HIV AND ALCOHOL

In this Issue...
Unhealthy alcohol use is prevalent among people infected with HIV and has been associated with morbidity and mortality, as well as with negative effects on HIV transmission and treatment adherence.

In this issue we discuss recent data describing the role of alcohol use in HIV transmission risk, medication adherence, and disease progression; how individual beliefs about antiretroviral and alcohol interactions effect medication-taking behavior; the effects of alcohol on liver disease in patients coinfected with HIV and those with HIV/HCV coinfection; and the results of a recent intervention for unhealthy alcohol use in an HIV primary care setting.

LEARNING OBJECTIVES

After participating in this activity, the participant will demonstrate the ability to:

- Describe the association between alcohol use and misuse and its relationship to medication adherence among persons with HIV.
- Discuss the impact of alcohol use on HIV transmission risk behaviors, HIV outcomes, and liver disease progression.
- Summarize recent data and interventions that support reduction in nondependent and dependent alcohol use in HIV treatment settings.

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IN THIS ISSUE

- **COMMENTARY** from our Guest Author

- **ALCOHOL USE AND ANTIRETROVIRAL ADHERENCE**

- **INTENTIONAL NON-ADHERENCE TO HIV MEDICATIONS**

- **ALCOHOL USE AND RISKY SEXUAL BEHAVIORS AMONG INDIVIDUALS WITH HIV**

- **ALCOHOL USE, VIRAL LOAD, ART DISRUPTION AND CD4 RESPONSE**

- **ALCOHOL USE ASSOCIATED AND ADVANCED HEPATIC FIBROSIS**

- **MOTIVATIONAL INTERVIEWING ENHANCED WITH INTERACTIVE VOICE RESPONSE SELF-MONITORING TO REDUCE ALCOHOL USE**

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**COMMENTARY**

Unhealthy alcohol use (also termed risky or hazardous alcohol use), defined as alcohol use at levels that increase the risk for negative health consequences, is prevalent among people infected with HIV and varies from 8%-11% in general HIV clinical settings\(^1,2\) to 38% in U.S. Veterans Administration (VA) samples.\(^3\) The National Institute of Alcoholism and Alcohol Abuse defines unhealthy alcohol use as consumption of more than 14 standard drinks per week or \(\geq 5\) drinks on one occasion for men, and greater than...
7 drinks per week or ≥ 4 drinks per occasion for women. Binge drinking is defined as ≥ 4 or 5 drinks per occasion in women and men respectively. In the studies reviewed in this issue, unhealthy alcohol use, including binge drinking, among people who have and those who are at risk for HIV, was shown to affect HIV transmission, treatment adherence, and HIV treatment outcomes.

Sexual transmission of HIV is multifactorial, but increasing evidence suggests that alcohol use is one factor that contributes to risky sexual behaviors. In a meta-analysis conducted by Shuper and colleagues, any alcohol use was associated with 1.6 times the odds of unprotected sex, and alcohol use in sexual contexts was associated with twice the odds of unprotected sex among those with HIV. The work by Hutton and colleagues (reviewed herein) adds further depth to these findings, demonstrating a strong association between frequent/binge alcohol use and receptive anal sex among HIV infected women and insertive anal sex among MSM infected with HIV. These studies among persons living with HIV, in combination with studies of alcohol use among MSM and IDU at risk for HIV, provide a compelling link between alcohol use and HIV transmission behaviors and underscore the importance of counseling about alcohol use in the context of risky behaviors.

In addition to the link between alcohol use and HIV sexual transmission behaviors, numerous studies have demonstrated a relationship between hazardous alcohol use, binge drinking, and worse antiretroviral therapy (ART) adherence. In their meta-analysis, Hendershot and colleagues found that any alcohol use was associated with lower ART adherence compared to no or lower levels of use. Another study conducted among United States veterans found a strong relationship between binge drinking and ART nonadherence. Specifically, on binge-drinking days, 14% of patients missed their ART, compared to 6% on nonbinge drinking days and 4% on days when they did not drink. Thus, encouraging reduction in both weekly consumption and binge drinking episodes is important to improve ART adherence. In addition, as highlighted by Kalichman and colleagues, patients who drink alcohol may intentionally skip ART or alter their ART-taking behaviors. Thus, exploring patients' beliefs about interactions between ART and alcohol and how these affect ART-taking behaviors is an important component of adherence counseling.

