# Updates on Hepatitis C & B co-infections in HIV patients

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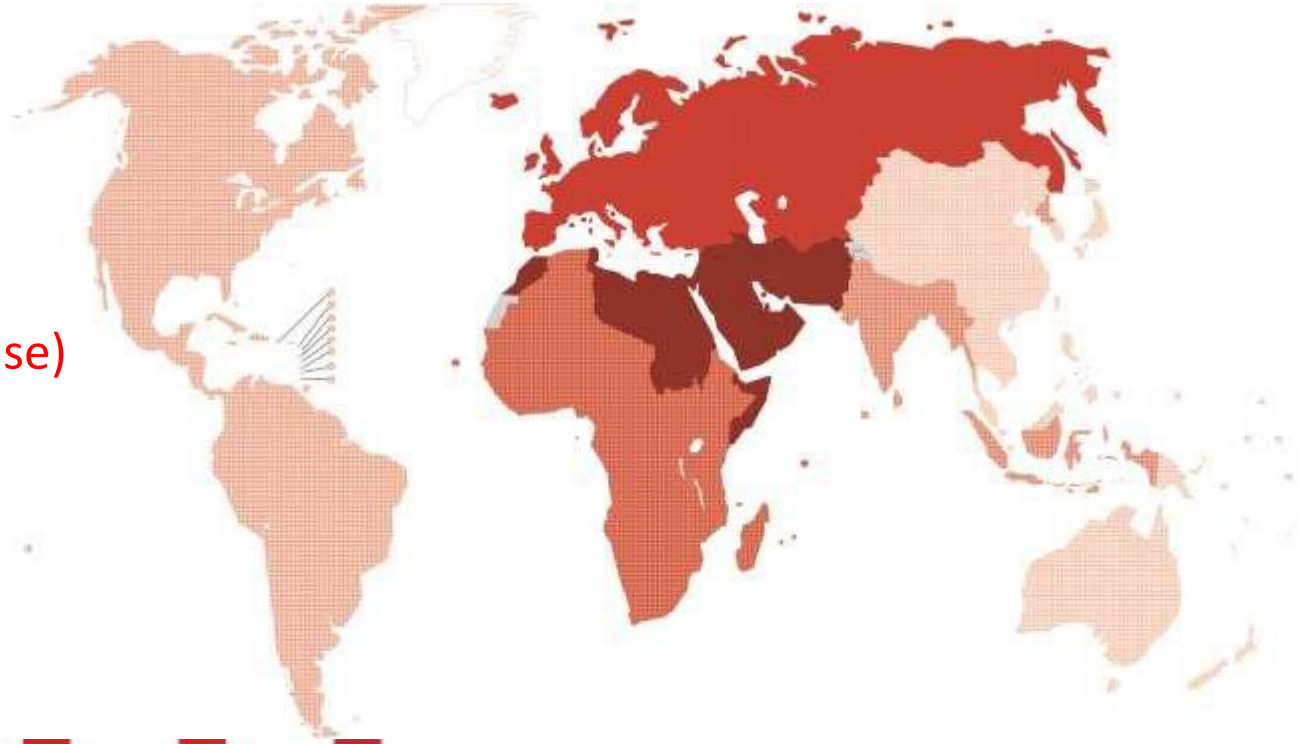
# Global Status of HCV Infection

HCV

**Incidence:**

1.25 million new infections / year

(Unsafe health care and injection drug use)

