



Epidemiology of Pathogenesis of HCV

A Focus on HIV

Presented by MayaTech
in conjunction with
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Our Speaker

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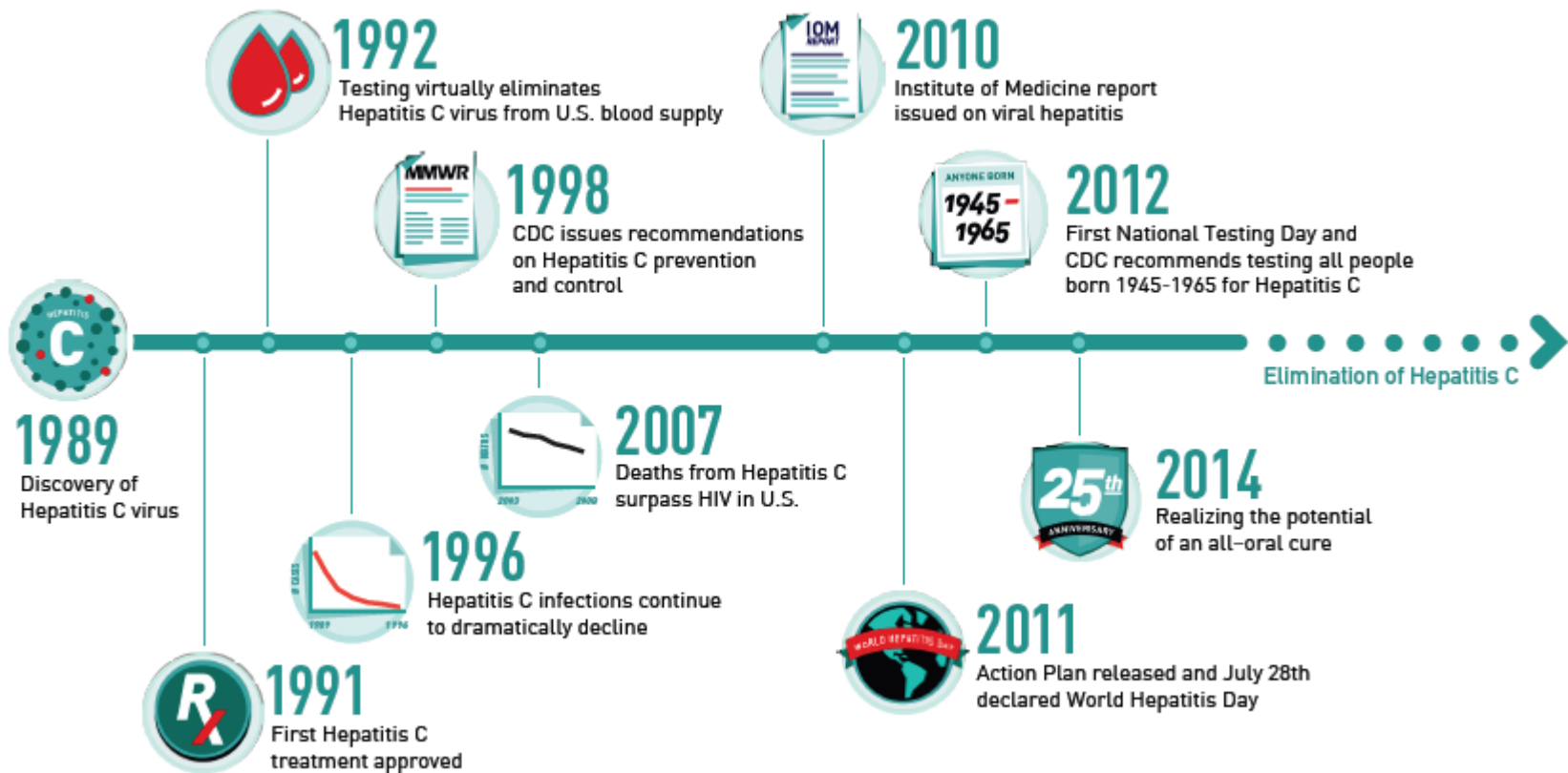
Boston, MA