Given the relationship between alcohol use and ART adherence, it is not surprising that heavy alcohol use would be associated with ART interruption and subsequent viral nonsuppression in the study conducted by Conen and colleagues. Notably, Conen et al did not find an association between alcohol use and viral suppression independent of ART interruption and nonadherence. Furthermore, among those on ART, no association between alcohol consumption and lower CD4 count was found. These findings are consistent with prior studies demonstrating the potency of ART in immunologic recovery, even in the setting of alcohol use, reinforcing the importance of ART initiation among those who drink to optimize immunologic response to ART.

Finally, with a significant proportion of patients with HIV coinfected with hepatitis C virus (HCV) and liver disease a leading cause of morbidity and mortality, assessing alcohol use in HIV care settings is critical not only in managing HIV but also in managing HCV coinfection. Lim and colleagues' work demonstrates that alcohol use at all levels is not only associated with advanced hepatic fibrosis among patients with HIV and HCV coinfection (compared to those without HIV/HCV and nondrinkers), but also among those with HIV monoinfection.

These studies highlight the importance of addressing alcohol use among patients with HIV. Given the association between alcohol use and HIV risk behaviors, it is imperative to initiate ART among those with unhealthy alcohol use to decrease HIV transmission risk and improve long-term clinical outcomes.

There is an increased emphasis on moving alcohol treatments into primary care settings. The United States Preventive Services Task Force (USPTF) recommends screening for alcohol use in clinical settings, and the use of brief behavioral interventions to reduce drinking among individuals with hazardous or risky use. Hasin and colleagues demonstrated that brief advice or motivational interviewing-based interventions are effective in reducing drinks per drinking day among nondependent (those without severe
alcohol use disorder) patients with HIV. These brief interventions can be delivered during an office visit. Among those with dependent use, this study found a more intensive intervention, including both motivational interviewing and daily monitoring, to be effective in reducing alcohol use. Another means of augmenting behavioral interventions for those with alcohol use disorders is the use of pharmacotherapy, such as naltrexone or acamprosate, particularly to maintain abstinence or prevent relapse. A recent systematic review and meta-analysis of 122 randomized controlled trials highlights the effectiveness of these therapies. However, despite a good evidence base for both brief intervention and alcohol pharmacotherapy for the treatment of alcohol use disorders, these interventions remain underused in both HIV and general primary care settings. 

In summary, these recent studies highlight the compelling reasons to screen for alcohol use among individuals living with HIV. Alcohol use may increase the risk of HIV acquisition and transmission through its association with high-risk sexual behaviors. In addition, it interferes with adherence to antiretroviral therapy and is associated with increased markers of hepatic fibrosis among HIV-monoinfected and HIV/HCV-coinfected individuals. Screening for alcohol use among HIV-infected individuals and exploring ART adherence and HIV risk-taking behaviors within the context of drinking, is integral to the primary care management of persons living with HIV and HIV/HCV co-infection. Finally, brief provider advice for unhealthy alcohol use may reduce drinking in HIV care settings. More intensive interventions, including consideration of pharmacotherapies for alcohol use, may be of use among those individuals with more severe alcohol use disorders.

References

back to top
ALCOHOL USE AND ANTIRETROVIRAL ADHERENCE


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Alcohol use has been associated with antiretroviral nonadherence across several studies. The purpose of this study was to systematically review and quantitatively evaluate the association between alcohol use and antiretroviral adherence. The authors included 40 studies, encompassing over 25,000 individuals, published between 1998 and 2007. The majority of studies were conducted in the United States (N = 33), while the remaining studies were conducted in France, Canada, Brazil, India, and Italy.

In meta-analysis across 40 studies, those who consumed alcohol were significantly less likely to be adherent to antiretroviral therapy compared with non-users or those who drank relatively less (OR: 0.55, 95% CI: 0.49-0.61; P < 0.001). When alcohol use was stratified by drinking level, those with at-risk drinking or a probable alcohol use disorder (defined by NIAAA guidelines of > 14 drinks per week or > 4 drinks per occasion for men; or > 7 drinks per week or > 3 drinks per occasion for women; CAGE score of ≥ 2 or AUDIT score ≥ 8) were less likely to be adherent compared to nondrinkers and lower-risk drinkers (OR 0.47, 95% CI: 0.41-0.55; P < 0.001); those with moderate alcohol use were less likely to be adherent compared to abstainers (OR: 0.48, 95% CI: 0.36-0.64; P < 0.001). Among studies examining any alcohol use in the past year versus none, any alcohol use was also significantly associated with lower adherence compared to none (OR: 0.60, 95% CI: 0.54-0.69; P < 0.001).

