

Please Stand By

You will hear silence until the
presentation begins

The HIV/STD/TB/Hepatitis Program, Division of Disease Control, conducts Lunch and Learn Webinars for health-care professionals in North Dakota.

Each month a new topic will be held from 12:00 p.m. to 1:00 p.m. CST on the **fourth Wednesday of the month.**

Next month's L&L : June 22th, 2016

Topic: Tuberculosis (TB)

Register: <http://www.ndhealth.gov/HIV/events.htm>

Please complete the post-test to receive CEU's for this presentation. You must score at least 70% to receive credit.

This presentation will be archived and available for review on:

www.ndhealth.gov/HIV/Resources/resources.htm

For questions or comments contact:

Gordana Cokrljic

701.328.2379

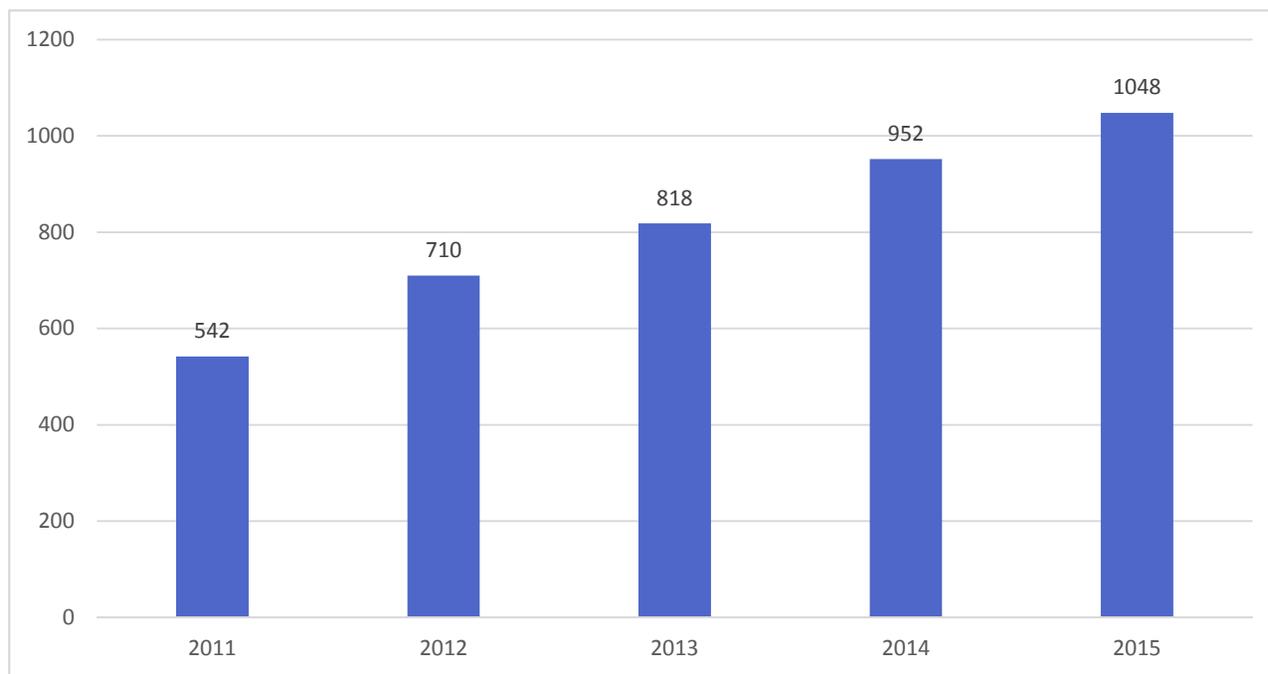
gcokrljic@nd.gov

HEPATITIS C IN NORTH DAKOTA

Gordana Cokrljic
Ryan White Part B Program Coordinator
HIV/STD/TB/Hepatitis Program
May 25, 2016

