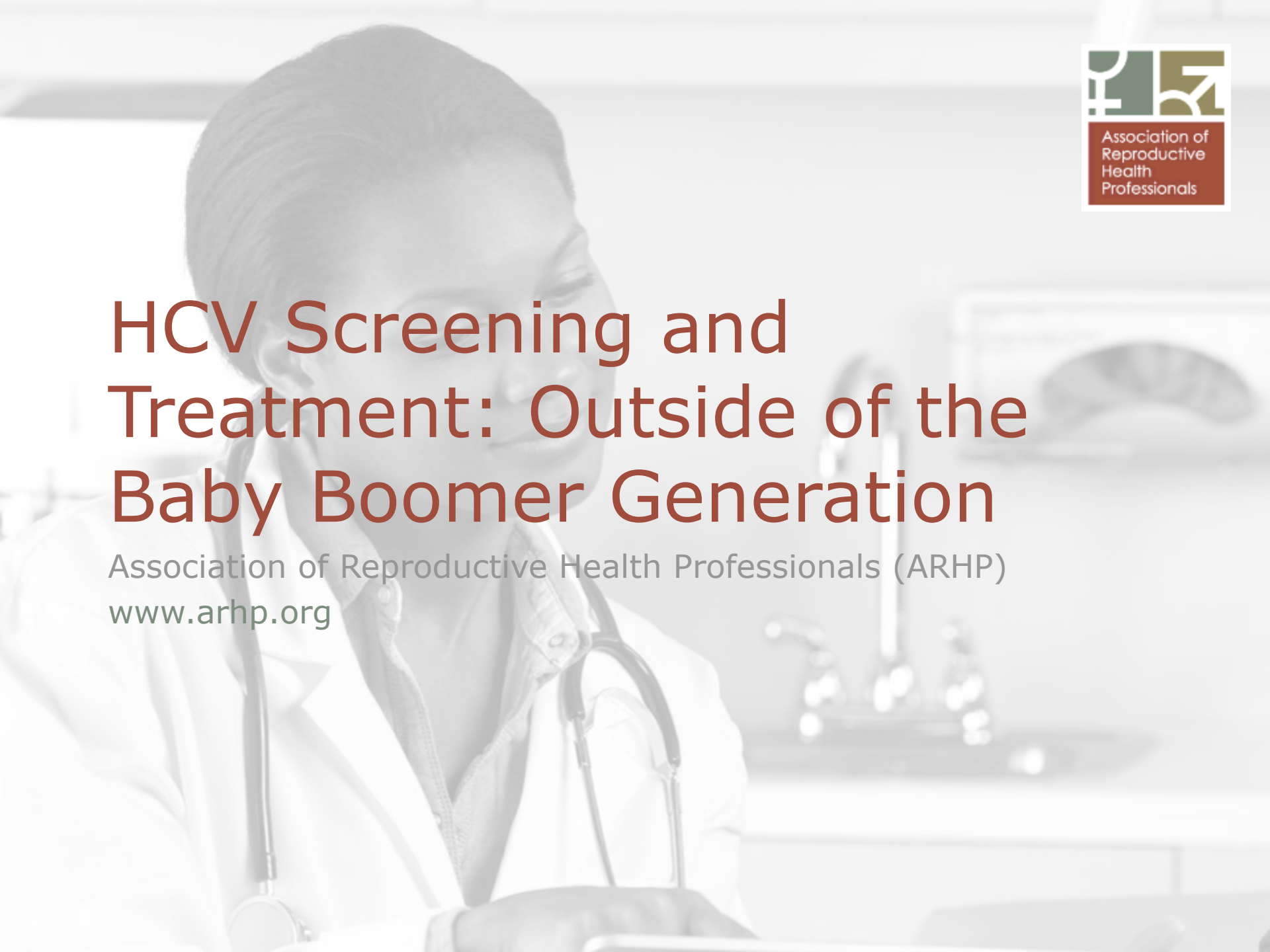


HCV Screening and Treatment: Outside of the Baby Boomer Generation

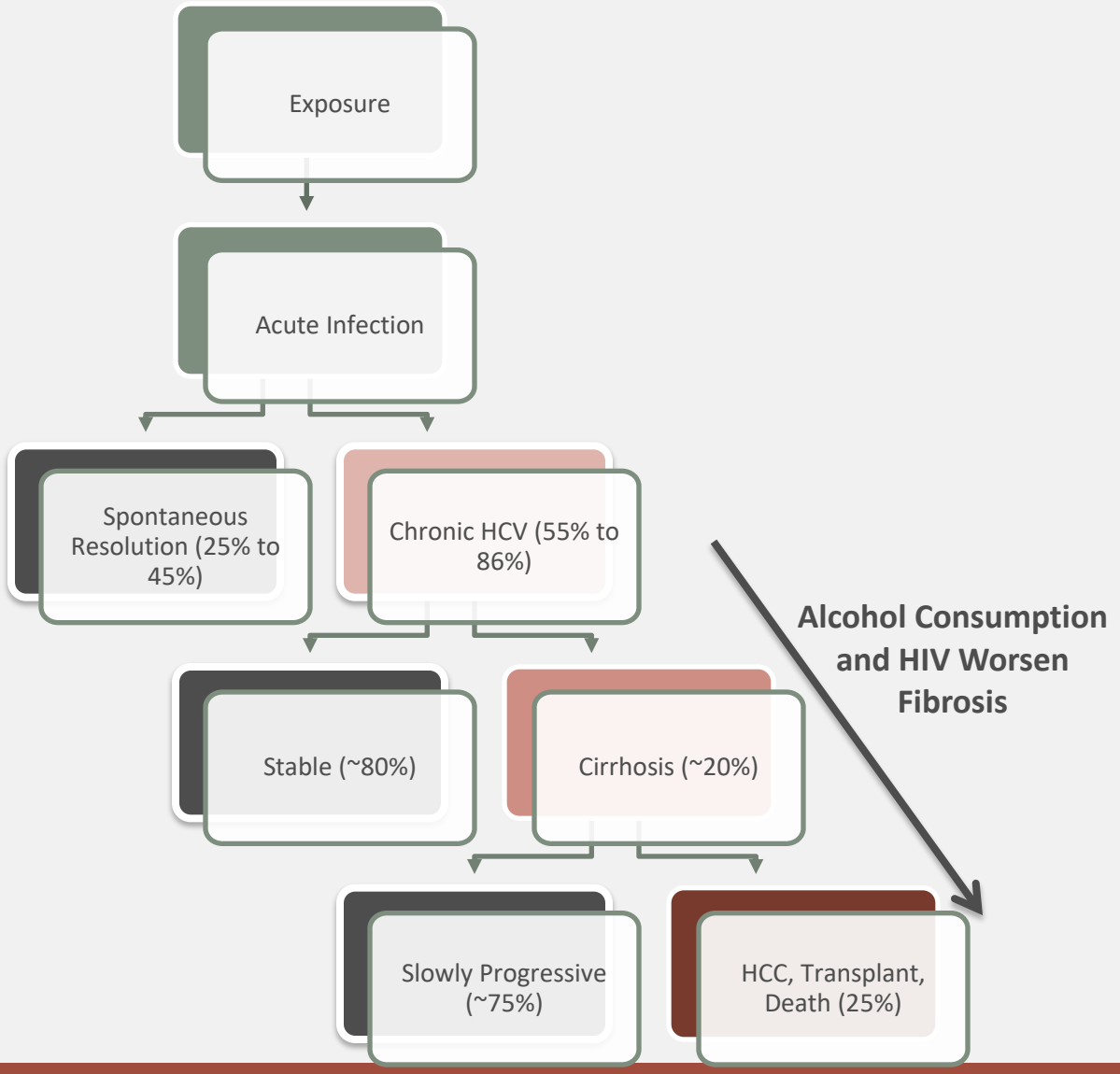
Association of Reproductive Health Professionals (ARHP)