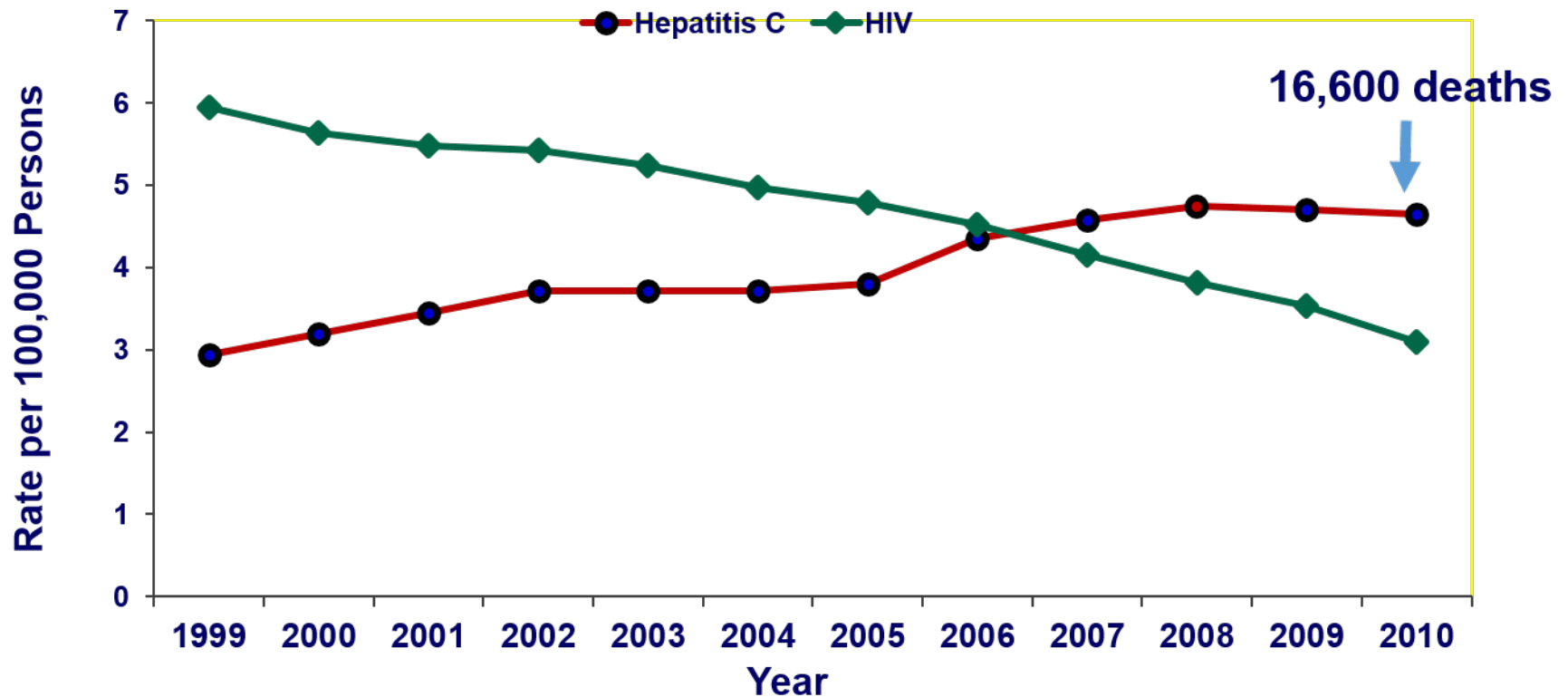
Objectives

- Identify who is at risk for HIV/HCV co-infection and HCV re-infection
- Recognize co-factors and co-morbidities that contribute to liver disease progression in HIV/HCV co-infection which are amenable for intervention
- Recognize the need for HCV treatment in co-infected populations

Working Towards the Elimination of Hepatitis C Virus (HCV)



Deaths Due to HCV Infections Now Exceed Those Due to HIV Infection



Number of HCV-related deaths may be over 60,000 because of under-reporting on death certificates

Ly KN, Xing J, Klevens RM, Jiles RB, Holmberg SD. Causes of death and characteristics of decedents with viral hepatitis, United States, 2010. *Clin Infect Dis*. 2014 Jan;58(1):40-9. Mahajan, IDSA 2013 0

National Academy of Sciences Consensus Report on Feasibility of HCV Elimination

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FOR IMMEDIATE RELEASE

U.S. Could Be Rid of Hepatitis B and C as Public Health Problems, Preventing Nearly 90,000 Deaths by 2030, With Better Attention to Prevention, Screening, Treatment, and Creative Financing for Medicines

National Academy of Sciences Consensus Report on Feasibility of HCV Elimination (cont)

- It is feasible to eliminate HCV in the US¹
 - Approximately 10% of patients with HCV infection (including those currently undiagnosed) have been treated with DAAs in the US
- Barriers to elimination include:
 - Lack of screening
 - Insufficient linkage and retaining patients in care
 - Ongoing stigma (especially against people who inject drugs) and lack of care in Corrections Facilities
 - High price of HCV regimens

