

Public Health Impact of Hepatitis C

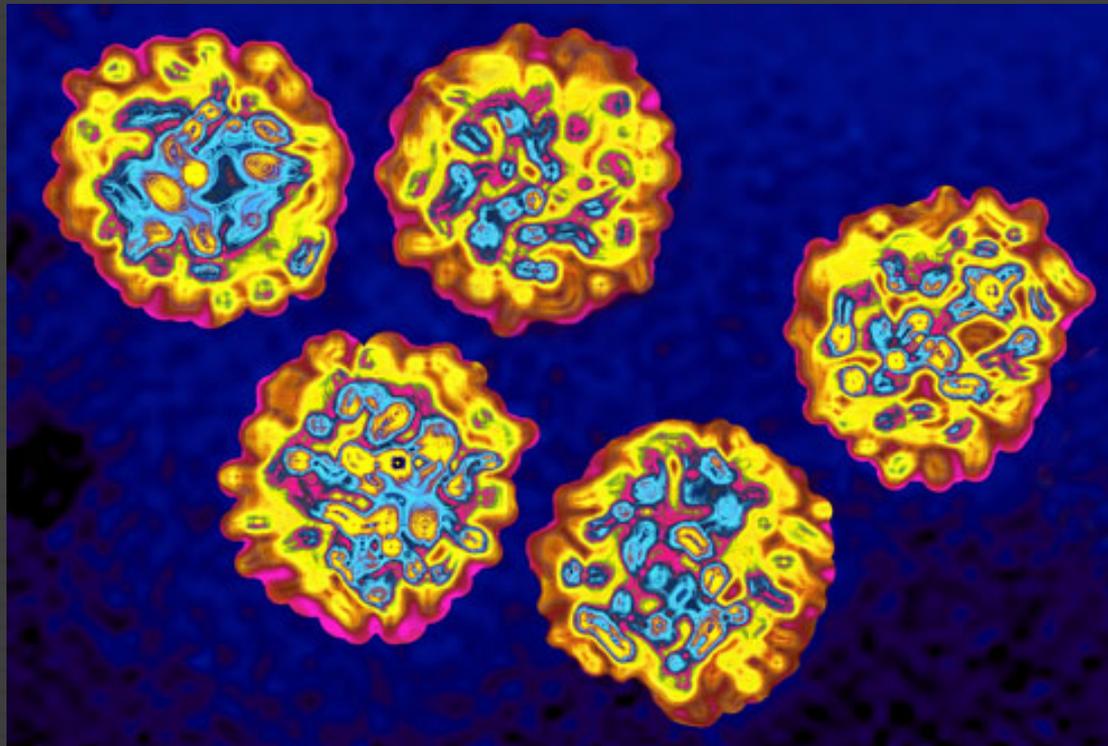


www.michigan.gov/hepatitis

May 15, 2014

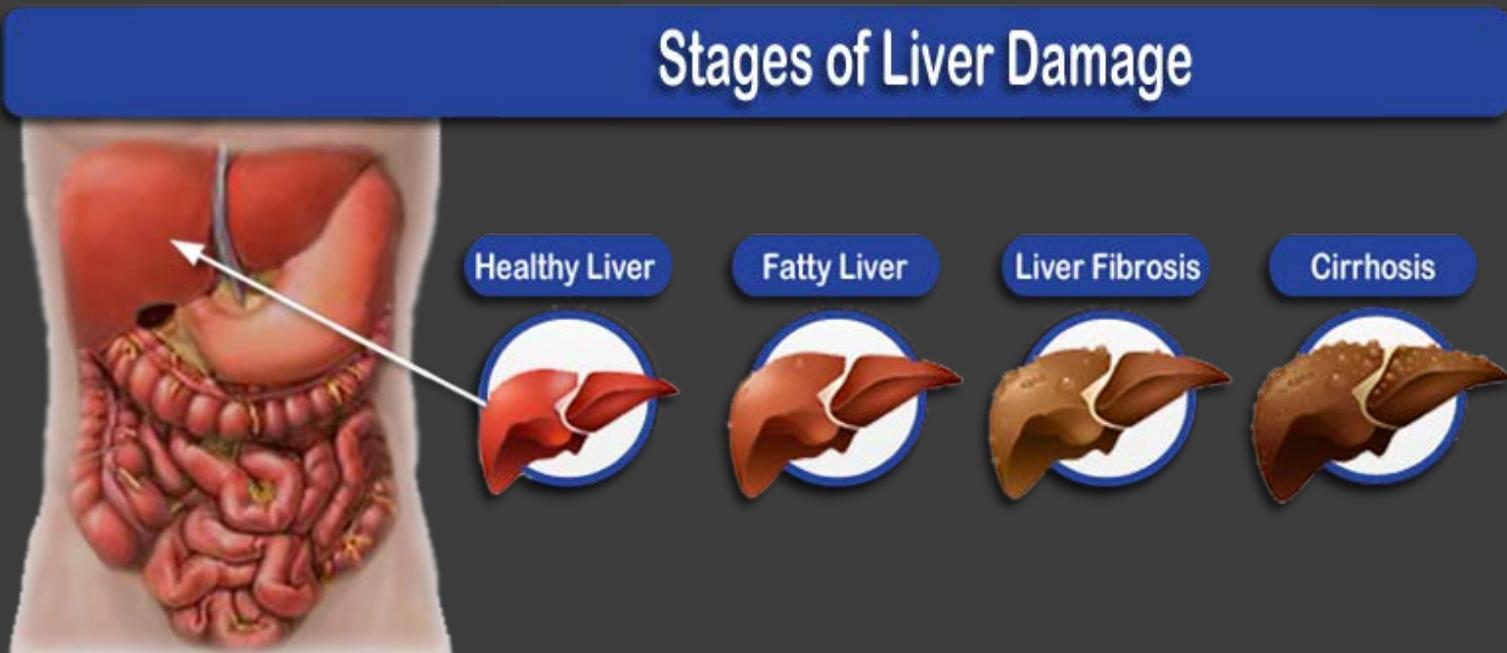
Joe Coyle, MPH

The Virus and the Disease



Hepatitis

- Hepatitis is characterized by inflammation of the liver which is a result of cellular damage
- Inflammation of the liver can impair liver function



Causes of Hepatitis

- The most common cause of hepatitis are the hepatitis viruses (hepatitis A, B, C, D, E)
- Non-infectious hepatitis can be caused by:
 - ▣ Alcohol consumption
 - ▣ Toxins and drugs (acetaminophen)
 - ▣ Autoimmune diseases

Table 3. Hepatitis symptoms.^{1-3,5-7,9,11,12,15}

Flu-like Symptoms	Other Symptoms
<ul style="list-style-type: none">• Fever• Fatigue• Nausea• Vomiting• Loss of appetite• Joint pain	<ul style="list-style-type: none">• Dark urine• Clay-colored stool• Abdominal pain• Jaundice

Viral Hepatitis

Table 2. Important characteristics of common hepatitis viral infections.^{1-5,7,9,11,12,15,16}

	HAV	HBV	HCV	HDV	HEV
Source of Virus	Feces	Blood / some body fluids	Blood / some body fluids	Blood / some body fluids	Feces
Route of Transmission	Fecal-oral	Percutaneous or permucosal	Percutaneous or permucosal	Percutaneous or permucosal	Fecal-oral
Chronic Infection	No	Yes	Yes	Yes	No
Prevention	<ul style="list-style-type: none"> • Pre / post exposure immunization • Hand hygiene • Total Ig 	<ul style="list-style-type: none"> • Pre / post exposure immunization • HBIg • Risk behavior modification 	<ul style="list-style-type: none"> • Risk behavior modification 	<ul style="list-style-type: none"> • Pre / post exposure immunization with HBV vaccine • Risk behavior modification 	<ul style="list-style-type: none"> • Access to clean drinking water • Hand hygiene
Vaccine	Yes	Yes	No	No	No

Ig: immunoglobulin; HBIg: hepatitis B immunoglobulin

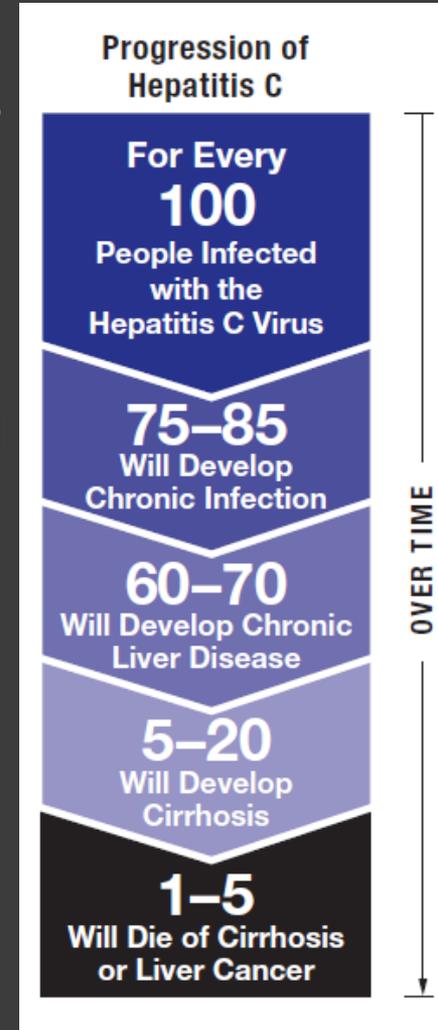
Hepatitis C Virus

- Hepatitis C is a disease of the liver caused by the Hepatitis C Virus (HCV)
- Called “non-A non-B hepatitis” until its identification in 1989
- HCV is a blood-borne pathogen meaning it spreads from person-to-person via contaminated blood