www.arhp.org

Learning Objectives

- Identify key patient populations at risk for hepatitis C virus (HCV) infection and implement screening strategies to detect and treat for HCV
- Communicate with patients about the importance of HCV screening as well as the implications of positive antibody results, and effectively describe the treatment options and long-term outcomes
- Recognize common comorbidities of HCV and unique patient populations who will benefit from additional counseling or treatment regimen modifications
- Discuss barriers pertinent to HCV management, including treatment access and cost, adherence, and re-infection

Natural History of HCV Infection



Modified from: Alter MJ. *Semin Liver Dis*. 1996;15:5-14.

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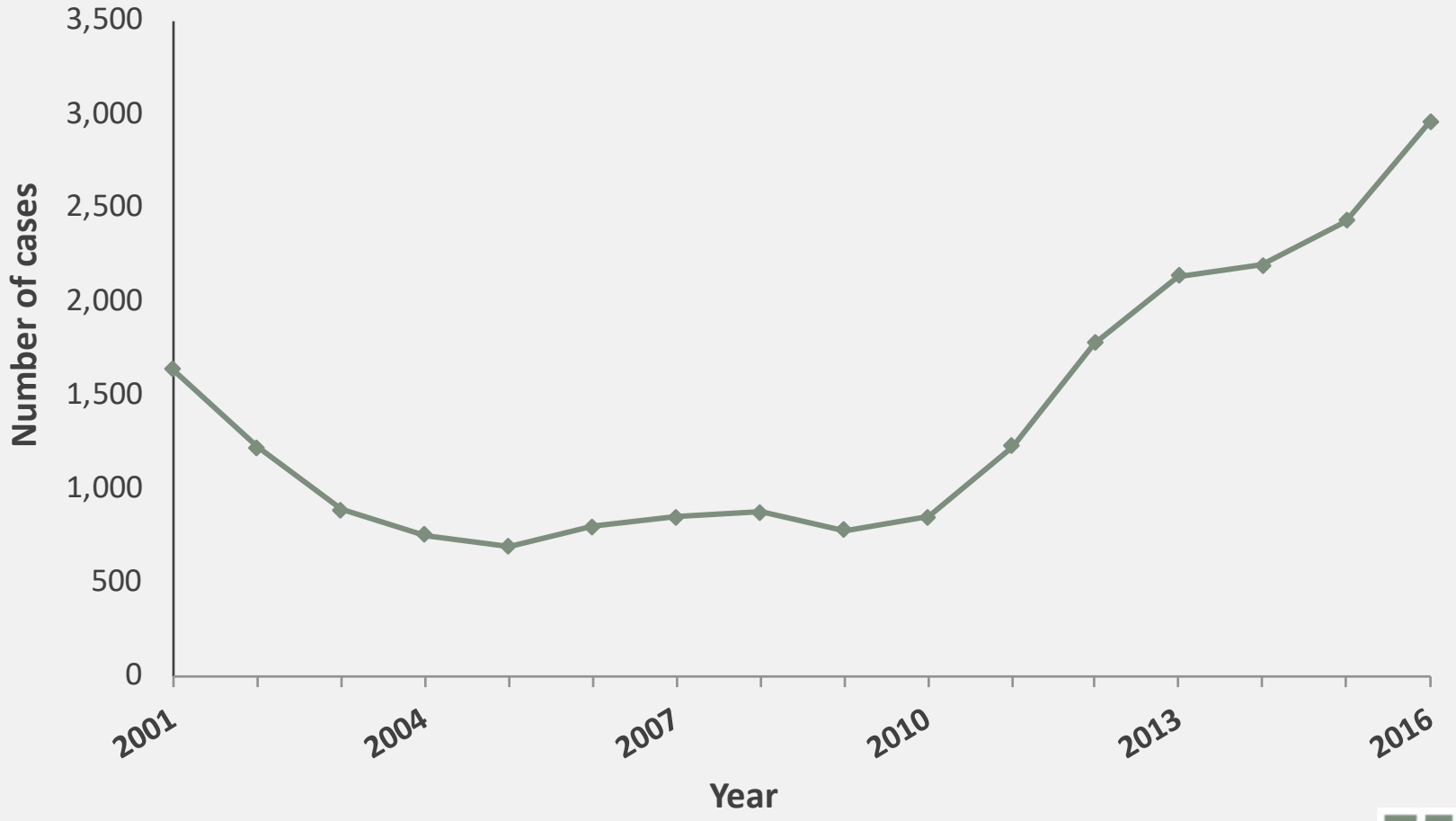
Reported number of acute hepatitis C cases — United States, 2001–2016



