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Diagnosis and Treatment of Unhealthy Alcohol Use in People with HIV

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Diagnosis and Treatment of Unhealthy Alcohol Use in People with HIV

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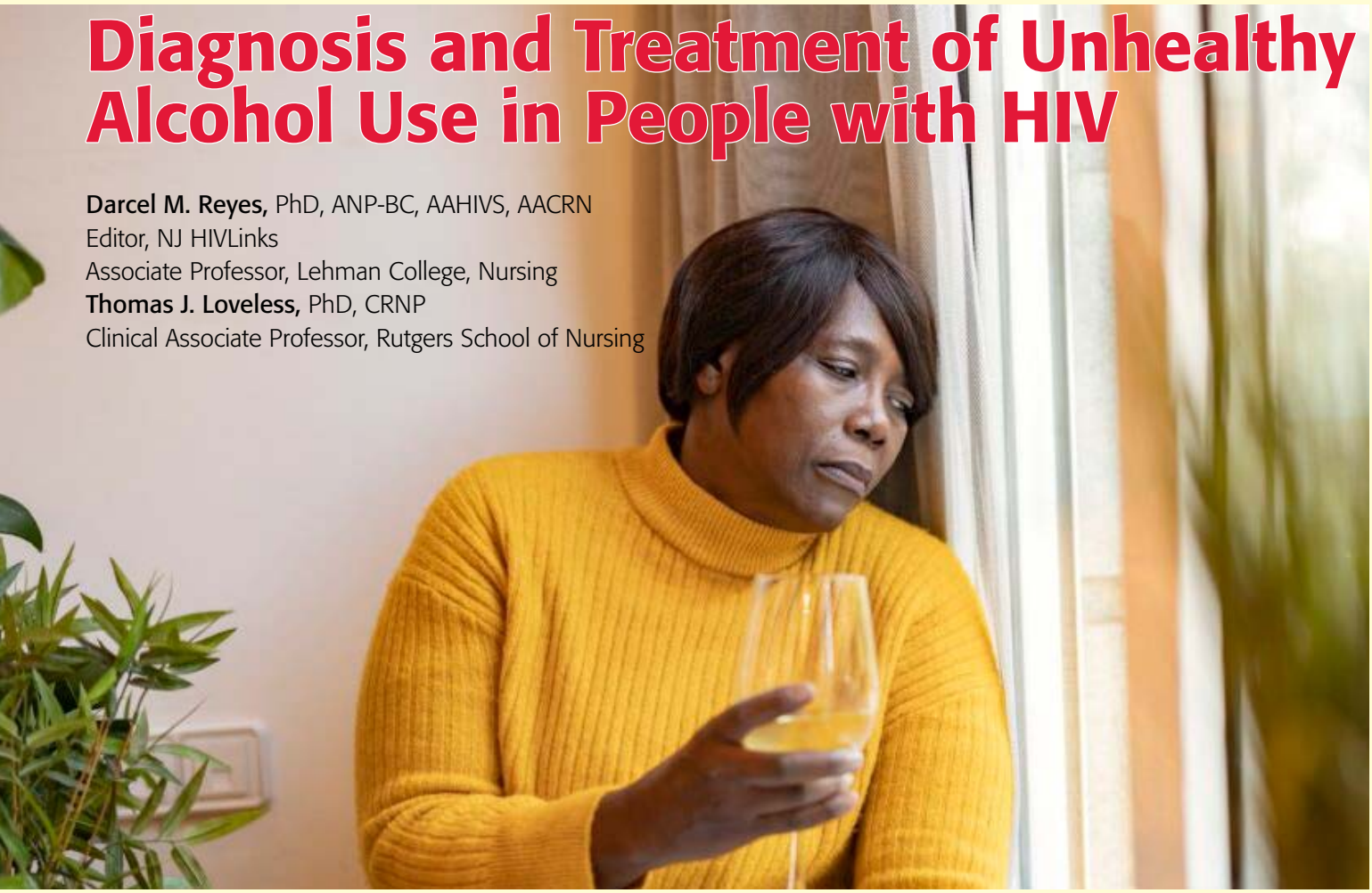
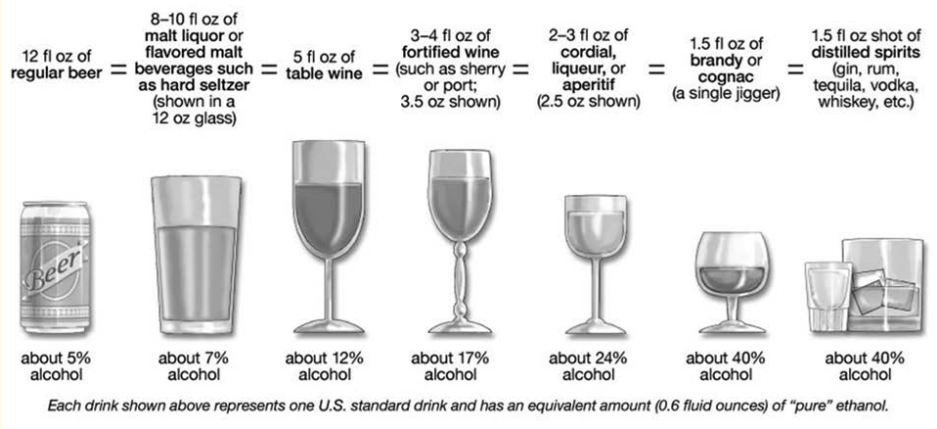


Unhealthy alcohol use (UAU) can have a detrimental effect on people's health and may pose a transmission risk. Rates of alcohol use among people with HIV (PWH) range from 54% to 67%, comparable to people who do not have HIV (53.5%).[1,2] Approximately 30% to 50% of PWH who use alcohol suffer from UAU, which leads to reduced adherence to antiretroviral therapy (ART) and is associated with higher rates of condomless sex due to the lessening of inhibitions, the loss of viral suppression, and viral rebound.[1-8] Clinicians need to understand how to identify and treat UAU to lessen its impact on the health of PWH. This article discusses UAU among PWH, describes the various forms of UAU, reviews the detrimental effects of alcohol on the health of PWH, and presents treatment options.

Types of Unhealthy Alcohol Use

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) defines UAU as alcohol intake exceeding the recommended daily or weekly limits. Healthy adult men ages 21 to 64 should limit alcohol to four drinks a day or 14 drinks a week; healthy men ages 65 or older should not drink more than three drinks a day or more than seven drinks a week. Healthy adult women of all ages should not consume more than three drinks a day or more than seven drinks a week. Standard



drink measurements are 12 ounces [oz] of beer, 5 oz of wine, or 1.5 oz of 80-proof liquor (see Figure 1). Alcohol consumption beyond these limits increases the risk of physical, psychological, or social harm.[9,10]

NIAAA defines *binge* or *heavy drinking* as a pattern of imbibing that brings blood alcohol concentration (BAC) levels to 0.08 g/dL, which occurs about two hours after four drinks for women and five drinks for men. The Substance Abuse and Mental Health Services Administration (SAMHSA) defines *heavy drinking* as five or more occasions in a month when an individual consumes five or more alcoholic drinks.[9]

Alcohol dependence occurs[9] when individuals need to drink significantly more alcohol to get the same effect and experience withdrawal symptoms after stopping alcohol use. Alcohol dependence affects physical and mental health and can cause problems with family, friends, and work (See Table 1).[10]

Alcohol Use Disorder (AUD)[9] is a maladaptive pattern of alcohol use resulting in clinically significant impairment with differing levels of severity (mild to severe) dependent on the number of symptoms present in the individual. The presence of two or more symptoms in a person during one year qualifies as an AUD diagnosis (See Table 2).

Table 1: Alcohol Dependence

A person endorses at least three of the following criteria within one year
1. A strong desire or sense of compulsion to drink alcohol
2. Difficulties controlling drinking in terms of its onset, termination, or levels of use
3. A physiological withdrawal occurs when the person stops or reduces alcohol intake.
4. The person drinks more to achieve the effects originally produced by lower doses.
5. Progressive neglect of alternative pleasures or interests and increased amount of time spent to obtain alcohol or to recover from its effects
6. Ongoing alcohol use despite clear evidence of overtly harmful consequences.

Table 2: Alcohol Use Disorder

The patient endorses two or more of the following symptoms in one year.
1. The patient reports that they drank more or longer than intended.
2. The patient tried to cut down or stop more than once but could not.
3. Spends a lot of time drinking, sick from drinking, or recovering from the after-effects.
4. Reports wanting to drink so badly that they could not think of anything else.
5. Reports that drinking (or being sick from drinking) interferes with family responsibilities, causes problems at work, or causes problems at school.
6. The person continues to drink despite trouble with family and friends.
7. The person has given up or cuts back on important or enjoyable activities to drink.
8. More than once, the person has gotten into situations while or after drinking that increase the chances of getting hurt (e.g., driving, swimming, unsafe sexual behavior).
9. Although alcohol made the person depressed or anxious and caused other health problems or blackouts, the individual continued to drink.
10. Reports increased drinking to get the desired effect or finding that the usual number of drinks had much less impact than previously.
11. The person experiences withdrawal symptoms after the effects of alcohol wear off, such as insomnia, tremors, restlessness, nausea, sweating, racing heart, or seizure.
2-3 symptoms indicate mild AUD, 4-5 are moderate AUD, and 6 or more symptoms indicate severe AUD.

Consequences of Unhealthy Alcohol Use in PWH

Although there is no direct causal relationship, UAU is linked to poorer ART adherence and less health care use.[11-14] In some cases, ART nonadherence results from the amount of alcohol consumed.[15] Studies of alcohol use among men with HIV found that frequent or heavy drinking was not significantly different between gay and heterosexual men; however, for both groups, it was strongly associated with nonadherence.[6] Research hints at a gender difference in the brain's neurochemistry; regardless of the amount of alcohol consumed, men have a higher dopamine release than women, potentiating alcohol's rewarding effect.[17] As PWH age, UAU becomes more prevalent, and ART nonadherence worsens, resulting in reduced health care use and poor treatment outcomes.[18]

Women of color living with HIV cope with unique forms of stigma, stress, and vulnerabilities, which may lead to consuming unsafe amounts of alcohol, negatively influencing adherence and HIV outcomes or resulting in adverse outcomes such as blackouts and body habitus changes.[19-21] Results of studies of African American women reported that their struggle to self-manage pain or distress led to UAU and, ultimately, nonadherence.[19] A qualitative study of women identified psychological issues that led to UAU, such as poor coping, low self-esteem, getting through bad experiences, or social influences of friends and families.[20] A study in Kenya of female sex workers with HIV found that feeling drunk was frequently associated with lower condom use. Compared with non-drinkers, women who drank heavily had a 4.1-fold higher risk of sexual violence and an 8.4-fold higher risk of physical violence.[21]

Excessive alcohol consumption, notably binge drinking, is linked to risky sex-

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ual behaviors among PWH.[12] A survey of sexual behavior in PWH conducted in Ethiopia indicated that 79.8% (CI: 75.3% - 83.9%) of the respondents had at least one risky sexual encounter within the previous three months, and multivariable analysis found that the odds of risky sexual practices were higher among individuals who consumed alcohol.[22] A national survey of 8,012 MSM found that the prevalence of sexual risk behaviors was significantly higher among those who binge drank than among non-binge drinkers, including receptive and insertive condomless intercourse with a discordant partner, exchanging sex for drugs or money, and having concurrent partners.[23] PWH of all genders who indulged in heavy drinking days were more likely to engage in unprotected sex, with increased unprotected sex frequency among women.[24] Regardless of sexual identity, gender, or years of living with HIV, excessive alcohol consumption is consistent with adherence difficulty and ultimately results in poorer outcomes. [12,13, 24,25]

Alcohol and Comorbidities in People with HIV

PWH have heightened morbidity and mortality at lower levels of alcohol consumption compared with HIV-uninfected persons.[26] Heavy alcohol use in PWH is associated with a risk of accelerated aging and fragility, increasing the risk for comorbidities and geriatric syndromes.[24,25] Alcohol misuse increases the risk for the development of neuropathology, cardiovascular and metabolic diseases, geriatric syndrome, and mental health issues in PWH.[24]

Neurological. MRI studies of PWH who use alcohol show abnormalities in brain structure and neurotransmitter deficits, which impaired working memory, decision-making ability, visuospatial abilities, and movement speed.[27,28] Another neurological condition, neuropathic pain, contributes to alcohol misuse by PWH, which also contributes to neuropathic pain.[29]