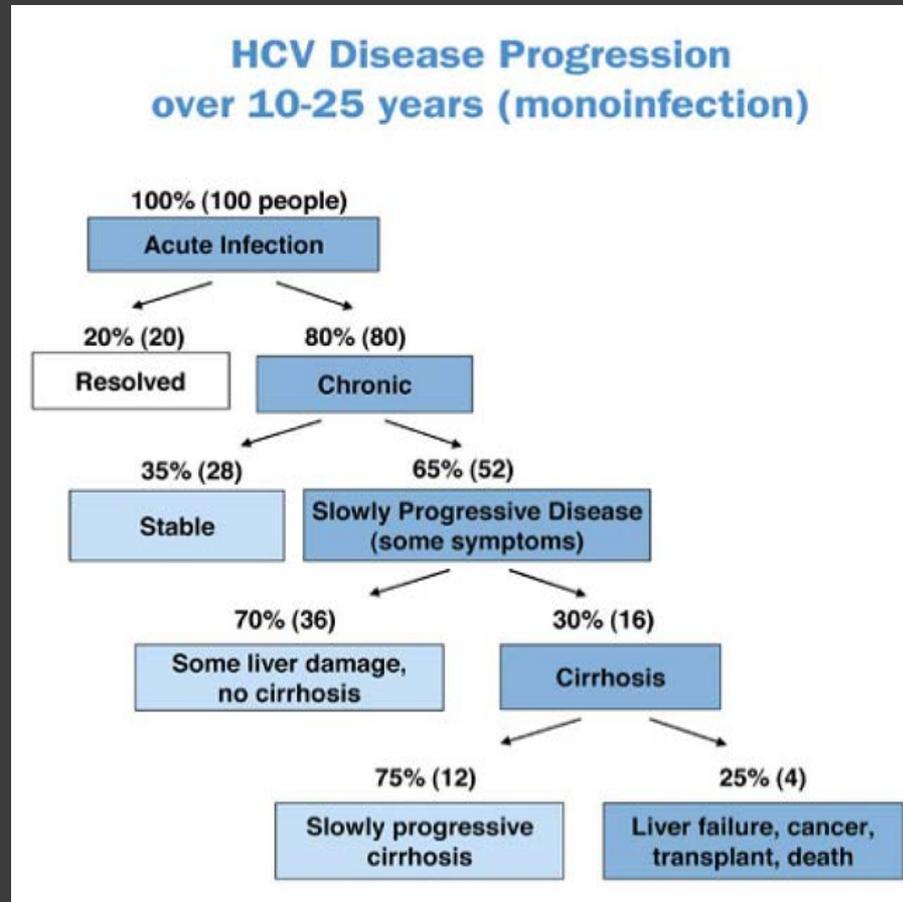


HCV Infection

- There are two stages of Hepatitis C:
 - Acute – short-term illness presenting 2 weeks to 6 months after exposure to HCV
 - Symptomatic in only 15% of cases
 - Symptoms: fever, fatigue, loss of appetite, nausea, abdominal pain, dark urine, grey-colored stool, and jaundice
 - Chronic – long-term illness that can last a lifetime
 - Over time chronic HCV infection can lead to liver damage, liver cirrhosis, liver failure and liver cancer



HCV Infection



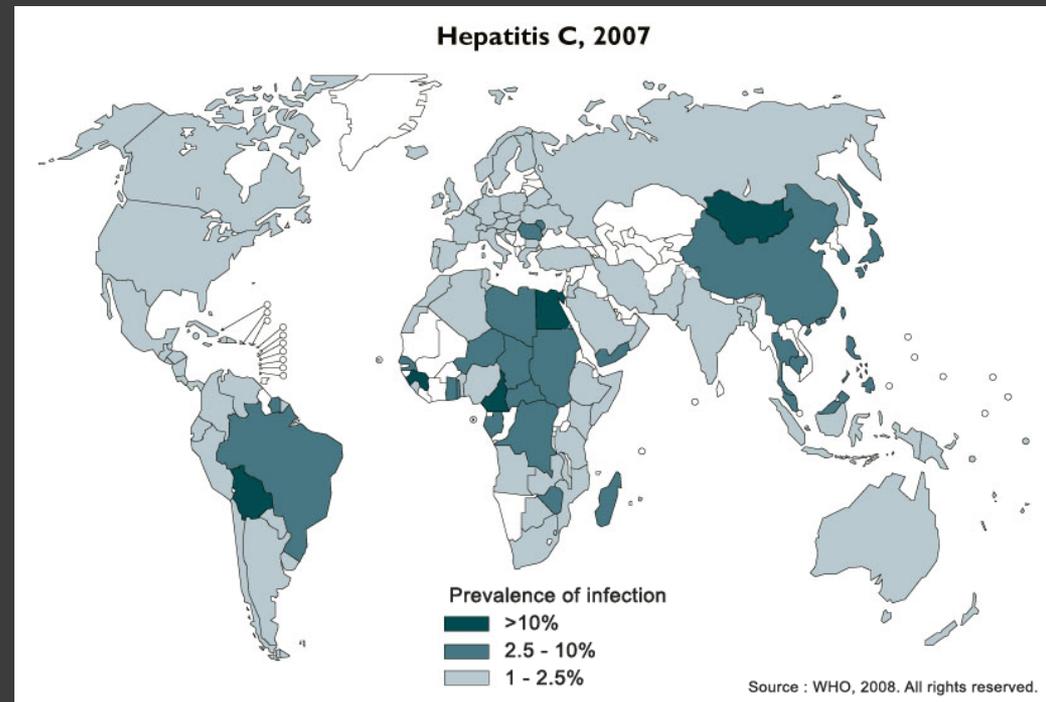
[Alter, MJ. Epidemiology of Hepatitis C in the West. *Semin Liver Disease*. 1996; 15: 5-14.](#)
[Management of Hepatitis C: NH Consensus Statement. *Hepatology*. 1997; 26\(3\): 2S-10S](#)



Epidemiology and Health Impact

Global Burden of HCV

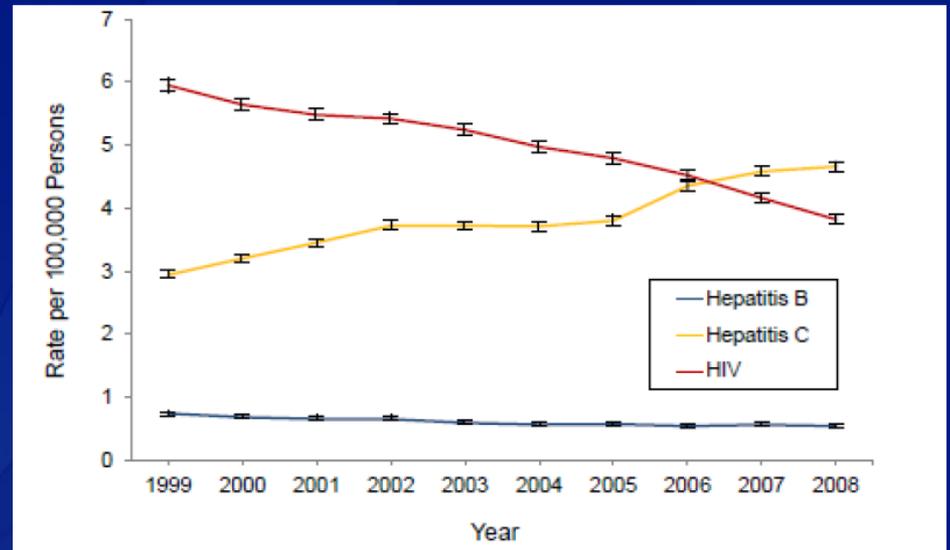
- 180 million people are infected with HCV
- 3-4 million new HCV infections each year
- 350,000 attributable deaths each year



HCV in the U.S.

- CDC estimates that 2.7-3.9 million persons in the U.S. have chronic HCV infection (1.3-1.9% of the population)
- HCV plays a role in ~12,000 deaths per year
- US citizens with HCV died 22-23 years earlier than those without HCV

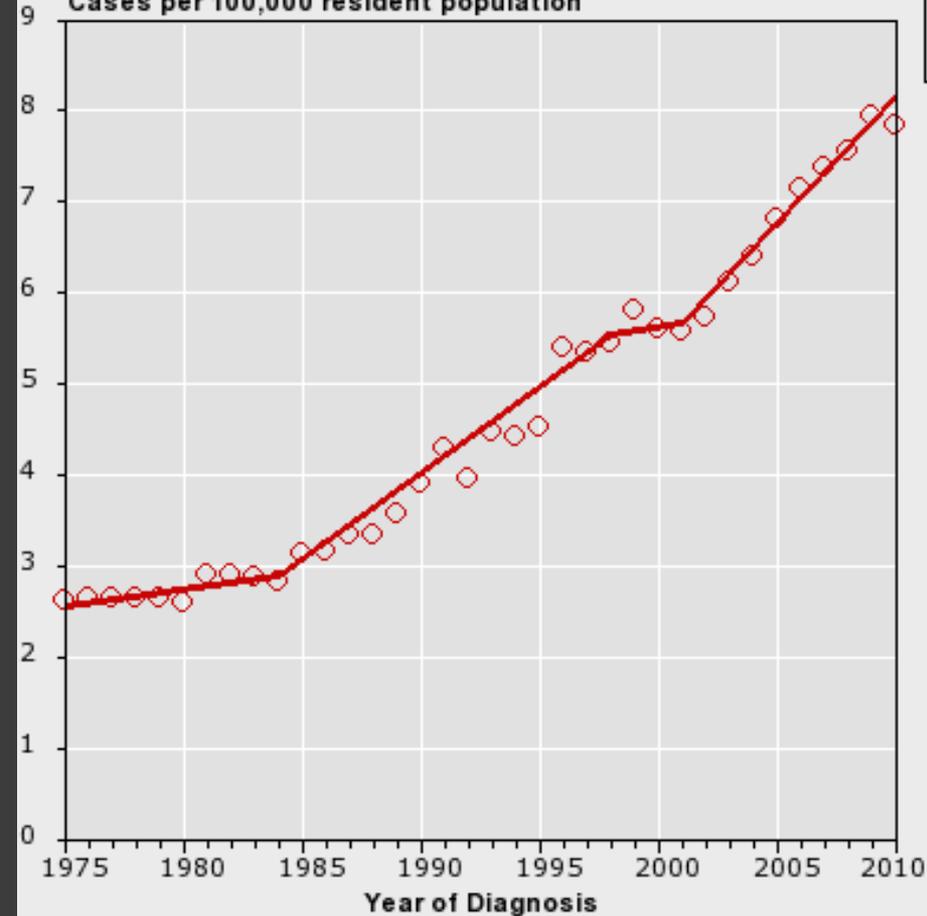
Mortality associated With Hepatitis B, Hepatitis C, and HIV
United States, 1999 – 2008