This meta-analysis of 40 studies highlights the consistent association between alcohol use and antiretroviral nonadherence, underscoring the importance of routine screening for alcohol use among patients with HIV infection.

back to top

INTENTIONAL NON-ADHERENCE TO HIV MEDICATIONS


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Among people with HIV infection who use alcohol, ART adherence may be affected by a person's belief that mixing alcohol with ART is toxic. These beliefs are referred to as alcohol-ART interactive toxicity beliefs and behaviors (AAITB). The purpose of this study was to examine alcohol-ART interactive toxicity beliefs among drinkers treated with ART and their association with intentional ART nonadherence.

This was a prospective study of people with HIV infections in Atlanta, Georgia. Eligibility included those who were age ≥ 18, taking ART, and had consumed alcohol in the past week. AAITB were assessed by asking about skipping or stopping medications when participants were drinking. Alcohol-ART interaction beliefs were assessed by the following statements:

"If I drink alcohol then I know my medicines are not going to work as well."
"Alcohol dilutes HIV medicines so the medicines don't work."

Alcohol use was assessed using the alcohol-use disorders identification test (AUDIT), and adherence was assessed using unannounced telephone-based pill counts approximately monthly, as well as three-day retrospective adherence recall.
Of 178 participants, 22% were female, 93% African American; 71% drank once per week or less, 21% drank two to three times per week, and 8% drank four or more times per week. Forty-four percent drank more than three drinks per occasion. Twenty-five percent had an AUDIT score above 8, indicating hazardous or at-risk alcohol use. Overall, 43% of participants reported skipping medications if they drank, and 34% reported stopping medications if they knew they would be drinking. Individuals who stopped or skipped medications when drinking (n = 90) were significantly more likely to endorse the ART-alcohol interaction belief that alcohol decreased the effectiveness of ART compared to those who did not stop or skip medications (P = 0.01).

Those who stopped or skipped medications when drinking were significantly more likely to adapt ART-taking behaviors when drinking, endorsing the following statements:

- "I wait at least a couple of hours after I take my medicine to drink alcohol."
- "I get sick if I mix HIV medications and alcohol together."
- "I do not mix alcohol and HIV medications because it is not safe."
- "I do not take my medications if alcohol is not completely out of my system."
- "I will not take medications if I am hung over from drinking alcohol."

Patients who intentionally stopped or skipped medications when drinking were significantly more likely to report < 85% medication adherence on unannounced pill counts (odds ratio [OR]: 1.67, 95% confidence interval [CI]: 1.06-2.62), and on self-reported adherence (OR: 1.10 95% CI: 1.01-1.21). Finally, those who endorsed skipping or stopping medications when drinking had significantly more days of concomitant alcohol consumption and missed medications (OR: 2.9: 95% CI: 1.09-7.68) compared to drinkers who did not intentionally stop medications when drinking.

This study illustrates that a proportion of patients with HIV infection who consume alcohol intentionally skip ART when drinking. Furthermore, those with intentional nonadherence are more likely to endorse alcohol-ART interaction beliefs and alter their ART-taking behavior when drinking. These findings underscore the importance of exploring ART-alcohol interactive toxicity beliefs and behaviors with patients who consume alcohol, as they may play a definitive role in alcohol-related medication nonadherence.

**ALCOHOL USE AND RISKY SEXUAL BEHAVIORS AMONG INDIVIDUALS WITH HIV**


This 2013 study examined the relationship between alcohol use and specific sexual behaviors, including vaginal sex and receptive and insertive anal sex in an HIV clinic-based sample of women and heterosexual and gay and bisexual men.