Cardiovascular and Metabolic. Although the combined effect of HIV disease and alcohol on cardiovascular disease has not been well researched, studies suggest that the risk for cardiovascular disease in PWH ranges from 37% to 78% with excessive alcohol use.[30] With regard to diabetes and complications of metabolic disease, some studies suggest that moderate alcohol use may be protective, but heavy drinking increases the risk.[31] Similarly, the results of the New Orleans Alcohol use in HIV (NOAH) study indicated that heavy alcohol use is a risk factor for the development of prediabetes and diabetes.[32] In a recent study, investigators found that PWH who use alcohol excessively were more likely to experience pancreatic dysfunction.[33] As expected, Kahler et al. found significant effects of heavy drinking on liver fibrosis in PWH, as indicated by increased FIB-4 scores, which in turn, increased the five-year mortality risk for PWH, as measured by the VAC index (Veterans Aging Cohort Index), a measure of mortality in PWH.[34]

Mental Health. There is limited research on the effects of unhealthy alcohol use on mental health. Research investigating alcohol use among PWH found that the severity of alcohol use is related to stress and HIV stigma and exacerbates anxiety and depressive symptoms.[35-37] Results of one study found that limited consumption of alcohol did not prevent PWH from receiving treatment for depression; however, risky alcohol use was associated with less resolution of depressive symptoms.[38]

Screening for Unhealthy Alcohol Use

The US Preventative Task Force recommends screening all patients for alcohol use. Clinicians can use brief questionnaires such as the abbreviated Alcohol Use Disorders Identification Test–Consumption (AUDIT-C) and the NIAAA-recommended Single Alcohol Screening Question (SASQ). The AUDIT-C is in the public domain; it screens for UAU and AUD.[39] The SASQ is a variation of the third question of the AUDIT-C, "How often do you have six or more drinks on one occasion?"[40] The most commonly used screening

questionnaire, the CAGE (Cut Down, Annoyed, Guilty, Eye-Opener), screens for alcohol dependence but does not capture the full spectrum of UAU.[39] Health care providers should avoid general questions such as, "How much do you drink?" which has less than a 50% sensitivity for uncovering UAU. An additional question may be helpful when screening for AUA:

- Have you ever had a drinking problem?
- When was your last drink? (Less than 24 hours is a red flag).
- Do you use alcohol to relieve pain, anxiety, or insomnia?
- Have you ever been arrested for drinking, such as driving under the influence?
- Have you ever lost friends or partners because of your drinking?
- Have you ever been to an Alcoholics Anonymous (AA) meeting?

There are screening instruments that target specific populations. Questionnaires for pregnant women include the TWEAK (Tolerance, Worried, Eye-Opener, Amnesia, Kut Down); the T-ACE (Tolerance, Annoyed, Cut Down, Eye-Opener); Parents, the 4Ps Plus (Partner, Past, Present Pregnancy); and the NET (Normal Drinker, Eye-Opener, Tolerance). The CRAFFT (Car, Relax, Alone, Forget, Family, Friends, Trouble) is a questionnaire for identifying risky substance use in adolescents. For older adults, ask if their drinking increased after someone close to them died or if alcohol made them so sleepy that they often fall asleep sitting in a chair. For adolescents, consider asking them if they ever drink alcohol alone, missed school to go drinking, or because they had a hangover. Tables 3 and 4 list common complaints and presentations suggestive of unhealthy alcohol use.

Table 3: Complaints Suggestive of Unhealthy Alcohol Use

Frequent absences from school or work
History of recurring trauma or accidental injuries
Depression or anxiety
Labile hypertension
Gastrointestinal symptoms
Sexual dysfunction
Sleep disorders

Clinically, laboratory abnormalities such as elevated gamma-glutamyl transpeptidase (GGT), mean corpuscular volume (MCV), aminotransferases, low platelet count, and carbohydrate-deficient transferrin (CDT) may indicate excessive alcohol use but have a sensitivity of approximately 50%. GGT is the most widely used test, but other conditions, such as nonalcoholic liver disease, hyperthyroidism, and the use of anticonvulsants, can elevate GGT levels.[41] MCV is less sensitive than the GGT level, but an elevated MCV level with an elevated GGT level should raise suspicion about heavy alcohol use. CDT tests are available but not often used; four to seven drinks per day for at least one week can significantly

Table 4: Clinical Presentation Suggestive of Unhealthy Alcohol Use

Signs of Unhealthy Alcohol Use
Mild tremor
The odor of alcohol on the breath
Enlarged or shrunken tender liver
Labile blood pressure
Tachycardia
"Aftershave/mouthwash" syndrome (to mask the odor of alcohol)
Signs of Alcohol Withdrawal
Nausea and vomiting
Diaphoresis
Headache
Tremor
Seizures
Visual and auditory hallucinations
Signs of Delirium Tremens
Tachycardia
Hypertension
Temperature elevation
Delirium
Tactile Hallucinations of Itching, Burning, or Numbness
Signs of Chronic Alcohol Use
Gynecomastia
Spider angiomas
Dupuytren contractures
Testicular atrophy
Enlarged or shrunken liver
Enlarged spleen
Ataxia
Asterixis and confusion: signs of hepatic encephalopathy

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elevate CDT levels in patients with UAU. Direct alcohol biomarkers include alcohol itself and ethyl glucuronide (EtG). EtG is a metabolite of alcohol formed by the conjugation of ethanol with activated glucuronic acid. EtG can be detected in urine for up to five days after heavy binge drinking, even in small amounts.[41]

Management of Unhealthy Alcohol Use in PWH

Ongoing alcohol use is not a contraindication for ART. Integrating AUD treatment with HIV care increases the number of patients who receive alcohol treatment, medication, and counseling, improving the likelihood that a PWH will achieve viral suppression. A randomized controlled trial of 128 individuals with HIV and AUD compared an integrated model of alcohol treatment in Veterans Administration HIV clinics to treatment as usual. At 24 weeks, the integrated model resulted in more participants receiving pharmacotherapy for AUD and participating in counseling. At 52 weeks, the integrated model was associated significantly with increased alcohol-abstinent days, decreased drinks per drinking day, and fewer heavy drinking episodes. In addition, the patients in the integrated model had increased odds of achieving viral suppression (odds ratio [OR] 5.58; 95% confidence interval [CI], 1.11–27.99).[42]

Pharmacotherapy for Alcohol Use

Pharmacotherapy for UAU in PWH demonstrates a reduction in alcohol use. The Food and Drug Administration (FDA) approved three pharmacotherapies for AUD: Naltrexone, Disulfiram, and Acamprosate. While there is limited research on the use of Naltrexone in PWH, data on the use of Disulfiram and Acamprosate among PWH are lacking. Table 5 presents a summary of pharmacological treatment for AUD.

Naltrexone. Naltrexone is an opioid antagonist that reduces the rewarding effect of alcohol. Because it is an opioid agonist, clinicians should not prescribe it to people on opioid analgesics for chronic pain or those on opioid agonist therapy for opioid misuse (e.g., methadone). Naltrexone appears to be safe to use in people with HIV. It is not associated with significant drug-drug interactions or irreversible hepatotoxicity.[43,44] Clinicians should not use Naltrexone in patients with decompensated liver disease. Clinicians should prescribe Naltrexone with caution in individuals with elevated transaminase levels. Naltrexone effectively reduces the number of heavy drinking days among PWH and AUD. In a randomized placebo-controlled trial of 100 prisoners with HIV who met the criteria for AUD, those provided with Naltrexone upon release from prison were more likely to achieve viral suppression at six months compared with a placebo group (56.7% vs.30.3%).[43] Patients start on an oral dose of 25mg daily for two days, then a standard dose of 50mg/day. Naltrexone is also formulated as an injectable that is administered monthly. Patients should start on oral Naltrexone for three to five days before the first injection. Patients should be free of opioid medication for at least seven to ten days before their first dose of Naltrexone to avoid precipitated withdrawal.

Disulfiram. Disulfiram creates an adverse reaction to alcohol within 10 minutes of drinking that may last several hours. The symptoms include flushing, headache, anxiety, nausea, vomiting, sweating, dizziness, palpitations, hyperventilation, and confusion. Disulfiram is contraindicated in patients with significant coronary artery disease or heart failure. Clinicians should educate patients to prevent a disulfiram alcohol reaction by avoiding preparations containing alcohol, such as sauces, cough mixtures, vinegar, and foods containing vinegar. Patients on metronidazole or paraldehyde should not take Disulfiram. Caution is necessary for patients with a history of liver disease.

Acamprosate. Acamprosate is safe and well-tolerated. It is as effective as Naltrexone but with fewer adverse reactions. Acamprosate modulates alcohol-related changes in the brain, reducing withdrawal symptoms that can lead to relapse, and may be more effective when combined with Naltrexone or Disulfiram. Acamprosate is safe for patients with liver disease because the liver does not metabolize it. Unlike Naltrexone, patients on opioid treatment for pain or opioid use disorder can safely use acamprosate. In addition, it does not interact with benzodiazepines and can be continued if a patient relapses and returns to drinking.

Table 5: Pharmacological Treatment for Alcohol Use Disorder

Naltrexone 1 pill daily or monthly injection	• Mu-opioid receptor antagonist • Decreases the reinforcing/pleasurable effects of alcohol • Helps prevent relapse and decreases current use • Can start if someone is still drinking ➢ **DO NOT START if PATIENT IS ACTIVELY USING OPIOIDS; the patient will experience withdrawal**
Acamprosate 2 pills 3x daily	• Helps prevent relapse after detoxification • Relatively safe option with minimal side-effects • Can be used in combination with Naltrexone

Disulfiram
1 pill daily
	• Prevents the breakdown of alcohol in the body
	• With alcohol consumption causes an adverse reaction that includes nausea, vomiting, sweating, palpitations, hypotension, tachycardia
	  • A patient needs to be highly motivated
	  • PRN use in episodic high-risk situations

One drawback to Acamprosate is the required dosing of two capsules three times a day, which may reduce adherence by PWH, who may be taking numerous medications. Additionally, clinicians should not prescribe acamprosate for patients with a creatinine clearance of less than 30 mL per minute.

Non-Pharmacological Interventions

The United States Preventive Services Task Force recommends that all adults in primary care who screen positive for unhealthy alcohol use and have risky drinking behaviors receive a brief counseling intervention.[39] Any treatment team member, such as physicians, PAs, NPs, RNs, and Social Workers, can administer brief interventions. Although research has demonstrated that brief interventions can reduce self-reported drinking for patients in primary care, brief interventions are not as effective in hospital or emergency room settings because of trauma, lack of a long-term relationship with providers, or the severity of the patient's UAU. SAMHSA's "Enhancing Motivation for Change in Substance Use Disorder Treatment" is a protocol for brief interventions based on Prochaska's five stages of change and motivational interviewing (https://www.ncbi.nlm.nih.gov/books/NBK571071/).

For patients who recognize a problem and want to consider an alternative to medication or support in remaining sober, the most accessible option is Alcoholics Anonymous (AA). This 12-step approach involves psychosocial techniques to change behavior. Each new person is assigned an AA sponsor, a person recovering from alcohol use, which supports the recovery of the new member. Other sources of treatment include FindTreatment.gov (https://findtreatment.gov/), sponsored by SAMHSA.