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

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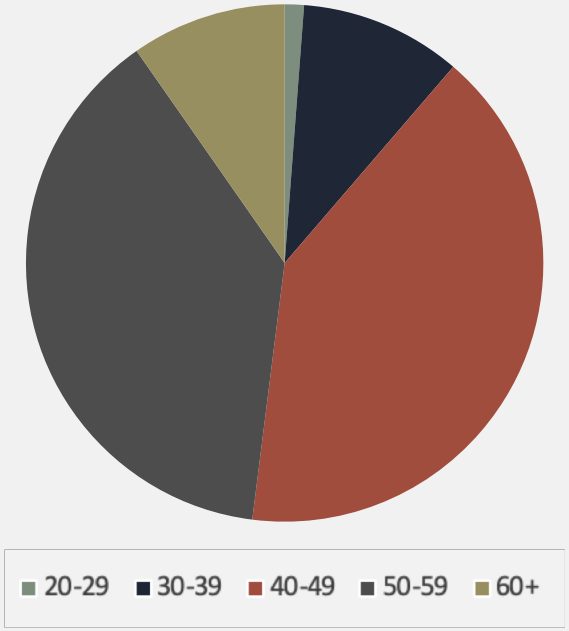
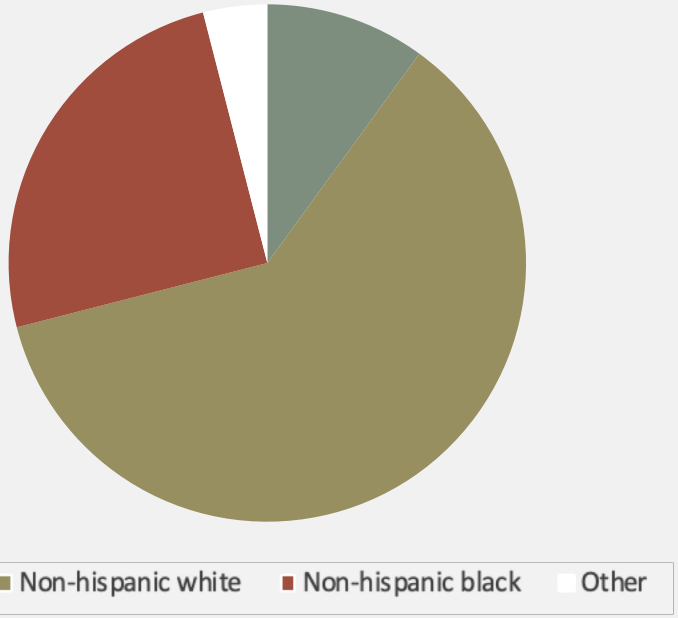
Epidemiology & U.S. Statistics

HCV Incidence By Age[1,a]



HCV Incidence By Race[1,a]



3.5 million people are chronically infected with HCV in the United States, and 4.6 million are HCV antibody positive.[2,b]

[a]Based on the results of the National Health and Nutrition Examination Survey 2003-2010 data. Of note, this survey has a poor representation of homeless and incarcerated populations.
[b]Estimate includes homeless and incarcerated populations.
1. Denniston et al, *Ann Int Med.* 2014;160:293-300; 2. Edlin et al, *Hepatology.* 2015;62:1353-1363.

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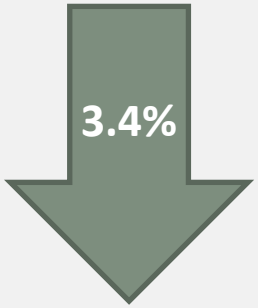
Rising HCV-Related Mortality

Between 2003 and 2013, the HCV-related mortality increased more than 60 other nationally notifiable infectious conditions (ONNICs) combined.

Incidence of ONNICs



Incidence of HCV

Ly KN et al. *Clin Infect Dis*, 2016;62(10):1287-1288.

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Evidence-Based Reinfection Rates

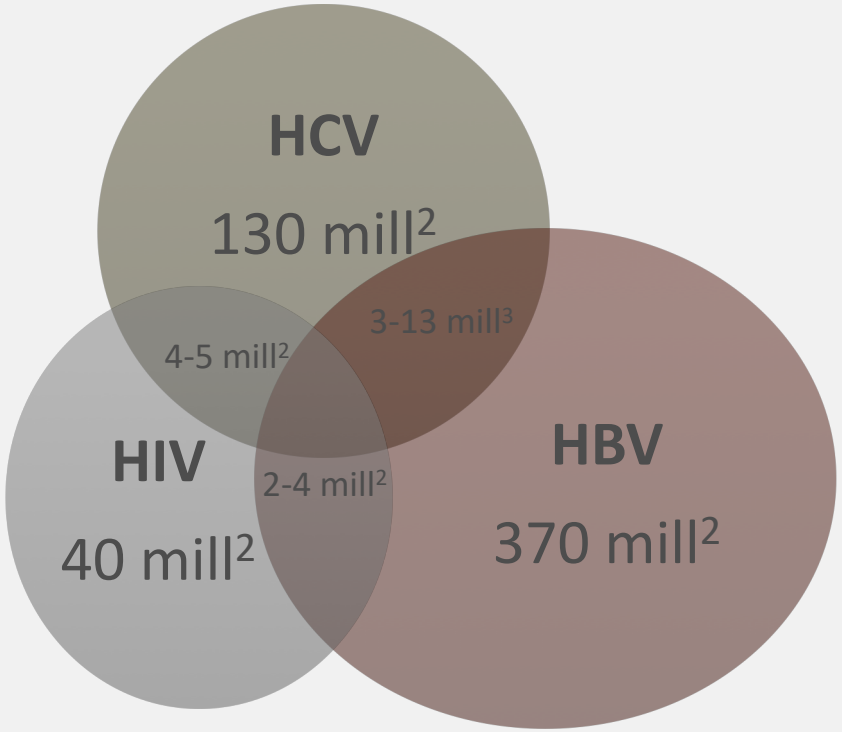
Reinfection rate: 1.27 people per 100 person-years

Higher Risk	Hazard Ratio
Among people with HIV coinfection	2.25
Among people who inject drugs	1.53
Lower Risk	
Among people on opioid substitution therapy	0.73
Among people in mental health counseling	0.71

Islam N et al. *Lancet Gastroenterol Hepatol.* 2017;2(3):200-210.

Preventive Care: Evaluation for Co-Infections

Worldwide Prevalence of Co-Infections



Co-infection with HIV or HBV are associated with worse outcomes among people with HCV.[1-3]

1. French AL et al, *J Acquir Immune Defic Syndr.* 2009;51(4):399-406; 2. Alter MJ, *J Hepatol.* 2006;44(S1):S6-S9; 3. Chu CJ, Lee SD, *J Gastroent Hepatol.* 2008;23:512-520.

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Preventive Care: Education on Limiting HCV Transmission

Clinicians are responsible for educating patients on preventing the spread of HCV

For most patients, education should focus on the potential for blood contact

For men who have sex with men, patients should be counseled on safe sex practices

Patient education resource: http://harmreduction.org/issues/hepatitis-c/overview/hepatitis-c-transmission/

Fraser S et al, *Drugs Educ Prev Polic.* 2014;21(1):88-92.

