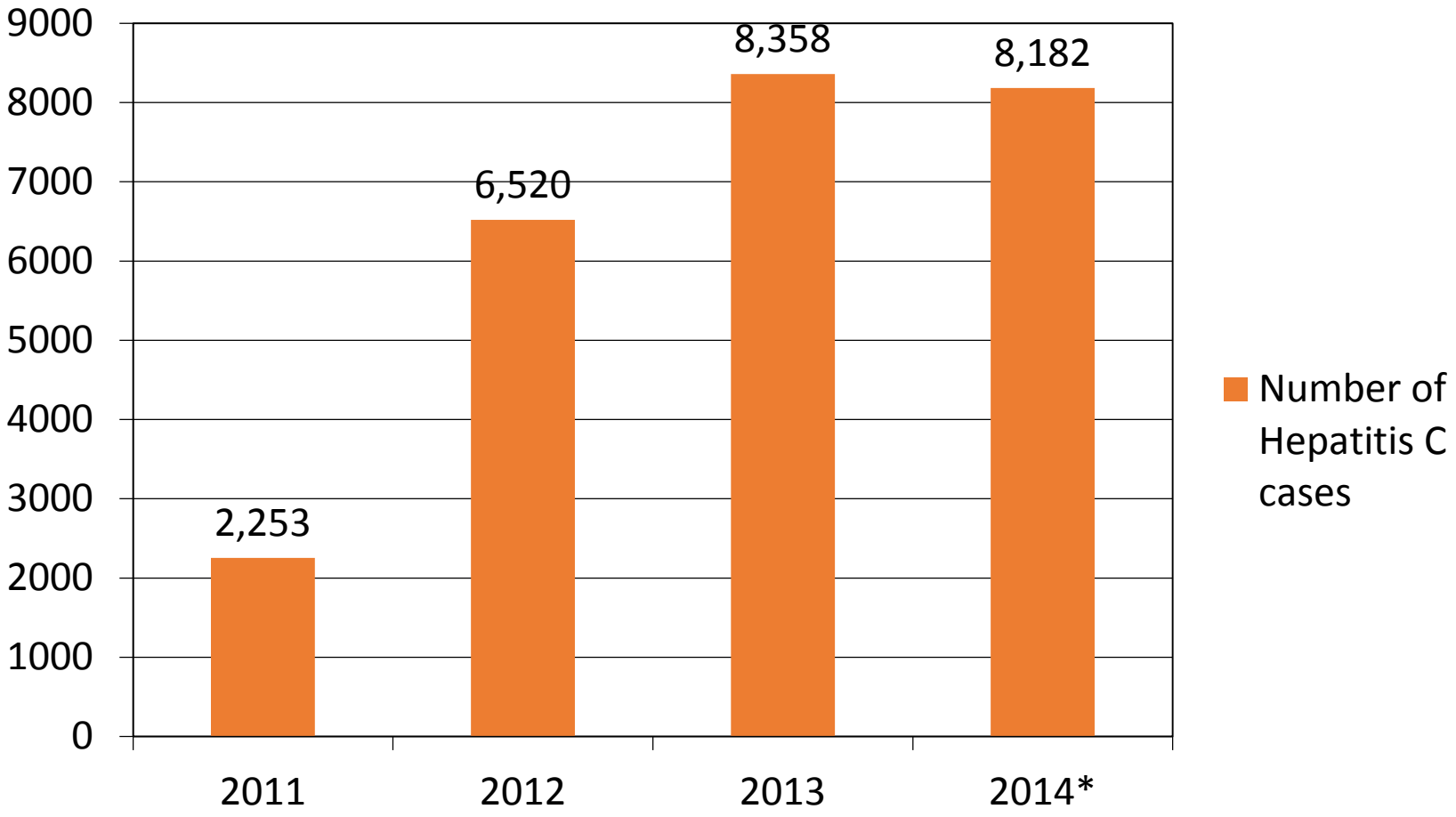
Source: CDC, National Notifiable Diseases Surveillance System (NNDSS)

Texas 2016: Presenting to their primary care physician with a new Dx of HCV already have cirrhosis



Davis G. : Baylor Medical Center Proceedings

Number of Newly Reported HCV Cases, Houston, TX



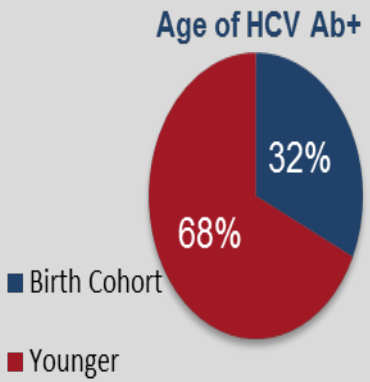
*The 2014 data is incomplete (as of 12/10/2014)

Finding Younger HCV Patients

- City Health Department provides the largest number of STD screenings in the city through its 3 city-wide STD clinics, mobile unit, and 6 community-based partners.
- Utilizing existing HIV service linkage infrastructure and staff to link HCV RNA positive patients to care.
- Central city laboratory provides HCV RNA testing.
- STD clinics now operational with electronic medical record system, facilitating screening.

QUICK FACTS

- Integrated STD screening, including HIV and HCV.
- Implemented at 3 city-wide STD clinics and one mobile clinic.
- Providing follow-up RNA confirmatory on all HCV screening tests.