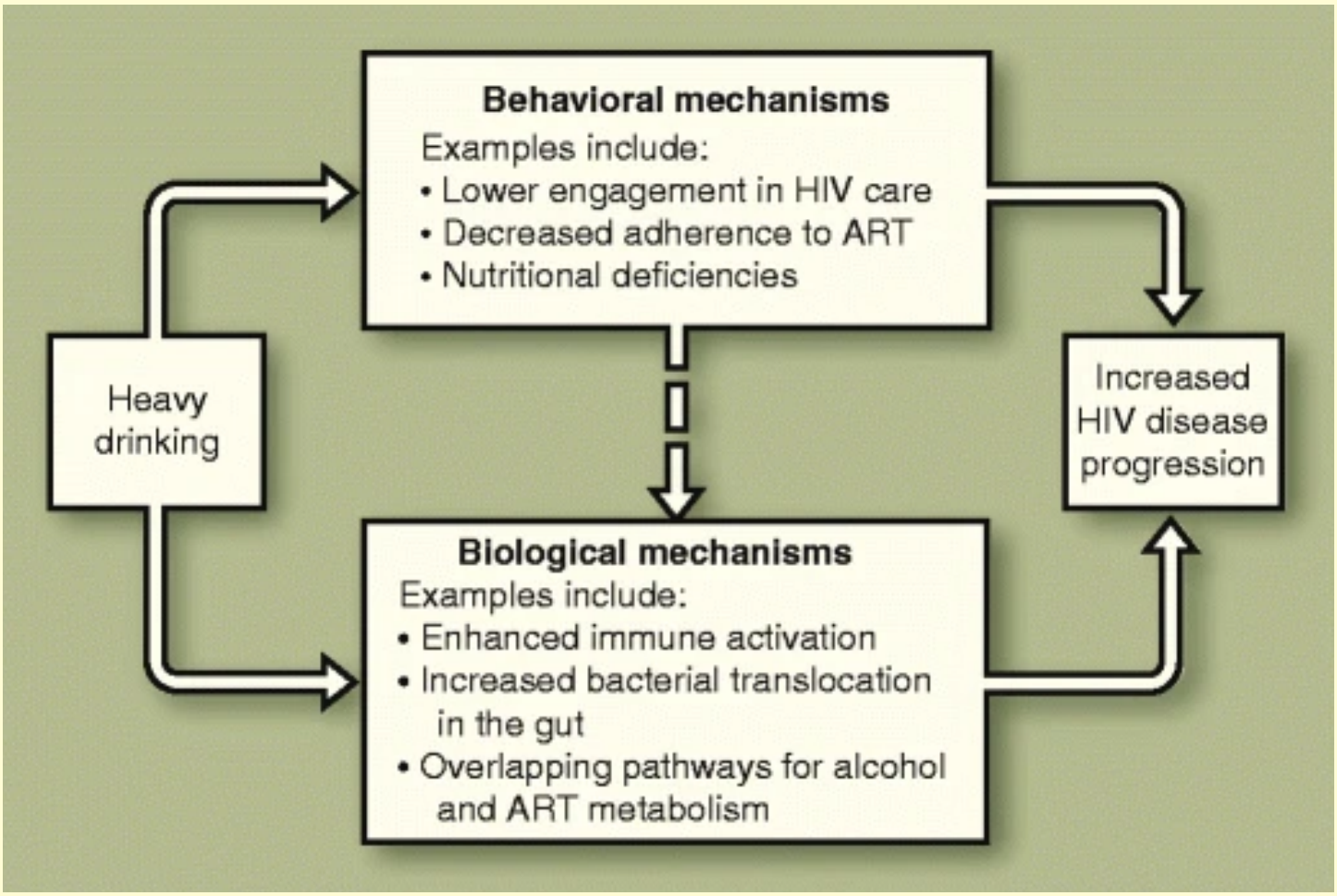
Conclusion

Excessive drinking disinhibits people, and its use can lead to risky behaviors, increasing the possibility of HIV transmission and infection. When a patient's complaints suggest excessive alcohol use, screening tools such as the AUDIT-C or the CAGE can help confirm the diagnosis. If excessive alcohol use is suspected, examination of the patient may reveal signs of alcohol misuse, such as tremors, enlarged liver, tactile hallucinations of itchiness, or spider angiomas. SAMHSA recommends that the treatment team address excessive alcohol with brief interventions based on the five stages of change. Pharmacological treatment for alcohol use includes Naltrexone, Disulfiram, and Acamprosate. AA is an accessible and low-cost support system for patients with alcohol use disorder who choose not to use medications. Alternatively, clinicians can refer patients for short or long-term detoxification and rehabilitation treatment. Recognition and treatment of alcohol use disorder may be another way to address the HIV epidemic.

References

1. Edelman EJ, Williams EC, Marshall BDL. Addressing unhealthy alcohol use among people living with HIV: recent advances and research directions. *Curr Opin Infect Dis.* 2018;31(1):1-7.
2. Duko B, Ayalew M, Ayano G. The prevalence of alcohol use disorders among people living with HIV/AIDS: a systematic review and meta-analysis. *Subst Abuse Treat Prev Policy.* 2019;14(1):52.
3. Williams EC, Hahn JA, Saitz R, Bryant K, Lira MC, Samet JH. Alcohol Use and Human Immunodeficiency Virus (HIV) Infection: Current Knowledge, Implications, and Future Directions. Alcohol Clin Exp Res. 2016;40(10):2056-2072.

4. Fuster D, Sanvisens A, Bolao F, Rivas I, Tor J, Muga R. Alcohol use disorder and its impact on chronic hepatitis C virus and human immunodeficiency virus infections. *World J Hepatol*. 2016;8(31):1295-1308.
5. Stall R, McKusick L, Wiley J, Coates TJ, Ostrow DG. Alcohol and drug use during sexual activity and compliance with safe sex guidelines for AIDS: the AIDS Behavioral Research Project. *Health Educ Q.* 1986;13(4):359-371.
6. Stall R, Wiley J. A comparison of alcohol and drug use patterns of homosexual and heterosexual men: the San Francisco Men's Health Study. *Drug Alcohol Depend.* 1988;22(1-2):63-73.
7. Lefevre F, O'Leary B, Moran M, et al. Alcohol consumption among HIV-infected patients. *J Gen Intern Med.* 1995;10(8):458-460.
8. Galvan FH, Bing EG, Fleishman JA, et al. The prevalence of alcohol consumption and heavy drinking among people with HIV in the United States: results from the HIV Cost and Services Utilization Study. *J Stud Alcohol.* 2002;63(2):179-186.
9. National Institute of Alcohol Abuse and Alcoholism. Drinking levels defined. https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/moderate-binge-drinking Accessed on May, 8, 2023.
10. Saitz R. Clinical practice. Unhealthy alcohol use. *N Engl J Med* 2005;352(6):596-607. doi: 10.1056/NEJMcp042262.
11. Kahler CW, Liu T, Cioe PA, et al. Direct and Indirect Effects of Heavy Alcohol Use on Clinical Outcomes in a Longitudinal Study of HIV Patients on ART. *AIDS Behav.* 2017;21(7):1825-1835.
12. Hendershot CS, Stoner SA, Pantalone DW, Simoni JM. Alcohol use and antiretroviral adherence: review and metaanalysis. *J Acquir Immune Defic Syndr.* 2009;52(2):180-202.
13. Azar MM, Springer SA, Meyer JP, Altice FL. A systematic review of the impact of alcohol use disorders on HIV treatment outcomes, adherence to antiretroviral therapy and health care utilization. *Drug Alcohol Depend.* 2010;112(3):178-193.
14. McKusick L, Horstman W, Coates TJ. AIDS and sexual behavior reported by gay men in San Francisco. *Am J Public Health.* 1985;75(5):493-496.
15. Cook RL, Zhou Z, Kelso-Chichetto NE, Janelle J, Morano JP, Somboonwit C, Carter W, Ibanez GE, Ennis N, Cook CL, Cohen RA, Brumback B, Bryant K. Alcohol consumption patterns and HIV viral suppression among persons receiving HIV care in Florida: an observational study. *Addict Sci Clin Pract.* 2017;12(1):22. doi: 10.1186/s13722-017-0090-0.
16. Shuper, P.A., Joharchi, N., Bogoch, I. et al. Alcohol consumption, substance use, and depression in relation to HIV Pre-Exposure Prophylaxis (PrEP) nonadherence among gay, bisexual, and other men-who-have-sex-with-men. *BMC Public Health* 2020; 1782. https://doi.org/10.1186/s12889-020-09883-z
17. Urban NB, Kegeles LS, Slifstein M, et al. Sex differences in striatal dopamine release in young adults after oral alcohol challenge: a positron emission tomography imaging study with [11[C]raclopride. *Biol Psychiatry.* 2010;68(8):689-696
18. Deren S, Cortes T, Dickson VV, Guilamo-Ramos V, Han BH, Karpiak S, Naegle M, Ompad DC, Wu B. Substance Use Among



Older People Living With HIV: Challenges for Health Care Providers. *Front Public Health.* 2019;7:94. doi: 10.3389/fpubh.2019.00094.

19. Lipira L, Rao D, Nevin PE, et al. Patterns of alcohol use and associated characteristics and HIV-related outcomes among a sample of African-American women living with HIV. *Drug Alcohol Depend.* 2020;206:107753.
20. Cook RL, Cook CL, Karki M, et al. Perceived benefits and negative consequences of alcohol consumption in women living with HIV: a qualitative study. *BMC Public Health.* 2016;16:263-016-2928-x.
21. Chersich, M.F., Bosire, W., King'ola, N. et al. Effects of hazardous and harmful alcohol use on HIV incidence and sexual behaviour: a cohort study of Kenyan female sex workers. *Global Health* 2014; 10(22). https://doi.org/10.1186/1744-8603-10-22
22. Wondemagegn F, Berkessa T. High level risky sexual behavior among persons living with HIV in the urban setting of the highest HIV prevalent areas in Ethiopia: Implications forinterventions. *PLoS ONE* 2020, 15(11): e0242701. https://doi.org/10.1371/journal.pone.0242701
23. Hess KL,Chavez PR, Kanny D, Elizabeth DiNenno E, Lansky A, Paz-Bailey G, 2015, Binge drinking and risky sexual behavior among HIV-negative and unknown HIV status men who have sex with men, 20 US cities. *Drug and Alcohol Dependence* 2015; 147, 46–52
24. Molina PE, Simon L, Amedee AM, Welsh DA, Ferguson TF. Impact of Alcohol on HIV Disease Pathogenesis, Comorbidities and Aging: Integrating Preclinical and Clinical Findings. *Alcohol Alcohol.* 2018;53(4):439-447. doi: 10.1093/alcalc/agy016.
25. Kelso-Chichetto NE, Plankey M, Abraham AG, et al. Association between alcohol consumption trajectories and clinical profiles among women and men living with HIV. *Am J Drug Alcohol Abuse.* 2018;44(1):85-94.
26. Edelman EJ, Williams EC, Marshall BDL. Addressing unhealthy alcohol use among people living with HIV: recent advances and research directions. *Curr Opin Infect Dis.* 2018; 1,1-7. doi: 10.1097/QCO.0000000000000422.
27. Rosenbloom MJ, Sullivan EV, Pfefferbaum A. Focus on the brain: HIV infection and alcoholism: comorbidity effects on brain structure and function. *Alcohol Res Health.* 2010;33(3):247-257
28. Paolillo EW, Inkelis SM, Heaton A, Saloner R, Moore RC, Moore DJ. Age of Last Alcohol Use Disorder Relates to Processing Speed Among Older Adults Living with HIV. *Alcohol Alcohol.* 2019;54(2):139-147. doi: 10.1093/alcalc/agz008.
29. Tsui JI, Cheng DM, Coleman SM, et al. Pain is associated with risky drinking over time among HIV-infected persons in St. Petersburg, Russia. *Drug and Alcohol Dependence*. 2014; 144:87–92.
30. Kelso NE, Sheps DS, Cook RL. The association between alcohol use and cardiovascular disease among people living with HIV: a systematic review. *American Journal of Drug and Alcohol Abuse.* 2015; 41:479–488.
31. Tiozzo E, Konefal J, Adwan S, et al. A cross-sectional assessment of metabolic syndrome in HIV-infected people of low socio-economic status receiving antiretroviral therapy. *Diabetology & metabolic syndrome.* 2015;7:1.
32. Welsh DA, Ferguson T, Theall KP, Simon L, Amedee A, Siggins RW, Nelson S, Brashear M, Mercante D, Molina PE. The New Orleans Alcohol Use in HIV Study: Launching a Translational Investigation of the Interaction of Alcohol Use with Biological and Socioenvironmental Risk Factors for Multimorbidity in People Living with HIV. *Alcohol Clin Exp Res.* 2019;43(4):704-709. doi: 10.1111/acer.13980
33. Simon L, Ferguson TF, Vande Stouwe C, Brashear MM, Primeaux SD, Theall KP, Welsh DA, Molina PE. Prevalence of Insulin Resistance in Adults Living with HIV: Implications of Alcohol Use. *AIDS Res Hum Retroviruses*. 2020;36(9):742-752. doi: 10.1089/AID.2020.0029. Epub 2020 Jun 22. PMID: 32449647; PMCID: PMC7482115.
34. Kahler CW, Liu T, Cioe PA, Bryant V, Pinkston MM, Kojic EM, Onen N, Baker JV, Hammer J, Brooks JT, Patel P. Direct and Indirect Effects of Heavy Alcohol Use on Clinical Outcomes in a Longitudinal Study of HIV Patients on ART. *AIDS Behav.* 2017;21(7):1825-1835. doi: 10.1007/s10461-016-1474-y.
35. Felker-Kantor EA, Wallace ME, Madkour AS, Duncan DT, Andrinopoulos K, Theall K. HIV Stigma, Mental Health, and Alcohol Use Disorders among People Living with HIV/AIDS in New Orleans. *J Urban Health.* 2019;96(6):878-888. doi: 10.1007/s11524-019-00390-0.
36. Armoon, B., Fleury, MJ., Bayat, AH. et al. HIV related stigma associated with social support, alcohol use disorders, depression, anxiety, and suicidal ideation among people living with HIV: a systematic review and meta-analysis. *Int J Ment Health Syst* 2022; 16,17. https://doi.org/10.1186/s13033-022-00527-w
37. Crockett, K.B., Kalichman, S.C., Kalichman, M.O., Cruess, D.G., Katner, H.P., 2019. Experiences of HIV-related discrimination and consequences for internalised stigma, depression and alcohol use. *Psychology & Health* 2019 34, 796–810. https://doi.org/10.1080/08870446.2019.1572143
38. DiPrete BL, Pence BW, Bengtson AM, Moore RD, Grelotti DJ, O'Cleirigh C, Modi R, Gaynes BN. The Depression Treatment Cascade: Disparities by Alcohol Use, Drug Use, and Panic Symptoms Among Patients in Routine HIV Care in the United States. *AIDS Behav.* 2019;23(3):592-601. doi: 10.1007/s10461-018-2282-3.
39. US Preventative Taskforce. Screening and Behavioral Counseling Interventions to Reduce Unhealthy Alcohol Use in Adolescents and Adults US Preventive Services Task Force Recommendation Statement. *JAMA,* 2018 20(18).
40. Peter C. Smith, P.C., Schmidt, S.M., Donald Allensworth-Davies, D., &Richard Saitz, R. Primary Care Validation of a Single-Question Alcohol Screening Test. *J Gen Intern Med* 2009; 24(7):783–8, DOI: 10.1007/s11606-009-0928-6
41. Mersey, D. J. Recognition of Alcohol and Substance Abuse. *Am Fam Physician* 2003; 67 (7).
42. Edelman EJ, Maisto SA, Hansen NB, Cutter CJ, Dziura J, Deng Y, Fiellin LE, O'Connor PG, Bedimo R, Gibert CL, Marconi VC, Rimland D, Rodriguez-Barradas MC, Simberkoff MS, Tate JP, Justice AC, Bryant KJ, Fiellin DA. Integrated stepped alcohol treatment for patients with HIV and alcohol use disorder: a randomised controlled trial. *Lancet HIV.* 2019; 6(8):e509-e517. doi: 10.1016/S2352-3018(19)30076-1.
43. Edelman EJ, Moore BA, Holt SR, et al. Efficacy of Extended-Release Naltrexone on HIV-Related and Drinking Outcomes Among HIV-Positive Patients: A Randomized-Controlled Trial. *AIDS Behav.* 2019;23(1):211-221. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30073637.
44. Springer SA, Di Paola A, Azar MM, et al. Extended-Release Naltrexone Improves Viral Suppression Among Incarcerated Persons Living With HIV With Opioid Use Disorders Transitioning to the Community: Results of a Double-Blind, Placebo-Controlled Randomized Trial. *J Acquir Immune Defic Syndr.* 2018;78(1):43-53. Https://www.nci.nim.nih.gov/pubmed/29373393