**Prevalence:**

58 million infected, all regions

# Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis

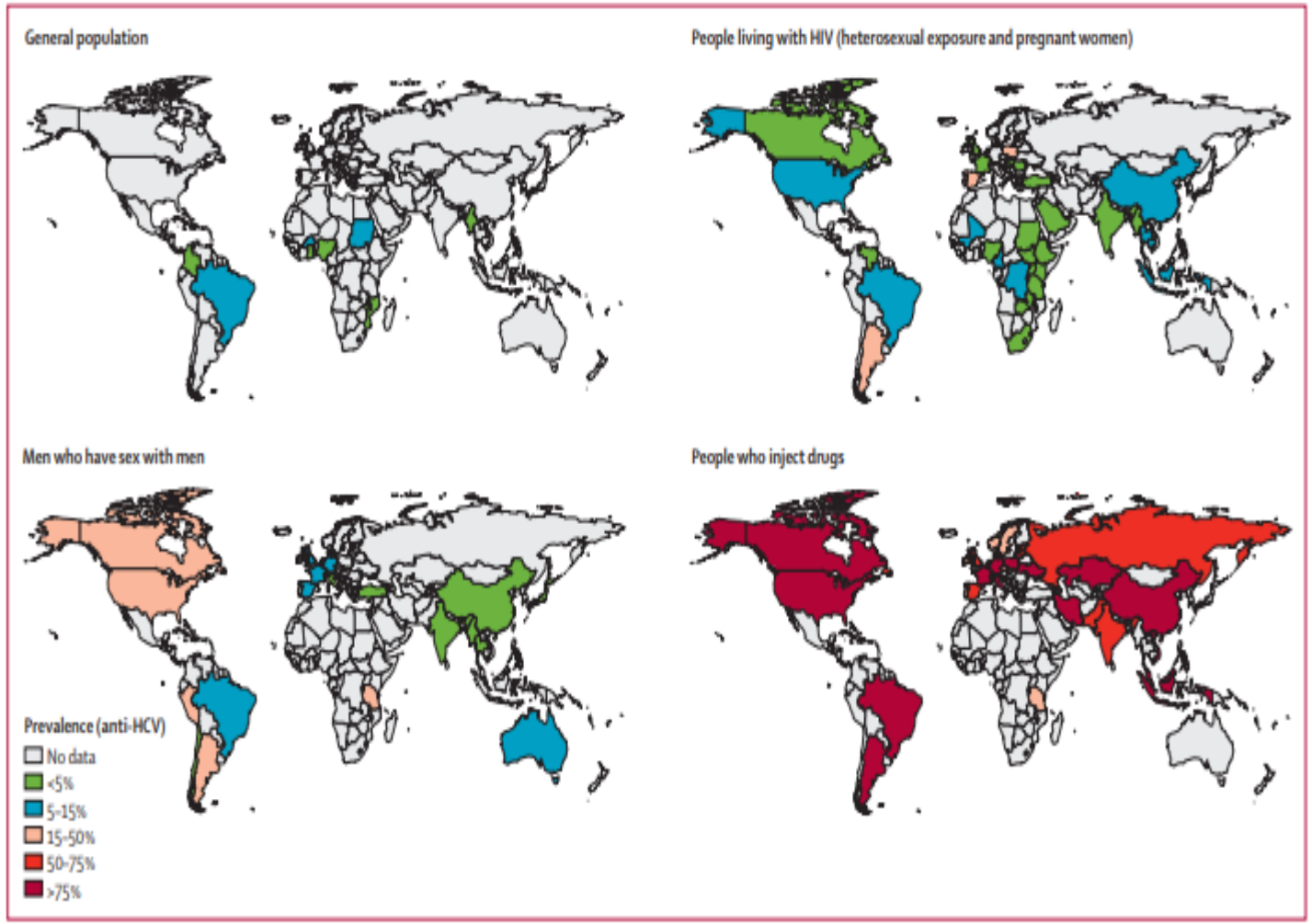



*Figure 2:* Best estimates of prevalence of hepatitis C virus (HCV) co-infection in four population samples

In HIV-infected individuals, HIV–HCV co-infection in

- 2·4% within general population samples
- 4·0% within pregnant or heterosexually exposed
- 6·4% in MSM, and
- 82·4% in PWID.

Worldwide, 2 278 400 HIV–HCV co-infections of which 1 362 700 are in PWID.

South and Southeast Asia:
Total HIV-infected individuals= 3 134 400
HIV Infected (excluding PWID) = 2 899 800
HIV-HCV co-infected = 89 900 (3%)

HIV-HCV PWID= 234 600
HIV-HCV co-infected= 195 700 (83%)

Lancet Infect Dis 2016

# Coinfection of HBV and HCV in HIV patients in Pakistan

Across multiple studies in PWIDs:

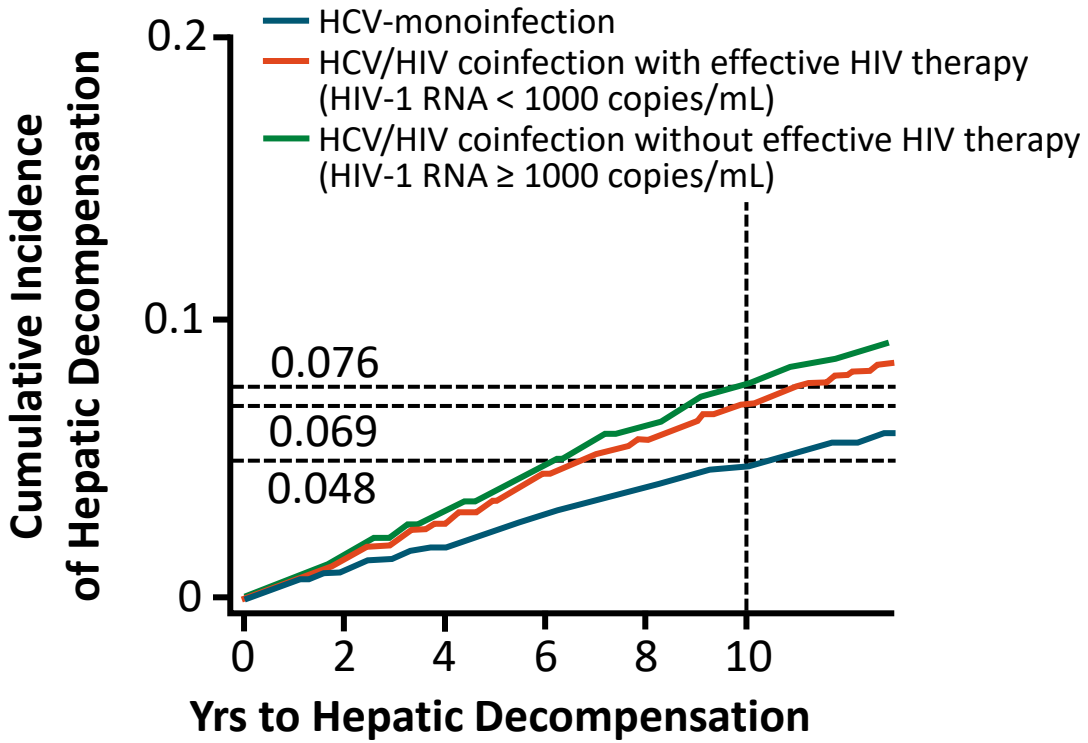
- HCV Infection:  54 – 72%.
- HIV Infection:  8.6 - 74%
- HBV Infection:  3.6- 5%
- HIV-HCV Co-Infection:  24 - 93%
- HIV-HBV Co-Infection:  ~ 5%

- Age: 16-30 yrs
- Education level: Low

# Disease Progression in HCV Monoinfection vs HCV/HIV Co-infection With or Without HIV Suppression

- Retrospective cohort study of HCV-infected, treatment-naive patients in the Veterans Health Administration (N = 10,359)

**Time to Decompensation by Maintained HIV RNA Level**




- If HIV-1 RNA < 1000 copies/mL: +65% excess risk
- If HIV-1 RNA ≥ 1000 copies/mL: +82% excess risk

Lo Re III V, et al. Ann Intern Med. 2014;160:369-379.