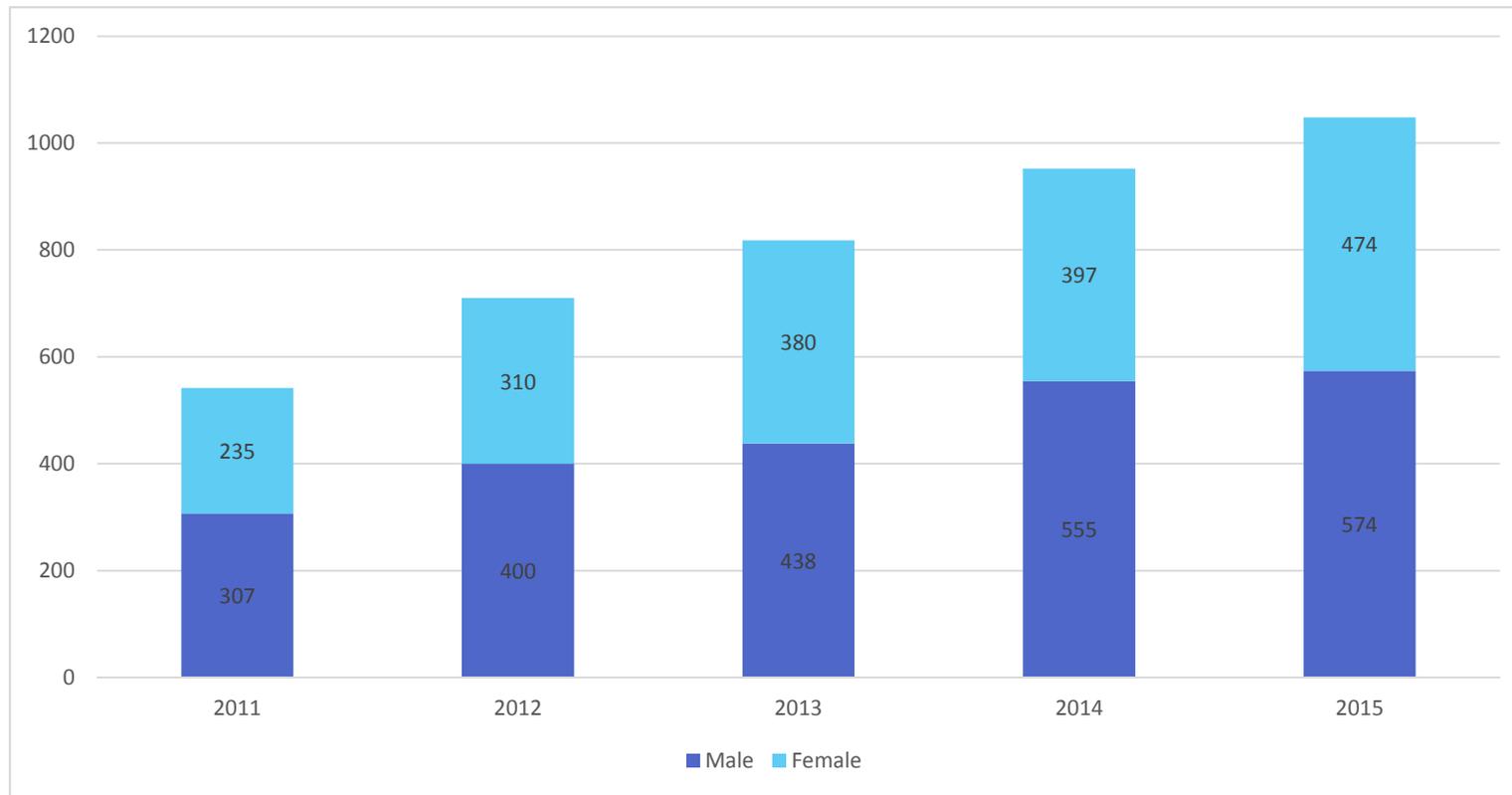


Reported Hepatitis C Cases* by Year, 2011-2015



* Includes acute and “past or present” infections

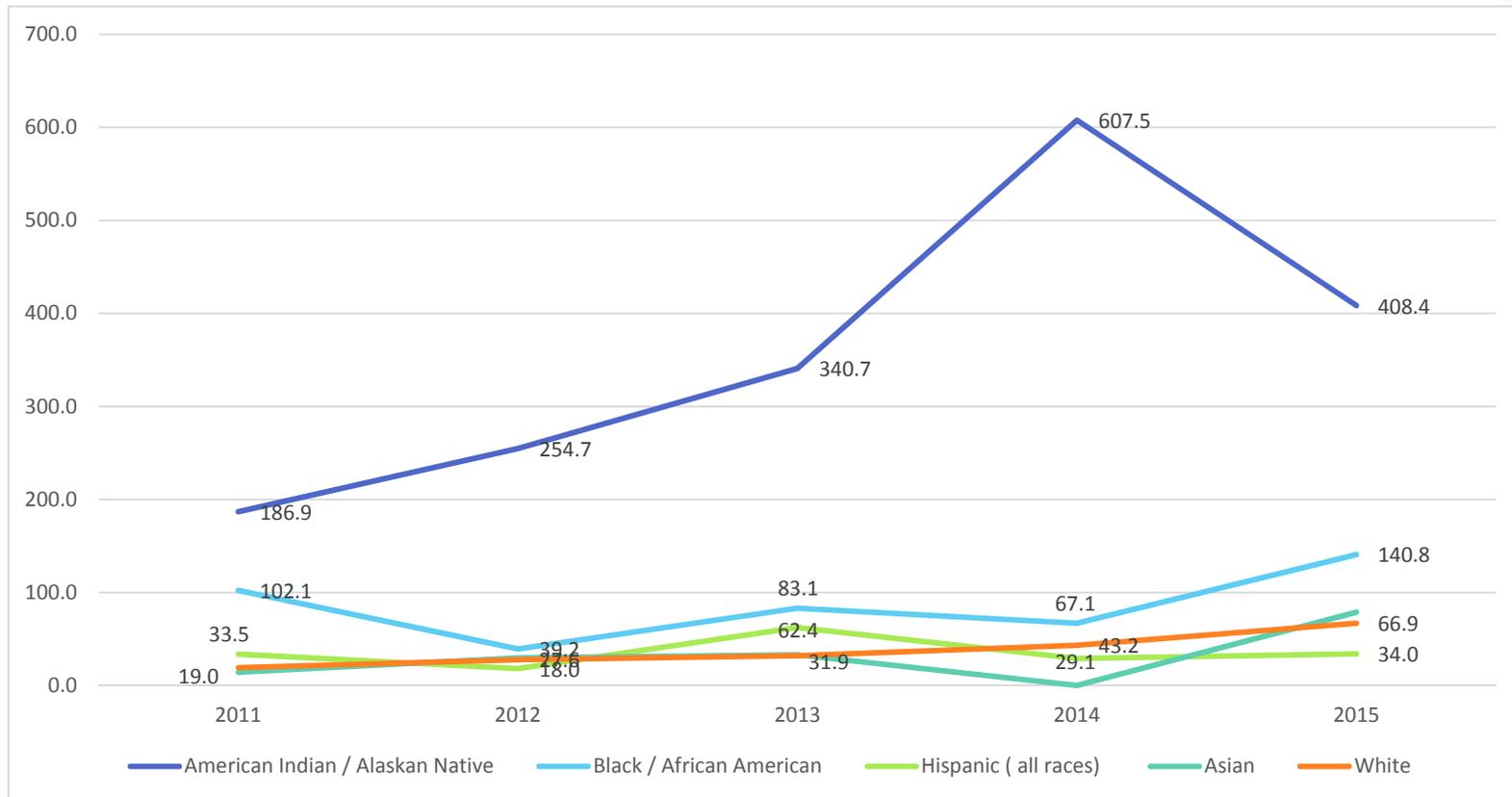
HCV Cases by Gender, 2011-2015



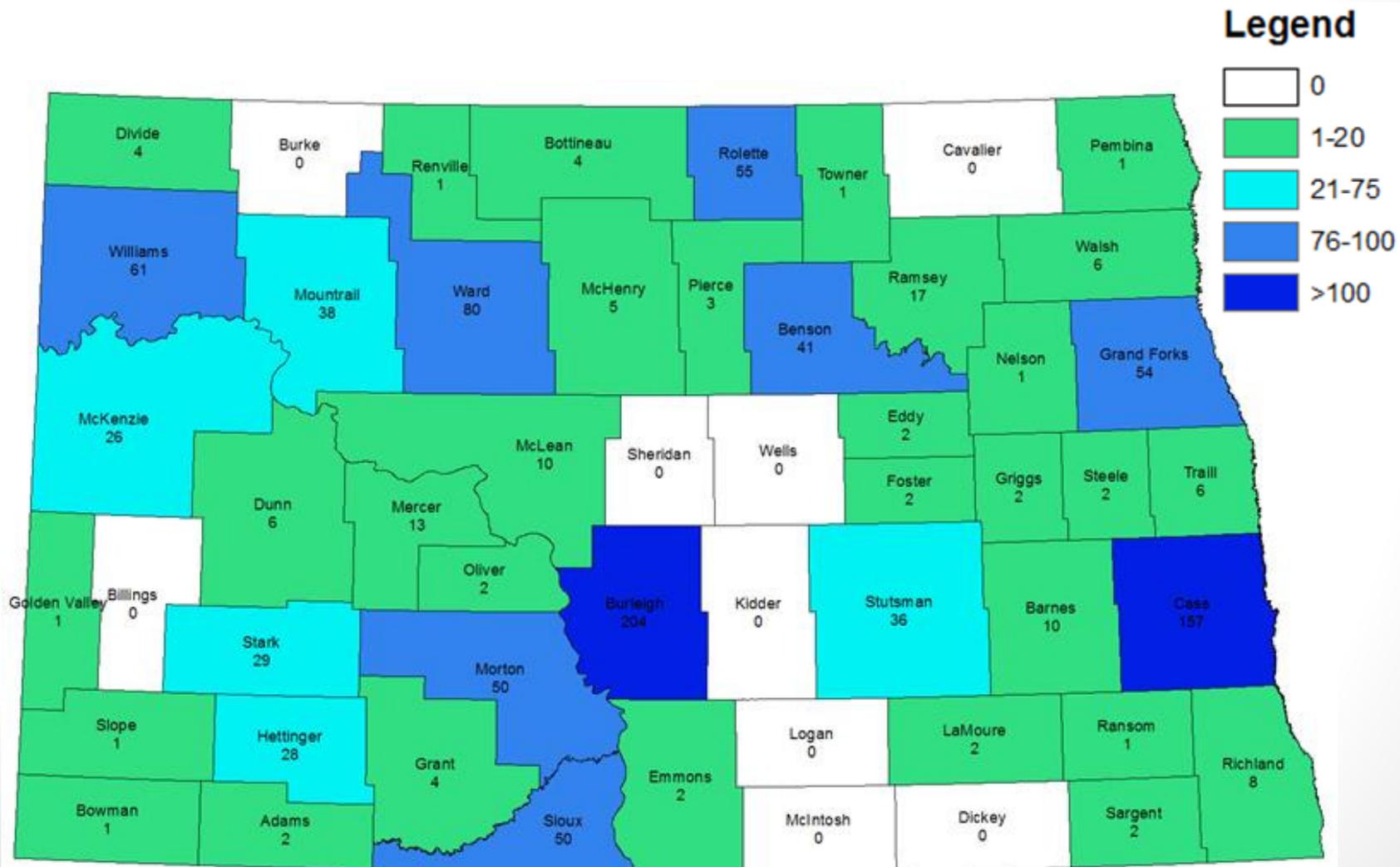
HCV Cases by Age

- The average age of reported cases in 2015 was 39 years.
- Cases reported ranged in ages between 17 and 71 years.
- Nationally, acute HCV outbreaks are being reported across the country in persons aged 20-29 years primarily due to high rates of injection drug use among this age cohort.