Focusing on Mental Health to End the HIV Epidemic

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Mental health disorders—which include substance use disorders[1]—are persistent barriers to reducing HIV incidence and sustaining viral suppression (VS).[2] The combination of improved health care data systems and a shift in focus to treating the whole person has led to greater awareness of untreated mental health conditions as major challenges to optimal HIV continuum outcomes. Disorders common among people with HIV (PWH) include major depression, anxiety disorders, posttraumatic stress disorder, psychotic disorders, and alcohol or other substance use disorders.[3] Collectively referred to as behavioral health (BH) disorders, they can interfere with all steps along the HIV prevention and care continuum.[4,5] Unless we focus on addressing these undertreated comorbidities, the Ending the HIV Epidemic (EHE) initiative,[6] launched in 2019 by the U.S. Department of Health and Human Services (HHS), is unlikely to reach its goal of reducing new HIV infections in the U.S. by 90% by 2030 through scaling up key HIV prevention and treatment strategies. Incorporating BH into EHE efforts can be accomplished using three approaches New Jersey pioneered: implementing a combined BH and HIV continuum, using collaborative planning and resource development processes focused on BH and HIV, and building a workforce that can ably address BH and HIV.

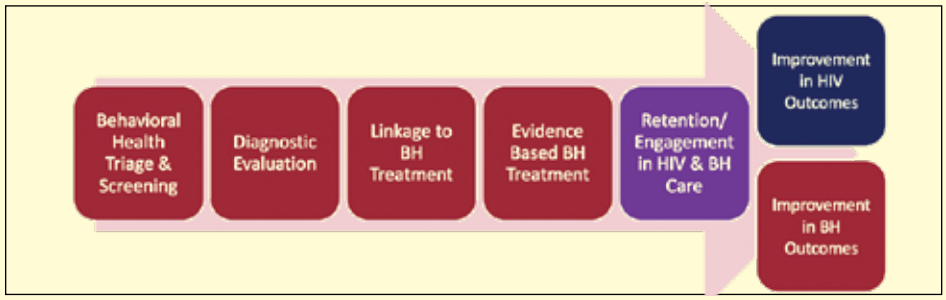
Barriers to integrating BH and HIV care

Optimal HIV service delivery includes screening for undiagnosed BH disorders. HIV care team members are not routinely trained to screen and effectively refer clients to appropriate BH services. The shortage of BH specialists compounds long wait lists for BH services. Communities of color are the leading population affected by HIV,[7] and implicit bias. A lack of robust cultural humility training can challenge delivering BH services to PWH in communities of color. Insufficient standardization of whether and how BH services are offered, delivered, and monitored creates systemic gaps. This accumulation of barriers creates a care disparity among PWH who have comorbid BH disorders and are disadvantaged in navigating services for their multiple complex conditions.[8]

New Jersey is a leader in helping HIV care teams integrate BH services.

The HIV care continuum places rightful emphasis on linkage to care as a critical step toward achieving VS. A statewide initiative in New Jersey demonstrated that linkage to BH care is inextricably connected to engagement and retention in HIV medical care. HIV care teams can place BH screening, diagnosis, and treatment as steps along a combined care continuum to improve access and quality of care (Figure 1).

Figure 1: Combined Behavioral Health and HIV Care Continuum[9]



The New Jersey Behavioral Health and Primary Care HIV Integration Project (NJ-BHIP)[10] was a four-year Learning Collaborative (LC) to support Ryan White-funded health care sites throughout New Jersey to implement a model for providing or referring clients to BH services. NJ-BHIP introduced a framework that enabled organizations to identify multiple ways to achieve integration through provider- and system-level changes. It created a forum for diverse HIV care sites to learn from their peers how to improve their care systems, better manage workflows, expand referral networks, and achieve better patient outcomes. The Northeast/Caribbean AIDS

Education and Training Center (NECA AETC) supported the LC with training, technical assistance, and practice facilitation coaching.

NJ-BHIP sites completed tools such as an organizational readiness self-assessment[11] (Figure 2 shows a sample page) to identify gaps in service delivery for those with BH needs and to evaluate the site's preparedness for BH service integration.

Quality improvement in NJ-BHIP was evaluated through performance measures that included depression and substance use disorder screening using validated tools; tracking referrals of positive screens; BH care retention; and VS rates of clients with both HIV and BH disorders. Other jurisdictions seeking to end the HIV epidemic look to New Jersey as a model for innovative approaches to meeting their EHE goals.

Setting priorities for ending the HIV epidemic

The Health Resources Services Administration has invested some of its EHE initiative funding in the AETCs across the U.S. NECA AETC serves HHS Region II, comprised of New Jersey, New York, Puerto Rico, and the U.S. Virgin Islands. This region is home to over 31.6 million people and nearly one in five PWH[12] and contains seven priority EHE jurisdictions, two of which are in New Jersey: Hudson and Essex counties. With EHE funding, NECA AETC expanded its infrastructure and scope of work to strengthen the capacity of the HIV workforce to address EHE goals in these jurisdictions: increase HIV testing and linkage to care; increase the number of providers who can administer prevention strategies such as pre-exposure prophylaxis; and increase the capacity of providers to deliver structurally and culturally competent care and treatment along the HIV care continuum to achieve sustained VS.

The Hudson and Essex counties' EHE

Figure 2. Sample Page of the Mental Health/Substance Use Care: Clinic/Health Center Readiness Assessment

AETC AIDS Education & Training Center Program

Mental Health/Substance Use Care[1]
Clinic/Health Center Readiness Assessment[2]

The following checklist contains information about recommended capacities to consider in implementing mental health/substance use care strategies in a clinic or health center. Services to address these conditions are often referred to as behavioral health. In the blank spaces provided, indicate which statement is the **best fit** for the given statement. This assessment may be completed individually by each member of your clinic team or collectively as a group to assist your team in planning and providing best practice mental health/substance use care for persons living with HIV (PLWH) in your program. Since every clinic and every client population is different, there is no single best-practice. Providing best-practice care is an ongoing process of evaluation, implementation, and re-evaluation. For help using this tool in your clinic, please email info@aidsetc.org.

Staff/Clinical Team Readiness	Not a current priority (indicate already addressed or not able to address at this time)	We have discussed this issue	We are developing a plan to address this issue	We are implementing a plan to address this issue	We are evaluating our implemented plan to address this issue	We are making adjustments to our plan to better address this issue	AIDS Education & Training Center services requested
1. There is ALL **STAFF recognition** of the **need** for **Mental Health/Substance Use Care** services in our clinic.							
2. Our clinic staff **knows** what Mental Health/ Substance Use Care includes **(Screening, Diagnosing, Treatment, and Follow-up - including referral to other services as needed)**.							
3. Our clinic has **leadership buy-in** to increase our Mental Health/Substance Use Care activities.							
4. Our clinic has **identified** an available Mental Health/Substance Use Care **champion**.							
5. **All** of our clinic **staff** is **invested** in improving our patient Mental Health/Substance Use Care.							

1 "Mental Health/Substance Use Care" refers to an evidence-based, comprehensive plan of care that efficiently and effectively identifies those with untreated mental illness including substance use disorders, engages them into evaluation, diagnosis, treatment, and follow-up to best manage their illness and improve their overall quality of life.

2 Based on a template from: Centers for Disease Control and Prevention (2005). Anti-Retroviral Treatment and Access to Services (ARTAS):An individual-level, multi-session intervention for people who are recently diagnosed with HIV: Implementation Manual. Retrieved from: www.cdc.gov/hiv/topics/cba/pdf/artas_implementation_manual.pdf

Mental Health/Substance Use Care Clinic/Health Center Readiness Assessment 1

continued on next page

plans[13] prioritize BH by calling for funding to train providers to ensure they can conduct BH assessments using a trauma-informed approach to care. Additional priorities include facilitating routine HIV testing in priority populations most vulnerable to HIV, including those with BH conditions, and engaging with relevant partners so that priority populations can access services known to prevent HIV acquisition, including housing and BH services.

Figure 3. The Collaborative Planning and Resource Development Process Used by NECA AETC to Create EHE Programming and Materials

To address BH and HIV, NECA AETC engaged in an extensive collaborative process to co-plan and co-create resources and training opportunities that increased capacity in a diverse and expansive workforce of providers and peers in many roles.

NECA AETC created working groups comprised of NECA AETC training partners and people with lived experience who identified regional training needs, key informants, and resources highlighting training gaps and barriers to care. Findings provided insight into previously underserved communities, including those needing integrated BH and HIV services, allowing NECA AETC to tailor EHE training sessions further. By conducting strategic webinars, hosting panel discussions, and producing toolkits and podcast episodes, NECA AETC centered its efforts on new topics as a way to support and contribute to EHE efforts, including:

- Social determinants of health, including homelessness, housing instability, and food insecurity
- Multiple intersecting stigmas
- Language biases effects on quality of care and engagement in care

Using this community-driven approach to mitigate health inequities, NECA AETC has increased the number of health care workers who can effectively provide HIV care and prevention in a culturally and structurally competent manner and ease the BH burden of PWH and those at risk for HIV.