Nearly 70% of all Ab+ are younger than 48

6.8% prevalence for HCV

RESULTS

Since implementing integrated screening at all city STD clinics and community-based testing sites:

- Conducted over 1,065 HCV Ab tests.
- Identified 89 HCV Ab+ patients (6.8%); of those with an RNA test, 30% chronic cases.
- Majority of Ab+ patients are younger than the birth cohort.
- 95% male; 70% African American

CONCLUSION

- Screening at STD clinics and using existing HIV service linkage structure is an efficient way to reach HCV patients, especially those younger than the birth cohort.
- To make screening sustainable, central lab will move to fee scale for screening and RNA to community agencies and individuals.

Project Leaders and Champions: Marlene McNeese, Lupita Thornton, Cynthia Turner, Cathy Wiley.

Who should be treated?

1. Hepatitis C infection ***IS CURABLE***
2. ***ALL*** HCV infected patients ***SHOULD*** receive treatment
3. Groups that should receive immediate therapy as they will derive the highest benefit
   a. Patients with a diagnosis of cirrhosis
   b. Liver Transplant recipients with active viremia
   c. HCV/HIV coinfected patients
   d. Extrahepatic manifestations of HCV
      - Cryoglobulinemia
      - B-cell Lymphoma
      - Porphyria

Who should be treated

- Special considerations to the following population groups
  1. Prison inmates
  2. HCV/HIV men who have sex with men
  3. Clinicians at high risk of transmission to patients
  4. IVD users

SVR-12 = Cure in Genotype 1 treatment naïve

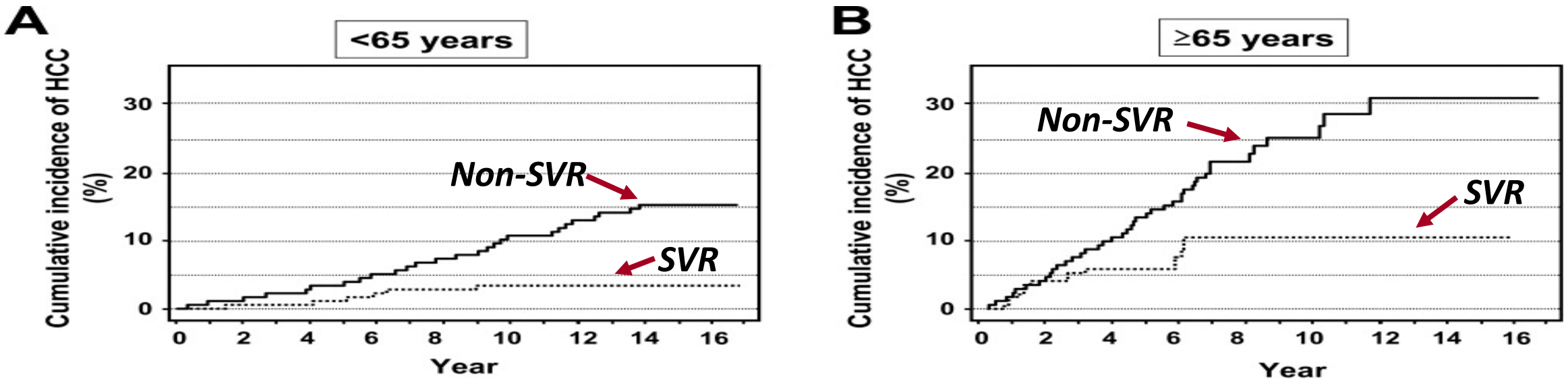
MEDICATIONS	SVR-12 rates
Ledipasvir + Sofosbuvir	94 – 99 %
Simeprevir + Sofosbuvir	91 – 94%
Ombitasvir + Paritaprevir + Dasabuvir + Ribavirin	91 – 100 %
Sofosbuvir + Daclatasvir	90 – 100 %
Elbasvir + Grazoprevir	94 – 100%

AASLD/IDSA. HCV guidelines. April 2016.

HCV Treatment Pri$$$$e tag

Estimated Cost* for Treatment of Genotype 1 Chronic HCV	
Regimen^ and Duration of Therapy	**Cost of Regimen***
Daclatasvir + Sofosbuvir x 12 weeks	$147,000
Daclatasvir + Sofosbuvir x 24 weeks	$294,000
Elbasvir-Grazoprevir x 12 weeks	$54,600
Elbasvir-Grazoprevir x 16 weeks	$72,800
Ledipasvir-Sofosbuvir x 12 weeks	$94,500
Ledipasvir-Sofosbuvir x 24 weeks	$189,000
Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir x 12 weeks	$84,000
Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir x 24 weeks	$168,000
Sofosbuvir + Simeprevir x 12 weeks	$150,000
Sofosbuvir + Simeprevir x 24 weeks	$300,000

Curing HCV reduces the incidence of HCC



Note: Even when HCV is Cured you still need to continue screening !

Summary

1. Hepatitis C is the leading cause of cirrhosis, HCC and liver transplantation
2. The incidence and mortality associated with HCV and HCC is increasing in US and specially in Texas.
3. We are doing a poor job in identifying and screening patients for Hepatitis C. And linkage to care is suboptimal
4. Hepatitis C is CURABLE. Treatment although expensive, is cost effective and decreases liver related complications