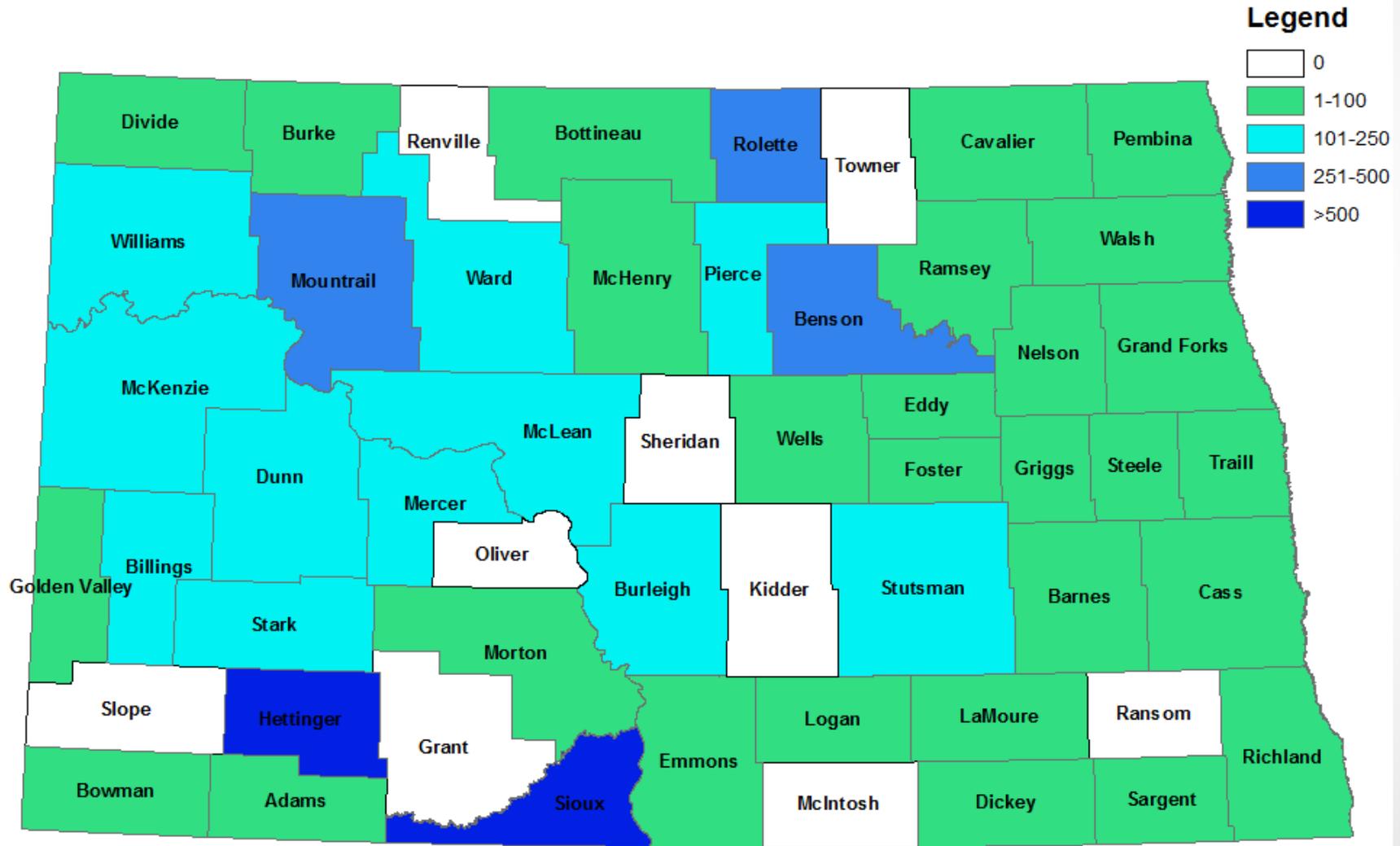
HCV Incident Rate by Race, 2011- 2015



HCV Cases by County, 2015



HCV Rates by County, 2014



HCV Reporting

- Hepatitis C is a mandatory reportable condition
 - All positive laboratory results of HCV Ab or RNA are reportable to NDDoH regardless of whether or not the case is the incident or prevalent case.
 - All instances of ACUTE PRESENTATION should be reported to NDDoH by calling the Division of Disease Control at 701.328.2378.

HCV Screening Recommendations

- Adults born during **1945 through 1965** should be tested once (without prior ascertainment of HCV risk factors)
- HCV-testing is recommended for those who:
 - **Currently inject drugs**
 - Ever injected drugs, including those who injected once or a few times many years ago
 - Have certain medical conditions, including persons:
 - who received clotting factor concentrates produced before 1987
 - who were ever on long-term hemodialysis
 - with persistently abnormal alanine aminotransferase levels (ALT)
 - who have HIV infection
 - Were prior recipients of transfusions or organ transplants, including persons who:
 - were notified that they received blood from a donor who later tested positive for HCV infection
 - received a transfusion of blood, blood components or an organ transplant before July 1992
- HCV- testing based on a **recognized exposure** is recommended for:
 - Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-positive blood
 - Children born to HCV-positive women

HCV Screening Recommendations Cont.

- Persons for Whom Routine HCV Testing is of **uncertain need**
 - Recipients of transplanted tissue (e.g., corneal, musculoskeletal, skin, ova, sperm)
 - Intranasal cocaine and other non-injecting illegal drug users
 - Persons with a history of tattooing or body piercing
 - Persons with a history of multiple sex partners or sexually transmitted diseases
 - Long-term steady sex partners of HCV-positive persons

HCV Screening Recommendations Cont.

- Persons for Whom Routine HCV Testing Is **Not** Recommended (unless other risk factor is present):
 - Health-care, emergency medical, and public safety workers
 - Pregnant women
 - Household (nonsexual) contacts of HCV-positive persons
 - General population

HCV Follow-Up by NDDoH

- N.D. Disease Intervention Specialists (DIS) do not follow-up non-acute cases of Hepatitis C given the course of the disease.
 - Only demographic information is collected for non-acute cases.

Hepatitis C and IDU Facts

- Nationally, rising HCV rates are being reported among young injection drug users, both male and female, primarily white, found in both suburban and rural settings, who started prescription opioid use (e.g. oxycodone) before transitioning to heroin injection.
- HCV prevalence among persons who inject drugs is between 30% to 70%
- HCV can survive long periods of time on inanimate objects
 - Filter and Foils: 1-2 days
 - Surfaces (i.e. tables): About 20 days
 - Water container: About 20 days
 - In a Syringe: Over 60 days

Resources

- ND 2015 Epidemiologic Profile of HIV, STDs, TB and Viral Hepatitis in North Dakota
- CDC Hepatitis C and Injection Drug Use Fact Sheet:
www.cdc.gov/hepatitis/HCV/PDFs/FactSheet-PWID.pdf
- Resources relating to HCV & IDU:
 - www.cdc.gov/mmwr/preview/mmwrhtml/mm6417a2.htm
 - www.cdc.gov/hepatitis/Populations/idu.htm

Program Contact Information

- Division of Disease Control
 - 701.328.2378
- Sarah Weninger, MPH
 - Viral Hepatitis and STD Program Coordinator
 - sweninger@nd.gov; 701.328.2366
- Shelby Loberg, PhD Candidate
 - HIV.STD.Viral Hepatitis Surveillance Coordinator
 - sloberg@nd.gov; 701.328.1059
- Lindsey VanderBusch
 - STD/TB/HIV/Hepatitis Program Manager
 - lvanderbusch@nd.gov; 701.328.4555

Current Management of HCV Infection

Noe B. Mateo, MD

ID Consultant / Sanford Bismarck

May 25, 2016

OBJECTIVES

- Describe and discuss the basic epidemiology and natural history of HCV infection.
- Review the diagnostic and staging strategies for acute and chronic HCV infection.
- Describe and discuss special features of HCV infection in pregnancy.
- Describe and discuss prior, current and future treatment regimens for HCV infection