1. <https://www.ncbi.nlm.nih.gov/books/NBK368067/>

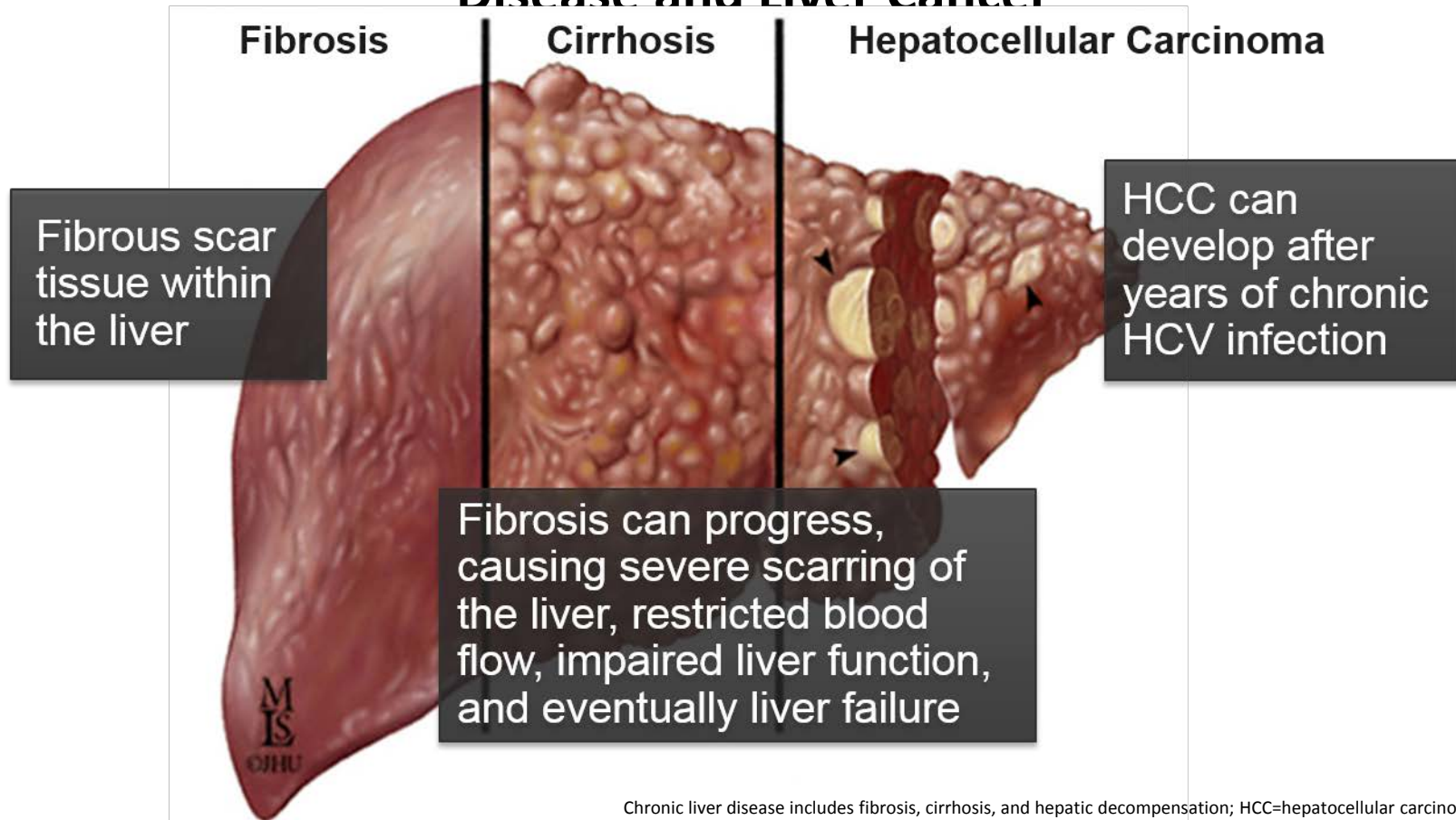
Who You Should Screen for HCV

- People who inject drugs (recent outbreak of HIV and HCV)
- Clotting factors before 1987
- Blood/organs before 1992
- Children born to HCV-infected mothers
- Needle stick injury
- Current sexual partner of an HCV-infected person (in particular MSM)
- Evidence of liver disease (elevated ALT)
- Born from 1945 through 1965
- Chronic hemodialysis
- **HIV**
- Incarcerated individuals

High Overlap Between HIV and HCV Risk Factors

- Common routes of transmission
- HIV is more transmissible through sex than HCV
 - Most cases of sexual transmission of HCV are in men who have sex with other men and rarely young women (from men with HCV infection)
- HCV is more transmissible through blood than HIV
 - Needle exchange programs dramatically decreased HIV transmission but HCV lives longer on environmental surfaces
 - Need to ensure people do not share ANY works (needles, syringes, cookers, cotton, ties, etc)

Chronic HCV Infection May Lead to Chronic Liver Disease and Liver Cancer



Chronic liver disease includes fibrosis, cirrhosis, and hepatic decompensation; HCC=hepatocellular carcinoma.