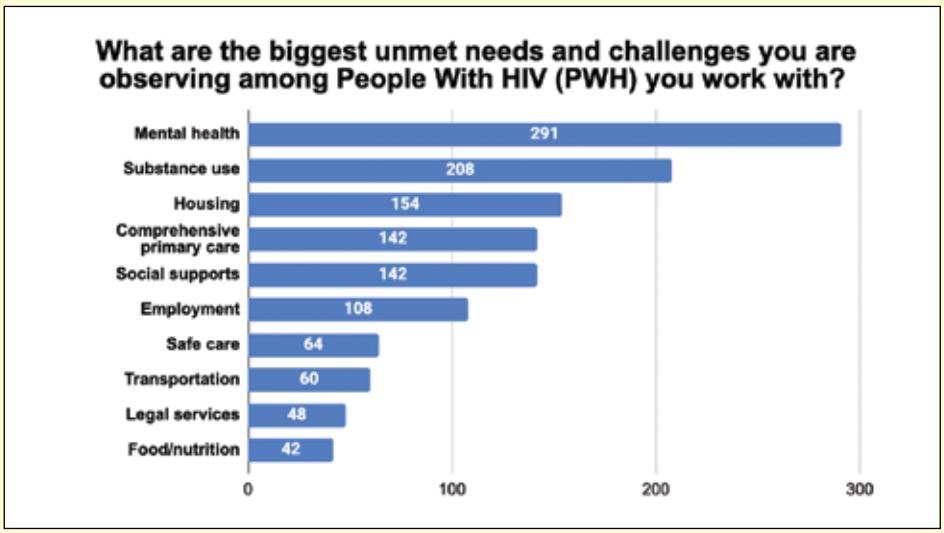
Building a workforce to end the HIV epidemic

First-generation HIV service providers are retiring in large numbers. Understanding who will take their place and how newer and, likely, a less specialized workforce will fill their decades of experience is a focus of the recently completed HIV Workforce Survey. NECA AETC assessed health care providers' attitudes and plans toward being part of the HIV workforce. The survey captured the needs, challenges, and gaps in providing high-quality HIV care, including BH care, in HHS Region II.

Of the 3133 survey respondents, 521 (17%) worked in New Jersey. Among them, 41% indicated that a better understanding of population-specific needs and resources would make providing optimal HIV services less challenging. Additionally, 56% of New Jersey respondents identified mental health as the most significant unmet need and challenge for the PWH they serve. Related challenges and unmet needs were substance use (40%) and social support (27%). The survey also revealed a need for increased training on mental health, substance use counseling, and trauma-informed care.

Regarding existing provider competencies, 41% of respondents reported being comfortable conducting a mental health screening, though only 20% felt they were experts in providing this service. While only 2% of the respondents worked in mental health clinics, social workers or case managers were the second largest group of respondents (13%). Figure 4 shows respondents' perceptions of

Figure 4. New Jersey's Top Unmet Needs and Challenges



their patients' most significant unmet needs and challenges.

Integrating BH services into HIV care is a challenging but critical step to providing optimal care for PWH. Increasing access to evidence-based interventions that address BH, cultural competence, and trauma-informed care is crucial, as is the use of data to promote person-centered services that tailor treatment and care to the specific needs of individual patients. By increasing the effective use of standardized screening and assessment tools, providers can identify patients likely to have BH needs and then develop individualized treatment plans. This approach can improve adherence to antiretroviral therapy, reduce viral load and onward transmission, and ultimately improve health outcomes.

Conclusion

New Jersey has taken many necessary steps toward ending the HIV epidemic and has been a leader in addressing BH as part of those efforts. From implementing a combined BH and HIV continuum to engaging in multiple community-driven processes designed to bring diverse perspectives to EHE planning to actively building a workforce that can ably meet both BH and HIV needs when providing services, concerted activities have put the state in a strong position to meet both federal and local jurisdictional EHE goals. Continued partnerships across city, county, tribal, and state health departments, local clinics and health care facilities, health care providers, providers of medication-assisted treatment for opioid use disorder, professional associations, advocates, community- and faith-based organizations, and academic and research institutions will allow for continued progress in achieving EHE goals.

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). *American Psychiatric Publisher,* 2013.
2. Glynn TR, Safren SA, Carrico AW, et al. High levels of syndemics and their association with adherence, viral non-suppression, and biobehavioral transmission risk in Miami, a US City with an HIV/AIDS epidemic. *AIDS Behav.* 2019;23:2956–2965. doi: 10.1007/s10461-019-02619-
3. Wainberg ML, McKinnon K, Cournos F. Epidemiology of Psychopathology in HIV. In J. Joska, D. Stein and I Grant (Eds.), *HIV/AIDS and Psychiatry,* London: John Wiley and Sons, 2014.
4. Chuah FLH, Haldane VE, Cervero-Liceras F et al. Interventions and approaches to integrating HIV and mental health services: a systematic review. *Health Policy Plan.* 2017;32(suppl_4):iv27-iv47. doi.org/10.1093/heapol/czw169
5. What is the HIV Care Continuum? HIV.gov. https://www.hiv.gov/federal-response/policies-issues/hiv-aids-care-continuum. Updated October 28, 2023
6. The Ending the HIV Epidemic Initiative. https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview/. Accessed March 3, 2023
7. HIV and African American People. Centers for Disease Control and Prevention. (https://www.cdc.gov/hiv/group/racialethnic/africanamericans/index.html). Last Reviewed February 16, 2023.
8. Remien RH, Stirratt MJ, Nguyen N, Robbins RN, Pala AN, Mellins CA. Mental health and HIV/AIDS: the need for an integrated response. AIDS. 2019; 15;33(9):1411-1420. doi: 10.1097/QAD.0000000000002227
9. Combined Behavioral Health and HIV Continuum. Conceptual Models & Frameworks. New Jersey Behavioral Health and Primary Care HIV Integration Project. https://www.njbhip.com/models-frameworks. Accessed March 10, 2023
10. The New Jersey Behavioral Health and Primary Care HIV Integration Project. https://www.njbhip.com/the-report. Accessed March 6, 2023.
11. Mental Health/Substance Use Care: Clinic/Health Center Readiness Assessment. AETC National Coordinating Resource Center. https://aidsetc.org/toolkit/mental-health/assessment-tool. Developed by the AETC Mental Health Committee in 2014-2015. Accessed March 10, 2023.
12. Kaiser Family Foundation. HIV diagnoses, adults and adolescents. https://www.kff.org/hivaids/state-indicator/hiv-diagnoses-adults-and-adolescents/?currentTimeframe=0&sortModel=%7B%22colId%22%3A%22Location%22%2C%22sort%22%3A%22asc%22%7D. Published April 30, 2021. Accessed March 10, 2023.
13. Ending the HIV Epidemic: New Jersey's Strategic Plan: Essex and Hudson Counties 2020-2030. https://nj.gov/health/hivstdtb/. Accessed March 10, 2023.

Polypharmacy and Older Adults with HIV: More Medications, More Problems

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Polypharmacy is associated with an increased risk of negative health outcomes, including adverse medication-related events, hospitalizations, and mortality. Understanding how polypharmacy affects persons with HIV (PWH) and mitigating its impact on their health should be a top priority for caregivers. In this article, we explore the drivers of polypharmacy, evaluate the literature on the effects of polypharmacy in PWH, and discuss current strategies health professionals can implement to ensure the right balance of risk versus benefit for each treatment.

Definition

Polypharmacy describes the coadministration of multiple medications, usually as a measure of overprescribing.[1] The method for quantitatively defining polypharmacy can differ regarding the number of agents needed to qualify and the technique for counting medications.[2-3] Studies apply various definitions, with most defining polypharmacy as the number of medications above a certain threshold. The threshold of five or more medications per day is the most common criterion for quantitative definitions of polypharmacy, although some studies use a threshold of 10 or 15 drugs per day.[2-4]

Studies evaluating polypharmacy in PWH generally only include non-antiretroviral drugs. Early in the combination antiretroviral (ART) era, challenges with the burden of medications were linked to ART and agents used to treat or prevent opportunistic infections (OI).[4-7] For many PWH in that era, the high pill burden and frequency (as well as pill size) of ART and OI therapy were more impactful to their quality of life and adherence than medications used to treat other conditions.[4] Fortunately for PWH, this is no longer the case for several reasons: a dramatic increase in co-formulated products, improvements in the pharmacokinetic and pharmacodynamic profiles of ART, and the growing body of data supporting two-drug (dual) therapy. Although pill burden has historically been an important issue, especially for PWH, polypharmacy usually accounts for all active medications a patient takes and administration routes. Nonetheless, health professionals should not overlook co-formulated products' advantages for patient satisfaction and adherence.

Another approach to defining polypharmacy is to consider whether a drug is clinically appropriate, focusing on identifying medications where risks may outweigh benefits.[1,3] It is logical to favor defining polypharmacy around the burden of inappropriate medications, particularly as the prevalence of polypharmacy continues to increase in older adults with HIV. This qualitative viewpoint is more relevant when polypharmacy is a consequence of having multiple comorbid conditions (or multimorbidity), which could lead to investigations into the root causes of increased comorbidities. Also, polypharmacy could be a symptom of comorbidity. Measuring polypharmacy based on appropriateness is inherently more difficult and time-consuming, especially when retrospectively analyzing records. In practice, an understanding of both quantitative and qualitative (inappropriate) polypharmacy can be helpful for clinicians in efforts to optimize patient care.

DRIVERS OF POLYPHARMACY

Chronic comorbidities and PLWH

There is a complex interplay of factors behind the greater burden of comorbidities earlier in life in this patient

population.[8,9] Studies have shown that people with HIV have a 1.5- to 2-fold higher risk of developing cardiovascular disease compared to their non-HIV counterparts.[10-12] Optimizing HIV treatment increases lifespan results in cumulative comorbidities requiring additional medications and drives polypharmacy. PWH are at an increased risk for comorbidities, such as cardiovascular chronic disease states (e.g., hypertension, diabetes, hyperlipidemia) and psychiatric disorders.[13]

Inequities across numerous determinants of health and stigmatization have historically contributed to the burden PWH deal with, along with their diagnosis. Additionally, rates of mental health disorders are higher in persons living with HIV compared to the general patient population. These two comorbidities are just a sliver of what one patient may deal with; both comorbidities are treated with multiple medications to prevent further complications, such as heart attacks or strokes or, on the side of mental health, suicidal ideation, or other depressive thoughts.

Fragmentation of Health care

PWH regularly receive care from multiple clinicians, which can increase the risk of polypharmacy. When the person managing the HIV care is not the primary care provider, there may be the potential to defer treatment decisions for non-HIV conditions to the other practitioner. Lack of medication review occurs more frequently as patients are increasingly referred to specialists to evaluate and manage other disease states.

Information on the patient's treatment history can be incomplete. Providers routinely take on the medical care of patients seen by practice colleagues (current or former) or for new patients transferring care to their facility. Indications or context behind initiating some medications are not always clear in progress notes or to patients themselves, often leading to the continuation of those agents. Acquiring medical records and a clear picture of the care received from other institutions can be a challenge.

Other Factors

There are several other contributing factors to polypharmacy. Guidelines for managing chronic medical conditions typically focus on a single disease state, primarily concentrating on treatment indications and highlighting which options are preferred based on literature and relevant factors. The same level of evidence and strength are rarely behind recommendations to discontinue a medication or at least reassessment of the benefits of continued use.

A prescribing cascade is another cause of polypharmacy. This phenomenon occurs when a drug-induced adverse effect leads to initiating another medication, with descriptions in the literature of multiple medications leading to a drug-related consequence when started.[16,17] Medications continued after discharge from a recent hospitalization can also add to polypharmacy. These medications may include appropriate short-term treatments that community prescribers should discontinue after a specified time, such as apixaban after a trauma-induced deep vein thrombosis or clopidogrel post-stent placement. Missed follow-up appointments with specialists can precipitate these situations, keeping patients on these therapies longer than warranted. Some medications may have been appropriate under previous circumstances, possibly based on older guidelines. The continued use of fenofibrate in PWH formerly on a PI-based therapy is an example of a prescribing cascade caused by adhering to guidance to treat moderately elevated triglycerides aggressively without reviewing on-going need for the medication. Prescribers should account for over-the-counter medications, vitamins, and natural supplements that can also contribute to polypharmacy and include them in all reviews of medication profiles.

CONSEQUENCES OF POLYPHARMACY

Accumulating multiple prescriptions for multiple comorbidities, possibly from multiple prescribers, can complicate care in PWH. Drug-drug interactions are one way polypharmacy can impact this population. The proportion of ART containing pharmacokinetic (PK) boosters has declined, yet many patients remain on these agents. These patients are often most at risk for contraindicated medications or those with substantial evidence of interactions.[3] Although the propensity and consequences are lower with other regimens without PK-boosters, potential interactions with select vitamins or minerals (i.e. magnesium, calcium) or acid suppressants remain a risk for serious drug-drug interactions. Thus, adding new drugs can lead to harm, especially by a provider that may not be aware of a person's whole medication list. Patients are also more likely to need clarification regarding dosing instructions as the number of prescriptions increase.