Disclosures

- Honoraria: Gilead

Brief History of Hepatitis C

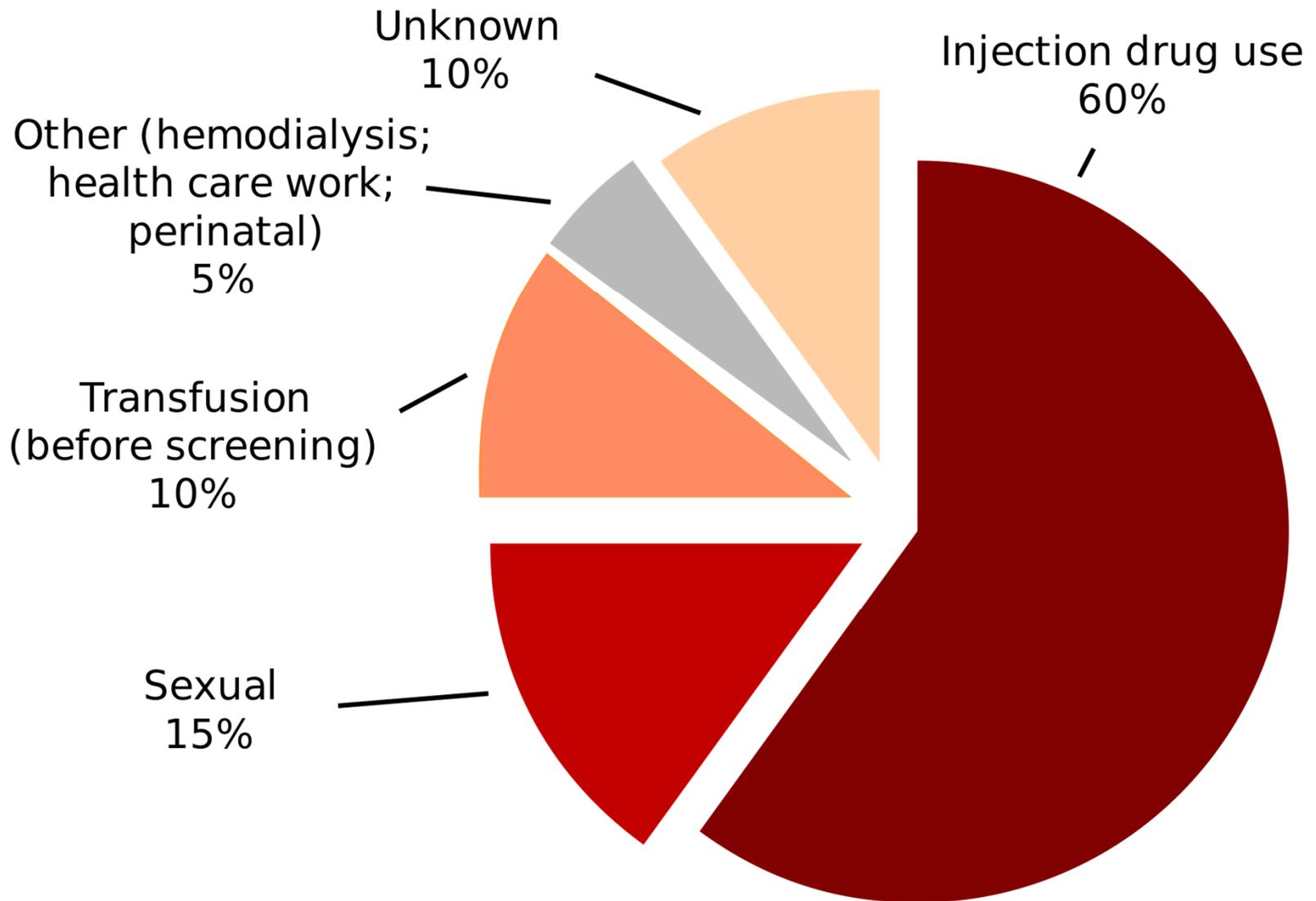
- In the mid-1970s, Harvey J. Alter and his research team at the NIH demonstrated how most post-transfusion hepatitis cases were not due to hepatitis A or B viruses.
- In 1987, Michael Houghton, Qui-Lim Choo, and George Kuo at Chiron Corporation, collaborating with Dr. D.W. Bradley at the CDC, used a novel molecular cloning approach to identify the unknown organism and develop a diagnostic test.
- In 1988, Alter confirmed the virus by verifying its presence in a panel of NANBH specimens.
- In April 1989, the discovery of HCV was published in two articles in the journal *Science*
- Drs. Alter and Houghton were honored with the Lasker Award for Clinical Medical Research for "pioneering work leading to the discovery of the virus that causes hepatitis C and the development of screening methods that reduced the risk of blood transfusion-associated hepatitis in the U.S. from 30% in 1970 to virtually zero in 2000

Risk Groups

Table 1: New Expanded Recommendations for Hepatitis C, August 2012⁵

All persons born from 1945 through 1965

- Existing, risk-based guidelines:
 - Anyone who has ever injected illegal drugs
 - Recipients of blood transfusions or solid organ transplants before July 1992, or clotting factor concentrates made before 1987
 - Patients who have ever received long-term hemodialysis treatment
 - Persons with known exposures to hepatitis C, such as:
 - Health care workers after needle sticks involving blood from a patient with hepatitis C
 - Recipients of blood or organs from a donor who later tested positive for hepatitis C
- People living with HIV
- People with signs or symptoms of liver disease (e.g., abnormal liver enzyme tests)
- Children born to mothers who have hepatitis C



Risk Groups

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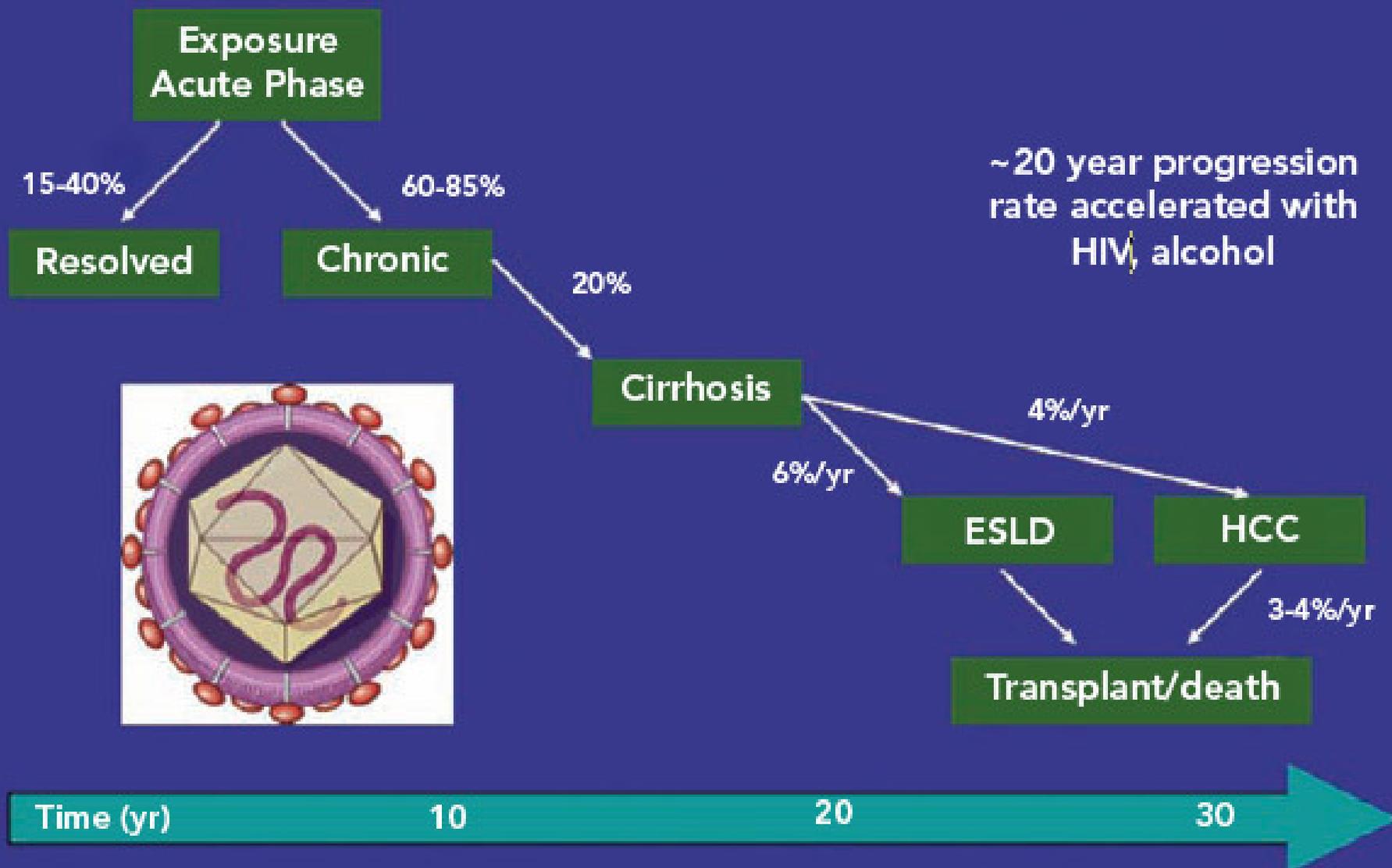
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Transmission of Viral Hepatitis

| Transmission Route | Hepatitis A | Hepatitis B | Hepatitis C | Hepatitis D | Hepatitis E |
|---------------------|-------------|-------------|-------------|-------------|-------------|
| Food - Borne | ● | ■ | ■ | ■ | ● |
| Fecal - Oral | ● | ■ | ■ | ■ | ● |
| Water - Borne | ● | ■ | ■ | ■ | ● |
| Raw Shellfish | ● | ■ | ■ | ■ | ● |
| Intra-Institutional | ● | ● | ● | ● | ● |
| I.V. Drug Use | ▲ | ● | ● | ● | ■ |
| Transfusion | ▲ | ● | ● | ● | ▲ |
| Hemodialysis | ■ | ● | ● | ● | ■ |
| Sexual | ▲ | ● | ▲ | ● | ▲ |
| Anal - Oral Contact | ● | ■ | ■ | ■ | ▲ |
| Oral - Oral Contact | ● | ▲ | ■ | ■ | ● |
| Household | ● | ▲ | ▲ | ▲ | ● |
| Mother to Newborn | ▲ | ● | ▲ | ● | ▲ |

