

Acute HCV Infection



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Disclosure Information



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Outline



- Rationale to identify acute HCV
- Definition of acute HCV
- Diagnosis of acute HCV
- Treatment of acute HCV

Case



A 22-year-old white female is seen in your clinic with a complaint of a 2 cm abscess on the antecubital fossa of her left arm.

On further questioning you learn she has a five-year history of injection drug use, but is adamant that she has never shared needles or syringes. She was tested for HCV approximately three years ago and was seronegative.

Her only symptom is fatigue and mild discomfort at the site of the small abscess. The rest of her exam is normal.

The patient has recently shared cotton/cookers with her new boyfriend.

HBsAg is non-reactive and her anti-HBc is non-reactive while her anti-HBs is reactive (>100 IU/mL); hepatitis A IgM and IgG is non-reactive, HIV nonreactive.

Her HCV antibody is reactive; her HCV RNA is 3,300 IU/mL; genotype 1a, ALT 120; AST 90.

Rationale to identify acute HCV



- For personal and public health benefit
 - Provision of education, HAV/HBV vaccines
 - Harm reduction, including HIV prevention
 - Knowledge of status critical
 - Interruption of transmission

HCV incidence is likely rising



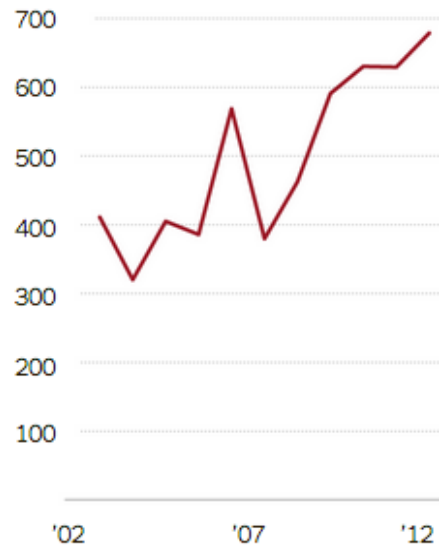
- Driven by opioid epidemic

The Resurgence of Heroin

The number of users of heroin has grown over the last decade.

Heroin users

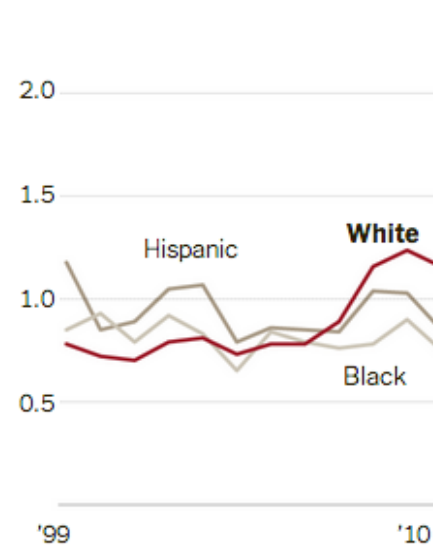
In thousands



Overdose deaths began to rise sharply in the latter half of the previous decade among young whites. Death rates since 2010 have not yet been compiled.

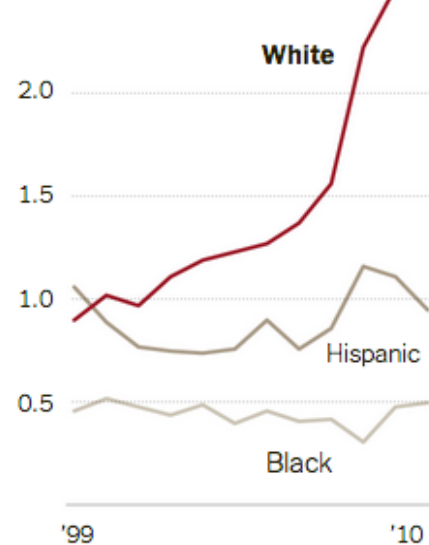
Heroin deaths by race

Per 100,000 population, age adjusted



Heroin deaths among 15- to 34-year-olds

Per 100,000 population

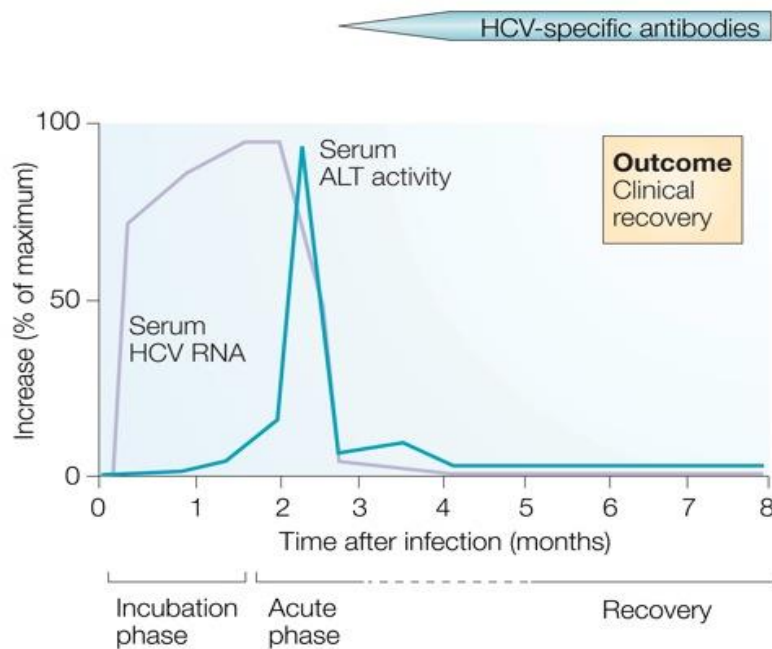


Source: Centers for Disease Control and Prevention; Substance Abuse and Mental Health Services Administration

What is acute HCV?