Numerous studies have associated polypharmacy with increases in morbidity and mortality.[18,19] In the general population, there is a potential association between increased use of medications and functional limitations, limitations with activities of daily living, confusion, and memory problems.[20] In PWH specifically, a higher prevalence of comorbidities and more medications show an increased risk of falls.[3] There is also evidence to suggest that polypharmacy may lead to an increased hospitalizations. Fukuba and colleagues studied the association between polypharmacy and time during hospitalization.[21] In patients prescribed at least five medications at admission, results indicated an increased length of stay for patients prescribed more medications. Although some study samples were people without HIV, regardless of the patient population,

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results emphasized the potentially severe consequences of polypharmacy. These consequences include an increased risk of mortality, with progressively escalating risk among individuals taking five or more medications.[19]

More research is needed to determine if polypharmacy reduces virologic control or if other factors drive it. Some studies found that polypharmacy negatively affects viral load suppression, suggesting the more medications a patient takes, the less in control of their HIV they may be. Not only do patients have the responsibility to manage their HIV, but have to manage their HIV along with other comorbidities, which poses a challenge.[4,22] On the other hand, a recent study suggested that patient frailty status, not polypharmacy, was associated with ART nonadherence.[23] Another cross-sectional review found high virologic control (95.9%) despite significant polypharmacy (46.6%) among PWH age 50 or older, although investigators did not analyze whether polypharmacy was an independent predictor.[24]

Reduced medication adherence related to pill fatigue is another potential consequence of polypharmacy. Pill fatigue, when a person becomes less motivated to take their medications based on the number of tablets or medications they must take, can occur with or without other exacerbating factors, such as toxicities or confusing dosing instructions. Decreased medication adherence often exacerbates their medical conditions, including HIV, requiring more frequent and higher levels of care. Krentz et al. found a strong association between polypharmacy and non-continuous ART, defined as discontinuing or switching ART, among PWH at their clinic.[7] More studies are needed to confirm these findings.

Drug costs may also contribute to the consequences of polypharmacy. For some patients, adherence may be impacted by prescription costs. With every increasing cost of living, the buildup of copays or high deductibles can leave patients with difficult choices, such as paying for medications or covering basic living costs. A report by AARP cited the HHS' Office of Health Policy's finding that more than 3,000 drugs increased in price between January and July 2022. The average increase in price was $150 per drug. Federal and state programs, specifically for PWH, such as AIDS Drug Assistance Program (ADAP), have provided patients with optimal coverage of ART regimens. Other resources, such as case managers and pharmacists, assist with drug costs or access should PWH need it. With the aging population of PWH and more variability in drug cost and drug coverage based on insurance, the uncertainty of prices may deter a patient from adhering to their medications.

EVALUATING PHARMACOLOGIC TREATMENT, REDUCING POLYPHARMACY

Regardless of the criteria set for polypharmacy, assessing each patient's medication profile at regular intervals should be incorporated into the standard of care. Although significant reductions in polypharmacy across society will likely require system-wide changes, health professionals have a vital role in this process. Changing our approach to patient care is increasingly critical as PWH age with a disproportionally greater comorbidity burden, placing them at risk of geriatric syndromes (e.g., frailty, dementia) earlier in life. As polypharmacy is often hard to disentangle from multimorbidity, providers should carefully weigh risks versus benefits when adding a medication, ensuring that the complaint(s) a patient is experiencing, or the symptoms are not due to another medication. Providers should also discontinue medications deemed ineffective for the prescribed indication before starting another agent and ensure that nonpharmacologic options are not preferable. Medication reviews should be ongoing rather than a discrete one-off activity. Clinicians can make small, incremental, carefully supported changes to decrease polypharmacy.

Medication reconciliation is an essential first step for addressing polypharmacy and involves using various resources to create a medication list that is as accurate and comprehensive as possible. Information should include over-the-counter medications, vitamins, and supplements. Medication reconciliation can be time-consuming, especially when there are multiple prescribers, recent hospitalizations, or when the patient is not a reliable source. Clinical teams can undertake an interdisciplinary approach to share the burden of conducting accurate medication reconciliation. Some facilities embed medication reconciliation software (e.g., Care Everywhere, Sure Scripts) within their electronic health records. Pharmacists can provide prescription fill records via fax or verbally. Clinicians should always confirm pharmacy records with patients as they may not be taking the dispensed medications. Once clinicians account for every medicine, they should ensure optimal use by checking the following:

- Clinical indication for each medication
- Drug-drug interactions
- Drug-disease interactions
- Duplications
- Recommended duration of use
- The risk-to-benefit ratio for the medication's indication (compared to alternative options)[25]

There are several approaches clinicians can use to reduce polypharmacy, with the overwhelming majority intended for use in older adults. Tools to address polypharmacy are often implicit- or explicit-based. Implicit-based approaches rely more heavily on

clinical judgment.[25] In contrast, explicit-based tools aim to provide objective criteria to define the appropriateness of therapy to minimize the extent of clinical assessment needed by clinicians.

The design of implicit-based tools streamlines the medication review process for clinicians (see table 1).[25,26] These protocols or algorithms can vary in their aim, with some explicitly emphasizing deprescribing while others provide general guidance toward judicious medication prescribing. Use of the ARMOR (Assess, Review, Minimize, Optimize, Reassess) protocol, created for use in long-term care facilities, maintains or restores functional capacity. General practitioners can use the Prescribing Optimization Method (POM), a series of six questions, to quickly assess medication use among older adults in the community. The Medication Appropriateness Index, another widely used tool comprised of 10 criteria, categorizes medications as appropriate, marginally appropriate, or inappropriate by assessing the drug effectiveness, dosing instructions, duplicative therapy, and relative costs[27,28]. A clinician's decision to use one of the approaches or another implicit-based option involves evaluating doses, drug-drug, drug-disease interactions, and the medication's risk-to-benefit ratio for the patient.

Explicit-based approaches are more common in practice than implicit-based ones due to their relative ease and objective criteria. These consensus guidelines are updated every few years, with recommendations based on the quality and strength of evidence to support it. The American Geriatric Society's (AGS) Beers Criteria lists potentially inappropriate medications (PIMs) for older adults.[29] It focuses on agents that could have more harm than benefit in this population, such as increasing fall risk, worsening cognitive impairment, bleeding, and hypoglycemia, to name a few. It also aims to limit drug-drug interactions and to ensure optimal dosing in persons with kidney impairment. The straightforward criteria set by this tool helped quantify the prevalence of PIMs, not just the extent of polypharmacy, in PWH. Using the AGS Beers Criteria, investigators with the Swiss HIV Cohort Study found that from January 2017 through December 2018, 31% of participants aged 65 or older had PIMs.[30] Another study found much higher rates of PIMs (63%) based on the same criteria among patients receiving care at San Francisco General Hospital (Ward 86).[31]

The STOPP/START (Screening Tool of Older Person's Prescriptions/Screening Tool to Alert to Right Treatment) criteria is another explicit-based tool that assesses the appropriateness of medication use in older adults. This tool guides medication use for various organ systems (i.e., cardiovascular, nervous, endocrine, etc.). The tool has two sections, one that provides which medications to stop (highlighted in red) and which medications to start (highlighted in green) and provides a rationale for each recommendation. After each organ system, they also reference the National Institute for Health and Care Excellence (NICE) guidelines, providing additional context for the recommendations offered to manage conditions in older adults. McNicholl and colleagues used the Beers and STOPP criteria to discontinue at least one medication in 69% of patients.[30] In one of 10 patients, this pharmacist-led initiative led to a discontinuation of at least six medications. These explicit-based criteria have inherent limitations, and thus treatment decisions must be made as part of a more comprehensive approach. Moreover, most tools have a discrepancy in the age cut-off. Criteria for PIMs in select situations are established for individuals 65 or older. Much literature on polypharmacy and multimorbidity in PWH focuses on those 50 and older. Clinicians should use judgment and consider comorbidity burden, functional status, years since HIV diagnosis, and other factors to guide decision-making.

Deprescribing is the planned and supervised process of dose reduction or stopping of a medication that may be causing harm or no longer is a benefit for the patient.[31] Deprescribing is common in palliative care, with increasing uptake in the older adult patient population. Several healthcare organizations have called for more widespread integration of deprescribing into routine practice, with some providing guidelines to streamline the evaluation of drug classes that are commonly scrutinized (https://deprescribing.org/resources/deprescribing-guidelines-algorithms/). These guidelines include recommendations for proton pump inhibitors, antihyperglycemics, antipsychotics, benzodiazepine receptor agonists, cholinesterase inhibitors, and memantine. Although most drugs on a patient profile will have an indication, it remains important to continually evaluate each drug's risks compared to other treatment options, the consequences of not treating the condition, and patient input into their care. The evidence around some therapies varies in weight (i.e., randomized controlled trial versus expert opinion), as can their risk-to-benefit ratio (i.e., improved survival but reduced quality of life of select treatment for prostate cancer).[16] Patient education and shared decision-making in this process are crucial. Discontinuation of medication may lead to a return of a symptom or may cause withdrawal. Discussions with patients about the benefits and risks of continuing or stopping a medication can strengthen provider trust and increase patient agency over their health. Discussions may include changes in treatment and reasons why a medication may no longer be indicated. Conversation with other specialists involved in the patient's care is often necessary. A plan should be agreed upon, with dose reductions or weaning when discontinuing select medications. Changes should be incremental, involve one medication at a time, and include close follow-up and monitoring. The plan should be

continued on next page

well documented and communicated to other providers and the patient's pharmacy.

Navigating through the deprescribing process can be a challenge.[16,17,32] Many of the same drivers of polypharmacy, such as incomplete records and inheriting care from a previous provider, can be a relative deterrent. Patients may be unaware of the indication for a medication, especially if a medication started years prior. Awareness of the side-effect profiles of medications and a low threshold to consider a patient's clinical picture to be drug-induced can greatly aid practitioners during this process. It is essential to consider that appropriate indications for some medications may have changed based on a person's age, functional status, co-administered medications, or new literature supporting a change in the standard of care. For example, the literature supporting using low-dose aspirin as primary prophylaxis for cardiovascular events has shifted over the years. The risk of bleeding is now well described, leading to recommendations against use without a specific indication (i.e., previous cardiovascular event).

Clinicians should consider re-evaluating the need for continued therapy as patients' health status improves or declines, or prescribing guidelines are updated. For example, previous hypertriglyceridemia guidelines and the prevalence of PI-containing regimens led to fibrates or omega-3 fatty acids prescribed for PWH. Clinicians should re-evaluate the need for continued therapy with these agents, particularly if the ART regimen no longer includes PIs and triglycerides are within normal limits. Clinicians may hesitate to discontinue therapy when the patient is stable, often not wanting to "rock the boat." Moreover, patients may be leery of these changes regardless of whether they understood the reason for select medications.

Conclusion

Time and resources are significant hurdles to addressing polypharmacy. Thoroughly collecting and evaluating each patient's history, the temporal relationship between the onset of symptoms and/or diagnoses with the start of current medications is time-consuming and laborious. It usually includes communication with other providers, who may have differing opinions on a patient's care or be unable to provide a timely response. Clinicians should discuss treatment histories with patients, determine their understanding of why a medication was prescribed, and explain indications for stopping medications no longer needed. This type of comprehensive care is increasingly difficult as the demand for health professionals that provide HIV care continues to grow. The shortage of geriatric care specialists exacerbates these needs as PWH age. Awareness of the polypharmacy crisis,

Table 1: Resources Used in Deprescribing and Mitigating Polypharmacy

Resource / Tool	Benefits	Limitations
ARMOR: Assess, Review, Minimize, Optimize, Reassess	- Provides guidance on which medications to be mindful of in assessing side effects - A universal tool to be used by any healthcare professional (not limited to prescribers) - Is not a process to be used once, encouraged to use at multiple visits, not just initial or singular visit	• Does not list all medications that could be a potential risk in PWH • Does not list all possible effects or potential ways to optimize the medication list • Only tested in a nursing facility
POM (Prescribing Optimization Tool)	• Includes open-ended questions • It also addresses adherence to medication • Ability to make real-time interventions while using the tool	• Limited to prescribers in terms of making interventions in real-time
START/STOPP (Screening Tool of Older Person's Prescriptions and Screening Tool to Alert Right Treatment)	• Provides guidance on what to potentially deprescribe and start • Can be administered by a provider and/or community pharmacist • Also is accompanied by the rationale behind proposed medication changes	• Limited to prescriber and community pharmacist • A limited number of medications are included in the tool
AGS' (American Geriatrics Society) Beers Criteria	• Can be used and referenced by prescribers and other healthcare professionals • Considers at risk medications, drug-drug/disease interactions risk, renal dose adjustments	• Limited to medications that may be at risk to the older adult population • Limited to guidance on certain medications, is not inclusive of all medications available
MAI (Medication Appropriate Index)	• Quick assessment (Y/N) questions about an indication of medication	• Limited to an indication of medication, does not necessarily provide guidance on discrepancies found • Given the questions provided, may be limited to prescribers
Deprescribing.org	• Provides resources outside of deprescribing algorithms (i.e., outside organizations, other programming) • Can be used as a reference tool for other healthcare professionals (not limiting)	• Limited to deprescribing algorithms for certain medications (i.e., PPI's)

shifting our approach to patient care, and embedding tools and criteria into processes are essential to improve patient quality of life and outcomes.