Audio-computer assisted self-interviews (ACASI) were conducted among 901 patients infected with HIV who were receiving care in Baltimore, MD and New York, NY. Alcohol use was queried over the three months prior to participation in the ACASI. If alcohol was not consumed, participants were classified into the "no alcohol use" group. The "low use" group included those who consumed alcohol less than monthly or one to three times a month, and never consumed five or more drinks on a single occasion. The "frequent/binge" use group included persons who had had more than five drinks on any occasion in the last three months (ie, binge use) and/or consumed alcohol at least once a week. Sexual risk behaviors that were examined included: 1) participating in vaginal or anal sex, 2) multiple partners, and 3) condom use. For women, sex was divided into vaginal sex and receptive anal sex. For men, sex was coded as vaginal sex with a female partner, insertive anal sex with a female partner, insertive anal sex with a male partner,
and receptive anal sex with a male partner. Results were adjusted for age, race/ethnicity, and other drug use.

Among the 319 women in the sample, 60% were sexually active, and frequent/binge drinkers were twice as likely to be sexually active compared with those who did not drink (adjusted odds ratio, AOR: 2.68, 95% CI 1.43–5.03, P = 0.002). Women who engaged in frequent or binge drinking were also more likely to report having multiple sex partners than did those who abstained (AOR: 2.46, 95% CI 1.05–5.78, P = 0.038) and low use drinkers (AOR: 3.03, 95% CI 0.89–10.31, P = 0.003). One-quarter (n = 49/192) of sexually active women who engaged in receptive anal sex and frequent or binge drinking had four times the odds of having anal sex compared with nondrinkers (AOR: 4.11, 95% CI 1.66–10.21, P = 0.002). Among heterosexual men (n = 254) there was no difference in sexual risk behaviors by level of alcohol use. Finally, among men who have sex with men (N = 337), frequent and binge drinkers were twice as likely to have insertive anal sex compared with infrequent and non-drinkers (AOR = 2.14, 95% CI 1.07–4.29, P = 0.32).

These findings underscore the association between frequent/binge drinking and risky sexual behaviors, particularly among women and gay/bisexual men. Providers should screen for quantity, frequency, and binge alcohol use among their patients and query risky sexual behaviors within the context of alcohol use to reduce the risk of transmission behaviors. Finally, given the association between alcohol use and receptive anal sex in women, queries about anal sex should be included.

ALCOHOL USE, VIRAL LOAD, ART DISRUPTION AND CD4 RESPONSE


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This 2013 study had two goals: 1) to evaluate the effect of alcohol use on ART discontinuation, viral failure, and CD4 count trajectory among patients initiating their first ART regimen and 2) to evaluate the relationship between alcohol use and CD4 trajectory among ART-naïve patients who remain untreated.

This was a prospective study of participants in the Swiss HIV Cohort Study who were either: 1) initiating their first ART regimen between 2005-2012 and answering an alcohol questionnaire within 12 months after starting ART or 2) ART-naïve participants whose first positive HIV test was between 2005-2012 and who had completed an alcohol questionnaire within 12 months of diagnosis. Alcohol use was categorized into WHO health risk categories, which included severe health risk drinking (> 40 grams/day for women; > 60 grams/day for men), moderate (20-40 g/d women, 40-60 g/d men), light (< 20 g/d women, < 40 g/d men), and none if they consumed < 1 drink per week. Outcomes included: 1) time to virological failure, defined as HIV-RNA > 400 copies/ml after 24 weeks; or > 50 copies/ml after 48 weeks of therapy or viral rebound; 2) ART interruption, defined as ART discontinuation for> 7 days; and 3) change in CD4 count over time.

Of the 2982 individuals initiating first ART, 75% were male, 2.2% were classified as severe health risk drinkers, 4.7% moderate risk, 45.9% light risk, and the remaining as non-drinkers. Eight percent did not achieve viral suppression or had viral rebound and 15% interrupted ART. Alcohol use was not associated with virological failure when individuals were censored for ART interruption; however, when not censored for ART interruption, severe-health-risk drinkers were more likely to experience virological failure (HR:1.66, 95% CI: 1.00-2.77) compared to non-drinkers. Severe-health-risk drinkers were also more likely to interrupt ART (HR:2.24, 95% CI 1.42-3.52, P < 0.01). Among first ART initiators there was no relationship between level of alcohol use and change in CD4 count over time. Among the ART-naïve group (n = 2 085), 79% were male, 2.2% were severe-health-
risk drinkers, 3.9% were moderate risk, 51.3% were light risk, and 42.4% were non-drinkers. There was no difference in CD4 over time by level of alcohol use in the ART-naïve group.