- Earliest phase of infection, defined as first 6 months
 - Spontaneous clearance possible
 - Responsiveness to exogenous IFN highest
- Often asymptomatic



~66% of spontaneous clearance occurs in first 6 months

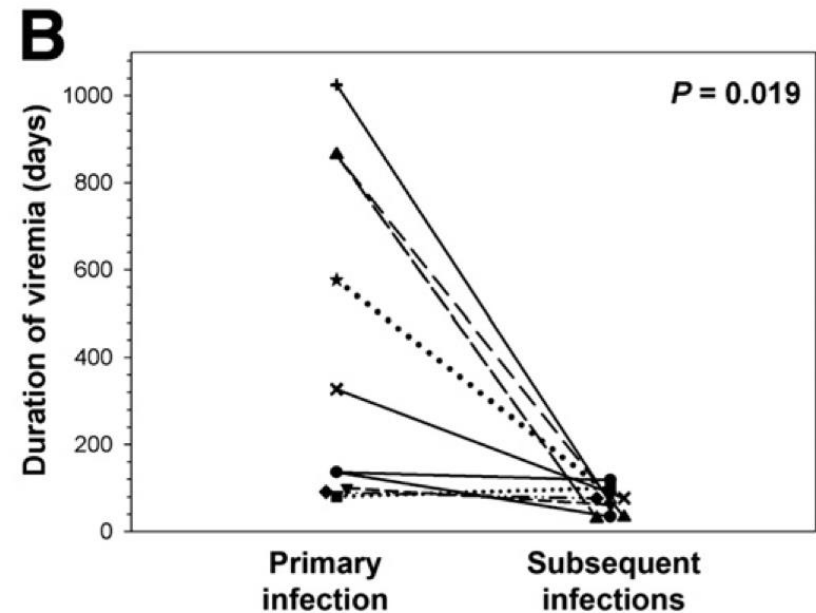
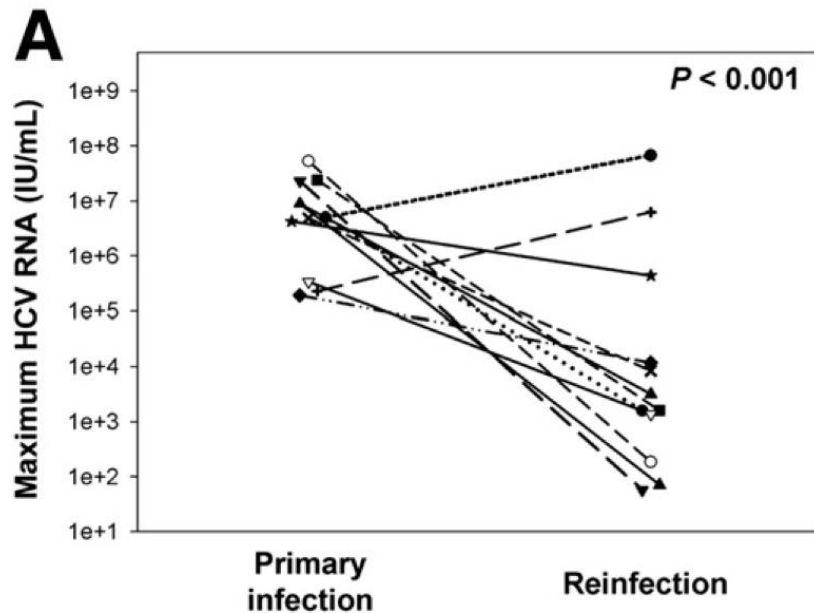
SC associated with:
female gender
young age
immunocompetence
non-African American race
IL28B CC and HLA genes
symptoms