References

1. Duerden M, Avery T, Payne R (2013) Introduction In: Brown A (ed) Polypharmacy and medicines optimisation - Making it safe and sound. p 1
2. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr.* 2017;17(1):230. doi:10.1186/s12877-017-0621-2
3. Freedman SF, Johnston C, Faragon JJ, et al. Older HIV-infected adults. Complex patients (III): Polypharmacy [published correction appears in Eur Geriatr Med. 2019;10(3):531-535]. *Eur Geriatr Med.* 2019;10(2):199-211. doi:10.1007/s41999-018-0139-y
4. O'Brien WA, Hartigan PM, Daar ES, et al. Changes in plasma HIV RNA levels and CD4+ lymphocyte counts predict both response to antiretroviral therapy and therapeutic failure. VA Cooperative Study Group on AIDS. *Ann Intern Med.* 1997;126(12):939-945. doi:10.7326/0003-4819-126-12-199706150-00002
5. Hasse B, Ledergerber B, Furrer H, et al. Morbidity and aging in HIV-infected persons: the Swiss HIV cohort study. *Clin Infect Dis.* 2011;53(11):1130-1139. doi:10.1093/cid/cir626
6. Yuan Y, L'italien G, Mukherjee J, Iloeje UH. Determinants of discontinuation of initial highly active antiretroviral therapy regimens in a US HIV-infected patient cohort. *HIV Med.* 2006;7(3):156-62. doi: 10.1111/j.1468-1293.2006.00355.x.
7. Krentz, H., Cosman, I, Lee, K, Ming, JM, Gill, J. Pill Burden in HIV infection: 20 years of experience. *Antivir Ther* 2012;17(5):833-840. doi:10.3851/IMP2076
8. Marcus JL, Leyden WA, Alexeeff SE, et al. Comparison of Overall and Comorbidity-Free Life Expectancy Between Insured Adults With and Without HIV Infection, 2000-2016. *JAMA Netw Open* 2020;3(6):e207954.
9. Kong AM, Pozen A, Anastos K, Kelvin EA, Nash D. Non-HIV Comorbid Conditions and Polypharmacy Among People Living with HIV Age 65 or Older Compared with HIV-Negative Individuals Age 65 or Older in the United States: A Retrospective Claims-Based Analysis. *AIDS Patient Care STDS* 2019;33(3):93-103.
10. Triant VA, Lee H, Hadigan C, Grinspoon SK. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. *J Clin Endocrinol Metab.* 2007;92(7):2506-2512. doi:10.1210/jc.2006-2190
11. Durand M, Sheehy O, Baril JG, et al. Association between HIV infection, antiretroviral therapy, and risk of acute myocardial infarction: a cohort and nested case-control study using Québec's public health insurance database. *J Acquir Immune Defic Syndr.* 2011;57(3):245-253. doi:10.1097/QAI.0b013e31821d33a5
12. Freiberg MS, Chang CC, Kuller LH, et al. HIV infection and the risk of acute myocardial infarction. *JAMA Intern Med* 2013;173(8):614-22. doi: 10.1001/jamainternmed.2013.3728
13. Courlet P, Livio F, Guidi M, et al. Polypharmacy, Drug-Drug Interactions, and Inappropriate Drugs: New Challenges in the Aging Population With HIV. *Open Forum Infect Dis.* 2019;6(12):ofz531. doi:10.1093/ofid/ofz531
14. El-Sadr WM, Lundgren JD, Neaton JD, et al. CD41 count-guided interruption of antiretroviral treatment. *N Engl J Med.* 2006;355(22):2283-2296. doi:10.1056/NEJMoa062360
15. Justice AC, McGinnis KA, Skanderson M, et al. Towards a combined prognostic index for survival in HIV infection: the role of 'non-HIV' biomarkers. *HIV Med.* 2010;11(2):143-151. doi:10.1111/j.1468-1293.2009.00757.x
16. Scott IA, Hilmer SN, Reeve E, et al. Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Intern Med.* 2015;175(5):827-834. doi:10.1001/jamainternmed.2015.0324
17. Farrell B, Galley E, Jeffs L, Howell P, McCarthy LM. "Kind of blurry": Deciphering clues to prevent, investigate and manage prescribing cascades. *PLoS One.* 2022;17(8):e0272418. doi:10.1371/journal.pone.0272418
18. Guaraldi G, Malagoli A, Calcagno A, et al. The increasing burden and complexity of multimorbidity and polypharmacy in geriatric HIV patients: a cross sectional study of people aged 65 –74 years and more than 75 years. *BMC Geriatrics.* (2018); 18:99. doi:10.1186/s12877-018-0789-0.
19. Leelakanok N, Holcombe AL, Lund BC, Gu X, Schweizer. Association between polypharmacy and death: A systematic review and meta-analysis. *Journal of the American Pharmacists Association* (2017) 1-10. doi:10.1016/j.japh.2017.06.002.
20. Charlesworth CJ, Smit E, Lee D, Alramadhan F, Odden MC. Polypharmacy Among Adults Aged 65 Years and Older in the United States: 1988-2010. *J Gerontol A Biol Sci Med Sci.* 2015;70(8):989-95. doi:10.1093/gerona/glv013.
21. Fukuba N, Nishida M, Hayashi M, Furukawa N. The Relationship Between Polypharmacy and Hospital-stay Duration: A Retrospective Study. *Cureus.* 2020 Mar; 12(3):e7267. doi:10.7759/cureus.7267.
22. Murray MM, Lin J, Stein AB, et al. Relationship of polypharmacy to HIV RNA suppression in people aged ≥ 50 years living with HIV. *HIV Medicine* (2021). doi: 10.1111/hiv.13122.
23. Olivieri-Mui B, Wilson I, Shi S, et al. Geriatric Conditions Associated with Nonadherence to Antiretroviral Therapy Among Older People with HIV: The Importance of Frailty. *AIDS Patient Care STDS*. 2022;36(6):226-235. doi:10.1089/apc.2022.0040
24. Pereira B, Mazzitelli M, Milinkovic A, et al. Evaluation of a Clinic Dedicated to People Aging with HIV at Chelsea and Westminster Hospital: Results of a 10-Year Experience. *AIDS Res Hum Retroviruses.* 2022;38(3):188-197. doi:10.1089/AID.2021.0083
25. Levy HB. Polypharmacy Reduction Strategies: Tips on Incorporating American Geriatrics Society Beers and Screening Tool of Older People's Prescriptions Criteria. *Clin Geriatr Med.* 2017;33(2):177-187. doi:10.1016/j.cger.2017.01.007
26. Scott I, Anderson K, Freeman C. Review of structured guides for deprescribing. *Eur J Hosp Pharm*. 2017;24(1):51-57. doi:10.1136/ejhpharm-2015-000864
27. Samsa GP, Hanlon JT, Schmader KE, et al. A summated score for the medication appropriateness index: development and assessment of clinimetric properties including content validity. *J Clin Epidemiol.* 1994;47(8):891-896. doi:10.1016/0895-4356(94)90192-9
28. Hanlon JT, Schmader KE. The medication appropriateness index at 20: where it started, where it has been, and where it may be going. *Drugs Aging*. 2013;30(11):893-900. doi:10.1007/s40266-013-0118-4
29. By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc.* 2019;67(4):674-694. doi:10.1111/jgs.15767
30. McNicholl IR, Gandhi M, Hare CB, Greene M, Pierluissi E. A Pharmacist-Led Program to Evaluate and Reduce Polypharmacy and Potentially Inappropriate Prescribing in Older HIV-Positive Patients. *Pharmacotherapy.* 2017;37(12):1498-1506. doi:10.1002/phar.2043
31. Reeve E, Thompson W, Farrell B. Deprescribing: A narrative review of the evidence and practical recommendations for recognizing opportunities and taking action. *Eur J Intern Med.* 2017;38:3-11. doi:10.1016/j.ejim.2016.12.021
32. Swinglehurst D, Hogger L, Fudge N. Negotiating the polypharmacy paradox: a video-reflexive ethnography study of polypharmacy and its practices in primary care. *BMJ Qual Saf.* 2023;32(3):150-159. doi:10.1136/bmjqs-2022-014963

HIV PrEP: Options for All

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There are currently three options for HIV Pre Exposure Prophylaxis (PrEP) approved by the Food and Drug Administration (FDA).[1-3] Although initial studies for HIV PrEP were done with tenofovir disoproxil fumarate/emtricitabine (TDF/FTC), additional studies have expanded the available options for PrEP to include tenofovir alafenamide/emtricitabine (TAF/FTC) and long-acting injectable cabotegravir (LA-CAB).[4-7] Recently updated guidelines for PrEP reflect the availability of these options, including appropriate patient selection and lab monitoring for each option. Providers who prescribe PrEP are encouraged to review these guidelines in detail.[8,9]

The End the HIV Epidemic Plan (EHE), established in 2019, focused on four science-based strategies designed to significantly reverse trends in HIV infections by reducing new HIV infections by 90% by 2030 while scaling up HIV prevention efforts and improving treatment and care retention. The four strategies include HIV Diagnosis, Prevention, Treatment, and Response.[10] As it relates to prevention, the use of PrEP for at-risk populations is the most important biomedical intervention available to reach the 2030 goals. However, despite widespread availability, recent data from CDC shows we are far below our goal of 50% of at-risk people on PrEP by 2030.[11] Many populations, including Black/African American MSM, Hispanic/Latino MSM, and cisgender women, are less likely to receive PrEP compared to white MSM. Black and Hispanic/Latino account for the majority of people for whom PrEP is recommended yet still have the lowest rates of PrEP use compared to other racial and ethnic groups. To illustrate disparities in HIV prevention and care, CDC data estimates that only 9% of the over 450,000 Black individuals who could benefit from PrEP received a prescription in 2020; only 16% of 313,000 Hispanic/Latino individuals received a prescription.[11] PrEP coverage is much lower for females as well. The CDC estimates that PrEP use was about three times higher in males (28%) compared to females (10%) in 2020.

PrEP Options for Patients

The three medications approved for PrEP allow for essentially four different PrEP options (see Table 1):

- TDF/FTC daily,
- TDF/FTC on-demand (2:1:1 or event driven dosing),
- TAF/FTC daily,
- LA-CAB injection every other month [8,9]

TDF/FTC Daily

TDF/FTC for PrEP, used across all at-risk populations for HIV, has been available since 2012.[1,4] In March 2021, it became available in a generic formulation, which has led to substantial reductions in the cost of this intervention. Despite its broad use and availability, the chronic use of TDF/FTC, primarily when used to treat HIV infection, can potentially cause renal tubular dysfunction and decreased bone mineral density.[8,9] Despite these concerns, a large metanalysis demonstrated safety when used for PrEP.[12] Clinicians should avoid prescribing TDF/FTC for patients with a confirmed Creatinine Clearance of less than 50ml/min.[1,8,9] Studies also indicate that TDF is weight neutral and may cause small decreases in LDL cholesterol.[13] For patients for whom cost is a consideration, generic TDF/FTC is currently one of the least expensive

FIGURE 1. On-Demand PrEP Dosing

1st Dose	2nd Dose	3rd Dose
2 TDF/FTC tablets 2-24 hours before sexual activity,	**1 TDF/FTC tablet 24 hours after 1st dose**	**1 TDF/FTC tablet 24 hours after 2nd dose**
TDF/FTC TDF/FTC	TDF/FTC	TDF/FTC

PrEP options.[14]

TDF/FTC on-demand

TDF/FTC on demand, is also known as 2:1:1 or event-driven dosing. The FDA and US Guidelines recommend daily dosing for TDF/FTC; however, there are off-label data supporting the use of on-demand dosing in MSM.[8,15] A study in France comparing daily dosing to on-demand PrEP demonstrated equivalent efficacy with no increased risk of HIV infection.[15] Despite the effectiveness of this strategy in MSM, on-demand dosing is NOT effective for cisgender females, should be used with caution in transgender women (TGW), and has not been studied in people who inject drugs (PWID).[8,9] This strategy is also not FDA approved and is not the preferred administration method based on recent guideline recommendations from the US Public Health Service (USPHS).[9] So, while patients should ideally take TDF/FTC for PrEP every day, event driven dosing provides flexibility for appropriate patients who may not be sexually active regularly and for PrEP candidates that may be concerned with ongoing toxicity of daily use of TDF/FTC (see a detailed description of on-demand dosing in Figure 1).