These findings show that individuals with severe-health-risk-drinking are more likely to interrupt their ART. Furthermore, lower viral suppression among severe-health-risk drinkers is likely due to alcohol-related ART interruption and poor adherence, suggesting that these behaviors are important targets for intervention. Alcohol use was not associated with CD4 cell count change over time, suggesting that factors other than alcohol may have a greater effect on CD4 response to ART and CD4 change over time in ART-naïve individuals.

ALCOHOL USE ASSOCIATED AND ADVANCED HEPATIC FIBROSIS


Alcohol consumption is associated with liver disease progression among individuals with HIV and chronic hepatitis C (HCV). The objective of this study was to evaluate the association between different categories of alcohol use and hepatic fibrosis by HIV and chronic HCV status.

This was a cross-sectional study of patients enrolled in the Veterans Aging Cohort Study (VACS) between June 2002 and September 2010 who had consumed alcohol in the 12 months prior to enrollment. Alcohol use was assessed using the AUDIT-C and ICD-9 codes for alcohol related diagnoses and categorized as either: 1) an alcohol-related diagnosis using ICD-9 codes for dependence or abuse between the previous 12 months and 6 months after enrollment into VACS; 2) hazardous/binge drinking, defined as an AUDIT-C score ≥ 4 or consumption of ≥ 6 drinks on one occasion in the prior year; or 3) nonhazardous drinking (AUDIT-C score < 4). The main outcome was hepatic fibrosis, defined as a FIB-4 Index > 3.25 (calculated using serum AST, ALT, platelets and age). Prevalence of fibrosis by category of alcohol use was examined by HIV and HCV status overall, and by categories of infection: HIV/HCV-coinfected, HIV-monoinfected, HCV-monoinfected and HIV/HCV-uninfected.

The sample included 3565 drinkers: 24% had an alcohol-related diagnosis, 35% were hazardous or binge drinkers, and 41% were nonhazardous drinkers. The majority were men (96.5%) and African American (64.7%). Seven-hundred-one individuals were HIV/HCV-coinfected, 1410 HIV-monoinfected, 296 HCV-monoinfected, and 1158 were HIV/HCV-uninfected.

The investigators found that the prevalence of advanced fibrosis increased by category of alcohol use among HIV infected compared to HIV uninfected individuals: 19% vs 8.6% for alcohol-related diagnosis, 9.5% vs 3.0% for hazardous use, and 6.7% vs 1.4% for non-hazardous use (P < 0.01 for trend). Among HCV infected individuals, the prevalence of advanced hepatic fibrosis increased by category of alcohol use, compared to HCV uninfected individuals: 22.1% vs 6.5% for alcohol-related diagnosis, 18.2% vs 3.1% for hazardous use, and 13.6% vs 2.5% for non-hazardous use (P < 0.01 for trend). When categorized by HIV/HCV co-infection the odds of hepatic fibrosis were increased in all alcohol use categories (95% confidence interval) in the HIV/HCV-coinfected group compared to uninfected, nonhazardous drinkers: alcohol-related diagnosis OR: 25.2, 95% CI: 10.6-59.7; hazardous OR: 18.9, 95% CI: 7.98-44.8; non-hazardous drinking OR: 14.2, 5.91-34.0). Among HIV-monoinfected persons, all three categories of alcohol use were significantly associated with advanced hepatic fibrosis compared to uninfected, non-hazardously drinking individuals. Finally, among HCV-monoinfected individuals, hazardous drinking and alcohol-related diagnosis were associated with advanced fibrosis.
These findings suggest that among HIV/HCV-coinfected and mono-infected individuals, alcohol use is associated with an increased prevalence of advanced hepatic fibrosis as measured by FIB4 Index. In the office or clinic, determination of hazardous alcohol use (as defined by the AUDIT-C), as well as alcohol-related disorders (determined through ICD-9 codes), can help identify people at risk for advanced hepatic fibrosis. Although this study is limited by the low proportion of women, these results support the need to screen for alcohol use among HIV/HCV-individuals and to counsel on reduction to reduce toxic effects of alcohol on the liver. Future longitudinal studies will help elucidate the role of alcohol in liver disease progression among HIV/HCV-coinfected and monoinfected persons and the relationship between level of alcohol use and advanced hepatic fibrosis in women.