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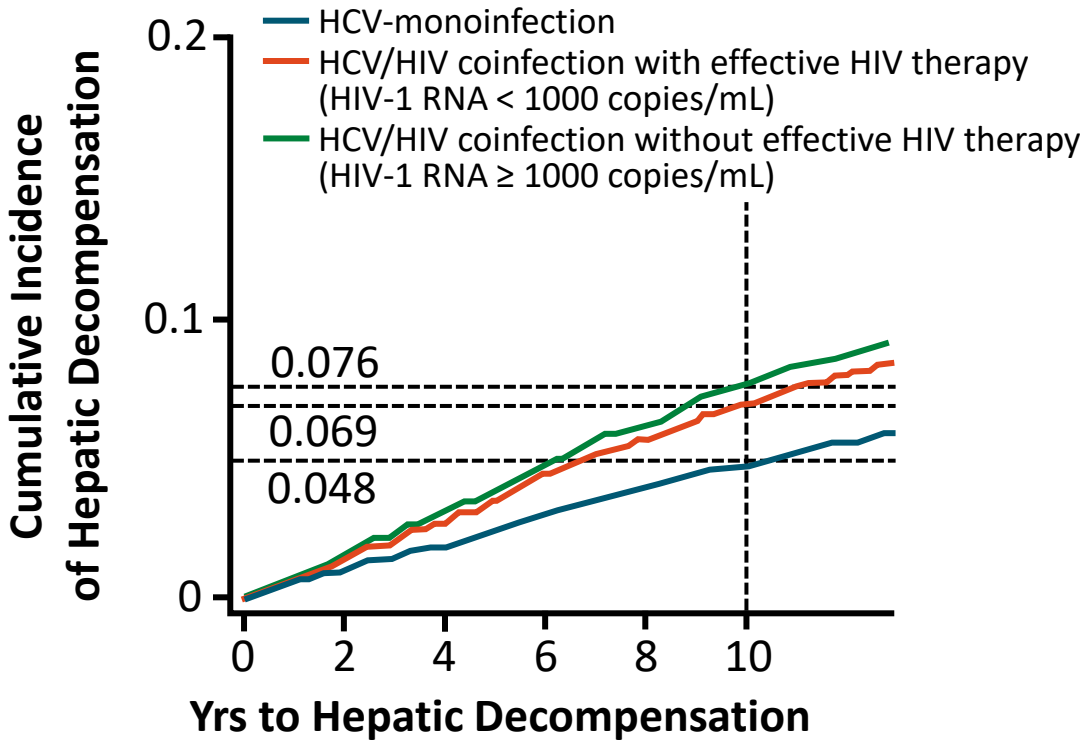
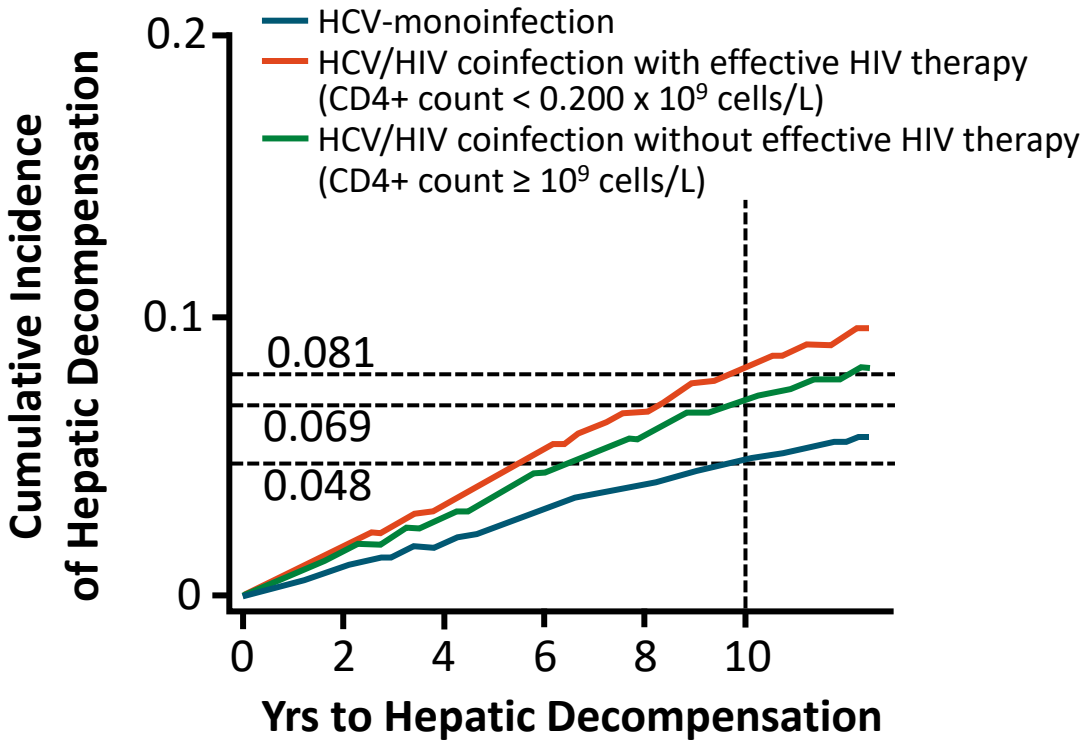



- If HIV-1 RNA < 1000 copies/mL: +65% excess risk
- If HIV-1 RNA ≥ 1000 copies/mL: +82% excess risk