U.S. Liver Cancer Incidence and Mortality

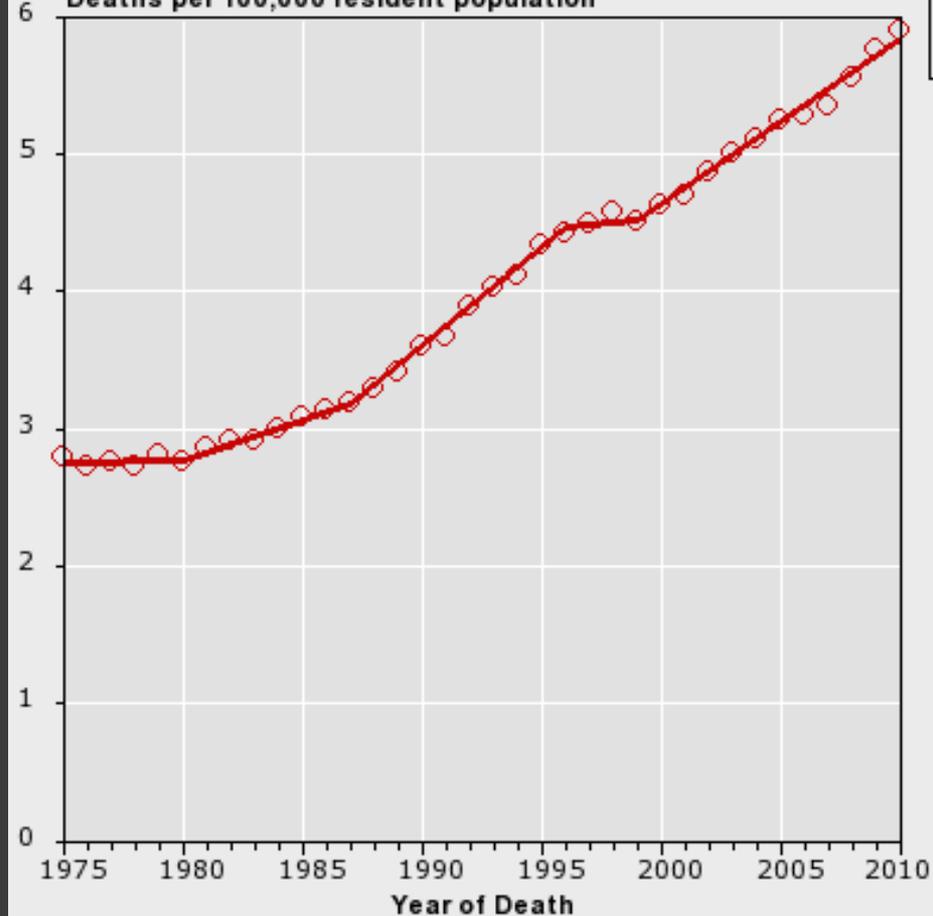
**Incidence, SEER 9 Registries
Liver & Bile Duct, All Races (incl Hisp)
Both Sexes, All Ages**

Cases per 100,000 resident population

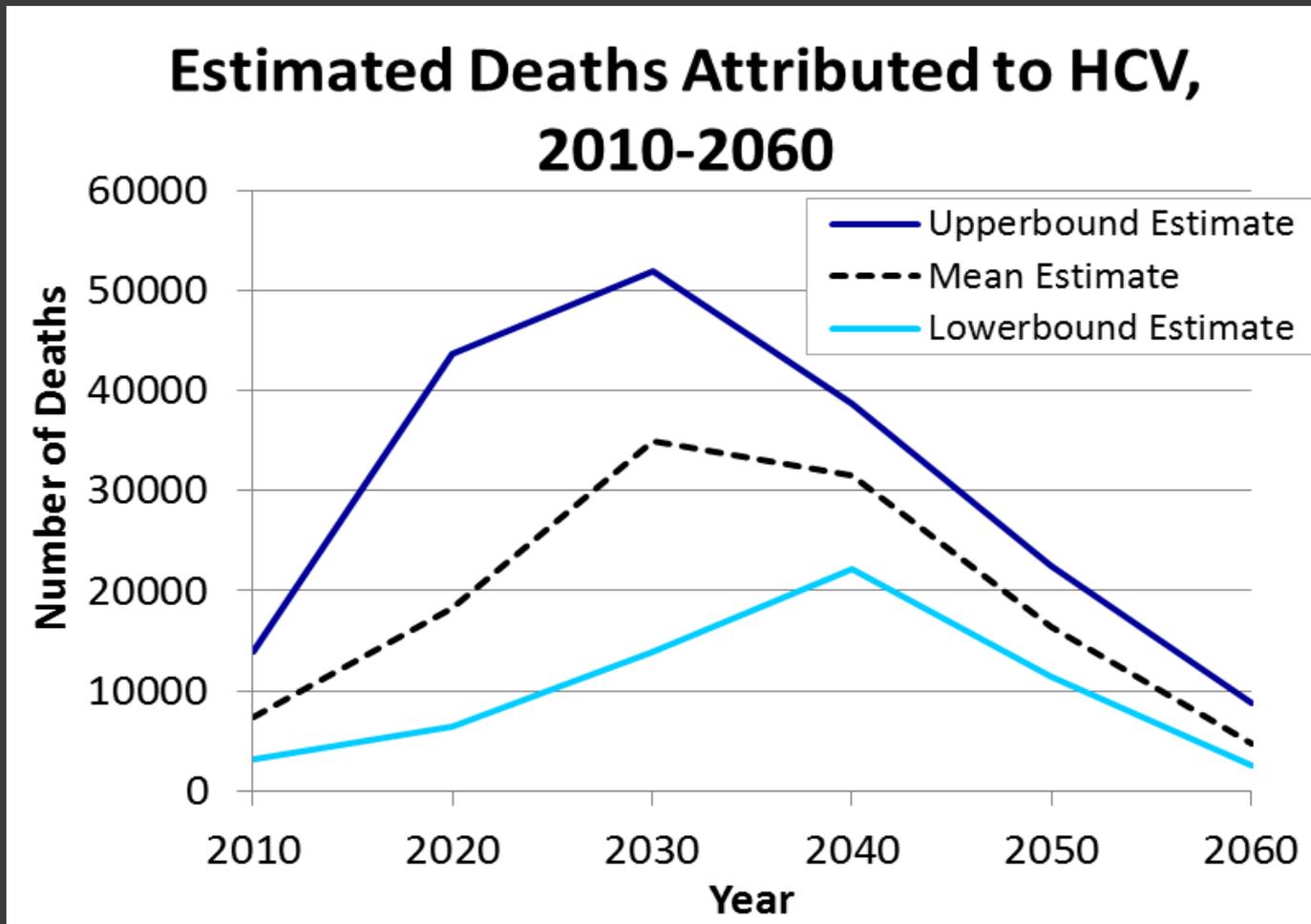


**Mortality, United States
Liver & Bile Duct, All Races (incl Hisp)
Both Sexes, All Ages**

Deaths per 100,000 resident population



Future of HCV Infection



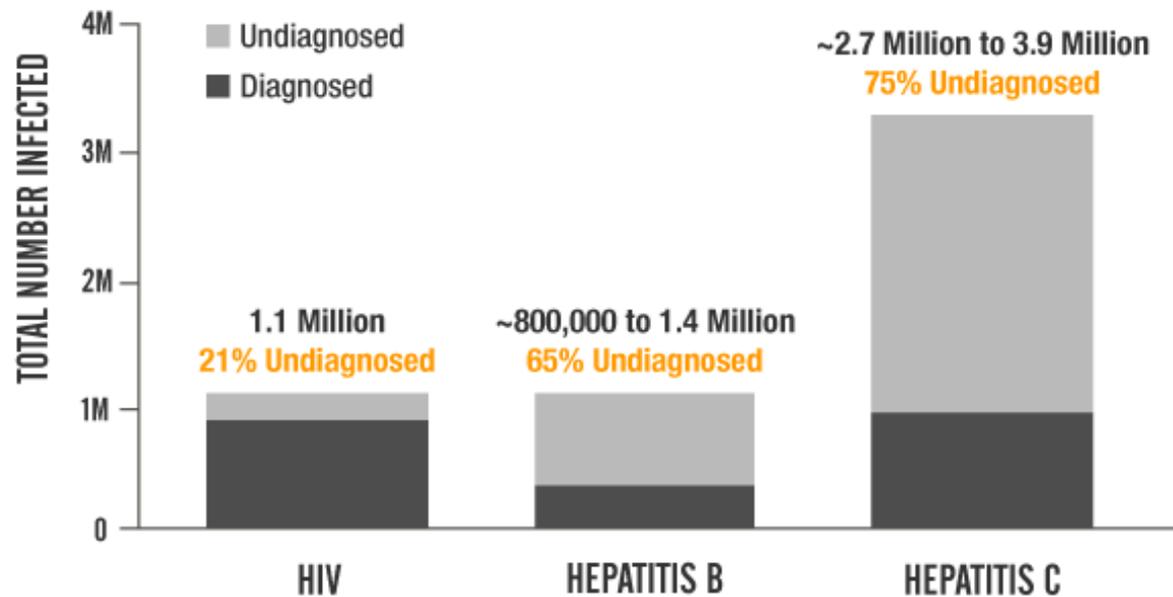
[Rein, DB et al. Forecasting the morbidity and mortality associated with prevalent cases of pre-Cirrhotic chronic hepatitis C in the United States. *Digestive and Liver Disease*. 2011; 43\(1\): 66-72.](#)

Testing

HEPATITIS C VIRUS IS NEARLY 4 TIMES AS PREVALENT AS HIV AND HEPATITIS B VIRUS IN THE UNITED STATES



Number of Infected Individuals vs
Number Aware They Are Infected (Diagnosed)



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://publications.milliman.com/research/healthrr/pdfs/consequences-hepatitis-c-virus-RR05-18-09.pdf>. Accessed August 28, 2012. This report was commissioned by Vertex Pharmaceuticals Incorporated.