Common Comorbidities Associated with HCV & Special Patient Populations

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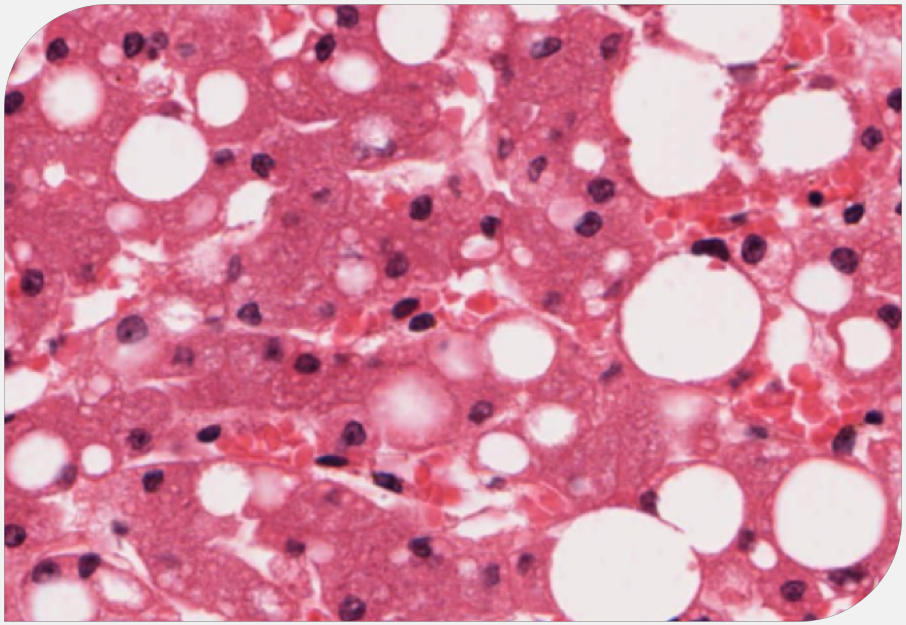
Hepatic Comorbidities



40X magnification of liver tissue with cirrhosis and fatty liver

- Non-alcoholic fatty liver disease (steatosis)
- Hepatocellular carcinoma

Louie et al, BMC Infect Dis, 2012

Extrahepatic Comorbidities

Comorbidity	Prevalence in HCV-Infected Individuals	Prevalence in Uninfected Individuals	Odds Ratio
Connective tissue disease	37.5%	27.7%	1.59
Depressive disorder	13.9%	4.2%	3.72
Essential hypertension	32.6%	25.8%	1.42
Esophageal disorders (primarily reflux)	20.5%	9.6%	2.47
Diabetes mellitus	13.8%	8.5%	1.8

Other manifestations: mixed cryoglobulinemia vasculitis, lymphoproliferative disorders, renal disease, sicca syndrome, cognitive impairment

Louie KS et al, *BMC Infect Dis.* 2012;12:86.

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Special Patient Populations: Renal Impairment

- Mild-to-moderate renal impairment
  - No dose adjustment for many of the DAAs

- Severe renal impairment
  - Recommended treatment for genotype 1a, 1b, or 4 with CrCl <30 mL/min: elbasvir/grazoprevir
  - Recommended treatment for genotype 1b with CrCl <30 mL/min: paritaprevir/ritonavir/ombitasvir/dasabuvir
  - Recommended treatment for patients with genotypes 2, 3, 5, or 6: Interferon + ribavirin

American Association of Liver Disease/Infectious Disease Society of America. 2018.

Special Patient Population: Decompensated Cirrhosis

Typically requires referral to specialist

Often requires addition of ribavirin to DAA regimens

For those who are ribavirin-ineligible, 24-week treatment regimens should be considered

American Association of Liver Disease/Infectious Disease Society of America. 2018.

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Case Study: Isabel

- 22-year-old presenting for contraceptive counseling
- History of 3 years of intravenous heroin dependence
- Has a job and lives with her parents
- Has severe cravings and withdrawal symptoms without heroin
- Consumes alcohol in excess on weekends
- Engages in high-risk sexual practices, including sexual intercourse under the influence of drugs and alcohol

Isabel

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Risk Factors Warranting Screening for HCV Besides Birth Date

- The CDC[1] recommends screening for:
  - Previous or current intravenous drug users
  - Adults who received clotting factor concentrated before 1987
  - HIV-infected individuals
  - Those with persistently abnormal alanine aminotransferase levels
  - Previous recipients of transfusions or organ transplants prior to 1992
- The AASLD/IDSA[2] further recommend screening for:
  - Intranasal drug users
  - Recipients of unregulated tattoos

1. Smith BD et al, *MMWR.* 2012;61(RR04):1-18; 2. American Association of Liver Disease/Infectious Disease Society of America, 2018

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Key Populations: Men Who Have Sex With Men

- Men who have sex with men (MSM) are at a high risk for HCV infection[1]
- Female partners of men who have sex with men should also be tested[1]
- Increased HCV prevalence in MSM is in part due to HIV infection[1]
  - HCV infection is negatively correlated with CD4+ T-cell count in HIV-infected patients
- **AASLD and IDSA recommend yearly screening in:[2]**
  - **Men who present for preexposure prophylaxis**
  - **Sexually active adolescent MSM**
  - **Adult MSM**

[1]Witt et al, Clin Infect Dis, 2013
[2]American Association of Liver Disease/Infectious Disease Society of America, 2018