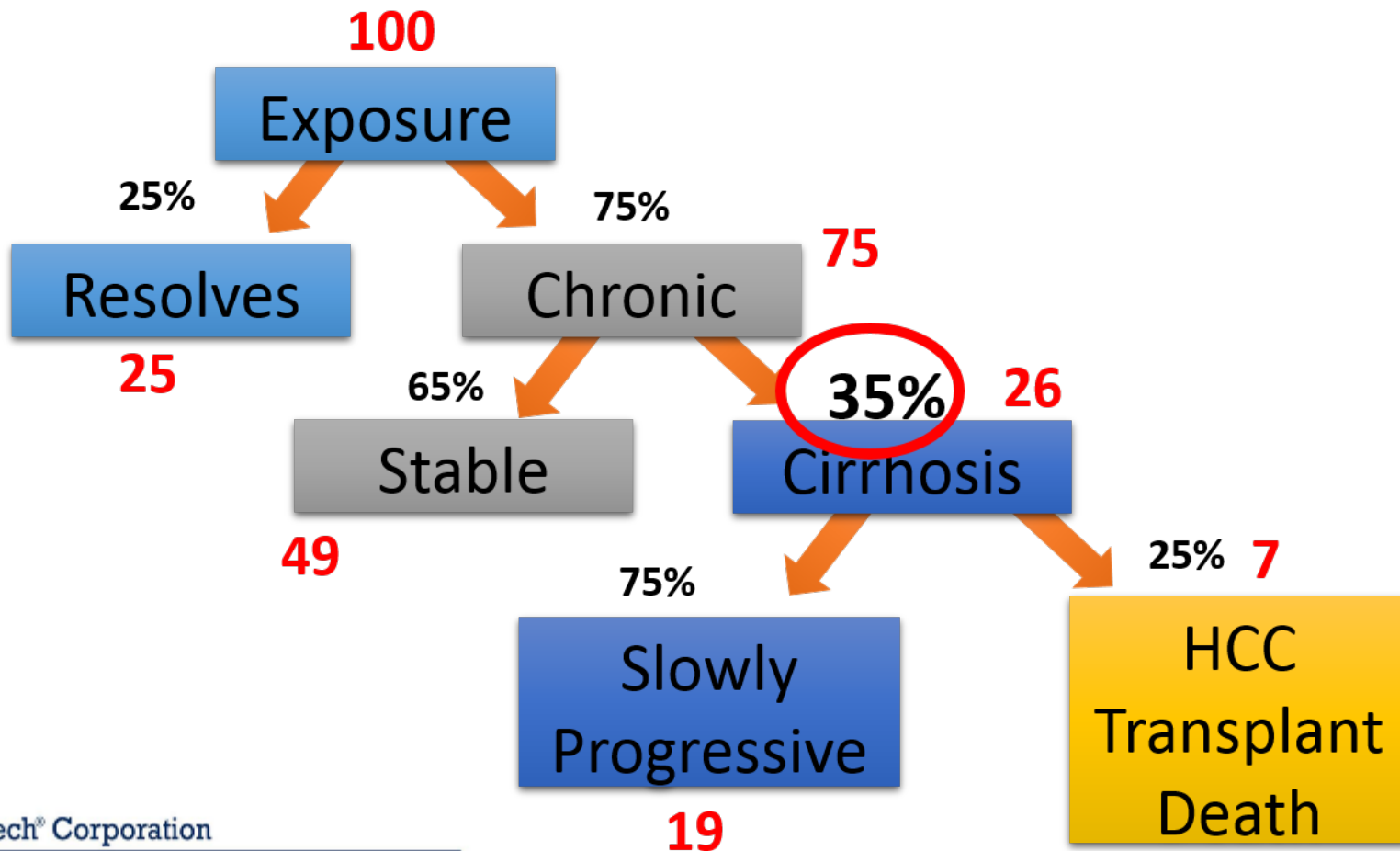
1. Highleyman L. Hepatitis C Support Project. http://www.hcvadvocate.org/hepatitis/factsheets_pdf/Fibrosis.pdf.

Accessed August 18, 2011; 2. Bataller R et al. *J Clin Invest*. 2005;115:209-218;

3. Medline Plus. <http://www.nlm.nih.gov/medlineplus/enxy/article/000280.htm>. Accessed August 28, 2012; 4.

Centers for Disease Control and Prevention. <http://www.cdc.gov/hepatitis/HCV/HCVfaq.htm>. Accessed May 8, 2012.

Natural History of HCV after 40 years (no HIV) or 20 - 30 year (HIV/HCV)



Factors that increase risk of liver disease progression in HIV/HCV coinfection

- Excessive alcohol use
- Non-alcoholic steatohepatitis (NASH)
 - Diabetes
 - Obesity
 - Hyperlipidemia
- Hepatitis B tri-infection (vaccinate!)
- Drug effect/liver toxicity
- Other causes (autoimmune, genetic diseases, etc)

FibroScan - Transient Elastography Has Replaced Liver Biopsy

- Ultrasound determines liver stiffness in kilopascal (kPa)
- Entire process requires 15 to 20 minutes, provides immediate results, and does not hurt
- RARELY is liver biopsy needed
- Falsely elevated results:
 - High ALT (>100)
 - Eating within 2 hours