● **Common**
 ▲ **Infrequent**
 ■ **Never**
 ● **Suspected**

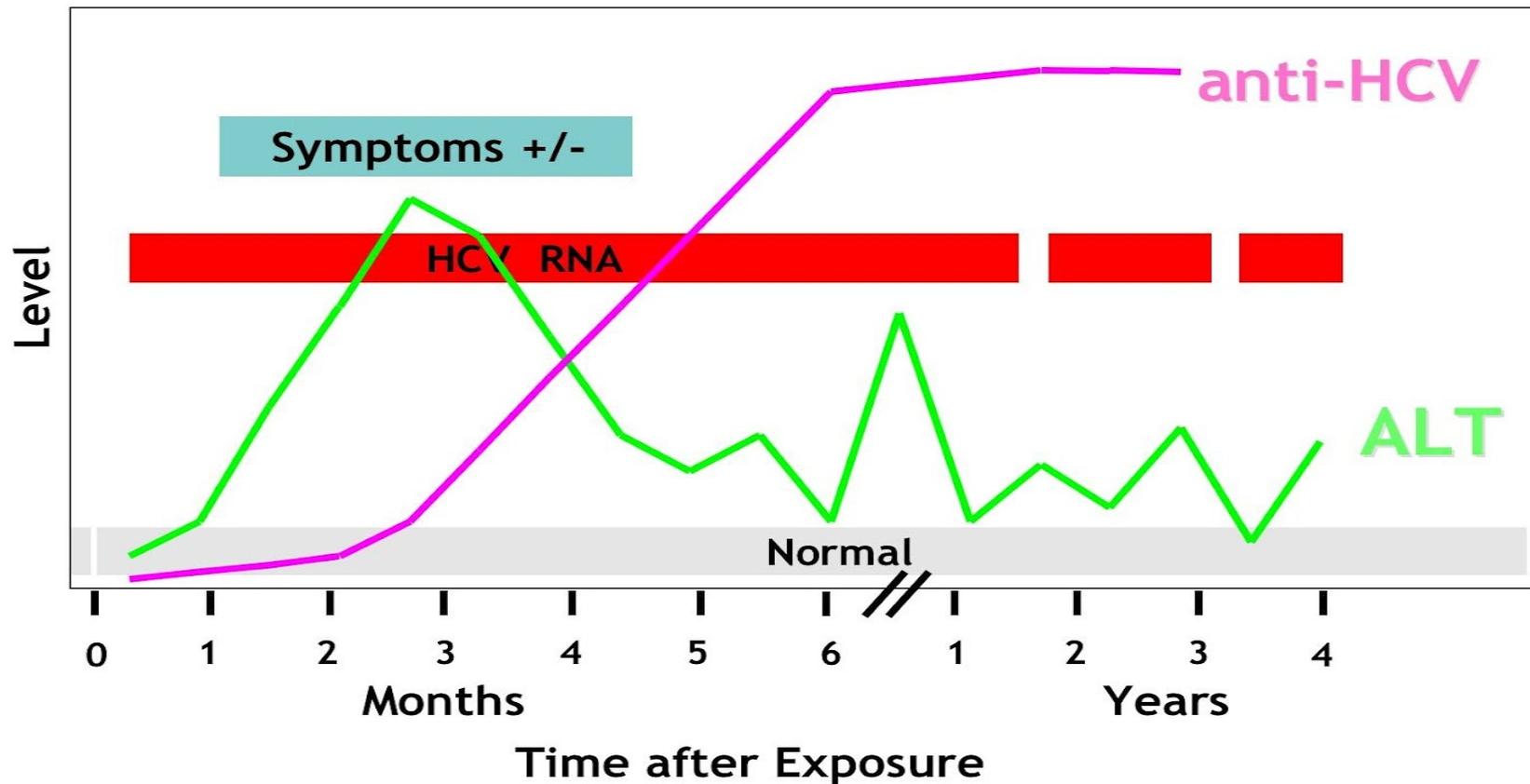
Natural History of HCV Infection



HCC = hepatocellular carcinoma
ESLD = end-stage liver disease

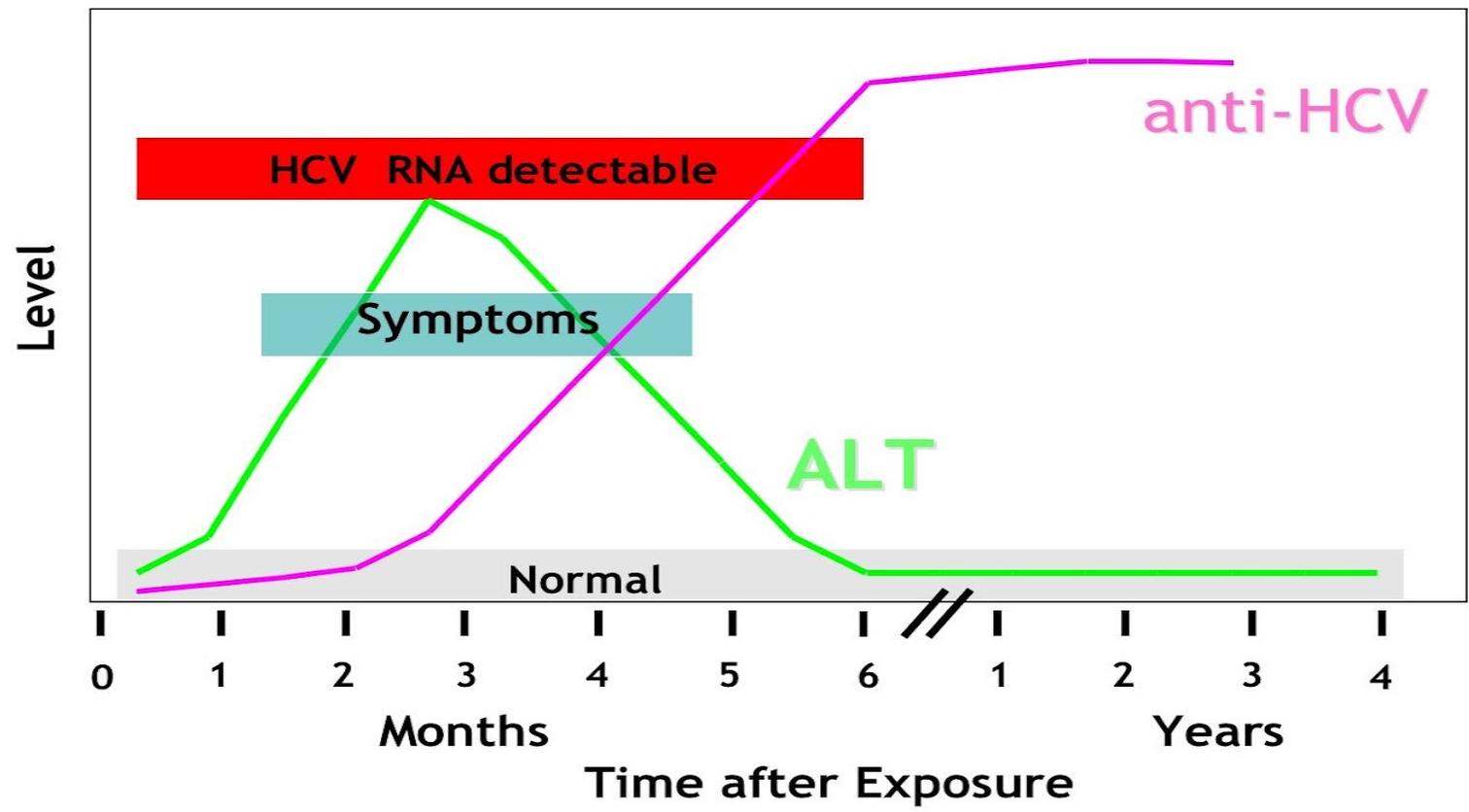
Adapted from: Di Bisceglle et al. *Hepatology*. 2000;31(4):1014-1018.