HCV RNA required to diagnosis
reinfection

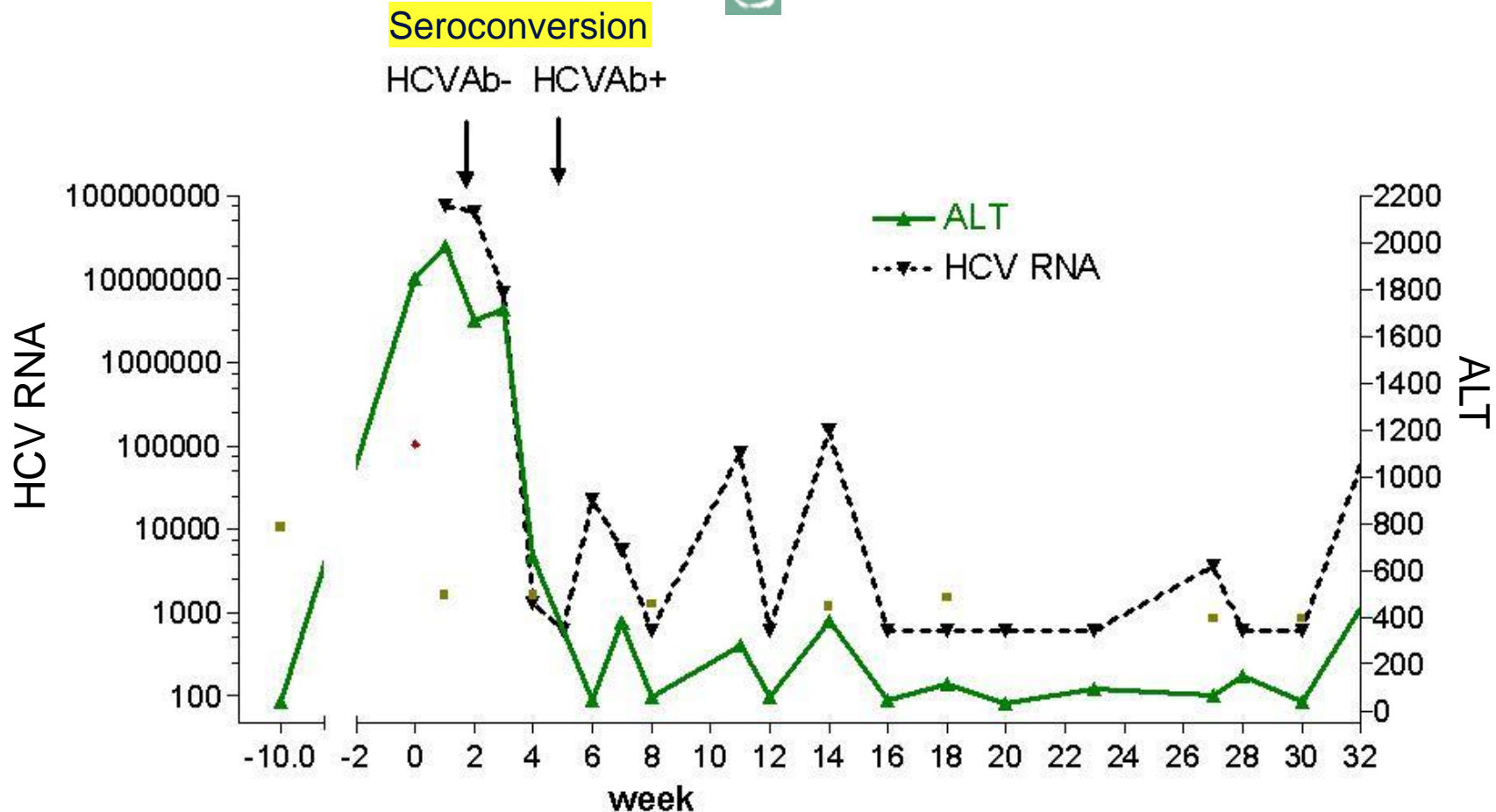
Clearance is associated with protection from reinfection



- HCV peak viral load (A) and duration of viremia (B) during reinfection in injection drug users



Acute HCV may exhibit a dynamic course



Dynamic changes
HCV RNA and ALT

Case



A 22-year-old white female with 5-year history of injection drug use, never shared needles/syringes, tested 3 years prior as negative now with new antibody.

The patient has recently shared cotton/cookers with her new boyfriend.

Her HCV antibody is reactive; her HCV RNA is 3,300 IU/mL; genotype 1a, ALT 120; AST 90

Serial monitoring of HCV RNA and LFTs:

baseline: HCV RNA 3,300 IU/mL; ALT 120; AST 90

week 4: HCV RNA 50,000 IU/mL; ALT 390; AST 270

week 10: HCV RNA 1,115 IU/mL; ALT 690; AST 425

bilirubin remains normal

Utility of IL28B testing



- Single nucleotide polymorphisms on chromosome 19 are associated with interferon-induced and spontaneous clearance of HCV
- rs12979860 SNP testing commercially available (not FDA-approved)
- CC type favorable, CT or TT unfavorable
 - CC about twice as likely to clear, correlates with jaundice
 - Not a perfect predictor
- Clinical utility likely less important in the novel direct-acting antiviral era due to high cure rates in chronic phase

Diagnosis of acute HCV



- High clinical suspicion + supporting laboratory data
 - Seroconversion, fluctuating HCV RNA > 1 log, or value $< 10^5$ IU/mL
 - HCV RNA for seronegative window, reinfections
- React to changes in LFTs
- Screen for high-risk behaviors
 - PWID: sharing of paraphernalia
 - HIV+MSM: Bloody practices, exposure to semen
- Screen those engaging in high-risk behaviors
 - Yearly antibodies recommended and cost-effective

Should we treat acute HCV?