**MOTIVATIONAL INTERVIEWING ENHANCED WITH INTERACTIVE VOICE RESPONSE SELF-MONITORING TO REDUCE ALCOHOL USE**


This 2013 randomized trial tested the efficacy of motivational interviewing (MI) and MI + HealthCall, an interactive voice response (IVR) self-monitoring system, in reducing drinking among primary care patients with HIV.

This was a three-arm, randomized trial of patients recruited from an urban HIV clinic who had consumed ≥4 drinks on one occasion in the past 30 days. Eligible individuals were randomized to an a) advice/education control condition, b) MI, or c) MI plus HealthCall. Participants in the control group were informed that they drank more than medically advised, watched a 30 minute HIV self-care DVD, and received an NIAAA (National Institute on Alcohol Abuse and Alcoholism) pamphlet on safer drinking. At 30- and 60-day follow-up, drinking reduction was encouraged. The MI-only group received a 20-25 minute, MI-based counseling session focused on alcohol reduction, and at 30 and 60 day follow-up they received 15 minutes of counseling where drinking behaviors and goals were reviewed. The MI + HealthCall group, in addition to receiving MI, called into an IVR system where they answered questions about their drinking, mood, adherence, and well-being. At 30- and 60-day follow-up participants received MI and feedback on their HealthCall responses. The primary outcome was average drinks per drinking day over 30 days at the end of the 60-day treatment.

Of the 254 persons randomized, the mean age was 45; 22% were women, and 49% African American. The mean number of drinks per drinking days was seven. Participants drank on average 32% of the 30 days prior to their baseline visit. At the end of treatment, all three groups reduced their mean drinks per drinking day to 4.75 drinks in the control, 3.94 in MI, and 3.58 in MI + HealthCall. There was a statistically significant difference between the MI + HealthCall and control condition, favoring the intervention ($P = 0.01$) and a near-significant difference between MI and control ($P = 0.07$). A secondary analysis focused on patients who were alcohol-dependent found significant differences between treatment groups and the number of drinking days. At end of treatment, drinks per drinking day among those who were alcohol-dependent was 6.07 in controls, 5.12 in MI-only, and 3.55 in MI + HealthCall. End-of-treatment effects in the MI + HealthCall cohort were significantly different from MI only ($P = 0.03$) and from control ($P = 0.01$) among those with alcohol dependence. Among individuals without alcohol dependence, drinks per drinking days decreased in all groups, but there was no significant difference among the study arms. At three, six, and 12 months, the number of drinking days was lower from baseline in all groups however the intragroup differences were no longer significantly different.

**Significance:** In this study a 20 minute MI-based counseling session followed by IVR-based alcohol self-monitoring and feedback significantly reduced drinks per drinking day in
patients with HIV who were alcohol-dependent compared to MI only and control. Of note, among those who were nondependent, all three groups reduced their drinking. These results suggest that among dependent drinkers, MI is not sufficient to reduce alcohol use, and augmenting the intervention is important. Among those who were nondependent drinkers, brief advice and/or MI may be sufficient to reduce alcohol use to safer limits. Thus in evaluating alcohol use in HIV clinical care settings, assessing the severity of alcohol use can assist providers in determining whether a brief or more intensive alcohol intervention is necessary.

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April 30, 2015; activities expire 2 years from the date of publication.

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### STATEMENT OF NEED:

- As the demographics of HIV have shifted to include many older adults, clinicians require education regarding the treatment of common comorbidities.
- Clinicians may be unclear about issues specific to the diagnosis and treatment of women with HIV.
- Many clinicians require education regarding current treatment and new emerging hepatitis C medications in patients coinfected with HIV/HCV who require antiretroviral therapy.
- Clinicians may need an update on current recommendations for the treatment of HIV with HAART.

### INTENDED AUDIENCE

The target audience (clinicians) for this initiative includes infectious disease (ID) specialists, primary care physicians (PCPs), nurse practitioners (NPs), physician assistants (Pas), and other health care practitioners whose work/practice includes treating patients with HIV.

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