Acute HCV Infection Evolving to Chronic Infection



Source: Adapted from MMWR 1998; 47(No. RR19)

Acute HCV Infection with Recovery



Source: Adapted from MMWR 1998; 47(No. RR19)

CDC Case Definition for Acute HCV

- Acute HCV infection is usually defined as an **estimated duration of infection less than 6 months**.
- Most patients with acute HCV infection do not have a symptomatic illness or have very mild non-specific symptoms that may include malaise, anorexia, and abdominal pain.
- When patients develop symptomatic acute HCV infection (30-40%), they most often present with jaundice, dark urine, nausea, abdominal pain, and malaise.
- The key laboratory studies utilized in the evaluation of possible acute hepatitis C are **HCV RNA, anti-HCV, and alanine aminotransferase (ALT)**.
- With acute HCV, patients usually first have detectable HCV RNA, followed by elevation in ALT, and followed last by development of anti-HCV.
- **The gold standard for diagnosis is anti-HCV seroconversion combined with a positive HCV RNA test and elevated ALT. Acute HCV infection rarely causes a life-threatening illness.**
- The CDC has a well-established case definition for acute HCV that includes both clinical and laboratory criteria.

Acute Hepatitis C: 2012 CDC Case Definition

Clinical Description

An acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., anorexia, abdominal discomfort, nausea, vomiting), **AND** Jaundice/dark urine *or* serum alanine aminotransferase (ALT) levels greater than 400 IU/L

Laboratory Criteria for Diagnosis

Meets one of three criteria

- Antibodies to hepatitis C virus (anti-HCV) screening-test-positive, **OR**
- Hepatitis C Virus Recombinant Immunoblot Assay (HCV RIBA) positive, **OR**
- Nucleic Acid Test (NAT) for HCV RNA positive (including qualitative, quantitative or genotype testing)

And, if done, meets the following two criteria

- IgM antibody to hepatitis A virus (IgM anti-HAV) negative, **AND**
- IgM antibody to hepatitis B core antigen (IgM anti-HBc) negative

Case Classification

Confirmed: A case that meets the clinical case definition, is laboratory confirmed, and is not known to have chronic hepatitis C.

Tests Used in the Diagnosis of Hepatitis C

| Anti-HCV EIA* | HCV RNA** | Interpretation |
|------------------|-----------------|---|
| Negative | Negative | Not infected |
| Positive | Negative | Resolved HCV infection |
| Negative | Positive | Early acute HCV infection or chronic HCV infection in immune compromised person |
| Positive | Positive | Acute or chronic HCV infection |

* EIA = enzyme-linked immunoassay is the type of antibody test used to screen for hepatitis C.

** There are many different types of tests available to measure HCV RNA. When used to make or exclude a diagnosis of hepatitis C, the assay must have a lower limit of detection of 50 IU/ml or less of HCV RNA.

Diagnostic Tests Used in Persons with Chronic HCV Infection

| Test Type | What is the Test Used for? | How Result is Reported |
|---|---|--------------------------------|
| HCV antibody (anti-HCV) | To screen for prior exposure to HCV | Positive or Negative |
| HCV RNA qualitative tests | To confirm current infection with HCV To determine whether treatment resulted in clearance of HCV | Positive or Negative |
| HCV RNA viral load tests (also called quantitative tests) | At the beginning and during treatment to assess response | # of viral "copies" (in IU/ml) |
| HCV genotype | Determines likelihood of responding to the treatment and how treatment is carried out (dose and duration) | 1a, 1b, 2a, 2b, 3a, 4, 5, or 6 |

Evaluating for Treatment Suitability

- **Liver factors**
 - Liver ultrasound
 - Liver biopsy
 - Fibroscan
 - FibroTest
 - FibroSure
- **Cirrhotics [GI referral]**
 - Child-Turcotte-Pugh score [q 3-6 months]
 - MELD score [q 3-6 months]
 - EGD
 - Abdominal Ultrasound [q 6 months]
 - Transplant evaluation [if MELD score ≥ 12]

Evaluating for Treatment Suitability

- **Host factors:**

- Drug/alcohol use
- Depression
- Obesity
- Diabetes mellitus
- Hemodialysis
- Cirrhosis
- Immune suppression
- Co-infections [HIV, HBV]
- OTC / Herbal use

- **Laboratory testing:**

- CBC/diff/PLTs
- LFTs / PT-INR
- HAV, HBV serostatus
- HIV serostatus
- ANA
- 25-OH D3 level
- TSH
- Uric Acid
- Alpha-fetoprotein
- Ferritin

Pre-Treatment Factors

- Patient readiness
- Genotype
- Co-morbidities
- Prior therapy [? intolerance, ? non-responder, ? relapser]
- Cirrhotics / Dialysis / Auto-immune disorders
- Acute HCV infection
- HIV / HBV co-infection
- Funding

Hepatitis C and Pregnancy / I

- A low vertical transmission rate of 3–5%, a high rate of spontaneous clearance (25–50%) and delayed morbidity have resulted in HCV being overlooked in pregnant women and their infants.
- Factors known to increase the risk of perinatal transmission include HIV coinfection and higher maternal viral loads, while elective C-section and withholding breastfeeding have not been demonstrated to reduce vertical transmission.
- Current guidelines for the diagnosis of persistent perinatal infection require a positive anti-HCV test in infants born to infected mothers after 12 months or two positive HCV RNA tests at least 6 months apart.

Hepatitis C and Pregnancy / II

- Worldwide, the seroprevalance of HCV in pregnant women is thought to be anywhere from 0.15% to 2.4% in the United States and European countries and much higher in countries like Egypt where it is estimated to be as high as 8.6%.
- The prevalence of HCV infection in children ranges from 0.05% to 0.36% in studies carried out in the United States and Europe, and is much higher in developing countries where it can range from 1.8% to 5%.
- Given that most perinatal HCV infections are silent with long-term complications that present later in adulthood, it is a considerably underestimated childhood disease with a predicted significant economic and health burden on society.

Hepatitis C and Pregnancy / III

- Some studies have shown that there is a decrease in serum alanine transferase levels (ALT) in the 2nd and 3rd trimesters of pregnancy, along with a corresponding increase in HCV RNA during these trimesters.
- Conversely, HCV RNA titres tend to decrease in the postpartum period. A study from Japan on 22 pregnant HCV RNA-positive women noted that some women may have spontaneous resolution of viremia following parturition.
- Some authors have also recommended that this may be an optimal time to initiate antiviral treatment, which can augment the natural defense mechanism.