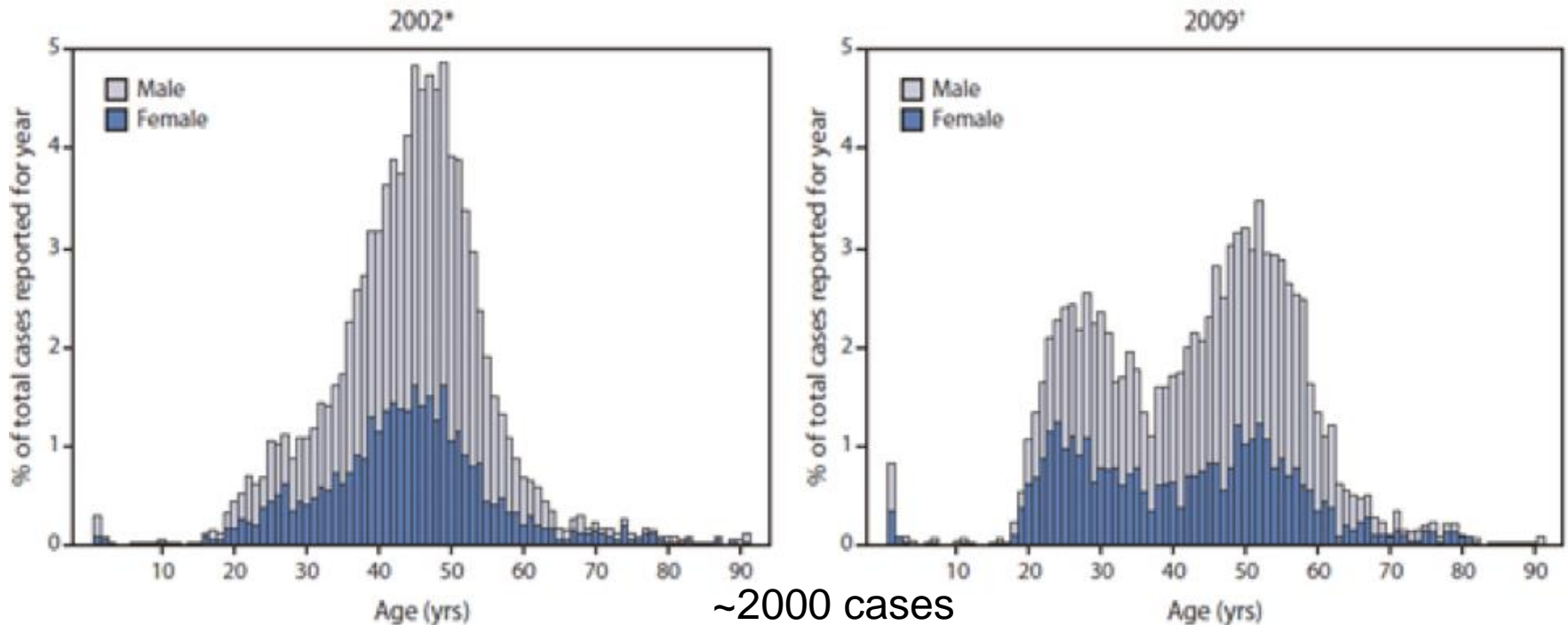
- Rarely fulminant, so unlikely to prevent acute liver failure/death
- Fibrosis accelerated for HIV+ individuals, more rationale to treat
- In past, rationale to treat early included cure rates of interferon-based therapies during acute phase >> chronic phase
- At this time, no data to indicate that less intensive courses of interferon-free based regimens are as effective for acute HCV
- Major rationale is to reduce transmission

Should we treat acute HCV?



- Burden of new infections is high and rising in the United States

Massachusetts surveillance data for HCV cases



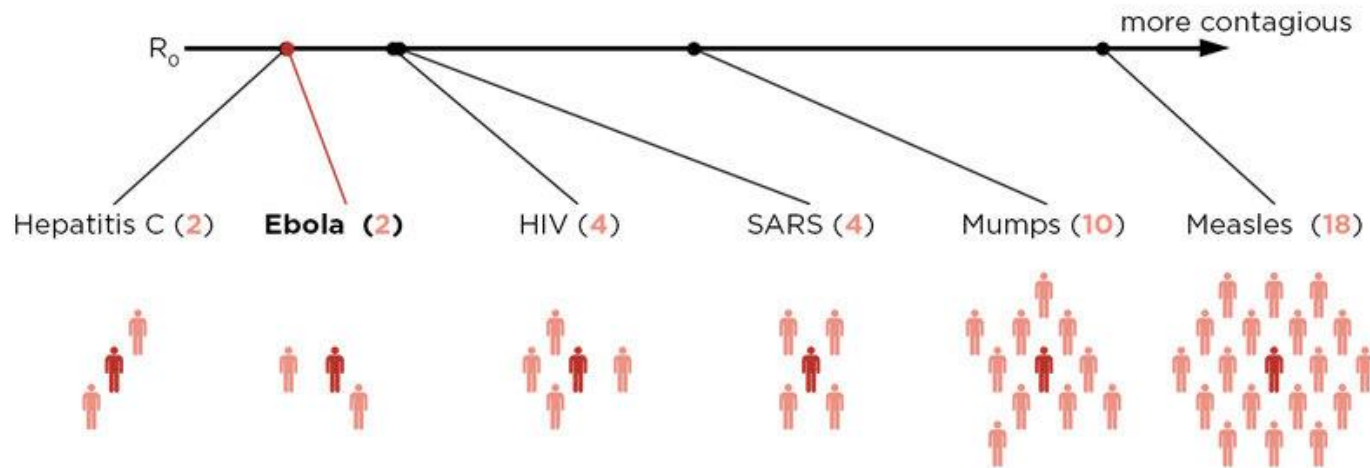
~2000 cases
<30 years annually

R₀ (basic reproductive number)