Baby-Boomers (Born 1945-1965)

Number of Chronic Hepatitis C Cases Reported to MDCH by Birth Year

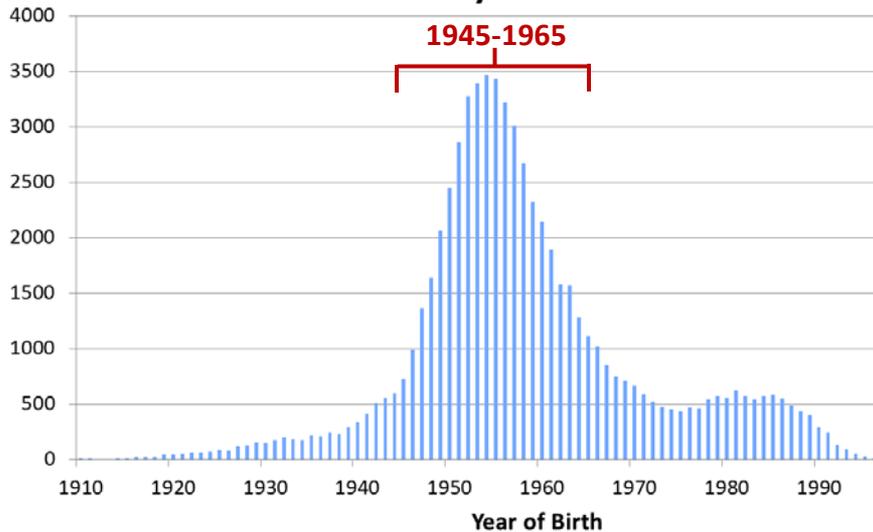
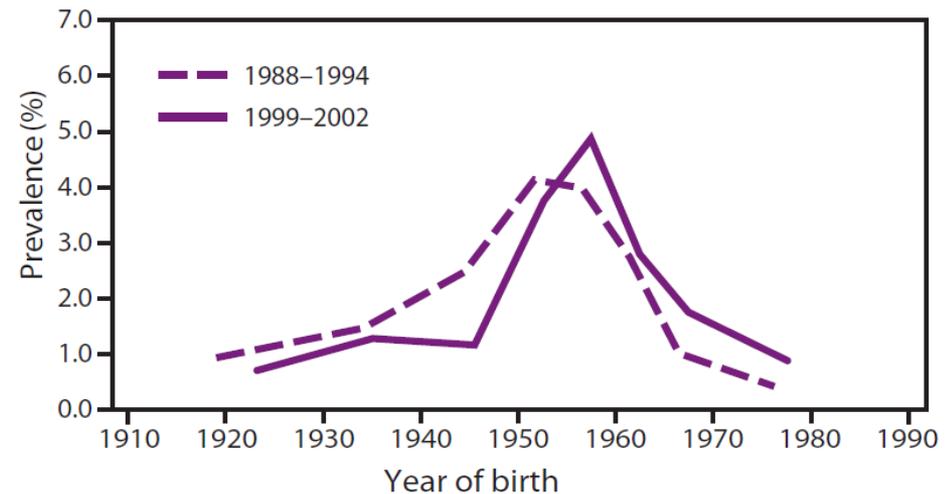


FIGURE 2. Prevalence of hepatitis C virus antibody, by year of birth — National Health and Nutrition Examination Survey, United States, 1988–1994 and 1999–2002



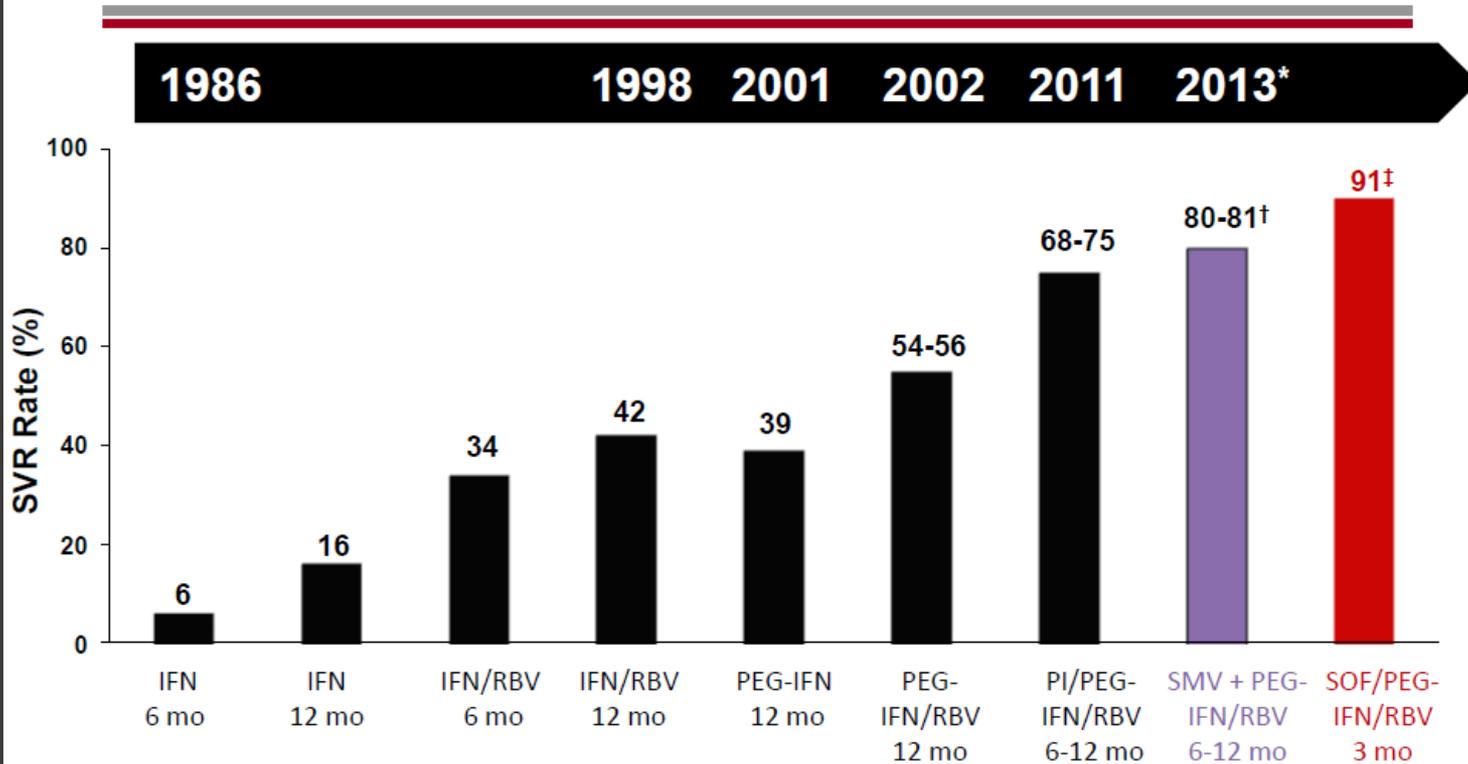
Source: Armstrong GL, Wasley A, Simard EP, et al. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Ann Intern Med* 2006;144:705–14. Modified and reprinted with permission from *Annals of Internal Medicine*.

Baby-Boomer HCV Screening

- August 2012 - CDC recommends all persons born between 1945 and 1965 receive one-time testing for HCV antibody
- June 2013 - United States Preventative Services Task Force recommends all persons born between 1945 and 1965 receive one-time testing for HCV antibody
- October 2013 - Legislation in NY State requires physicians to offer HCV test to patients born between 1945 and 1965