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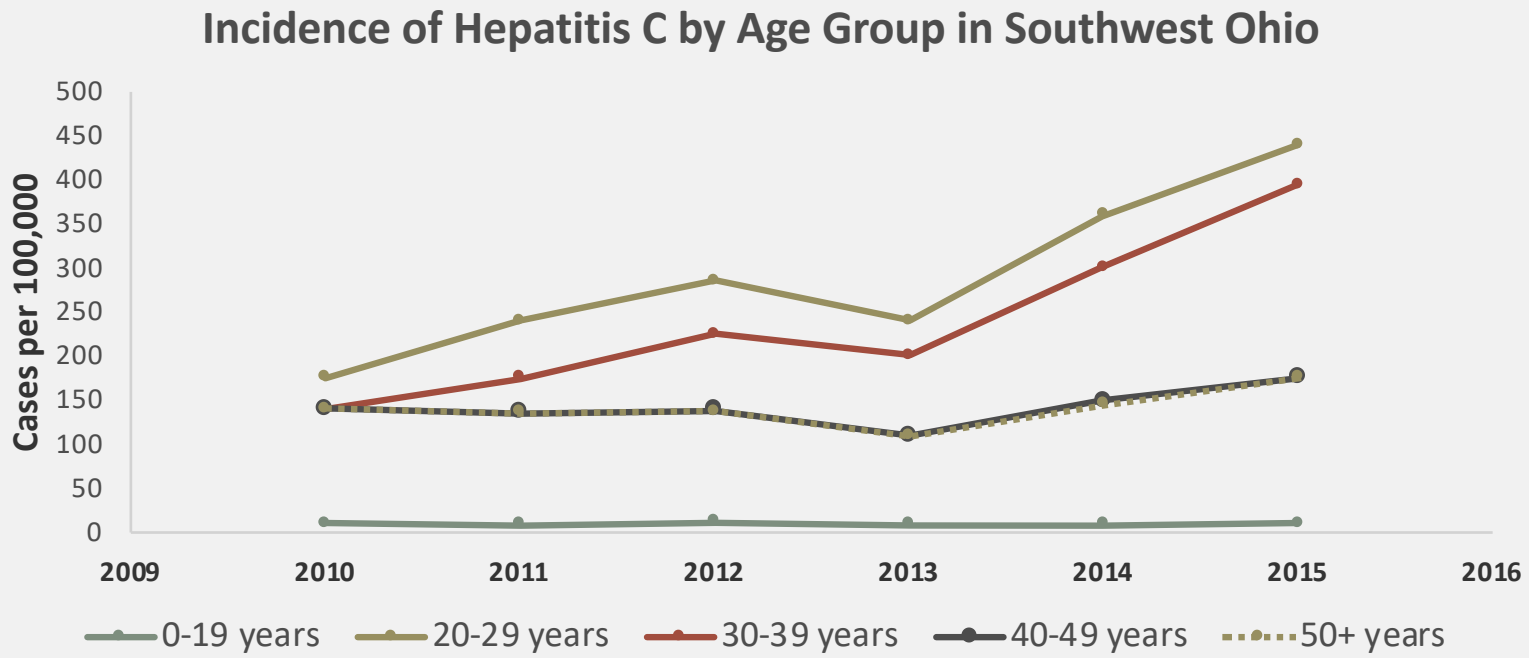
Key Populations: People Who Inject or Inhale Drugs



The opioid epidemic is driving higher incidence of HCV in new age groups, primarily 20- to 39-year-olds.

Woltman J et al, *Hepat Mon*, 2016;16(8):e37904.

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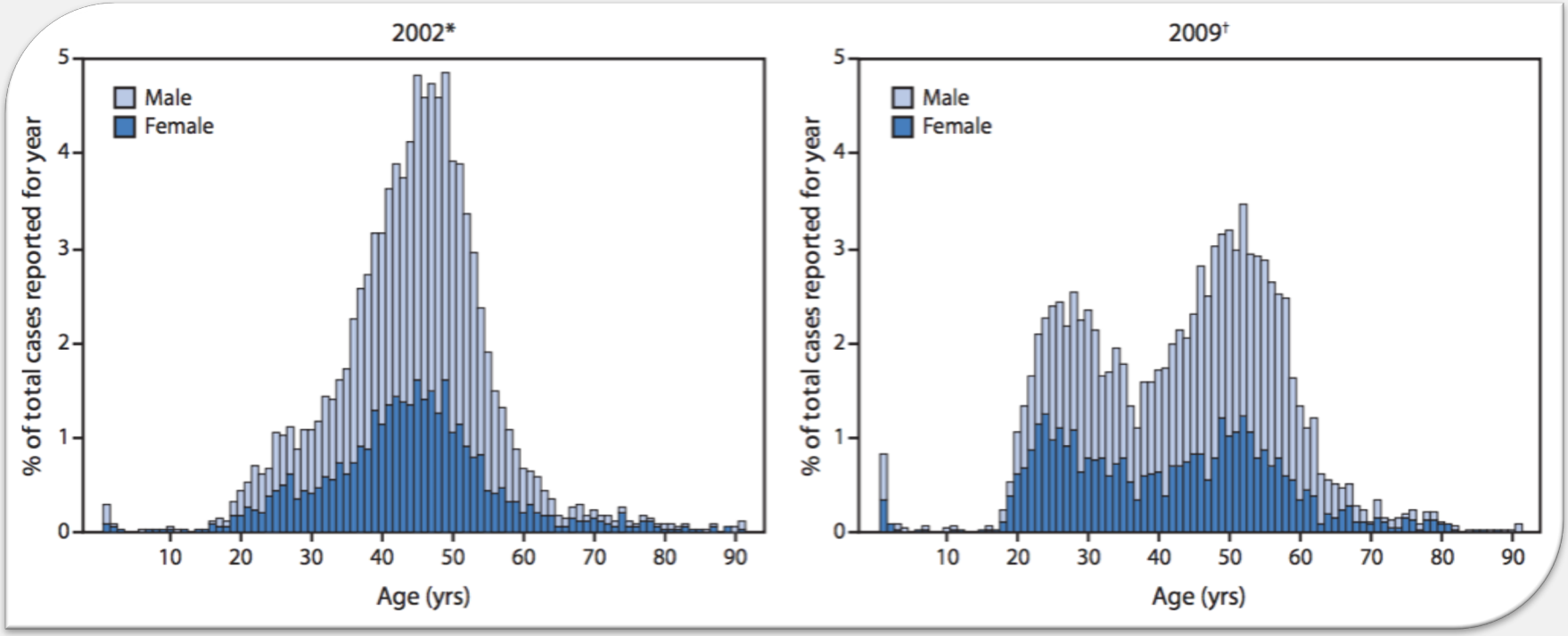
Key Populations: People Who Inject or Inhale Drugs



*n = 6281; excludes 35 cases with missing age or sex information
†n = 3904; excludes 346 cases with missing age or sex information

CDC, *MMWR.* 60(17):537-546.