**Time to Decompensation by Maintained CD4+ Cell Count**

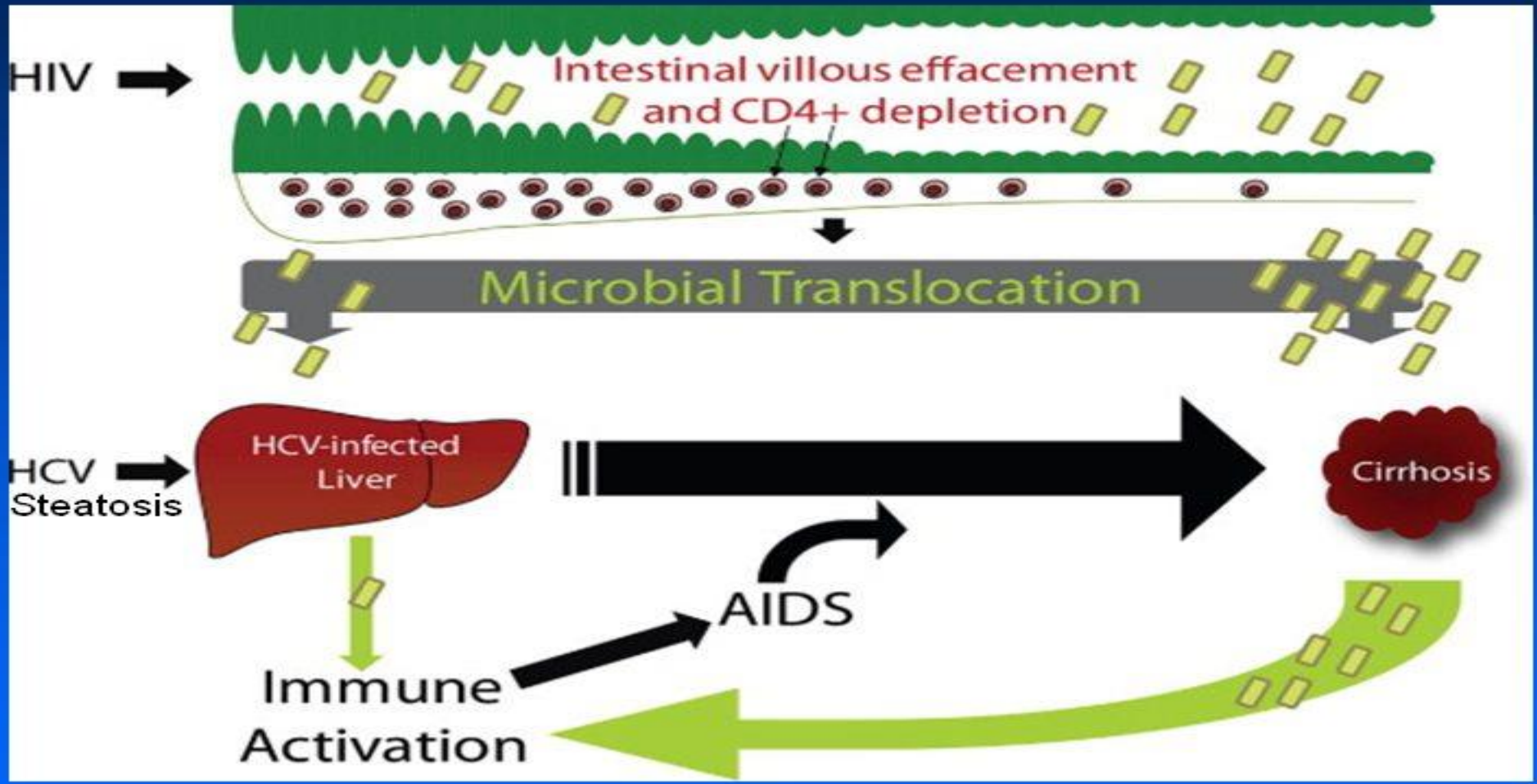



- If CD4+ < 200/$mm^2$: +203% excess risk
- If CD4+ ≥ 200/$mm^2$: +56% to 63% excess risk

Lo Re III V, et al. Ann Intern Med. 2014;160:369-379.