Improved Treatments

SVR Rates in Patients With HCV



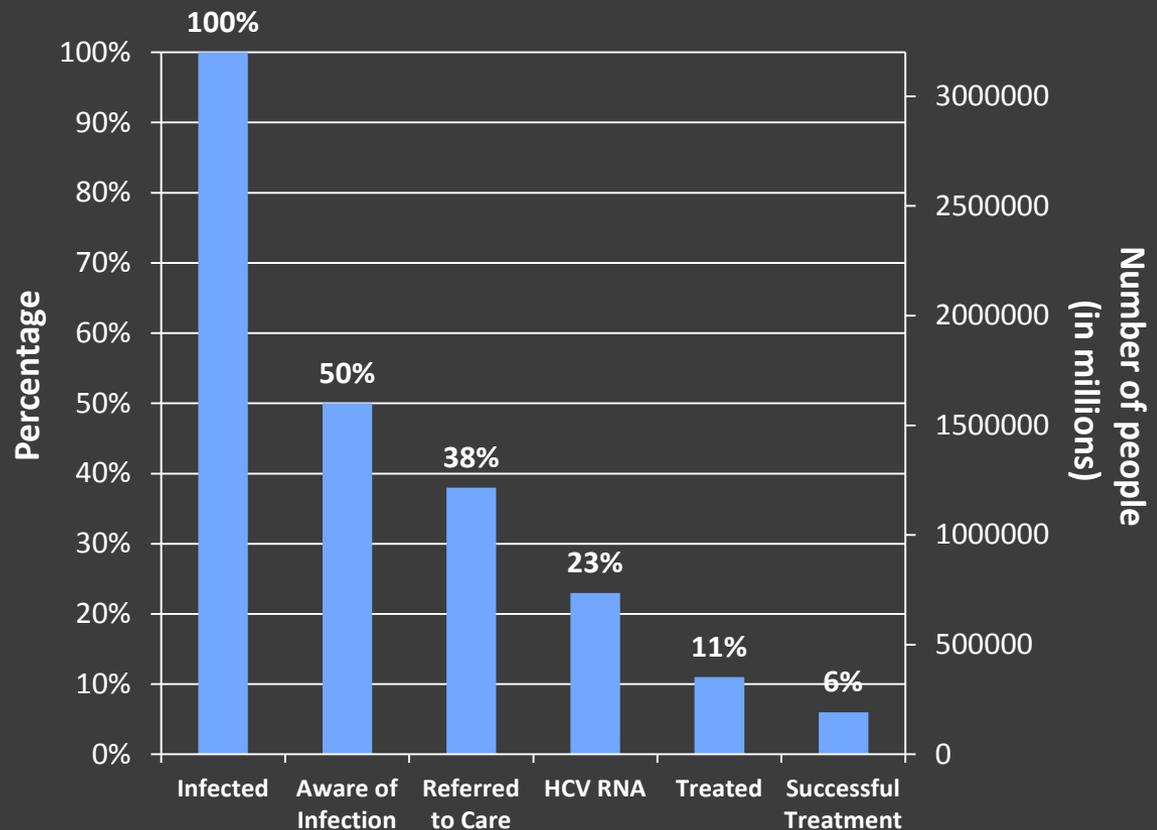
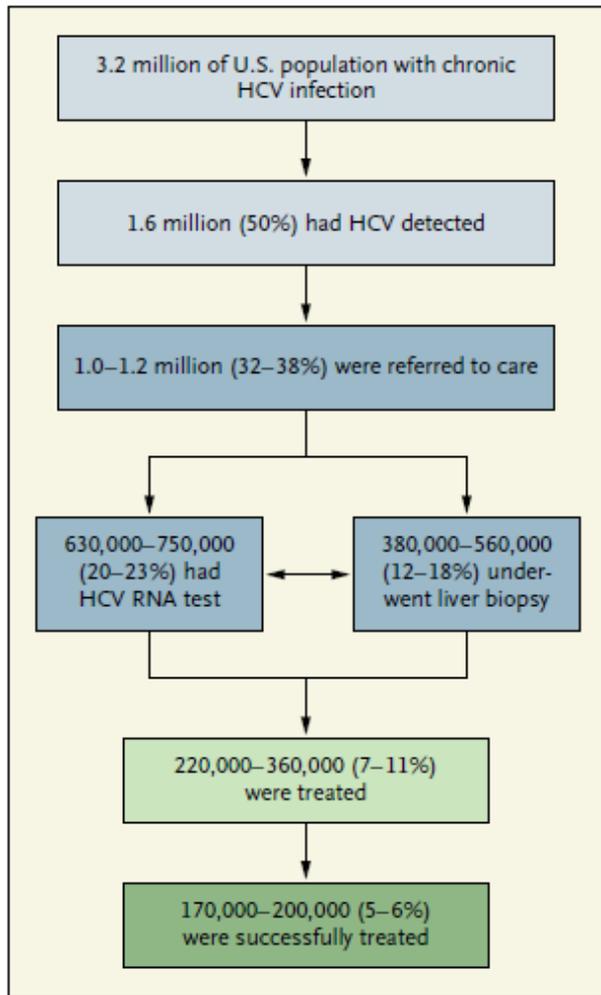
*Year of presentation of QUEST-1, QUEST-2, and NEUTRINO

†SVR12 rate of 80-81% among GT 1 patients in the Phase 3 studies QUEST-1 and QUEST-2 (24-48 weeks of SMV+PEG-IFN+RBV)

‡SVR12 rate of 90% among GT 1 patients in the Phase 3 NEUTRINO trial (12 weeks of SOF+PEG-IFN+RBV)

Adapted from Strader DB, et al. Hepatology 2004;39:1147-71. INCIVEK [PI]. Cambridge, MA: Vertex Pharmaceuticals; 2012. VICTRELIS [PI]. Whitehouse Station, NJ: Merck & Co; 2011. Jacobson I, et al. EASL 2013. Amsterdam. The Netherlands. Poster # 1425. Manns M, et al. EASL 2013. Amsterdam. The Netherlands. Oral #1413. Lawitz E, et al. APASL 2013. Singapore. Oral #LB-02