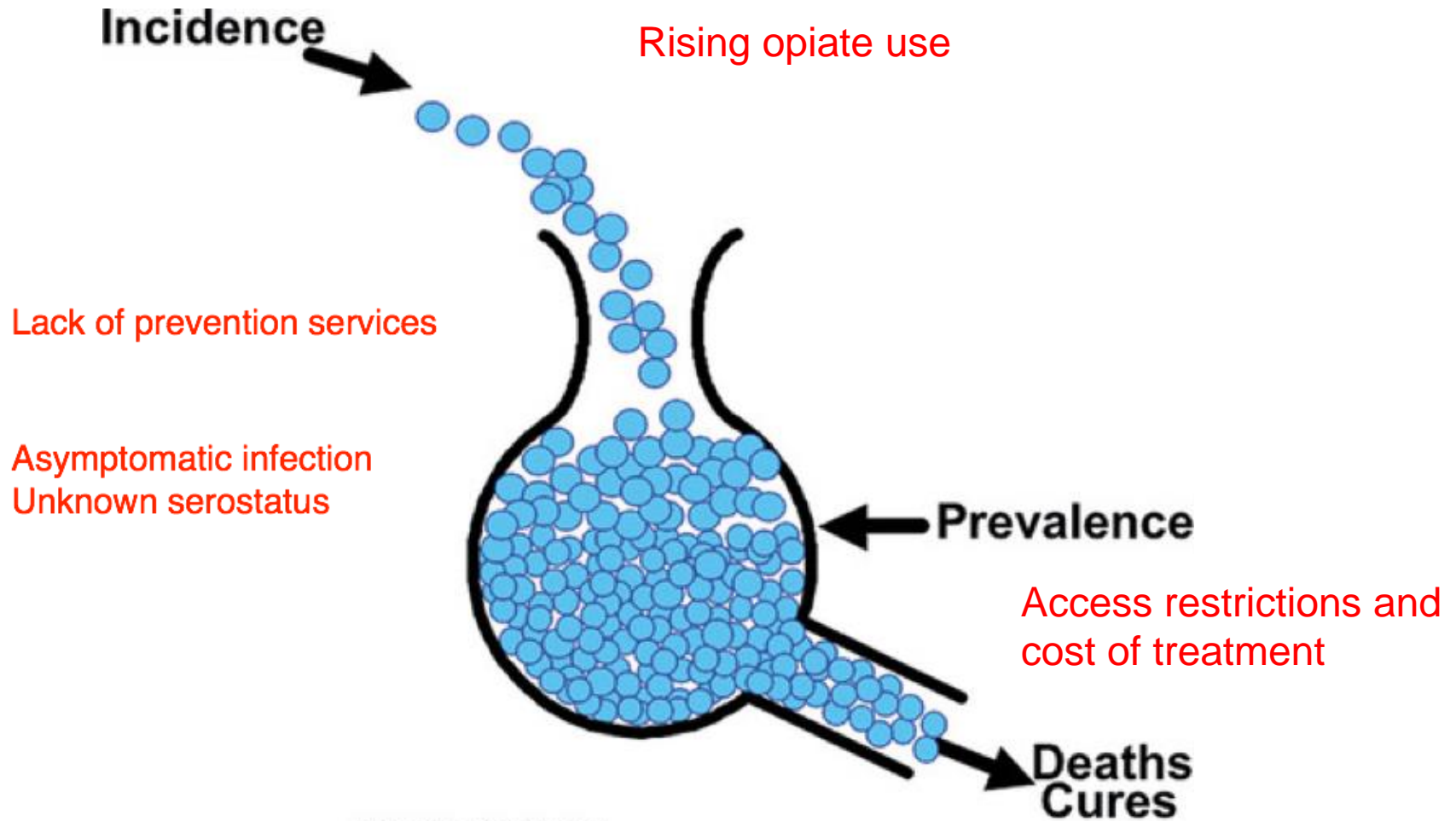


- C = # of contacts per unit of time
- P = probability of transmission per contact with infectious person
- D = duration that patient is infectious to others