Continuum of Fibrosis/Cirrhosis in HCV

<7 kPa = Stage 0-1

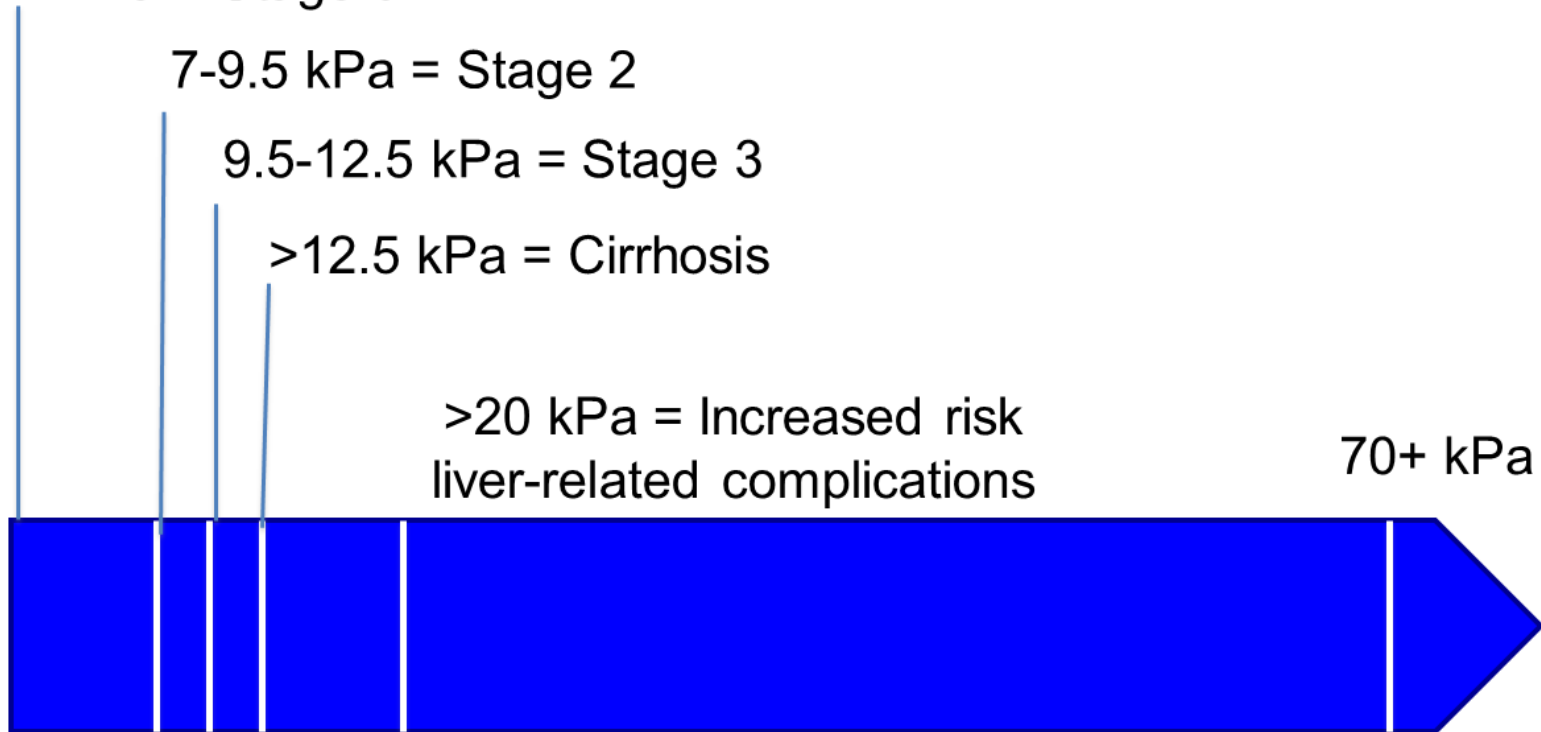
7-9.5 kPa = Stage 2

9.5-12.5 kPa = Stage 3

>12.5 kPa = Cirrhosis

>20 kPa = Increased risk
liver-related complications

70+ kPa



Management of Patients with Hepatitis C and Cirrhosis

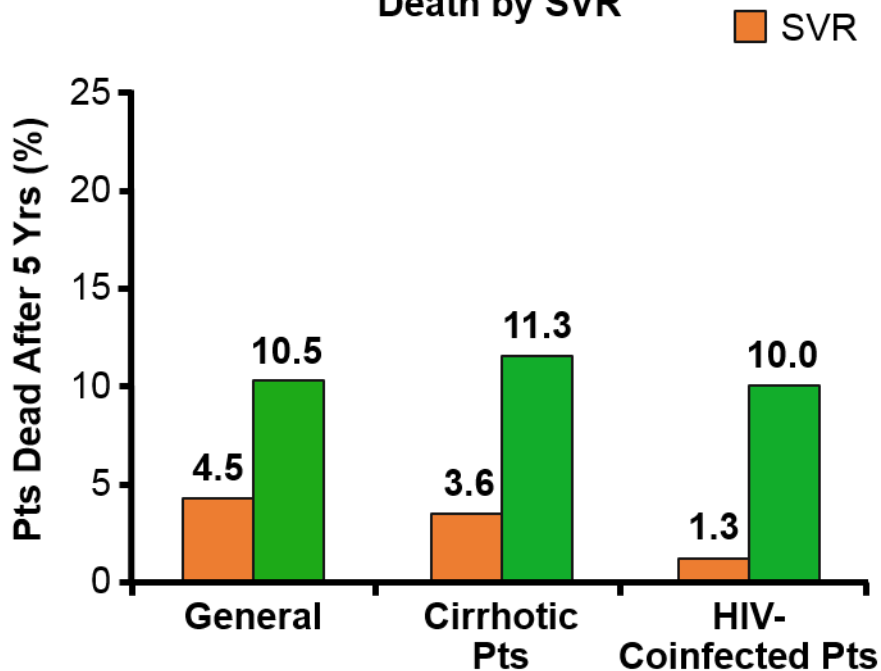
- Every 6 month screening for liver cancer
 - Usually ultrasound
 - Consider CT or MRI if highly nodular liver; first exam
- Screening for esophageal varices
 - Repeat every 1 -3 years depending on results
- Counsel on symptoms of hepatic encephalopathy
- Vaccination for pneumococcus
- Counseling around medication use to avoid overdose or adverse events (including common drugs like Tylenol and NSAIDs)
- Counseling about complete abstinence from alcohol
- Evaluation for antiviral treatment
 - Cure of HCV can reduce liver failure and liver cancer, even in patients with cirrhosis (+/- HIV coinfection)
- Possible referral for liver transplant services

Poor Adherence to Guidelines for Screening of HCC in HIV/Hepatitis C Virus–Coinfected Patients