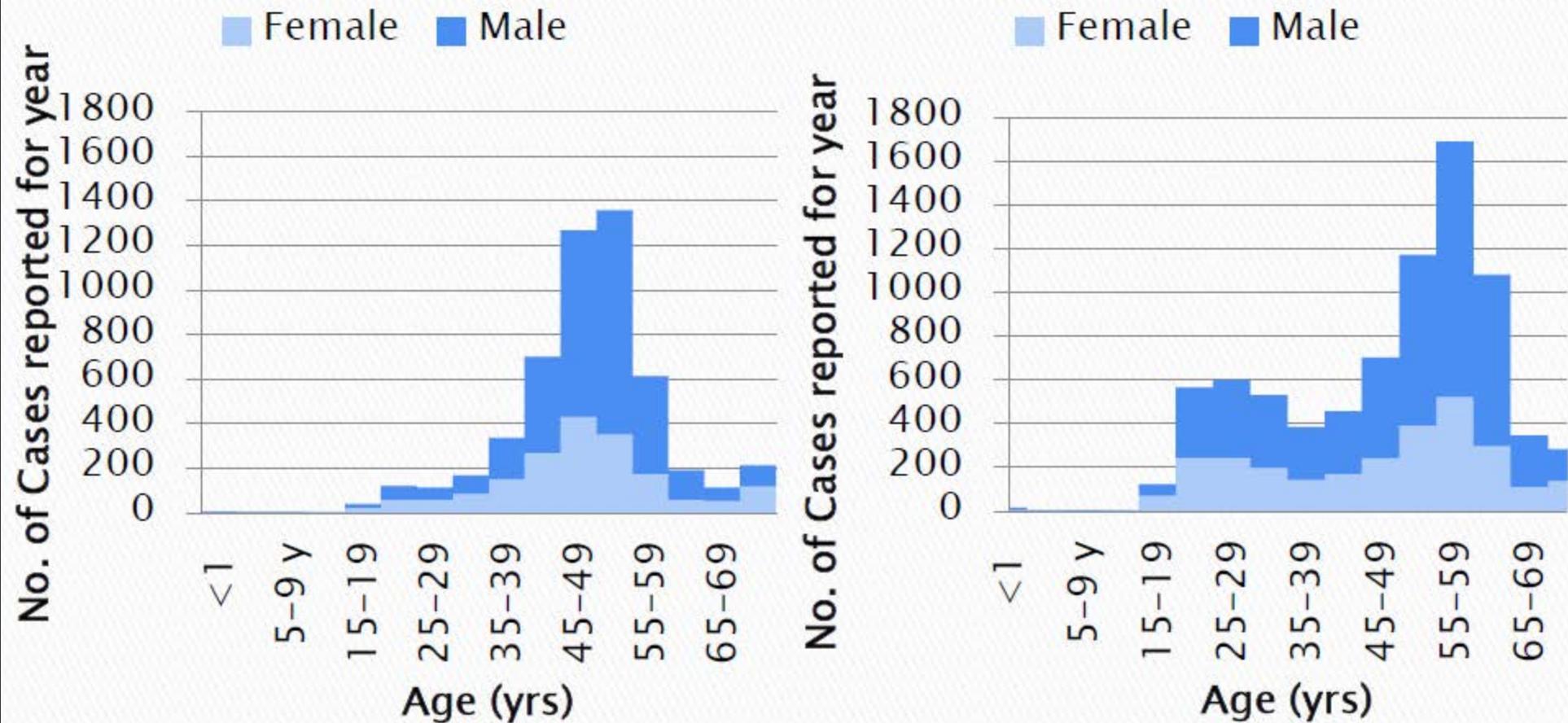
Treatment Cascade



Confirmed Cases of Hepatitis C Infection Michigan, 2004 and 2012

2004*

2012†

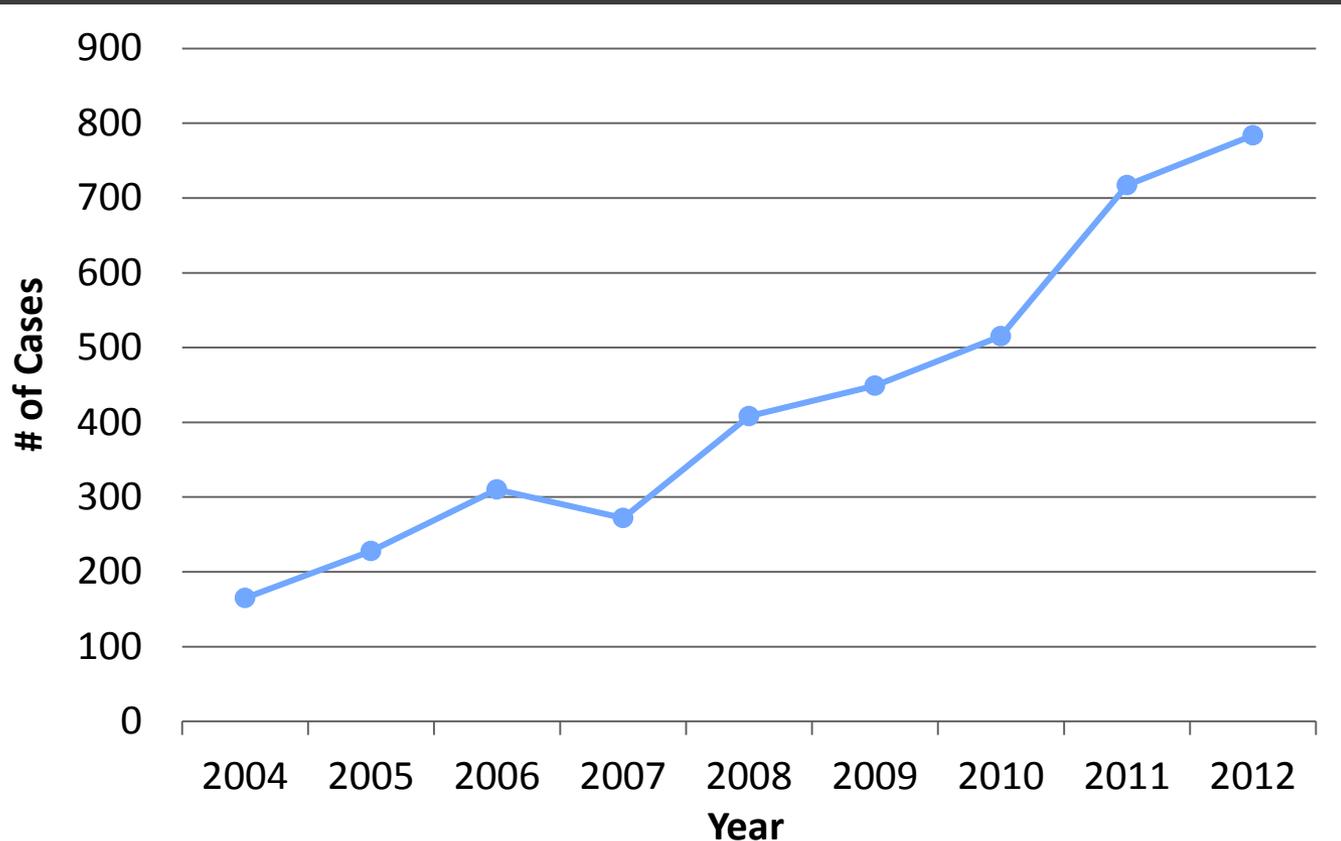


*N= 5,270; excludes 38 cases with missing age or sex information

†N= 7,968; excludes 56 cases with missing age or sex information

Young Adults with HCV Infection

Chronic Hepatitis C Cases among persons aged 18 to 25 reported to MDSS

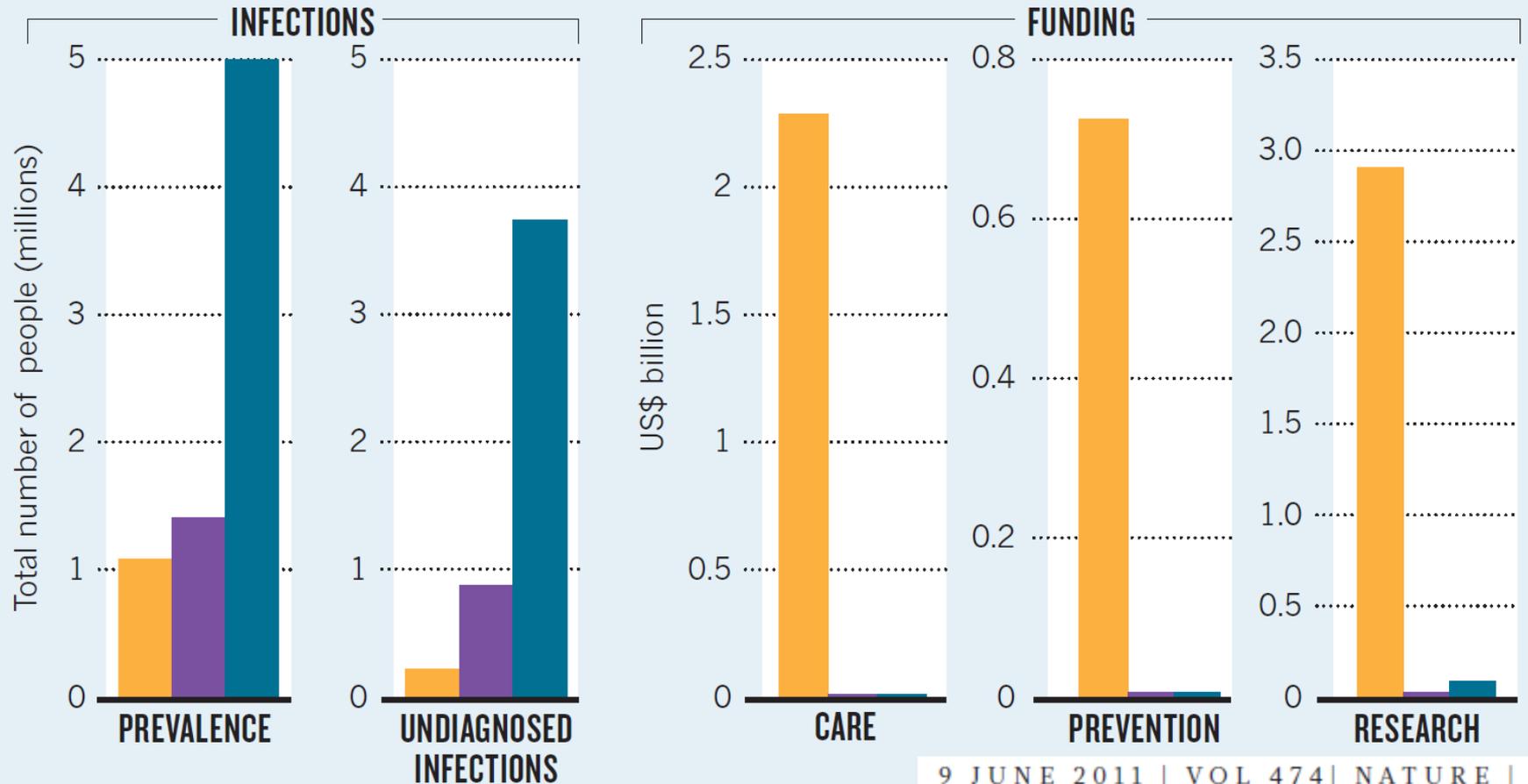


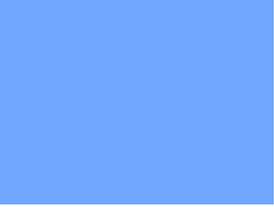
Year	Cases
2004	165
2005	228
2006	310
2007	272
2008	408
2009	449
2010	515
2011	717
2012	784

Funding?

US RESPONSE TO HIV AND VIRAL HEPATITIS EPIDEMICS

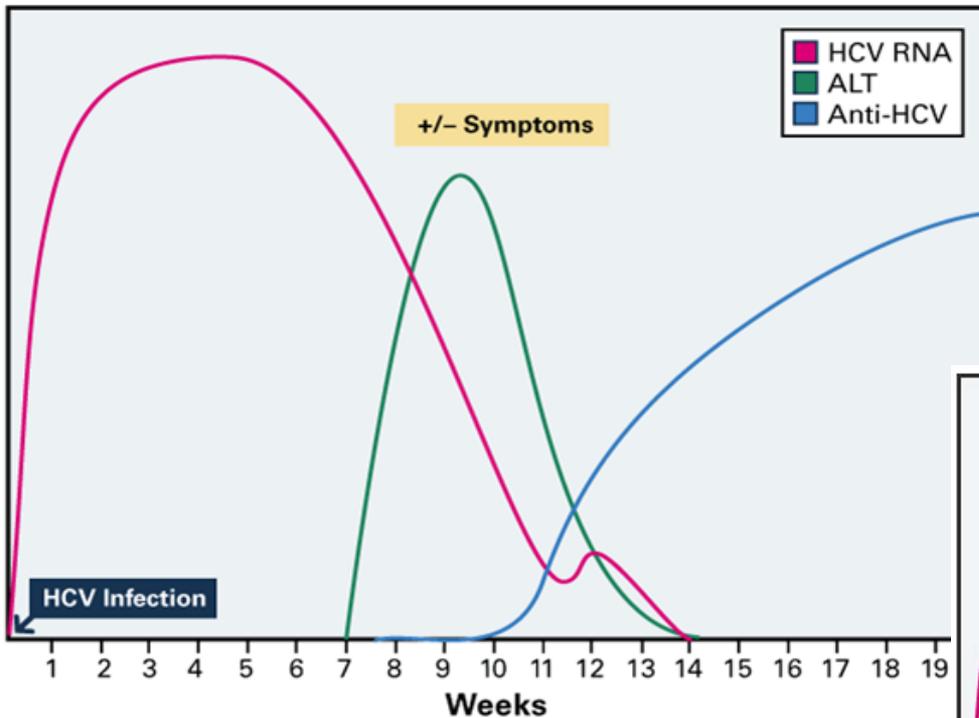
Hepatitis C infection is at least five times more prevalent as HIV infection in the United States, yet funding lags far behind.