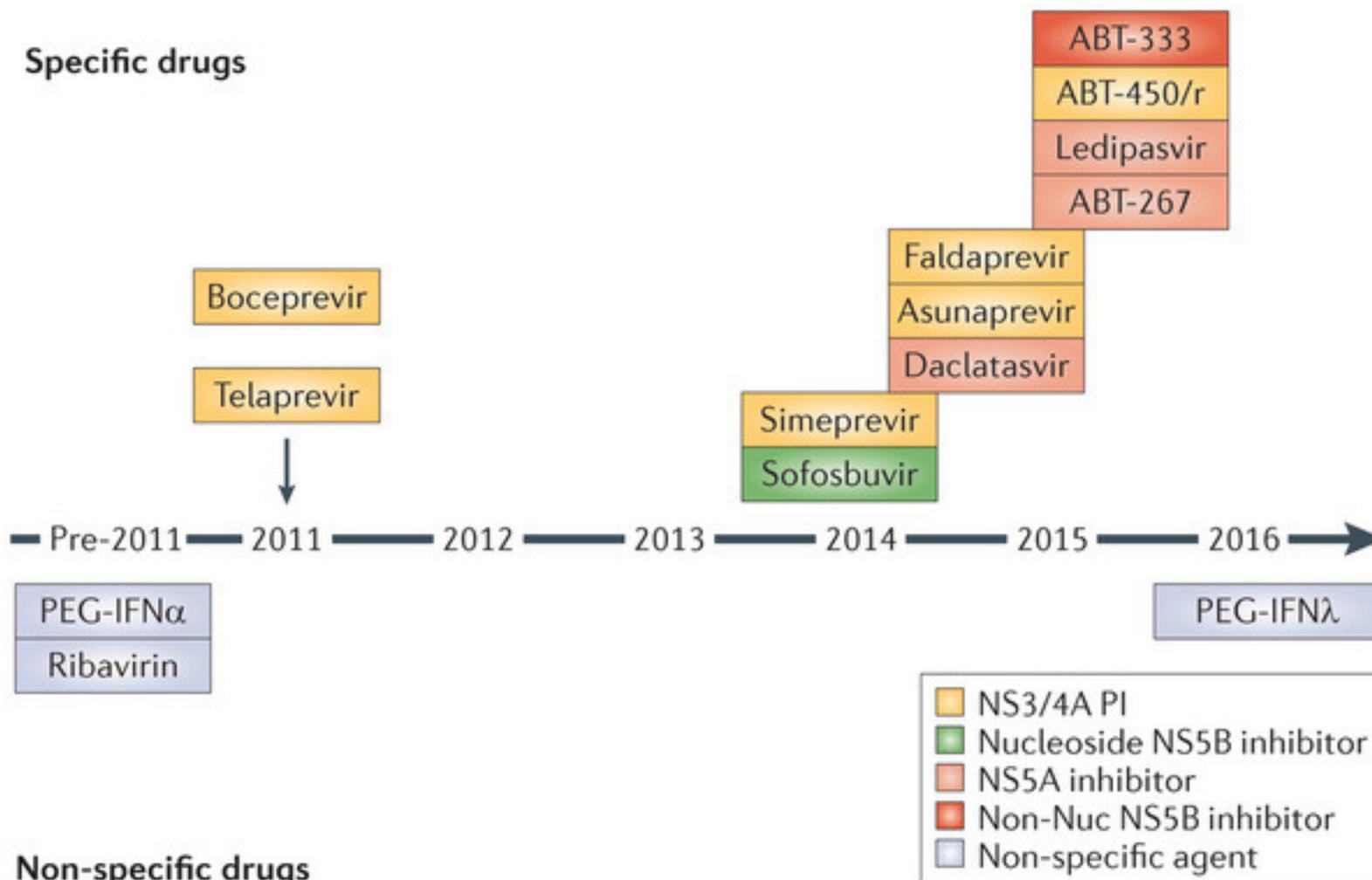
Hepatitis C and Pregnancy / IV

- In cases where vertical transmission occurs, it is likely that HCV is transmitted *in utero* at an early or middle stage of pregnancy.
- The incidence of HCV vertical transmission is approximately 3–5% in HCV RNA-positive-monoinfected mothers, but can be as high as 19% in HIV-coinfected mothers. Even when controlling for HIV, presence of HCV viremia increases the odds of vertical transmission by 2.82-fold. Studies have shown a 0% transmission, when maternal HCV RNA is negative.
- Rupture of membranes for more than 6 h has been significantly associated with viral transmission. However, there is lack of any statistically significant data on the impact of obstetrical procedures on intrapartum HCV exposure. There is some suggestion that use of scalp electrodes may lead to HCV exposure.

Hepatitis C and Pregnancy / V

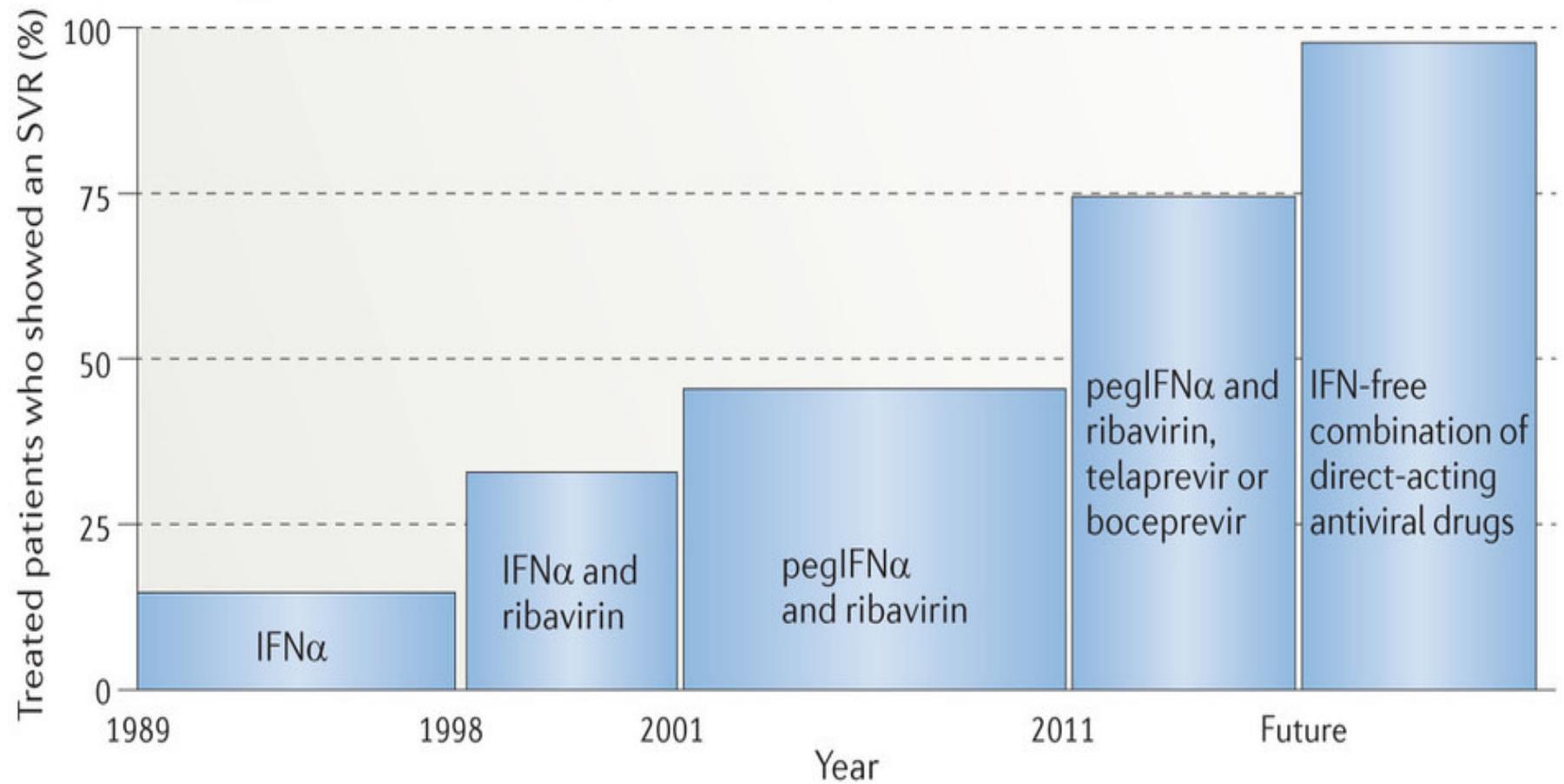
- The European Paediatric Hepatitis C Virus Network showed in a study carried out on 1758 mother–infant pairs that there was no significant difference ($P = 0.16$) in vertical transmission between elective C-section, vaginal delivery or emergent C-section.
- HCV RNA has been detected in breast milk and colostrum. However, there are only isolated studies that show some indication of HCV infection of the infant secondary to breastfeeding in mothers with a high viral load. Most studies indicate that even though theoretical transmission may be possible, the viral count in breast milk is extremely low and likely becomes inactivated in the digestive tract of the infant.
- There is no data yet on the efficacy and safety of newer antiviral agents to treat Hepatitis C during pregnancy [since PEG-IFN and RBV are contra-indicated].

Specific drugs



Non-specific drugs

Recombinant type I IFN-based therapy in chronic hepatitis C



PEGASYS® ProClick™
Autoinjectors prefilled with
PEGASYS 180 mcg or 135 mcg



Not actual size.

**Syringes prefilled
with PEGASYS**



Not actual size.