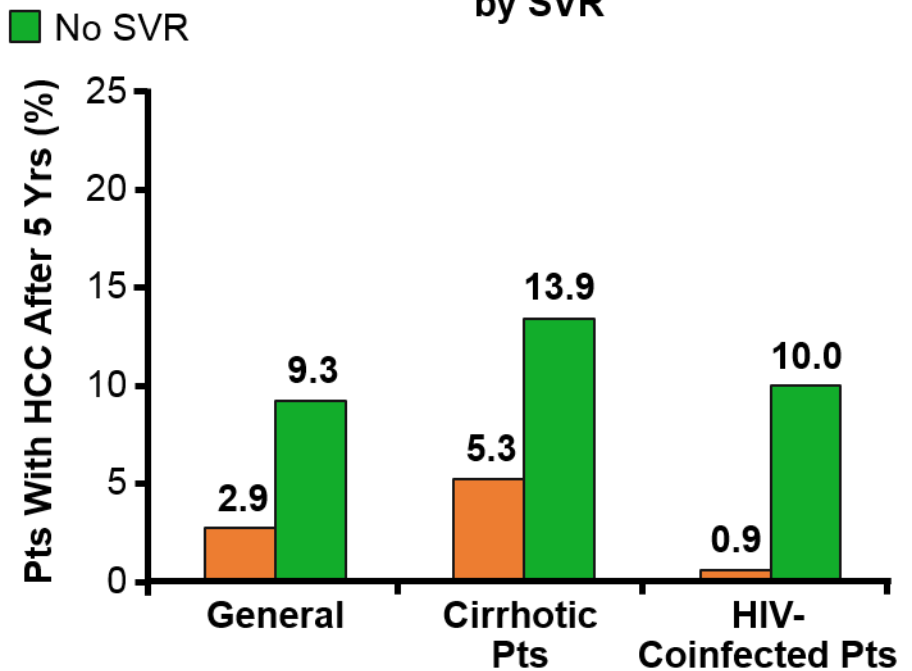
- Among patients with documented cirrhosis, 52 (36%) never had an abdominal ultrasound performed during study follow-up (median follow-up, 2.5 years)
- Median number of ultrasounds per patient per year was 0.4 (IQR, 0–0.9)
- There were 9 incident diagnoses of HCC, 2 of which occurred in patients without any documented abdominal ultrasound prior to diagnosis. HCC was screening-detected in 2 patients; for the remainder there were large gaps in screening between the last ultrasound and HCC diagnosis. Mortality among patients with HCC was 69%.
- Patients at centers with standardized systems for screening were more likely to have had an ultrasound performed

SVR Associated With Reduced 5-Yr Risk of Death and HCC in All Populations

5-Yr Risk of All-Cause Death by SVR



5-Yr Risk of HCC by SVR



HCV Treatment Overview

- Seven FDA-approved regimens for genotype 1
 - Three regimens can be used for genotypes 2 and 3
 - A few subgroups require ribavirin (anemia)
- Selection may be guided by insurance restrictions
- Most patients receive 12 weeks (range 8-24)
- Most receive 1 pill once a day
- All patient groups have a >90% SVR (virological cure) rate
 - HIV/HCV coinfection, all genotypes, decompensated cirrhosis

Key Issues in Treating HIV/HCV Coinfection

- Most people are candidates for HCV treatment with the proper support
- Most will have genotype 1 infection
- Treatment choice will likely depend on insurance coverage
- In most cases follow guidelines for HCV mono-infection
 - hcvguidelines.org
- Drug interactions with HIV medications most important difference

Using Similar Models of Care for HIV and HCV

- Readiness assessments
- Substance use
- Psychiatric comorbidity
- Unstable housing
- Inadequate insurance
- Adherence support
- Case management (can't use Ryan White for HCV mono-infection)

Treating HCV in HIV Coinfection

- Identify desired (reimbursed) HCV regimen
- Determine any drug interactions with current HIV regimen
- Switch to compatible HIV regimen (if needed)
- Wait 3 -4 weeks to look for adverse effects of new regimen and ensure ongoing suppression
- Start HCV regimen
- Monitor both HIV and HCV safety and viral suppression
- Consider switching back to original HIV regimen after completion of HCV treatment

Case Study: Holding on to a Complicated HIV Regimen

- 56 y/o man with HIV and HCV, genotype 3
- Refused pegylated IFN+RBV in the past
- On abacavir (300 mg twice a day) + Kaletra (2 tablets twice a day) + etravirine (2 tablets twice a day) + raltegravir (1 tablet twice a day)
- Needed to start sofosbuvir plus daclatasvir
- Reviewed a mountain of old records to determine reasons for every medication change – most were for adverse effects
- Switched to Triumeq (ABC+3TC+DTG) + rilpivirine
- Increased nausea initially; HIV remained suppressed
- Tolerated SOF+DCV well, now cured

Case Study: Contraindicated Regimen Anyway

- 63 y/o man with HIV, genotype 1a HCV and decompensated cirrhosis with encephalopathy (Child B)
- On TDF/FTC+atazanavir+RTV
- Atazanavir is contraindicated in Child B cirrhosis
- Switched to TDF/FTC + raltegravir
- Started sofosbuvir/ledipasvir+RBV 600 mg a day (slowly titrated RBV up to 1000 mg a day)
- Cured HCV; mental status dramatically improved, stopped lactulose and rifaximin