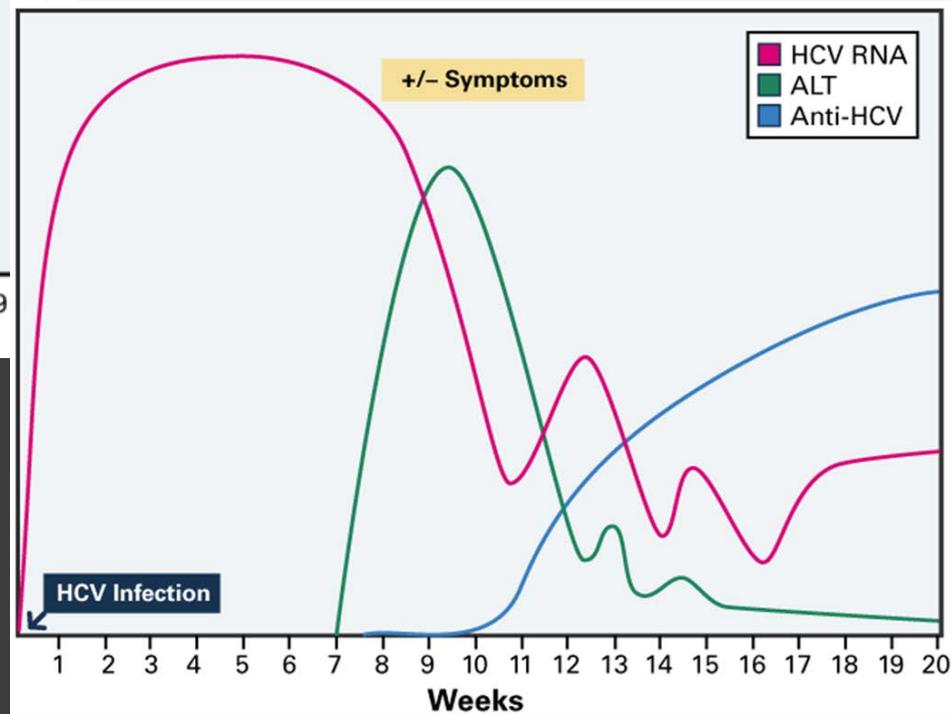


Hepatitis C Surveillance and Reporting

Clinical HCV Testing



Patient clears HCV infection (~15-25%)



Persistent HCV infection (~75-85%)



HCV Case Definitions

- Positive Hepatitis C tests are required to be reported:
 - HCV Antibody tests
 - Qualitative and Quantitative HCV RNA tests
 - HCV Genotype tests
- HCV cases are classified according CDC/CSTE case definitions

	Unknown	Suspect	Probable	Confirmed	Not a Case
Hepatitis C, Acute	✘	✘	✘	✓	✓
Hepatitis C, Past or Present	✘	✘	✓	✓	✓

HCV Labs

- HCV Antibody (Anti-HCV, HCV Ab) – detects the presence of antibodies against the Hepatitis C Virus:
 - With high S/CO Ratio:

Results	
Reported Test Name : HCV AB SER QL EIA/HEPATITIS C ANTIBODY	
Alternate Coded Result :	REACTIVE
Numeric Result :	
Reported Test Name : HCV AB S/CO SERPL EIA-RTO/SIGNAL TO CUT-OFF	
Numeric Result :	37 . 40
Abnormal Flags/Susceptibility Results:	H
<input type="button" value="Reset"/> <input type="button" value="Cancel"/> <input type="button" value="Help"/>	

- Without S/CO Ratio:

Results	
Reported Test Name :	
Coded Result :	Positive
Numeric Result :	
<input type="button" value="Reset"/> <input type="button" value="Cancel"/> <input type="button" value="Help"/>	

Signal to Cutoff Ratios

Screening Test Kit Name	Manufacturer	Assay Format	Signal-to-cut-off ratio predictive of a true positive \geq 95% of the time
Ortho HCV Version 3.0 ELISA Test System	Ortho	EIA (Enzyme Immunoassay)	≥ 3.8
Abbott HCV EIA 2.0	Abbott	EIA (Enzyme Immunoassay)	≥ 3.8
VITROS Anti-HCV	Ortho	CIA (Chemiluminescent Immunoassay)	≥ 8.0
AxSYM Anti-HCV	Abbott	MEIA (Microparticle Immunoassay)	≥ 10.0
Architect Anti-HCV	Abbott	CMIA (Chemiluminescent Microparticle Immunoassay)	≥ 5.0
Advia Centaur HCV	Bayer	CIA (Chemiluminescent Immunoassay)	≥ 11.0

HCV Nucleic Acid Tests

- An HCV Nucleic Acid Test (NAT) must be conducted to detect the Hepatitis C virus itself:
 - HCV RNA Quantitative PCR:

Results	
Reported Test Name : HCV RNA SERPL PCR-ACNC/HCV RNA, QUANTITATIVE REAL TIME PCR	
Numeric Result :	8810 IU/MLIU/MLL

- HCV RNA Qualitative PCR:

Results	
Reported Test Name : Hepatitis C virus RNA/HCV RNA	
Coded Result :	Detected
Alternate Coded Result :	Detected
Numeric Result :	
Abnormal Flags/Susceptibility Results:	N
Comments :	Reference Range: Not Detected Lower limit of detection is 1,000 IU/ml

- HCV Genotype:

Reported Test Name : HCV GENTYP SERPL PCR/HCV GENOTYPE, LIPA	
Alternate Coded Result :	GENOTYPE 1b
Numeric Result :	

HCV Quantitative Tests

❑ Negative / Not Detected

Results	
Reported Test Name : Hepatitis C virus RNA/HCV RNA	
Coded Result :	-Not Detected
Alternate Coded Result :	-Not Detected
Numeric Result :	
Abnormal Flags/Susceptibility Results:	N

❑ Some number IU/mL (e.g. 3,562,822 IU/mL)

Reported Test Name : Hepatitis C RNA Quant V-Load	
Text Result :	3360217
Numeric Result :	
Abnormal Flags/Susceptibility Results:	H

❑ < Some number IU/mL (e.g. <43 IU/mL)

Results	
Reported Test Name : HCV RNA SERPL BDNA-ACNC/HCV RNA QUANTIFICATION, S	
Numeric Result :	< 615 IU/ML
	THIS ASSAY CANNOT DETERMINE AN ACCURATE HCV RNA LEVEL BELOW THIS LIMIT.
Reported Test Name : HCV RNA	
Coded Result :	Positive
Text Result :	<43

Hepatitis C, Acute - Confirmed

- Option 1:

- ▣ Discrete onset of acute symptoms (fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, abdominal pain)

AND

- ▣ Jaundice **OR** serum alanine aminotransferase (ALT) > 400IU/L

AND

Hepatitis C, Acute - Confirmed

- One or more of the following:
 - Positive HCV antibody result with a signal-to-cutoff ratio predictive of true positive
 - Positive HCV nucleic acid test (quantitative, qualitative, genotype)

AND (if done)

- Negative Hepatitis A IgM Antibody AND
- Negative Hepatitis B core antigen IgM Antibody

Hepatitis C, Acute - Confirmed

- Option 2:
 - ▣ One or more of the following:
 - HCV antibody positive result with a signal-to-cutoff ratio predictive of true positive
 - HCV nucleic acid test positive (quantitative, qualitative, genotype)

AND

- ▣ A negative HCV antibody test in the 6 months preceding the positive result

Omar



Hepatitis C, Past or Present – Confirmed

- Must meet the following criteria:
 - ▣ One or more of the following:
 - HCV antibody positive result with a signal-to-cutoff ratio predictive of true positive
 - HCV nucleic acid test positive (quantitative, qualitative, genotype) – this must be true for patients <18 months old

AND

- ▣ Does not meet the definition for Hepatitis C, Acute

Hepatitis C, Past or Present – Probable

- Must meet the following criteria:
 - ▣ Positive HCV Antibody test with unknown signal-to-cutoff ratio

AND

- ▣ ALT values above the upper limit of normal

AND

- ▣ Does not meet the case definition for Hepatitis C, Acute

Evidence of acute illness with a discrete onset of any sign or symptom* consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, abdominal discomfort, diarrhea, nausea, vomiting)?