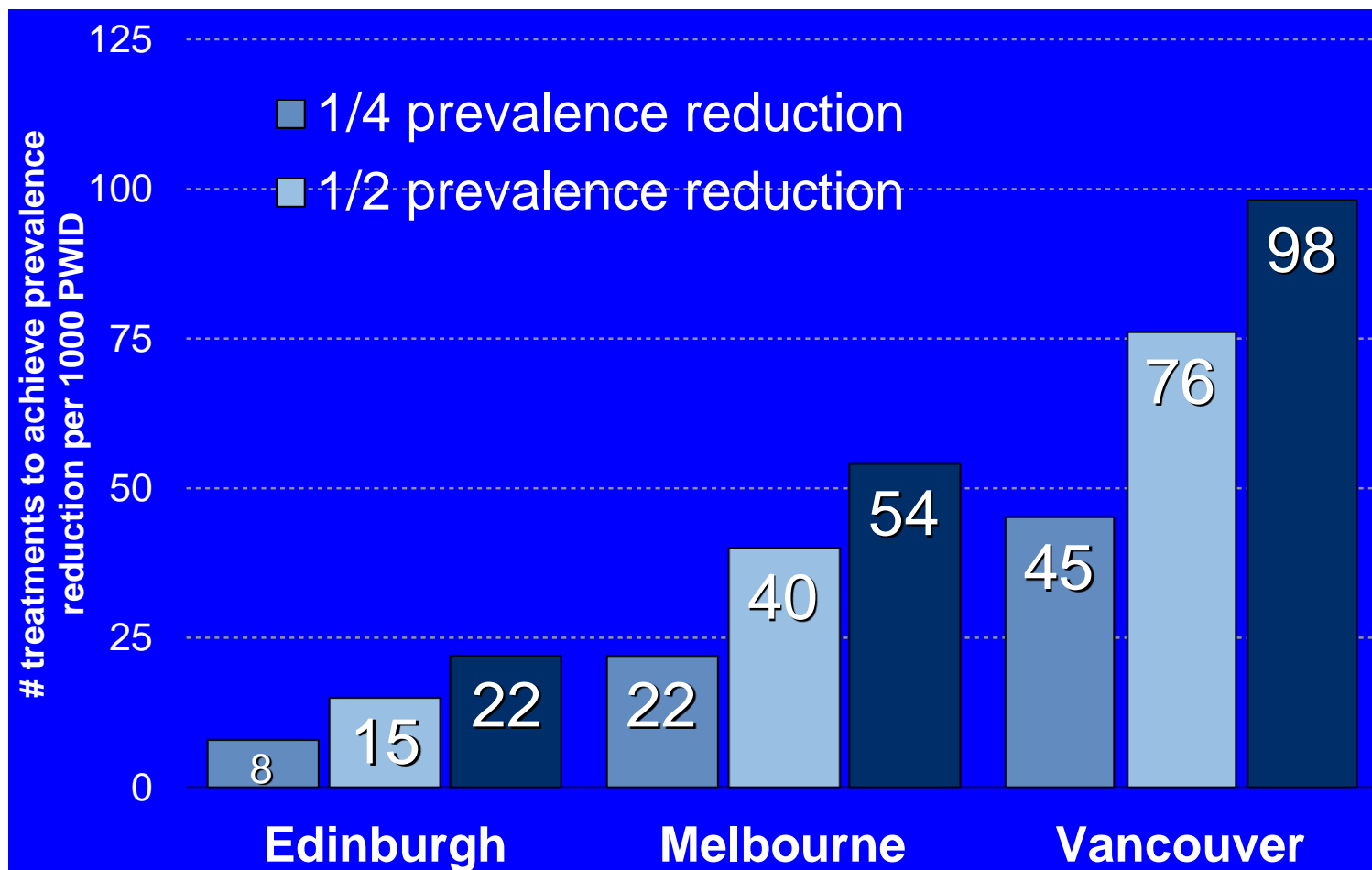
The number of **people** that **one sick person** will infect (on average) is called R₀. Here are the maximum R₀ values for a few viruses.



Incidence, prevalence, and sustaining an epidemic



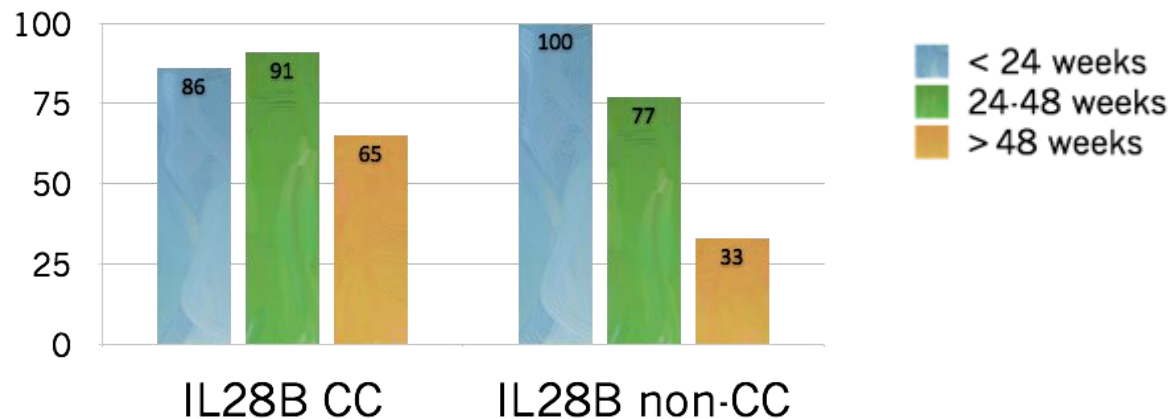
Can treatment as prevention be applied for HCV among people who inject drugs (PWID)? Modeling DAAs