# Why is liver disease more progressive in those with low CD4?

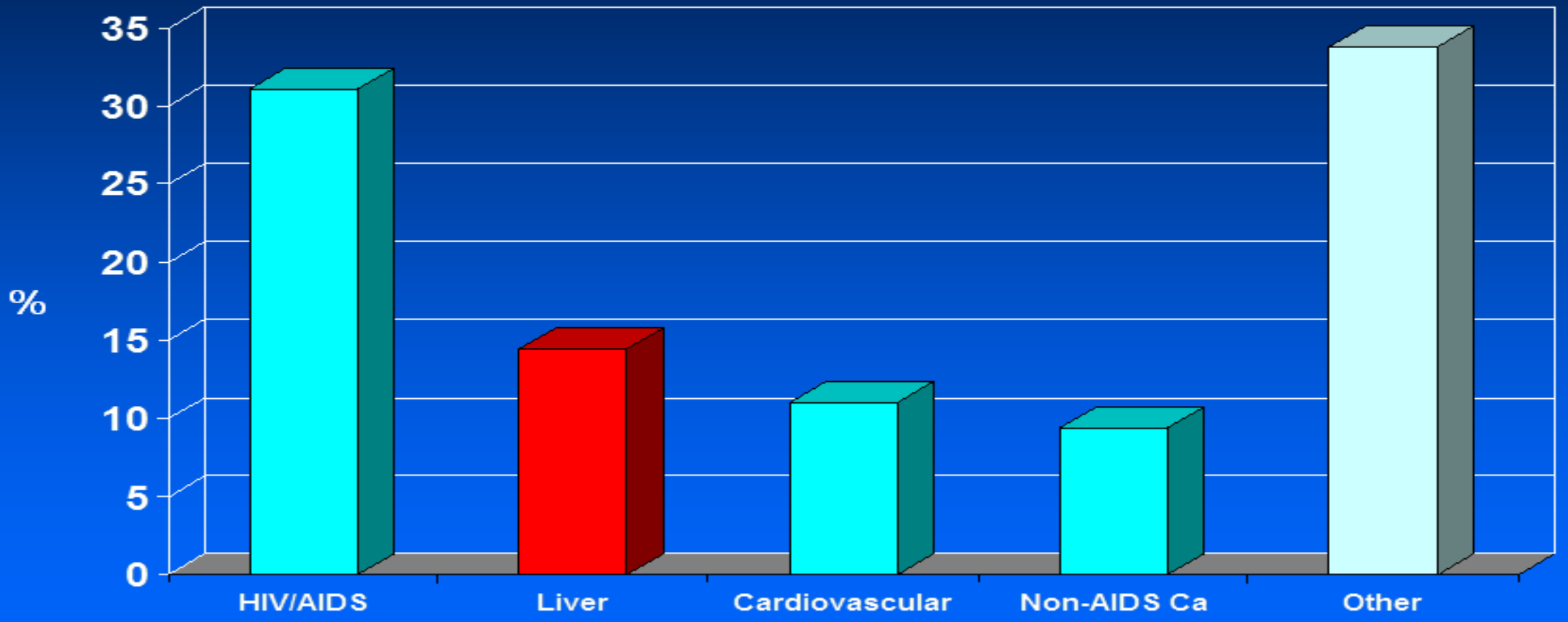
## Bacterial Translocation




Balagopal et al. Gastroenterology 2008;135:226-233

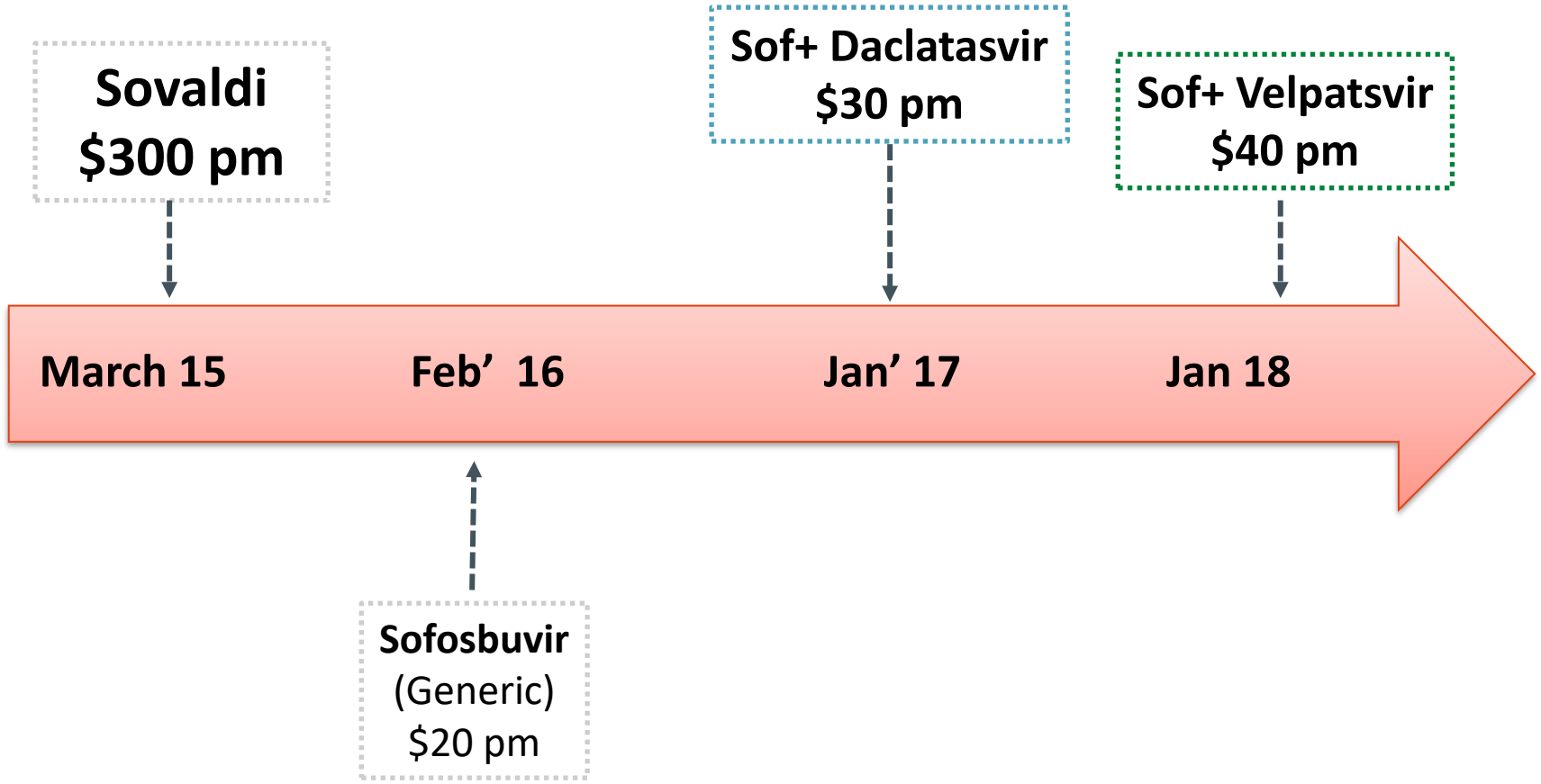
# Liver-Related Deaths in HIV

1246 deaths in 23,441 HIV+ pts followed for 3.5 yrs
22% HCV, 8% HBV




D:A:D Study Arch Int Med 2006

# DAA availability in Pakistan



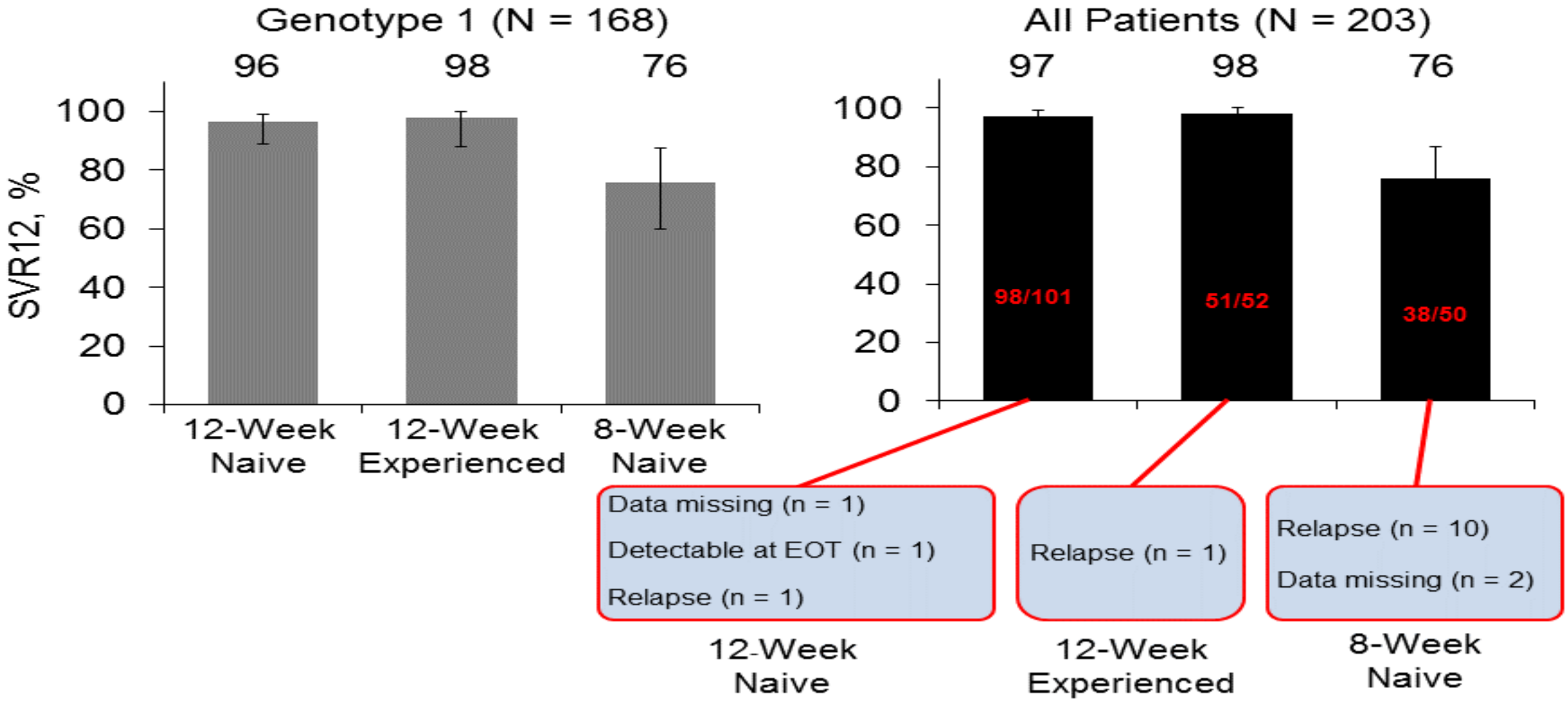
ORIGINAL ARTICLE

# Daclatasvir plus Sofosbuvir for HCV in Patients Coinfected with HIV-1

D.L. Wyles, P.J. Ruane, M.S. Sulkowski, D. Dieterich, A. Luetkemeyer, T.R. Morgan, K.E. Sherman, R. Dretler, D. Fishbein, J.C. Gathe, Jr., S. Henn, F. Hinestrosa, C. Huynh, C. McDonald, A. Mills, E.T. Overton, M. Ramgopal, B. Rashbaum, G. Ray, A. Scarsella, J. Yozviak, F. McPhee, Z. Liu, E. Hughes, P.D. Yin, S. Noviello, and P. Ackerman, for the ALLY-2 Investigators*

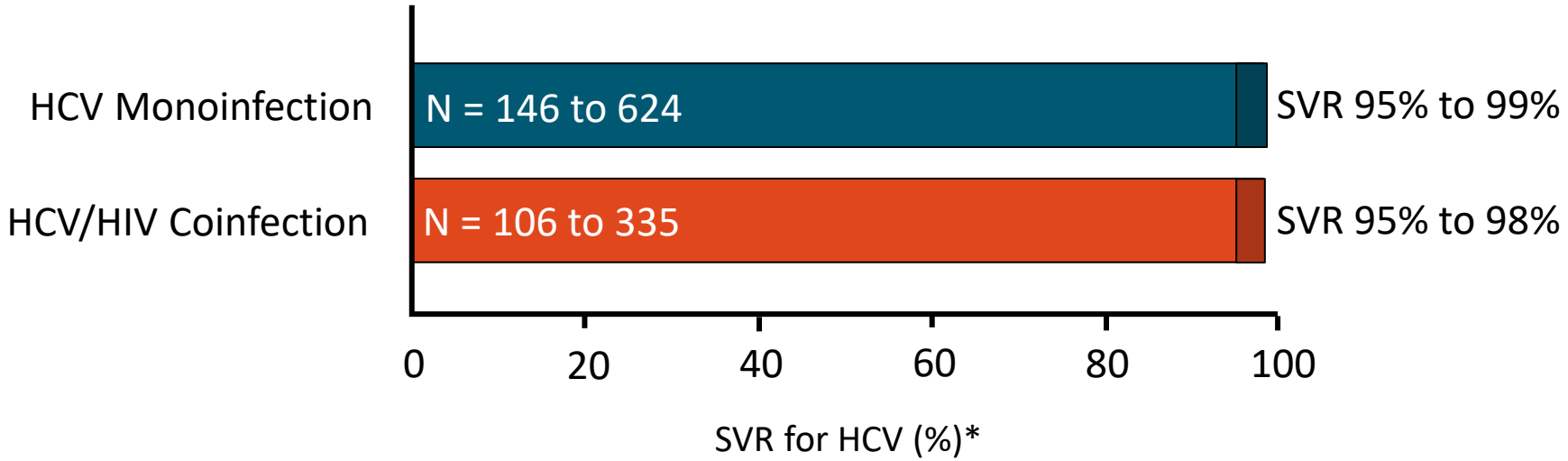
Wyles et al. N Engl J Med 2015

# ALLY-2: SVR12 by treatment duration and HCV treatment experience



# HCV DAAs Have Similar Efficacy in Persons With and Without HIV Coinfection

Efficacy Across Separate Phase III Studies of GT1-6 HCV Infection With GLE/PIB, GZR/EBR, SOF/LDV, or SOF/VEL




*Most data reported for these studies are from treatment-naive patients with GT1/4 HCV infection receiving 12-wk regimens.