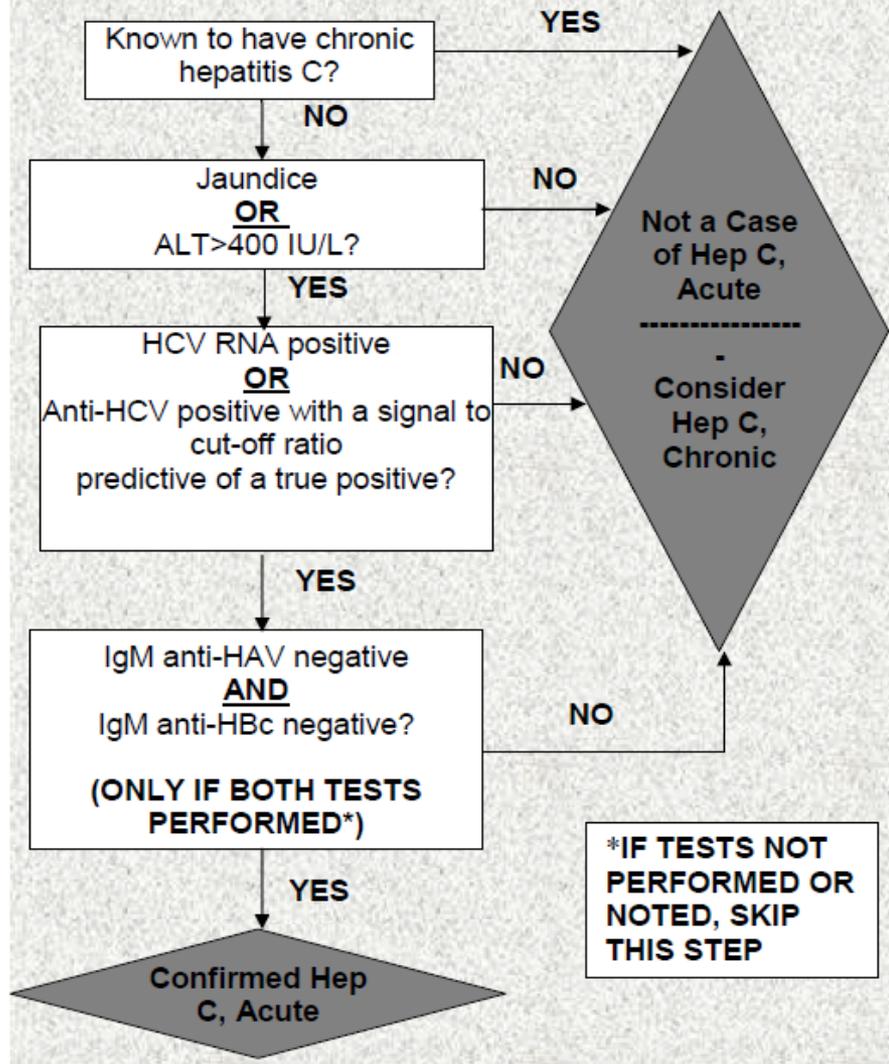
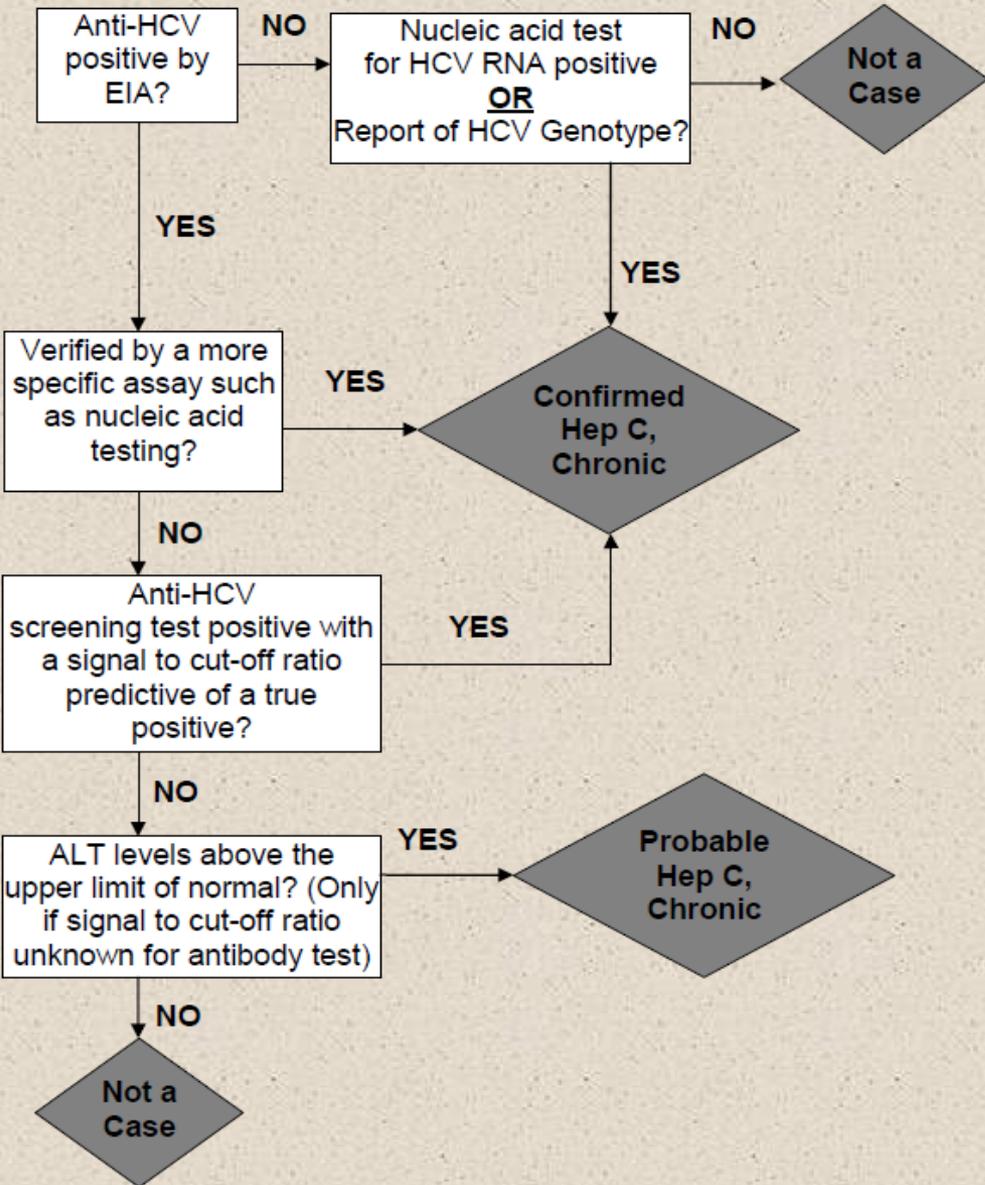
*A documented negative HCV antibody laboratory test result followed within 6 months by a positive test result does not require symptoms to meet acute case definition

NO or UNKNOWN

YES

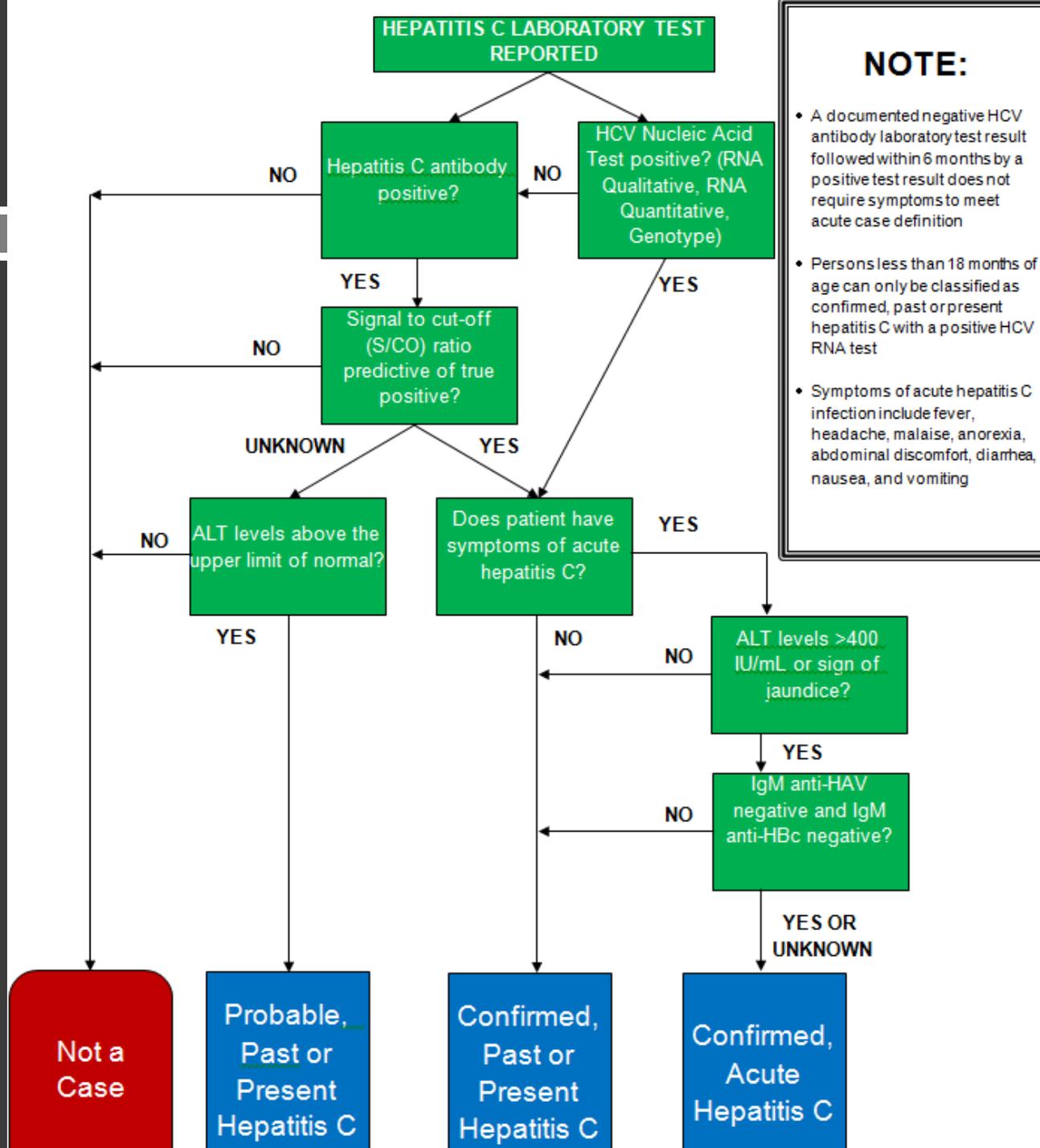
Chronic Hepatitis C Track

Acute Hepatitis C Track



*IF TESTS NOT PERFORMED OR NOTED, SKIP THIS STEP

Hepatitis C Reporting Flowchart



NOTE:

- A documented negative HCV antibody laboratory test result followed within 6 months by a positive test result does not require symptoms to meet acute case definition
- Persons less than 18 months of age can only be classified as confirmed, past or present hepatitis C with a positive HCV RNA test
- Symptoms of acute hepatitis C infection include fever, headache, malaise, anorexia, abdominal discomfort, diarrhea, nausea, and vomiting

Deduplication

- A person should only be counted once in their lifetime for chronic HCV
- For people with multiple HCV positive labs:
 - ▣ Merge the patient and merge the case
- A person can be an acute case and a chronic case if the labs are >6 months apart:
 - ▣ Merge the patient, create a new case

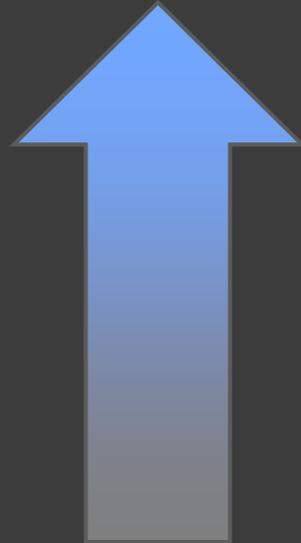
Case Follow-up

- For completed cases meeting a CDC/CSTE case definition:

Type of Case

Follow-up

Active



Passive

Hepatitis C Case

Acute Cases

Young Adults (ages 18-25)

Persons Born Before 1945

Other Groups

Resources

- CDC/CSTE Case Definitions -
<http://wwwn.cdc.gov/NNDSS/script/ConditionList.aspx?Type=0&Yr=2014>
- www.cdc.gov/hepatitis
- www.cdc.gov/knowmorehepatitis
- www.cdc.gov/knowhepatitisb
- www.michigan.gov/hepatitis
- www.michigan.gov/hepatitisb
- www.michigan.gov/cdinfo

Thanks!

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