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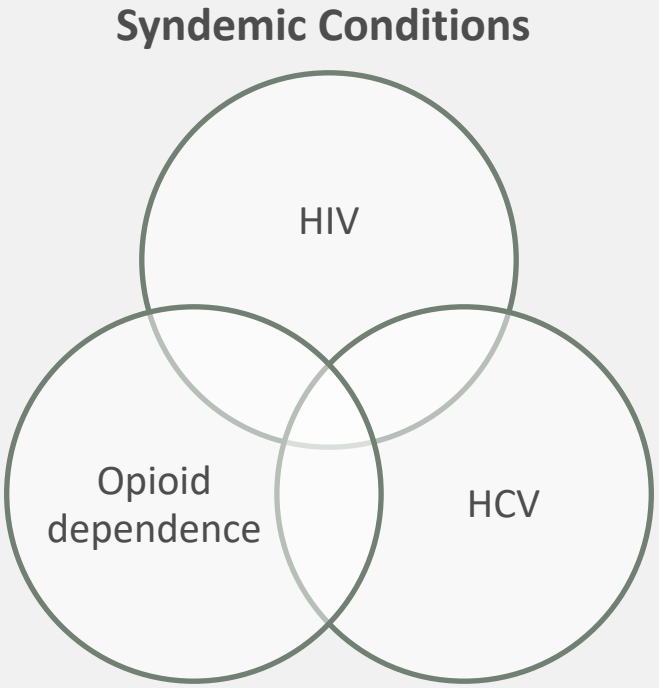
Key Populations: People Who Inject or Inhale Drugs



Opioid substitution treatment has been shown to reduce transmission of HCV and increase the uptake of antiviral therapy for HCV.

Midgard H et al. *PLoS One*. 2016;11(11):e0166451; Platt L et al. *Addiction*. 2018;113(3):545-563; Norton BL et al. *J Subst Abuse Treat*. 2017;75:38-42.

Key Populations: Women of Reproductive Age

- Since 2006, the number of reproductive-aged women with HCV infection has doubled (15,550 to 31,039 in 2014)[1]
  - Pregnant women in rural counties are more likely to be infected with HCV
- The AASLD and IDSA recommend that all pregnant women should be tested for HCV infection at the start of their prenatal care[2]
- Risk-based screening is not as reliable as universal screening[3]
  - In a retrospective chart study, 10% of HCV-positive pregnancies occurred in women with no reported risk factors

1. Ly et al, Ann Intern Med, 2017;166(11):775-782; 2. American Association of Liver Disease/Infectious Disease Society of America, 2018;
3. Boudova et al, Open For Infect Dis, 2018;5:ofy043.

Key Populations: Pregnant & Lactating Mothers

- Cesarean section should not be recommended as a method of reducing transmission risk[1]
- DAAs have not yet been adequately tested in pregnant women
  - Liver cirrhosis does not typically worsen during the course of pregnancy and may even improve[2]
- HCV infection in infants does not have a negative effect on growth and development of infants[1]
- HCV is not transmitted by breast milk[1]
  - Cracked and bleeding nipples may increase transmission risk

1. Yeung CY et al, *World J Hepatol.* 2014;6(9):643-651; 2. Jhavery R, Swami GK, *J Ped Infect Dis.* 2014;3(Suppl 1):S13-S18.

Risk of Transmission During Pregnancy

- Children born to mothers with HCV infections (5% to 15%)[1]
  - Testing at 12 to 18 months is primary diagnostic test
  - Risk factors for perinatal transmission:[2]
    - High maternal viremic load
    - Prolonged rupture of membranes
    - Maternal drug use[3]
    - Operative vaginal delivery (forceps or vacuum)
    - Fetal scalp electrode placement

1. American Association of Liver Disease/Infectious Disease Society of America, 2018; 2. Murakami et al, *Hepatol Res,* 2012;42:648-657; 3. Resti et al, *J Infect Dis*, 2002;185(5):567-572.

Key Populations: Heterosexual Partners of People With HCV

- HCV is primarily a bloodborne pathogen
- Sexual transmission can occur in heterosexual monogamous couples
  - A rare but important risk
  - Sexual transmission is 0.07% per year
  - Transmission is not associated with specific sexual practices
- Possible candidates for annual screening

Terrault NA et al, *Hepatology.* 2013;57(3):881-889.

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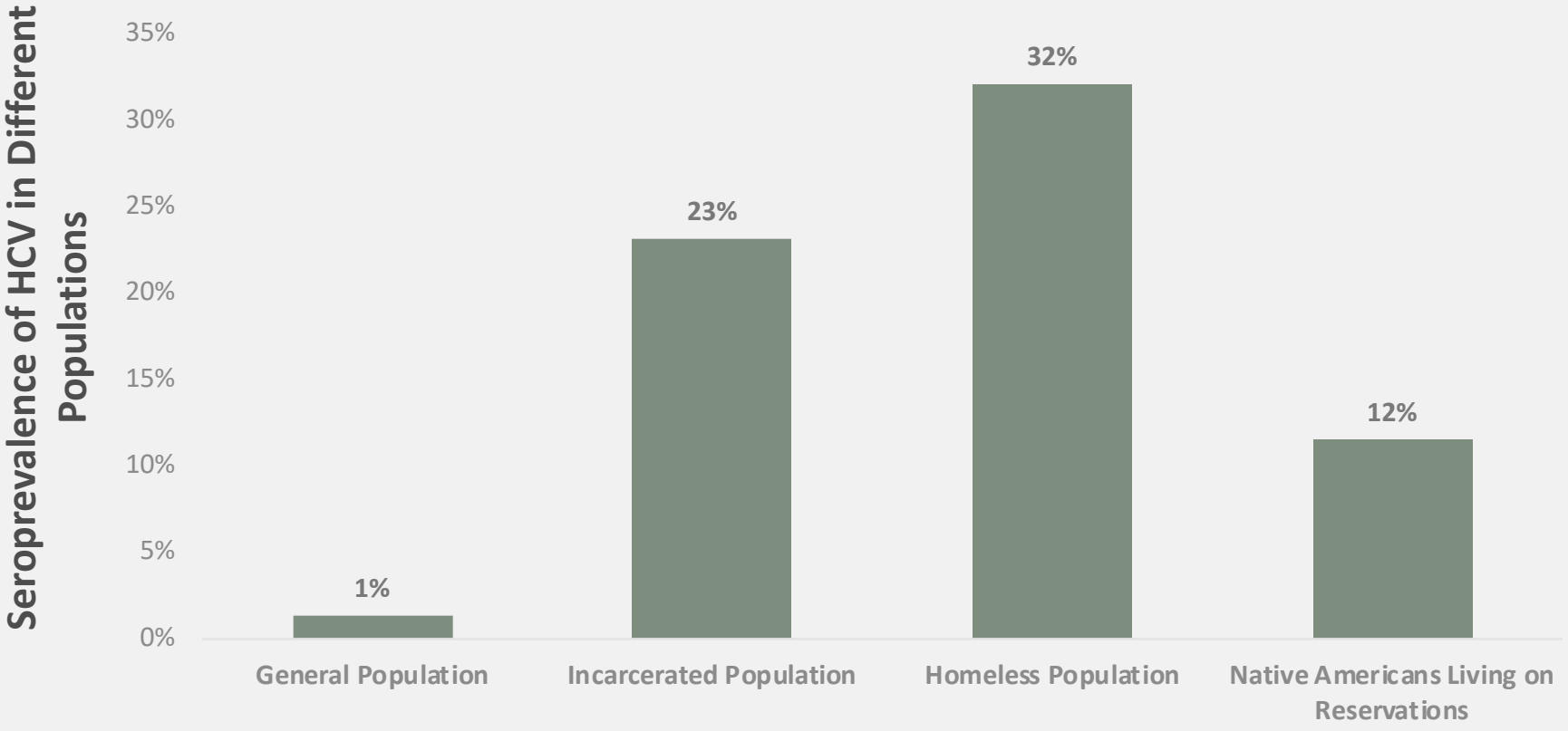
Underdiagnosed Populations