# Treatment of HCV and HIV in Co-infected Persons

- All persons with HIV should be treated with **potent ART,** especially those with HIV/HCV coinfection[1]
  - HIV infection is independently associated with HCV disease progression[2]
- **HCV treatment** should also be a priority for persons with HCV/HIV coinfection[2]
  - Efficacy and adverse event rates of HCV DAAs among those with HCV/HIV coinfection are similar to those observed with HCV alone
  - Cotreatment "requires continued awareness and attention to the complex drug–drug interactions that can occur between DAAs and antiretroviral medications"

1. DHHS Guidelines. 2018. 2. AASLD/IDSA HCV Guidelines. 2017.

# Common Scenarios for the Co-treatment of HCV and HIV Infection

1. Persons taking ART with HIV RNA suppression who plan to initiate HCV DAA therapy

- Decisions:
  - Selection of HCV DAA regimen
  - Adjustment of ART to facilitate a specific DAA regimen

2. Persons not taking ART who plan to initiate HCV DAA therapy

- Decision:
  - Which infection to treat first, or whether to start both treatments simultaneously

# Cotreatment of HIV and HCV coinfection

- For many patients, initiation of ART should be prioritized; however, HIV treatment and HIV-1 RNA suppression are not required before HCV DAAs
  - Treatment readiness for 8-12 wks of HCV DAAs may be different than for lifelong ART
  - HCV treatment and cure may serve to facilitate HIV care engagement
  - SVR may reduce the risk of drug-induced liver injury
- If ART is initiated first, consider delaying HCV DAAs for 4-6 wks to confirm tolerability and HIV-1 RNA response

AASLD/IDSA HCV Guidelines. 2017.

# Recommendations for Hepatitis C Virus/HIV Coinfection

## Updated March 2023

- All people with HIV should be screened for hepatitis C virus (HCV) infection**.**
- Patients at high risk of HCV infection should be screened annually and whenever incident HCV infection is suspected **(AIII).**
- ART should be initiated in all patients with HCV/HIV coinfection, regardless of CD4 T lymphocyte cell count **(AI).**
- The benefits of ART outweigh concerns regarding drug-induced liver injury
- The ARV and HCV treatment regimens should be selected with special consideration for potential drug–drug interactions and overlapping toxicities **(AIII)**
- Before initiating HCV therapy, patients with HCV/HIV coinfection and active HBV infection (HBsAg positive) should receive ART that includes two agents with anti-HBV activity **(AIII)**

***Rating of Recommendations:*** *A = Strong; B = Moderate; C = Weak*

***Rating of Evidence:*** *I = Data from RCTs trials; II = Data from well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

NIH Panel on Antiretroviral Guidelines for Adults and Adolescents

# HIV/HCV Drug–Drug Interactions

| ARV(s) | GLE/PIB | GZR/EBR | SOF/LDV | SOF/VEL | SOF/VEL/VOX |
|---|---|---|---|---|---|
| ATV + (RTV or COBI) | X | X | ✓* | ✓* | X |
| DRV + (RTV or COBI) | X | X | ✓* | ✓* | ✓*†‡ |
| LPV + RTV | X | X | ✓* | ✓* | X |
| EFV | X | X | ✓* | X | X |
| RPV | ✓ | ✓ | ✓* | ✓ | ✓ |
| BIC | –§ | –§ | ✓† | ✓† | ✓† |
| DTG | ✓ | ✓ | ✓* | ✓ | ✓ |
| RAL | ✓ | ✓ | ✓ | ✓ | ✓ |
| EVG/COBI/FTC/TDF | ✓*† | X | X | ✓* | ✓*† |
| EVG/COBI/FTC/TAF | ✓† | X | ✓ | ✓ | ✓† |
| 3TC/ABC | ✓ | ✓ | ✓ | ✓ | ✓ |
| TAF or TDF | ✓ | ✓ | ✓* | ✓* | ✓* |

*Monitor for tenofovir toxicity if used with TDF. †No clinically significant drug interaction per prescribing information. ‡Guidelines recommend monitoring liver enzymes owing to lack of clinical safety data. §No information in prescribing information.

DHHS Guidelines. 2018.

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| LPV + RTV | X | X | ✓* | ✓* | X |
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| EVG/COBI/FTC/TDF | ✓*† | X | X | ✓* | ✓*† |
| EVG/COBI/FTC/TAF | ✓† | X | ✓ | ✓ | ✓† |
| 3TC/ABC | ✓ | ✓ | ✓ | ✓ | ✓ |
| TAF or TDF | ✓ | ✓ | ✓* | ✓* | ✓* |

Coadministration of HCV and HIV PIs not currently recommended

*Monitor for tenofovir toxicity if used with TDF. †No clinically significant drug interaction per prescribing information. ‡Guidelines recommend monitoring liver enzymes owing to lack of clinical safety data. §No information in prescribing information.

DHHS Guidelines. 2018.

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| BIC | –§ | –§ | ✓† | ✓† | ✓† |
| DTG | ✓ | ✓ | ✓* | ✓ | ✓ |
| RAL | ✓ | ✓ | | | |
| EVG/COBI/FTC/TDF | ✓*† | X | | | |
| EVG/COBI/FTC/TAF | ✓† | X | ✓ | | ✓† |
| 3TC/ABC | ✓ | ✓ | ✓ | | ✓ |
| TAF or TDF | ✓ | ✓ | ✓* | ✓* | ✓* |

Coadministration of LDV or VEL with TDF, but not TAF, requires liver monitoring

*Monitor for tenofovir toxicity if used with TDF. †No clinically significant drug interaction per prescribing information. ‡Guidelines recommend monitoring liver enzymes owing to lack of clinical safety data. §No information in prescribing information.