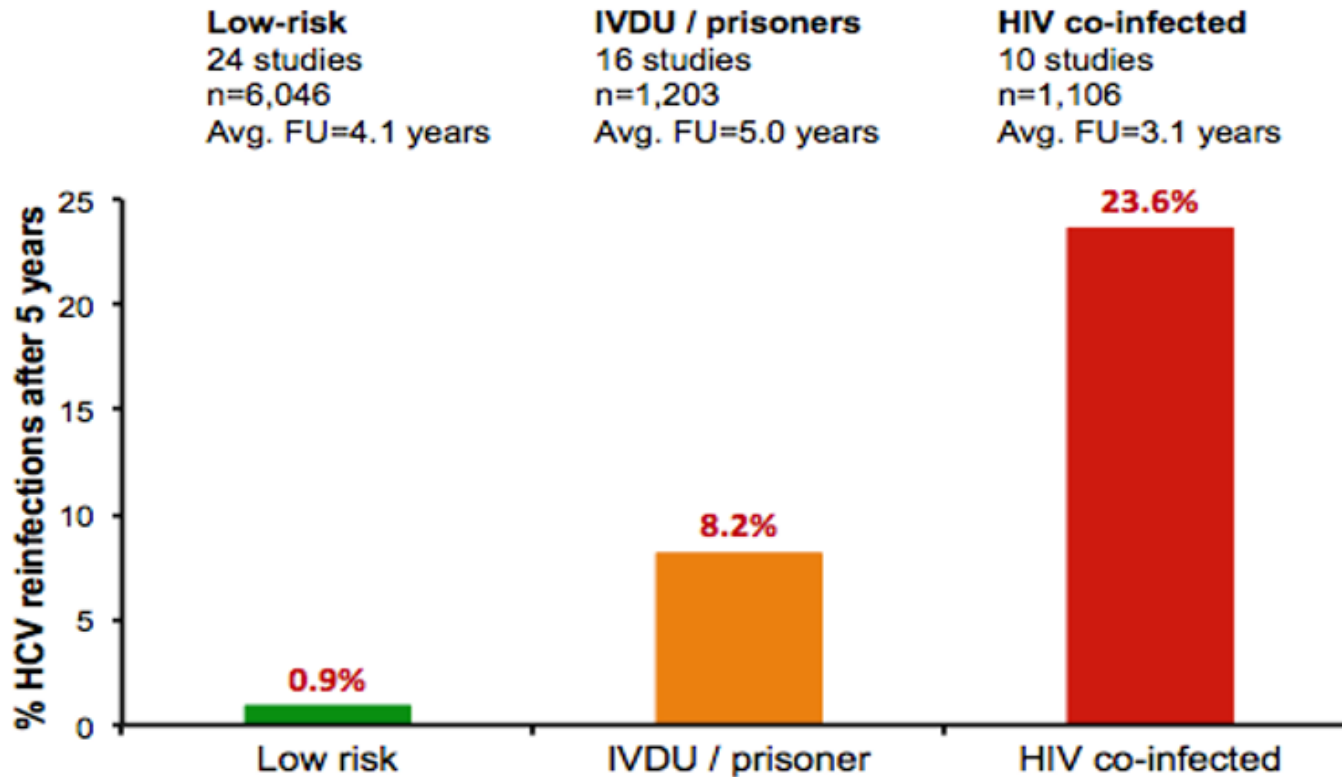
Case Study: Current Failing HIV Regimen

- 67 y/o woman with HIV, HCV genotype 1a (viral load 99 million), CKD on hemodialysis, porphyria cutanea tarda
- On AZT+3TC+Darunavir/r+Raltegravir with HIV VL 34,000 copies/mL
 - Mutations associated with decreased susceptibility to raltegravir (L74M, T97A) detected – DTG ok. No other significant mutations
- Missed days around HD
- Needed to use elbasvir/grazoprevir
- Switched to AZT+3TC+Dolutegravir with subsequent HIV VL 100 copies/mL
- Started ELB/GRZ; at week 4 HIV and HCV viral loads below limit of detection

Reminder: You Can Treat HCV!

- 47 year old woman sent to ID Clinic from Gastroenterology
- Referral: Change HIV regimen so we can treat her HCV
 - What HCV regimen is desired?
 - What is the ARV history – failure, resistance, intolerance, adverse effects, comorbidities, etc?
 - How long should new regimen be given prior to starting HCV regimen?
 - Does insurance cover desired HCV and HIV regimens?
 - If not, who will write the appeal to maintain a compatible combination of HIV and HCV regimens?
 - Who will monitor for tolerability and maintenance of HIV viral suppression while HCV DAAs are given?