Edlin et al, *Hepatology.* 2015;62(5):1353-1363.

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Reproductive Health & HCV

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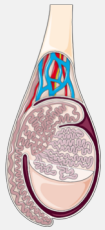
Effectiveness of Contraceptive Methods

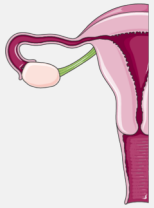
More effective

Less than 1 pregnancy per 100 women in one year

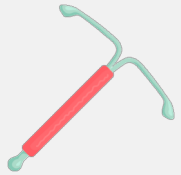
Implant



Vasectomy



Tubal ligation



IUD

6-12 pregnancies per 100 women in one year

Injectable

Pills

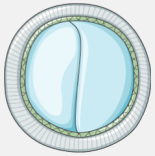
Patch

Ring

Diaphragm

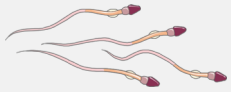
18 or more pregnancies per 100 women in one year

Condoms

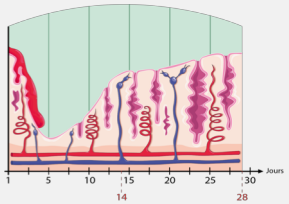


Sponge

Spermicides



Withdrawal



Fertility awareness-based methods

Less effective

Trussell J, et al. In: Hatcher RA, et al. *Contraceptive Technology,* 20th revised ed. 2011. Chart adapted from WHO 2007.

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Case Study: Isabel

- Counseling:
  - Discuss contraceptive options based on patient preferences
  - Encourage continued use of barrier methods
  - Counsel on high-risk sexual behaviors
  - Offer opioid substitution treatment
  - Offer HCV screening

Case Study: Isabel

- HCV antibody test: positive
- HCV RNA test: positive
- HCV genotype: 1a

CDC Medical Eligibility Criteria for Contraceptive Use 2016

Condition	Category 1 (No Restriction)	Category 2 (Advantages generally outweigh theoretical or proven risks)	Category 3 Theoretical or proven risks usually outweigh the advantages	Category 4 Unacceptable health risk (method not to be used)
Viral hepatitis: Acute or flare	• Progestin-only pill • Implant • LNG-IUD • Copper-IUD • Injection	Combined hormonal contraception: • Pill (C) • Patch (C) • Ring (C)	Combined hormonal contraception: • Pill (I) • Patch (I) • Ring (I)	
Viral hepatitis: carrier/chronic	• Progestin-only pill • Implant • LNG-IUD • Copper-IUD • Injection			

I = initiation of contraceptive method
C = continuation of contraceptive method

Curtis KM, MMWR, 2016;65(3):1-103.

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Case Study: Isabel

- Contraceptive options for chronic HCV:
  - Progestin-only pill
  - Implant
  - LNG-IUD
  - Copper-IUD
  - Injection
- Counseling on HCV treatment
- Connection with opioid substitution treatment clinics
- Counseling on HCV transmission, including sexual risk factors and needle sharing
- Counseling on alcohol consumption

Isabel

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Barriers to Standard of Care in HCV

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Medicaid Coverage Barriers

36 states required at least stage F2 fibrosis for reimbursement of DAAs

19 states required drug testing before treatment either in all patients (**16 states**) or in patients with a history of abuse (**3 states**)

25 states required abstinence from alcohol and drugs, either in all patients (**20 states**) or in patients with a history of abuse (**5 states**)

5 states did not allow people with decompensated cirrhosis to receive treatment

Ooka K et al, *Am J Gastroenterol.* 2017;112(6):828-832.