How to treat acute HCV



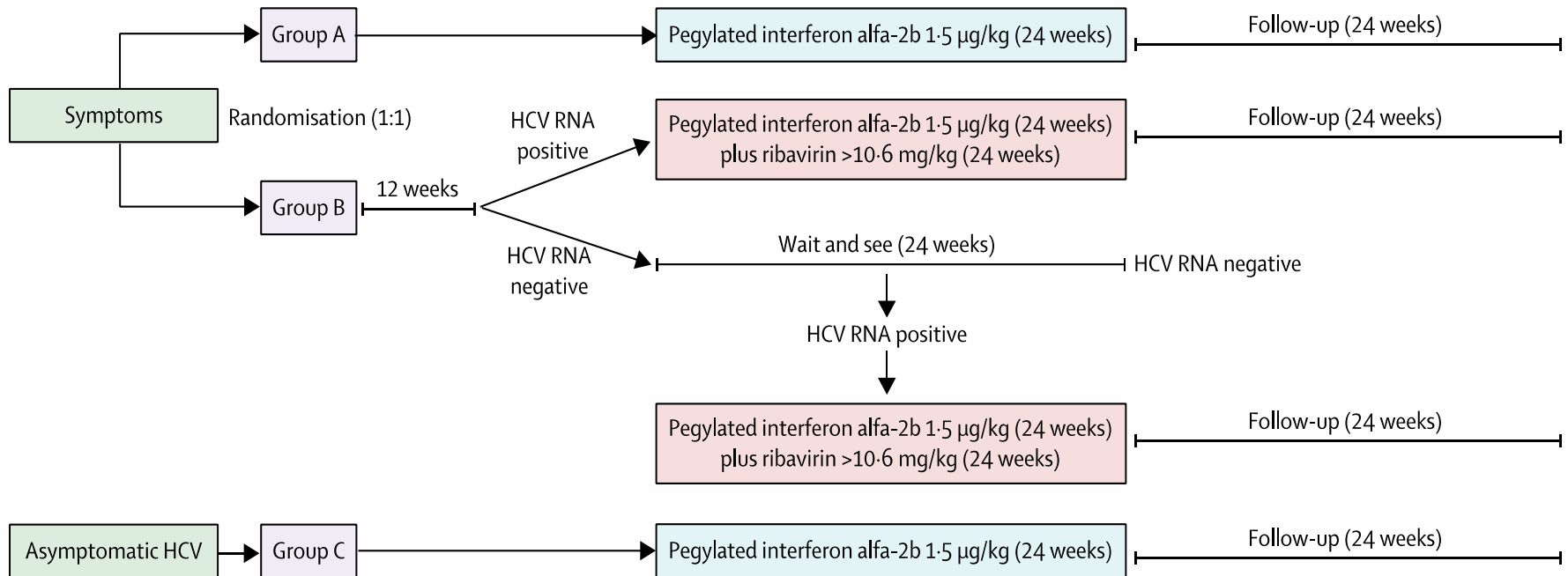
- Timing mattered in the interferon era
- 80 acute HCV patients treated in Italy
 - Timing determined by patient/provider preference
 - Shortened course < 24 weeks, standard course for chronic HCV if > 24 weeks



Timing of treatment, IFN-era



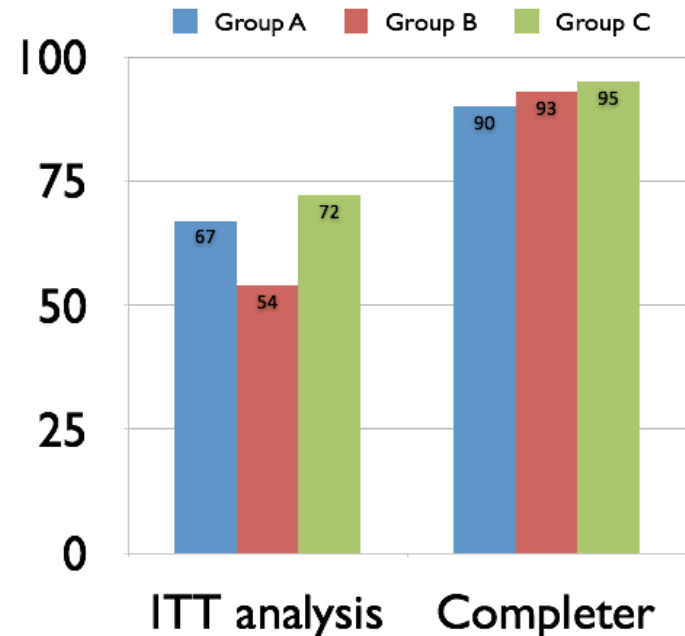
- Largest randomized-control trial of HCV therapy
 - Immediate PEG monotherapy vs. delayed PEG/RBV combination therapy



Hep-Net Trial shows delays not as effective, but completers of therapy did quite well



- Group A: immediate
- Group B: delayed
 - 11 or 52 on delayed arm spontaneously cleared
- Group C: immediate (if no symptoms)
- PEG/RBV not as effective, but highly dependent on adherence



PEG/RBV + telaprevir for total 12 weeks



- 41 patients with HIV + aHCV enrolled from 2011-2012
 - 7 non-GT1
 - 7 did not have access
 - 5 spontaneously cleared
 - 2 refused treatment
- 19 patients treated: median age 44
 - 12 IL28B genotype CC (63%)
 - SVR12: 16/19 84%
 - Historical SVR 63% with PEG/RBV

What to do while awaiting data from interferon-free regimens?