**Vials containing PEGASYS
and empty syringes**



Not actual size.











technivie™

ombitasvir, paritaprevir and ritonavir tablets
12.5mg/75mg/50mg



Estimated Medication Cost for Treatment of Genotype 1 Chronic HCV

| Regimen and Duration | Regimen Cost |
|--|--------------|
| Ledipasvir-Sofosbuvir x 8 weeks | \$63,000 |
| Ledipasvir-Sofosbuvir x 12 weeks | \$94,500 |
| Ledipasvir-Sofosbuvir x 24 weeks | \$189,000 |
| Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir +/- Ribavirin x 12 weeks | \$84,00 |
| Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir +/- Ribavirin x 24 weeks | \$168,000 |
| Sofosbuvir + Simeprevir +/- Ribavirin x 12 weeks | \$150,000 |
| Sofosbuvir + Simeprevir +/- Ribavirin x 24 weeks | \$300,000 |

Estimated Medication Cost for Treatment of Genotype 2 Chronic HCV

| Regimen and Duration | Regimen Cost |
|--|--------------|
| Sofosbuvir + Ribavirin x 12 weeks | \$85,000 |
| Sofosbuvir + Ribavirin x 16 weeks | \$113,000 |
| Sofosbuvir + Ribavirin + Peginterferon alfa x 12 weeks | \$97,000 |

Estimated Medication Cost for Treatment of Genotype 3 Chronic HCV

| Regimen and Duration | Regimen Cost |
|--|--------------|
| Sofosbuvir + Ribavirin x 24 weeks | \$169,000 |
| Sofosbuvir + Ribavirin + Peginterferon alfa x 12 weeks | \$97,000 |

Estimated Medication Cost for Treatment of Genotype 4 Chronic HCV

| Regimen and Duration | Regimen Cost |
|--|--------------|
| Ledipasvir-Sofosbuvir x 12 weeks | \$94,500 |
| Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir + Ribavirin x 12 weeks | \$84,000 |
| Sofosbuvir + Ribavirin x 24 weeks | \$169,000 |
| Sofosbuvir + Ribavirin + Peginterferon x 12 weeks | \$97,000 |
| Sofosbuvir + Simeprevir +/- Ribavirin x 12 weeks | \$150,000 |

Estimated Medication Cost for Treatment of Genotypes 5 and 6 Chronic HCV

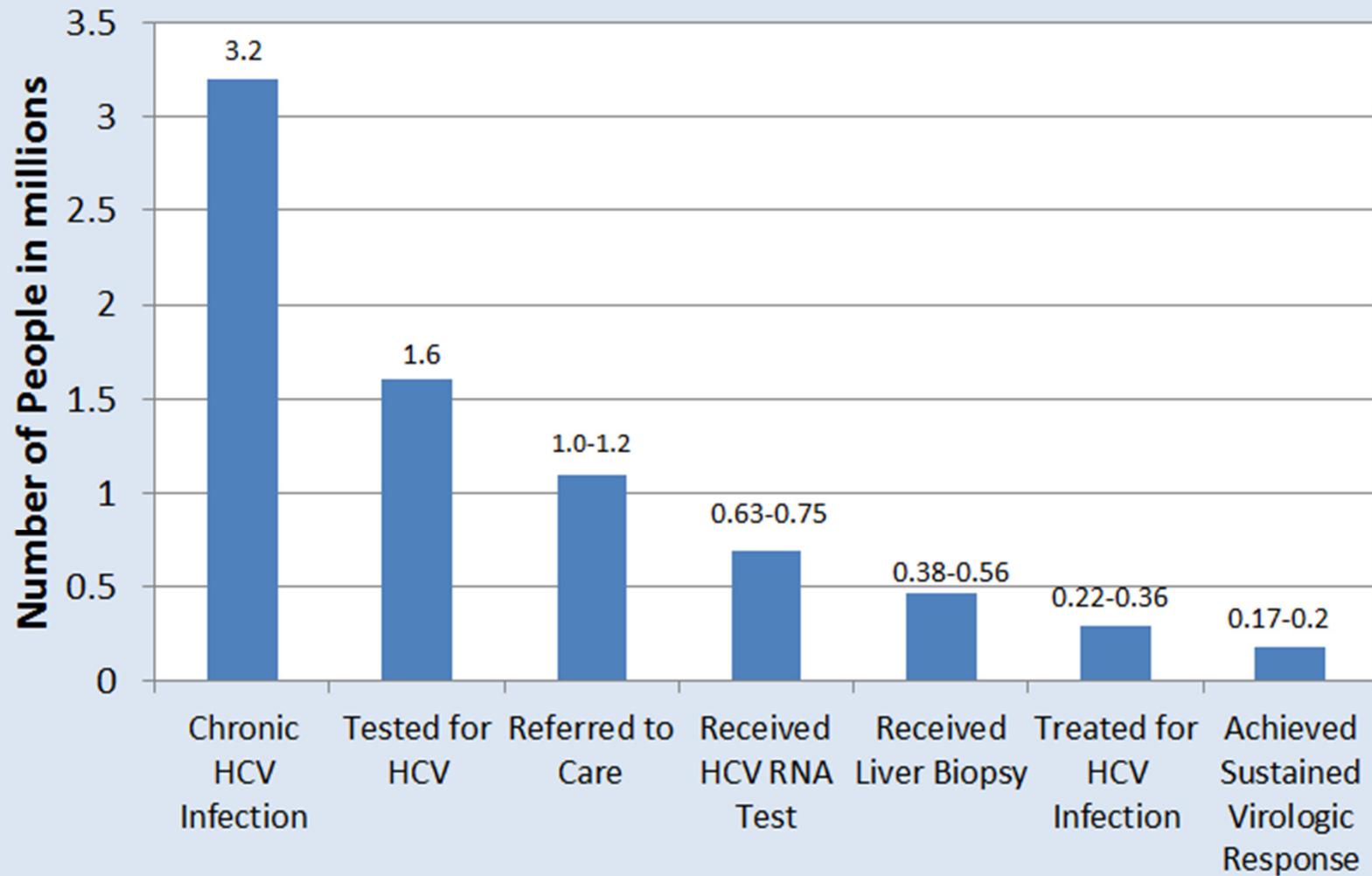
| Regimen and Duration | Regimen Cost |
|---|--------------|
| Sofosbuvir + Ribavirin + Peginterferon x 12 weeks | \$97,000 |
| Ledipasvir-Sofosbuvir x 12 weeks | \$94,500 |
| Ribavirin + Peginterferon x 48 weeks | \$27,000 |

HCV PREVALENCE IN 2013 BY HEALTH INSURANCE TYPE

| Health Insurance Type | Total U.S. Population (Thousands) | Estimated Prevalence of HCV-RNA+ | Estimated Number of HCV-RNA+ (Thousands) |
|-----------------------------|-----------------------------------|----------------------------------|--|
| Uninsured | 48,600 | 2.08% | 1,012 |
| Veteran Affairs | 5,600 | 5.40% | 302 |
| Commercial | 164,200 | 0.47% | 779 |
| Dual Medicare and Medicaid | 6,900 | 2.91% | 201 |
| Medicare (non-dual) | 37,600 | 0.31% | 117 |
| Medicaid | 43,300 | 0.87% | 377 |
| Other Military | 2,200 | 0.47% | 10 |
| Prison | 1,500 | 30.0% | 450 |
| Total | 310,000 | 1.05% | 3,249 |
| Total without Prison | 308,500 | 0.91% | 2,799 |

Sources: Milliman analysis of NHANES. Variable:LBXHCR - Hepatitis C RNA (HCV-RNA) in NHANES. Chien N, Dundoo G, Horani M et al. Seroprevalence of viral hepatitis in an older nursing home population. *J Am Geriatr Soc.* 1999;47:1110-3. Dominitz JA, Boyko EJ, Koepsell TD et al. Elevated prevalence of hepatitis C infection in users of the United States veterans medical centers. *Hepatology.* 2005;41:88-96. Chak E, Talal A, Sherman K et al. Hepatitis C virus infection in USA: an estimate of true prevalence. *Liver International.* 2011;10:1090-1101.

Number of Hepatitis C-Infected People in the U.S. and Estimated Engagement in Screening, Referral to Care and Treatment



Advice For Patients

DO:

1. Maintain a weight as close to your ideal body weight as possible (being overweight can be harmful to the liver)
2. Limit the amount of acetaminophen (Tylenol®) you use per day (24 hours) to 2000 mg daily (e.g., 4 extra-strength tablets) or less
3. Find out whether you need to be vaccinated against hepatitis A virus and hepatitis B virus
4. Consider participating in a Liver Support group or program

DON'T:

1. Drink alcohol, or if you do, limit your use to only 1 drink per day
2. Use marijuana daily
3. Use herbal remedies or supplements without checking first with your doctor
4. Eat raw oysters or other seafood if you have cirrhosis

References

- http://en.wikipedia.org/wiki/Hepatitis_C
- <http://www.roslin.ed.ac.uk/assets/profile-pages/peter-simmonds/the-origin-of-hcv.pdf>
- <http://www.nature.com/emi/journal/v3/n3/full/emi201419a.html>
- <http://www.clinicaloptions.com/HIV/Annual%20Updates/2011%20Annual%20Update/Modules/HCV%20Resistance/Pages/Page%204.aspx>
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References

- <http://www.epidemic.org/thefacts/hepatitisc/transmission.php>
- <http://www.hepatitisc.uw.edu/go/treatment-infection/treatment-genotype-1/core-concept/all>
- <http://www.hepatitisc.uw.edu/pdf/screening-diagnosis/acute-diagnosis/core-concept/all>
- <http://www.medscape.com/viewarticle/741439>