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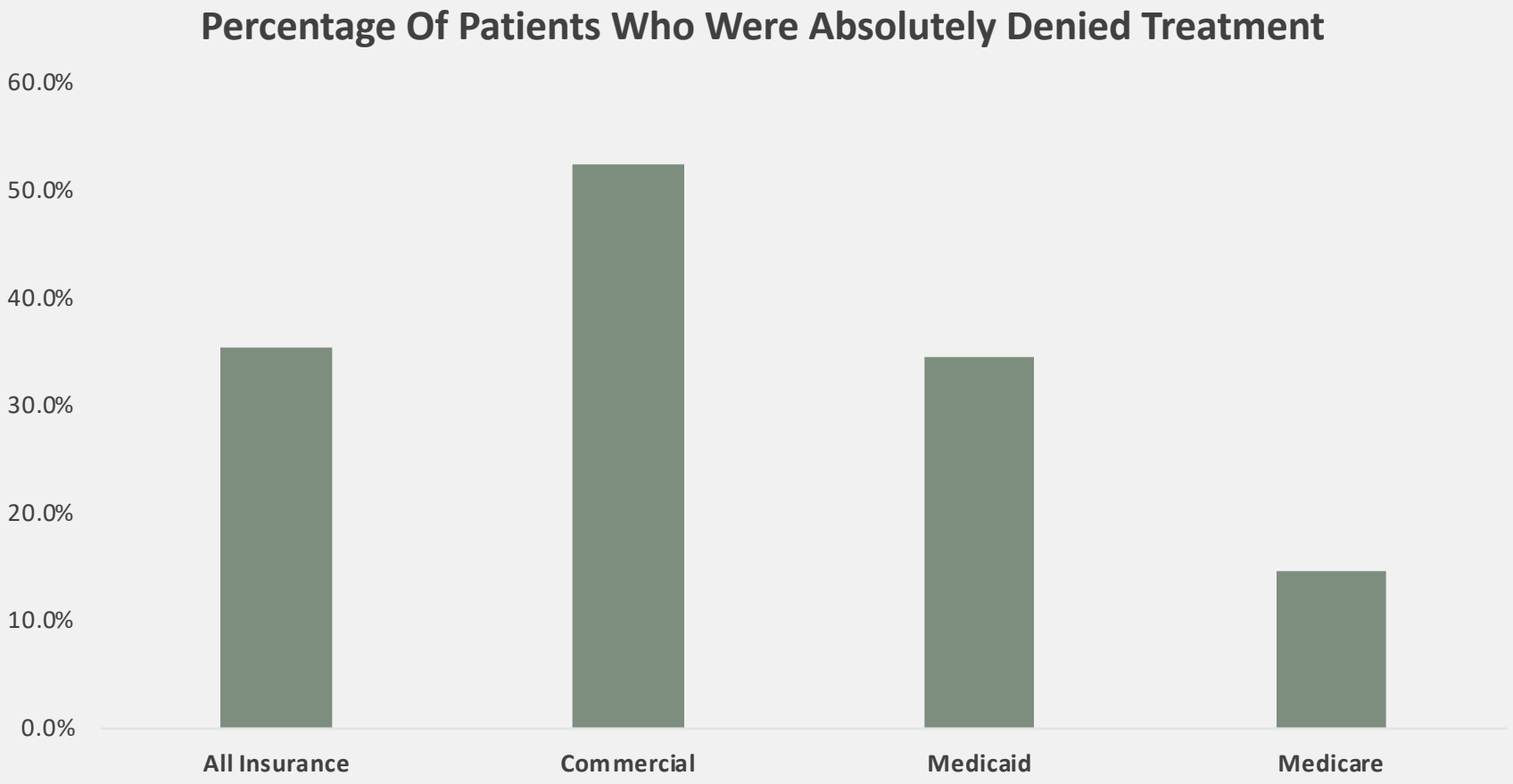
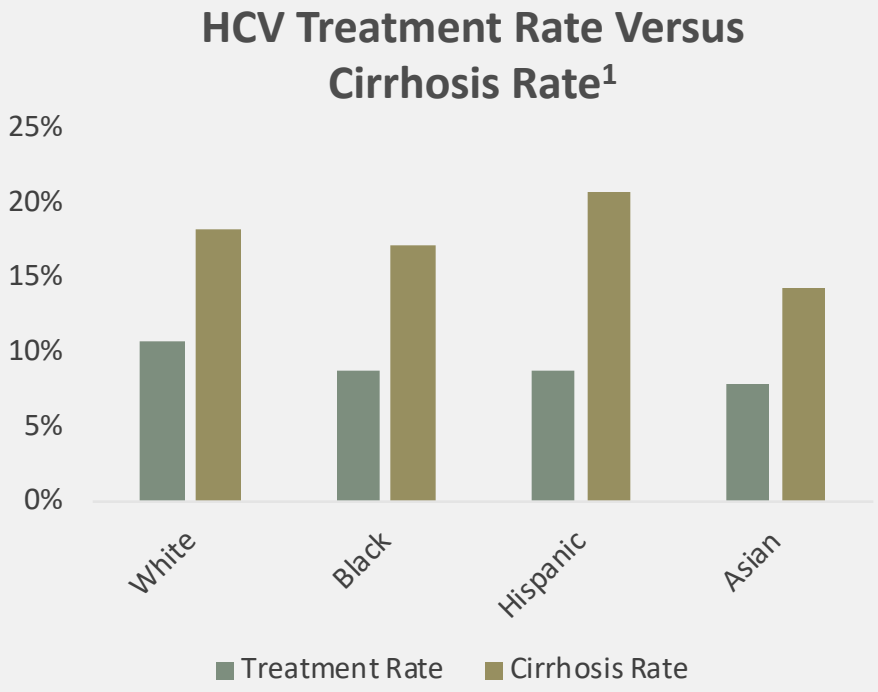
Barriers to Standard of Care: Cost



Gowda C et al, *Open For Infect Dis.* 2018;5:ofy076.

Barriers to Standard of Care: Socioeconomic Status & Race

- Black and Hispanic patients are more likely to be infected with HCV but are less likely to receive treatment[1]
- Black patients were more likely to be deemed treatment ineligible compared with white patients[2]
- Socioeconomic status is also correlated with HCV testing and access to care[3]



1. Vutien et al, *Medicine (Baltimore).* 2016;95(22):e3719; 2. Melia et al, *Hepatology.* 2011;54(1):70-78; 3. Tohme et al, *Am J Pub Health.* 2013;103:112-119.

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Barriers to Standard of Care: Adherence & Engagement

- Patients are often reluctant to receive treatment due to:
  - Treatment duration
  - Cost

- Engaged and educated patients are more likely to adhere to HCV treatment

- For patient engagement resources, visit www.prepc.org

Grebely J et al, *J Infect Dis*, 2013;207:S19-S25.

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Barriers to Standard of Care: Provider-Driven Reasons

- Clinicians who worry about re-infection, particularly for intravenous drug users, are less likely to prescribe treatment[1]
- Re-infection after SVR occurs but has a low incidence[2]
- SVR is achievable in patients who currently inject drugs[3]

Surveyed Providers Willingness to Treat Based on Drug Use[1]

Time Abstinent From Intravenous Drugs	Providers Willing to Treat
Currently Injecting	10%
<6 months	33%
≥12 months, used non-IDU	25%
≥12 months	55%

1. Asher AK et al, *Substance Use Misuse.* 2016;51:1218-1223; 2. Grady BP et al, *Clin Infect Dis.* 2013;57:S105-S110; 3. Aspinall EJ et al, *Clin Infect Dis.* 2013;57:S80-S89.

Barriers to Standard of Care: PWID & Young PWID

Stigma, fear of treatment, fear of biopsy

Dissatisfaction with provider interactions

Perceived lack of referral to treatment and care continuity

Logistical challenges (eg, imprisonment, distance to hospital)

Perceived need for treatment

Skeer MR et al. Drug Alcohol Depend. 2018; Crowley D et al. J Transl Int Med. 2017.

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Key Take-Aways

- Many people living with HCV are unaware—clinicians are responsible for knowing the risk factors and initiating dialogues about screening
- Interferon-based therapies are no longer preferred
- New DAAs with or without ribavirin are the preferred treatments
- Cost, access, and provider willingness are all barriers to care—clinicians should make strides to ensure equitable access to care
- Special patient populations may require different treatments