5-year risk of HCV re-infection post-SVR



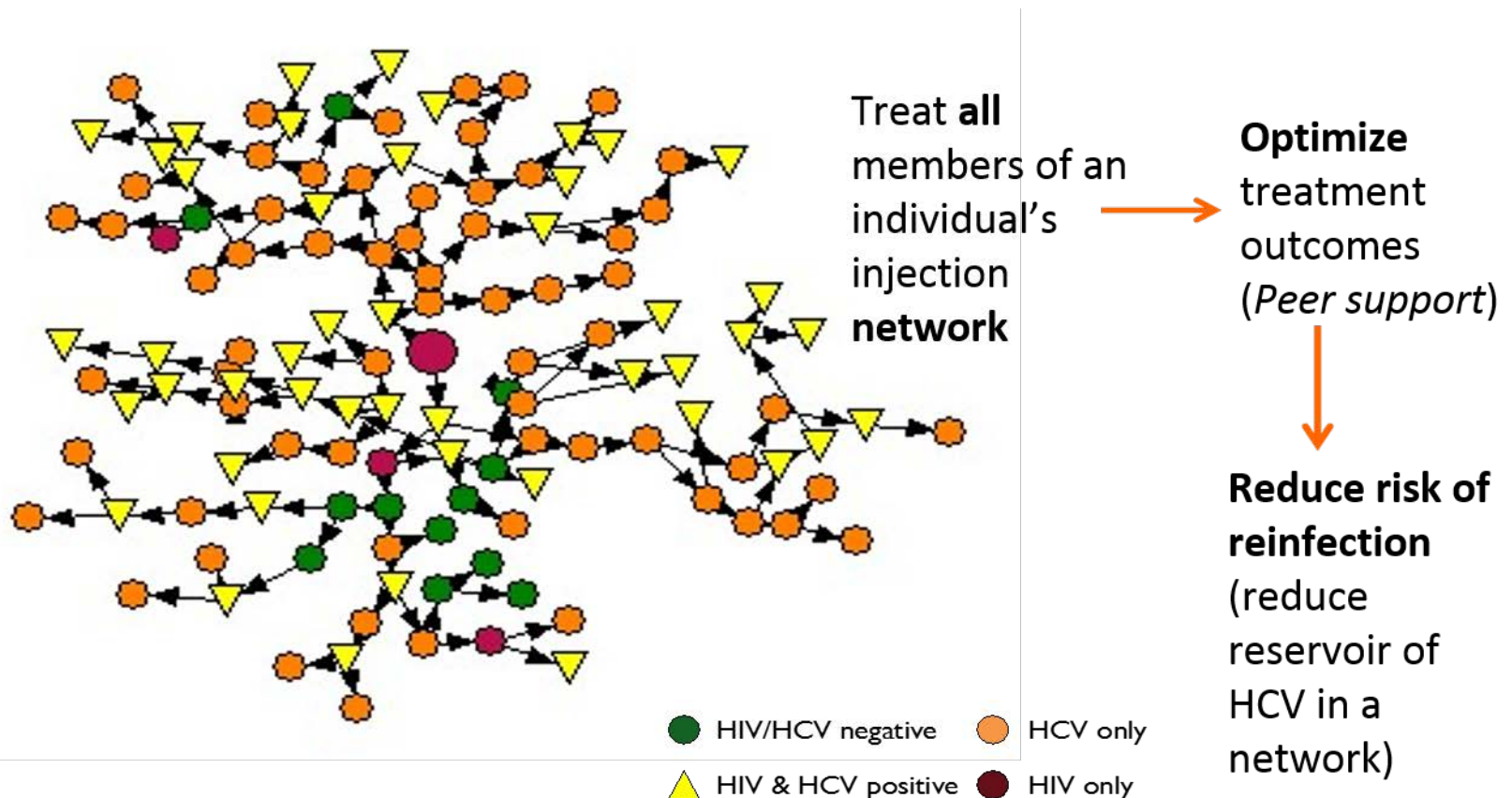
Treating HCV in PWID

- We have to treat PWID for their own health *and* to reduce HCV transmission
- People will get re-infected
 - If nobody gets re-infected, we have not been treating the right patients to reduce transmission
- Treating small numbers of patients increases the risk of reinfection
- Treat in setting of other harm reduction interventions
 - Needle exchange, opioid substitution therapy, counseling

We Lack Data on Effective Strategies to Reduce HCV Reinfection in MSM with HIV/HCV

- People will get re-infected
 - If nobody gets re-infected, we have not been treating the right patients to reduce transmission
- Treating small numbers of patients increases the risk of reinfection
- Counsel on barrier protection and specific sexual activities that may involve small amounts of blood
 - HCV has been found in rectal fluids
- Stimulants increase higher-risk sex and may involve injection

“Bring your friends” approach may optimize treatment and prevention outcomes



Key Points

- Persons living with HIV have an increased risk of hepatitis C infection and everyone needs to be tested
 - Men who have sex with other men and persons who inject drugs need to be tested at least annually if initially negative
 - If a patient previously cleared HCV (either with treatment or spontaneously) they need routine screening for reinfection with HCV RNA (viral load)
 - Ongoing harm reduction efforts are important
- Patients with HIV/HCV coinfection have an increased risk of developing cirrhosis, liver cancer, and liver failure
- Everyone with HIV/HCV coinfection needs to be treated for hepatitis C and needs to be cured
 - New all-oral regimens can cure 95% of patients with HIV/HCV
 - Patients who relapse need to be treated again
- Patients need support in order to successfully start and complete HCV treatment
 - Barriers to cure are similar to those for HIV treatment, but interventions last 12 weeks on average

Excellent Hepatitis C Resources

HCV Guidelines

<http://www.hcvguidelines.org/>

HCV Drug-Drug Interactions

<http://www.hep-druginteractions.org/>

HCV Learning

<http://www.hepatitisc.uw.edu/alternate>

WE NEED YOU!

Participate as Health Center co-presenter.

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Thank you for participating in this Webinar.

We hope that you are able to find the information provided useful as you continue your P4C project. We ask that you take a few moments to complete the feedback survey you will receive when you close out of this webinar.

If you have any additional questions, please email us:

P4CHIVTAC@mayatech.com