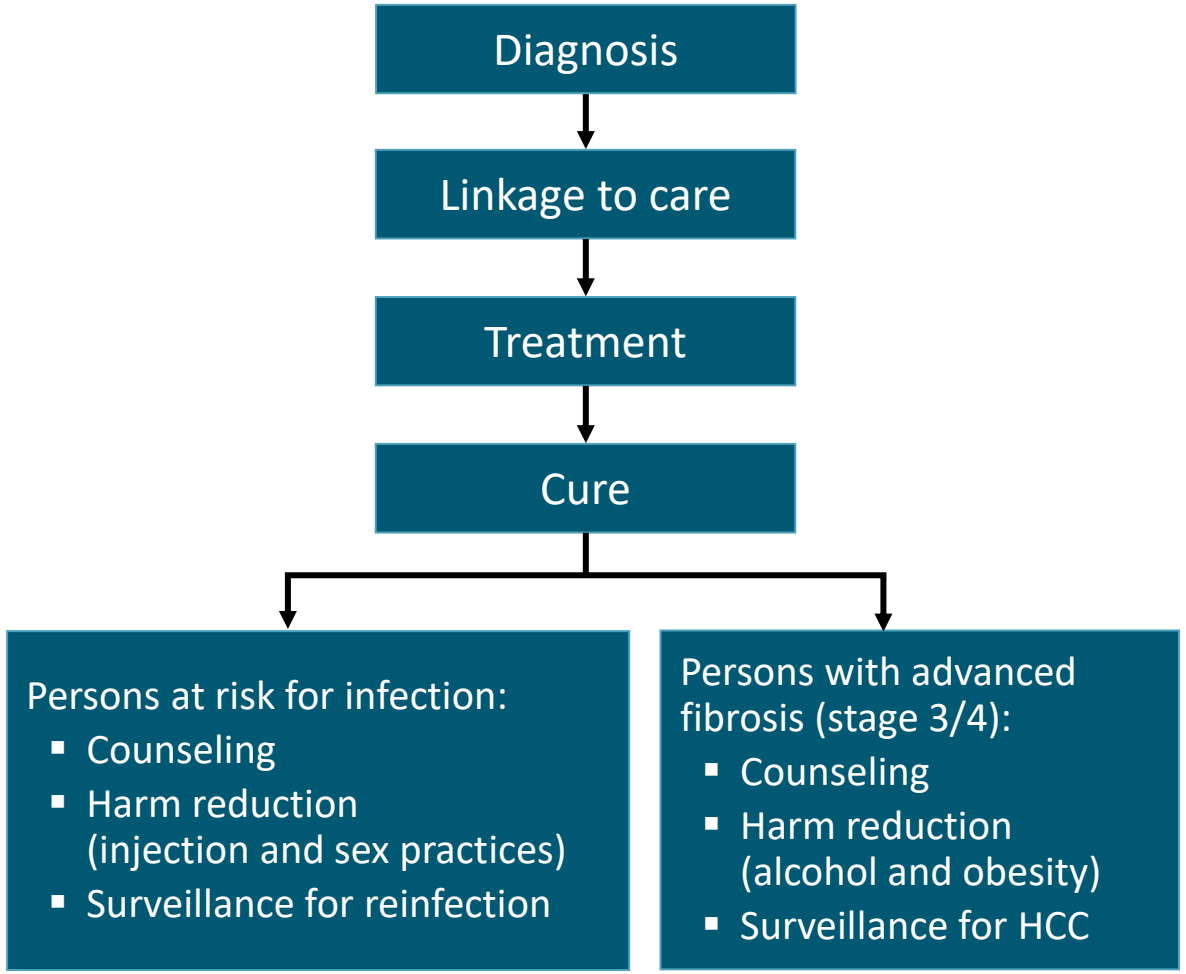
DHHS Guidelines. 2018.

# Consider Potential for HBV Reactivation

- Test all patients initiating HCV DAA therapy for HBsAg, anti-HBc, and anti-HBs[1]
- HIV-infected patients with active HBV infection (HBsAg positive) should receive dual NRTI therapy with anti-HBV activity[2]
  - (TAF or TDF) plus (3TC or FTC), or entecavir if TAF or TDF not feasible
  - Initiate ART before DAA therapy owing to risk of HBV reactivation with DAAs
- In patients positive for anti-HBc ± anti-HBs,[1] no consensus on approach
  - Risk of HBV reactivation is very low,[3] but consider monitoring transaminases at Wks 4 and 8 following HCV DAA initiation
  - Insufficient data to inform HBV DNA monitoring

1. AASLD/IDSA HCV Guidelines. 2017.
2. DHHS Guidelines. 2017.
3. Belperio PS, et al. Hepatology. 2017;66:27-36.

# HCV Care Continues Past Achievement of SVR




| Characteristic | Follow up After SVR |
|---|---|
| No advanced fibrosis (Metavir stage F0-F2), no or low risk of HCV reinfection | ▪ Standard medical care, as in someone without HCV |
| Advanced fibrosis (Metavir stage F3 or F4) | ▪ Ultrasound surveillance for HCC every 6 mos ± AFP |
| Moderate to high risk of HCV reinfection | ▪ Harm reduction<br>▪ HCV RNA every 12 mos |

Falade-Nwulia O, et al. J Hepatol. 2017;66:267-269. AASLD/IDSA HCV Guidelines. 2017.

# HBV / HIV Co-infection

- Serological evidence of previous exposure to HBV is found in more than 80% of HIV-positive patients, with considerable variation according to the geographical regions.

- HIV concurrent infection influences the natural course of HBV infection by impairing the quantity and quality of the innate and adaptive immune response.

- The higher chronicity rate and decreased rates of spontaneous resolution of anti-HBe and anti-HBs seroconversion after acute infection are common.

- The levels of HBV replication is increased in HIV-infected patients, causing more rapid progression of liver fibrosis and a higher rate of hepatic decompensation (but not HCC).

- The risk of liver-related mortality may be increased in HBV/HIV concurrent infection.

Brook MG, . HIV Med 2003, Rehermann B, Semin Liver Dis 2003, Di Martino V, Gastroenterology 2002, Bonacini M, AIDS 2004

# Treatment of HBV/HIV Co-Infection

- Treatment of HBV in the setting of HIV is straightforward.
- Three-drug ART containing tenofovir disoproxil or tenofovir alafenamide provides effective treatment for both viruses.
- If tenofovir is contraindicated, entecavir should be prescribed in addition to three effective ART drugs.

Umang Arora et al, Lancet Infect Dis 2021

# Conclusions and recommendations

- HIV-HCV infection common, particularly in PWIDs
- Liver disease now the leading cause of mortality and morbidity in HIV patients.
- Effective treatment available for both HCV and HIV
- Lack of integration between HIV and VH programs

- Define well the care pathway of co-infected patients.
- Educate the PWID/HIV population of vulnerability of liver disease.
- Simplify further the HCV treatment of co-infected patients.