- All published data are in interferon-era
 - Could use shortened course PEG-IFN +/- RBV
 - Many patients and providers may shun side effects
- Reasonable to wait for spontaneous clearance unless risk of transmission is high
 - Surgeon suffering aHCV after needlestick injury
 - Active PWID
- Can treat with same regimens used for chronic infection after waiting period
- Vital to provide knowledge, services and treatment to reduce further transmission



Recommendations for Testing, Managing, and Treating Hepatitis C



4. *Vaccination against hepatitis A and hepatitis B is recommended for all susceptible persons with HCV infection.*

Rating: Class IIa, Level C

5. *All persons with HCV infection should be provided education on how to avoid HCV transmission to others.*

Rating: Class I, Level C

- Vaccinate or ensure immunity against other hepatitis viruses
- Educate regarding avoidance of HCV transmission
 - Harm reduction for PWID: clean needles & equipment
 - Harm reduction for HIV+MSM: barriers, practices



Recommendations for Testing, Managing, and Treating Hepatitis C



When and in Whom to Initiate HCV Therapy Table 2. Persons At Elevated Risk of HCV Transmission* and in Whom HCV Treatment May Yield Transmission Reduction Benefits

Men who have sex with men (MSM) with high-risk sexual practices

Active injection drug users

Incarcerated persons

Persons on long-term hemodialysis

HCV-infected women of child-bearing potential wishing to get pregnant

HCV-infected health care workers who perform exposure-prone procedures

Rating: Class IIa, Level C

*Patients at substantial risk of transmitting HCV should be counseled on ways to decrease transmission and minimize the risk of reinfection.

- Decision to initiate earlier - preventing transmission (ie, needlestick to surgeon, PWID) - ? utility of IL28B genotype



Recommendations for Testing, Managing, and Treating Hepatitis C



Recommendations for medical management and monitoring in acute HCV infection.

Regular laboratory monitoring is recommended in the setting of acute HCV infection until the alanine aminotransferase (ALT) level normalizes and HCV RNA becomes repeatedly undetectable, suggesting spontaneous resolution.

Monitoring HCV RNA (eg, every 4 weeks to 8 weeks) for 6 months to 12 months is recommended to determine spontaneous clearance of HCV infection versus persistence of infection.

Counseling is recommended for patients with acute HCV infection to avoid hepatotoxic insults, including hepatotoxic drugs (eg, acetaminophen) and alcohol consumption, and to reduce the risk of HCV transmission to others.

Referral to an addiction medicine specialist is recommended for patients with acute HCV infection related to injection drug use.



Recommendations for Testing, Managing, and Treating Hepatitis C



If the practitioner and patient have decided that a delay in treatment initiation is acceptable, monitoring for spontaneous clearance is recommended for a minimum of 6 months. When the decision is made to initiate treatment after 6 months, treating as described for chronic hepatitis C is recommended

If a decision has been made to initiate treatment during the acute infection period, monitoring HCV RNA for at least 12-16 weeks is recommended to allow for spontaneous clearance before starting treatment.

For patients in whom HCV infection spontaneously clears, treatment is NOT recommended.

Rating: Class III, Level B



Recommendations for Testing, Managing, and Treating Hepatitis C



Recommended regimens for patients with acute HCV infection

Owing to high efficacy and safety, the same regimens recommended for chronic HCV infection (see Initial Treatment of HCV Infection and When and in Whom to Treat sections) are also recommended for acute infection.

- High rates of cure for novel regimens for chronic HCV
- Vast majority of data is with PEG-IFN, less costly, but far more side effects. Experts in U.S. generally would not recommend this option.

Summary



- Acute HCV incidence is rising in the United States
 - Achievement of viral clearance will be important to prevent new cases
- Diagnosis requires a high clinical suspicion
 - Yearly antibody recommended
 - ✦ People who inject drugs
 - ✦ HIV+MSM
- Acute HCV is a dynamic phase of infection
 - Longitudinal values may show elevated ALT and fluctuating HCV RNA
 - Spontaneous clearance
 - Determining outcome informs the patient's infectiousness to others
- IL28B genotyping available for prognosis, but currently less useful in clinical-decision making

Summary



- **Diagnosis of acute HCV requires a high clinical suspicion**
 - No single diagnostic test
- **Counseling points for newly-identified acute HCV**
 - Not likely to have fulminant disease
 - Possibility of spontaneous clearance
 - Able to transmit to others
- **Treatment decisions**
 - Most often we will be allowing for spontaneous clearance
 - No reason to believe that SVRs will be lower for the same regimens used for chronic HCV
 - Awaiting data of clinical trials of interferon-free regimens