TAF/FTC Daily

TAF/FTC has favorable bone and renal biomarker data compared with TDF/FTC. As a result, TAF/FTC is preferred in patients with underlying renal or bone disease, especially those with Stage 3 kidney disease (Creatinine Clearance 30-59 ml/min).[1,2,8,9] TAF/FTC was approved by the FDA for MSM, cisgender men, and TGW only and NOT for cisgender women. Currently, clinicians should not prescribe TAF/FTC for cisgender women based on FDA labeling.[2] The DISCOVER trial showed TAF/FTC to be non-inferior to TDF/FTC (DISCOVER); however, some participants experienced mild elevations in weight and small increases in LDL cholesterol.[5,8,9,16] The cost of TAF/FTC is much greater than TDF/FTC because it is not available in generic forms to date.[14]

Table 1. Comparison of PrEP Options

Characteristic	TDF/FTC Daily	TAF/FTC Daily	LA-CAB q2mo	On-Demand TDF/FTC
Effectiveness	++++	++++	++++	++++
FDA Approved	Yes	Yes	Yes	No
Populations FDA Approved	All	MSM and TGW only	All	MSM and TGW only
Time to protection (based on PK modeling)	7 days or earlier for rectal exposure	Unknown, but likely within 7 days	Unknown, but likely within 7 days	24 hours with 2 tablet TDF/FTC loading dose
Renal Safety	Potential adverse effect on renal tubules	Favorable renal safety compared to TDF/FTC	No effect	Potential adverse effect on renal tubules
Bone Safety	Potential adverse effect on bone mineral density	Favorable bone safety compared to TDF/FTC	No effect	Potential effect on bone mineral density
Effect on Weight	Neutral	Small increase	No effect	Neutral
Effect on LDL Cholesterol	Neutral	Small increase	No effect	Neutral
Dosing	Once daily	Once daily	Every month X 2 doses, then every other month, gluteal IM injections	2:1:1 see Figure 1
Dosing if higher BMI	No change	No change	No change; however, use a bariatric (2 inch) needle for IM dose if BMI>30	No change
Relative Cost	+	+++	++++	+
HIV Monitoring (Ag/Ab and HIV Viral Load)	Baseline and Q3 months	Baseline and Q3 months	TBaseline and Q2 months	Baseline and Q3 months
STI Monitoring	Baseline and Q3 months	Baseline and Q3 months	Baseline and Q4 months for most patients	Baseline and Q3 months
Renal Monitoring	Baseline and Q12 months if under 50 and CrCl over 90ml/min. Every six months for all other patients	Baseline and Q12 months if under 50 years of age and CrCl over 90ml/min. Every six months for all other patients	Not required	Baseline and Q12 months if under 50 years of age and CrCl over 90ml/min. Every six months for all other patients
LDL Monitoring	Not required	Baseline and Q12 months	Not required	Not required
Weight Monitoring	Not required	Baseline and Q12 months	Not required	Not required
Risk of Drug Interactions	+	+	++	+

LA-CAB (long-acting cabotegravir) or Injectable PrEP

LA-CAB or injectable PrEP is an

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attractive option for people who prefer every other month injections to oral tablets. Data from two large studies, HPTN-083 and HPTN-084, supported FDA approval for using LA-CAB in all populations, including MSM, TGW, and cisgender women.[6,7] Both studies showed LA-CAB superior to daily TDF/FTC, and it was added to guidelines upon FDA approval.[8,9] Despite the superior efficacy, there were rare cases of breakthrough HIV infections with the use of LA-CAB injections, despite on time administration.[17] Since LA-CAB has such a long elimination half-life, there is a risk of integrase resistance in these breakthrough cases. As a result, the guidelines highlight the importance of 4th generation HIV Ag/Ab testing and viral load testing when monitoring patients on LA-CAB for PrEP.[8,9,18] Providers are encouraged to review recent data that provides evidence based on comparisons of acute HIV infection (AHI) and Long Acting Early Viral Inhibition Syndrome (LEVI) described in detail elsewhere.[19]

Selecting PrEP Regimen for Patients

When selecting the appropriate PrEP regimen for patients, the most important principle is to provide all options for patients and to be sure to highlight the advantages and disadvantages of each option, understanding that most patients (especially MSM and TGW) will have multiple options for HIV prevention. Key factors that play into shared decision making when selecting an appropriate strategy include factors such as patient age, sexual activity, substance use issues (i.e., anal versus vaginal sex versus PWID), current renal and bone health, desire for oral versus injectable, willingness to take tablets on a daily, ongoing basis, and ability to pay for brand versus generic versions of PrEP. Insurance coverage for medications, associated tests, and PREP monitoring visits may determine the ultimate decision about the most appropriate option. For patients with limited financial resources, the USPHS Guidelines provide pathways for patients to obtain PrEP from various sources.[9]

Conclusion

In summary, although in the US, there are three excellent FDA-approved options for PrEP that provide protection for all of our at-risk populations, individuals at the highest risk for HIV often do not receive PrEP prescriptions. These data highlight the importance of ongoing and expanding HIV prevention efforts for all those involved with HIV care, including primary care settings.

References

1. Truvada (emtricitabine/tenofovir disoproxil fumarate) [package insert]. Foster City, CA: Gilead Sciences; 2020
2. Descovy (emtricitabine/tenofovir alafenamide) [package insert]. Foster City, CA: Gilead Sciences; 2022
3. Apretude (cabotegravir extended release injectable suspension) [package insert]. Durham, NC: ViiV Healthcare; 2023
4. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med.* 2010;363(27):2587-99.
5. Mayer KH, Molina J-M, Thompson MA, et al. Emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomised, double-blind, multicentre, active-controlled, phase 3, noninferiority trial. The Lancet. 2020;396(10246):239-254.
6. Landovitz RJ, Donnell D, Clement ME, et al. Cabotegravir for HIV prevention in cisgender men and transgender women. *N Engl J Med.* 2021;385(7):595-608.
7. Delany-Moretlwe S, Hughes JP, Bock P, et al; HPTN 084 Study Group. Cabotegravir for the prevention of HIV-1 in women: results from HPTN 084, a phase 3, randomised clinical trial. *Lancet*. 2022;399(10337):1779-1789.
8. Gandhi RT, Bedimo R, Hoy JF, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2022 recommendations of the International Antiviral Society-USA Panel. *JAMA*. 2023; 329(1):63-84.
9. Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf. Published December 2021.
10. Centers for Disease Control and Prevention: Ending the HIV Epidemic in the US. https://www.cdc.gov/endhiv/index.html. Published June 2022.
11. Centers for Disease Control and Prevention: Prep for HIV Prevention in the US. Fact Sheets. https://www.cdc.gov/nchhstp/newsroom/fact-sheets/hiv/PrEP-for-hiv-prevention-in-the-US-factsheet.html. Published November 2021.
12. Fonner, VA, Dalglish, Sl, Kennedy, CE, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. *AIDS.* 2016; 30(12):1973-1983.
13. Glidden DV, Mulligan K, McMahan V, et al. Metabolic Effects of Preexposure Prophylaxis With Coformulated Tenofovir Disoproxil Fumarate and Emtricitabine. *Clin Infect Dis.* 2018;67(3):411-419.
14. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. 2023. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Accessed (4/5/23) [Table 25]
15. Molina JM, Capitant C, Spire B, et al. On demand preexposure prophylaxis in men at high risk for HIV-1 infection. *N Engl J Med.* 2015;373:2237-2246.
16. Ogbuagu O, Ruane PJ, Podzamczer D, et al. Long-term safety and efficacy of emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV-1 pre-exposure prophylaxis: week 96 results from a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet HIV.* 2021; 8(7):e397-e407.
17. Eshleman SH, Fogel JM, Piwowar-Manning E, et al. Characterization of human immunodeficiency virus (HIV) infections in women who received injectable cabotegravir or tenofovir disoproxil fumarate/emtricitabine for HIV prevention: HPTN 084. *J Infect Dis.* 2022;225(10):1741-1749.
18. Eshleman S, Fogel JM, Halvas EK, et al. CA-LA PrEP: early detection of HIV infection may reduce InSTI resistance risk [Abstract LB95] in special issue: Abstracts From the 2022 Conference on Retroviruses and Opportunistic Infections. *Top Antiv Med*. 2022;30(1 suppl):36-
19. Eshleman S, Fogel JM, Piwowar-Manning E, et al. The LEVI Syndrome: Characteristics of early HIV infection with cabotegravir for PrEP. Abstracts from 2023 Conference on Retroviruses and Opportunistic Infections. Seattle, WA February 20-23, 2023. Abstract 194.

New Jersey HIVLinks 2023
HIV, STD, and TB news and information for health professionals

My PrEP Story: Jardel A.

Interview conducted by **Michelle Thompson**, Program Manager, New Jersey HIV Links Assistant Editor, Rutgers School of Nursing, FXB Center

Jardel is a 21-year-old cisgender white Mexican American male. He currently works as a Harm Reduction counselor. He has been on PrEP for four months. We discussed his experience.

How did you first hear or learn about PrEP?

The first time was about three years ago. I had a close friend who was an HIV counselor.

How did you decide that PrEP was the right choice for you?

When my friend initially educated me about the basics of HIV, I had an assessment of my sexual behavior that also evaluated my risk factors. When I tested negative for HIV, I decided PrEP was the right thing for me.

Tell me about your experience with finding a provider and how the provider discussed your sexual history with you.

I saw a PrEP counselor at Proceed, Inc. in Elizabeth and was referred to a provider in Newark. She is very professional when it comes to talking about sexual risks and behaviors, asking about the types of sex you have and if you use protection. She never tells you that you "need" to do something. It creates a non-judgmental environment. You get all the information and make your own decisions.

Is not being judged or feeling judged by a provider something that is important to you and why?

Yes, it is extremely important for me to feel comfortable with the health care provider. To be able to open myself up and honestly talk about my sexual behaviors without feeling judged or feeling ashamed is important. It creates a safe space. You have to trust a provider to get the service you need.

What method/drug/form of PrEP are you taking?

Apretude injections. I didn't think I could remember to take a pill every day when I have a lot of things going on in my life. I want to stay protected, and the shot was just better for me and my lifestyle.

What side effects, if any, have you experienced and how long did they last?

I never really had any side effects. The most I have experienced is pain at the injection site. It's not really bad and the pain is gone in a couple of days. I have been treated with penicillin before and that shot was more painful to me. I have heard stories from other people about different side effects, but that didn't happen to me.

Tell me about adherence. How did you make a decision on how and when to take PrEP?

I received my first and second shots back- to- back in February and March, then every two months for future shots. I had no trouble with taking my shots. I would schedule the time between my school and work to make sure I kept my appointments. I want to stay protected. I know I couldn't depend on taking that pill every day. Have a busy life. I am also in the Army Reserves, and it is important to me that I minimize the risk of HIV transmission in my personal life.

How do you pay for your medication?

I have private insurance that covers the cost of my medicine with no co-pay.

Do you have a message for someone considering PrEP?

Anyone considering PrEP should first be educated about the basics of HIV and how a positive diagnosis can change your life. PrEP minimizes the risk of HIV transmission.

My doctor explained a lot to me. You need a health care provider who makes you feel comfortable.

There needs to be more education to stop the stigma, misinformation and myths surrounding PrEP. It's not just for gay men.

**(Authors note: *Apretude* is generically known as cabotegravir extended-release injectable suspension)

Update: TB and HIV

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Tuberculosis (TB), a dreaded scourge of humanity since prehistoric times, has been known by many names throughout recorded history. The oldest recognized case of TB was found in human remains dating to before 9000 BCE. In 1882, when Robert Koch isolated *Mycobacterium tuberculosis*, tuberculosis diseases were responsible for one in seven deaths worldwide.[1] Public health and the advent of effective antibiotics led to moderate control of this plague in the early and mid-20th century. However, the HIV pandemic synergically fueled the TB pandemic, leading to a worldwide increase in infections, morbidity, and mortality, primarily concentrated in sub-Saharan Africa. In the early 1990s, over eight million people worldwide suffered from tuberculosis, and one to two million died yearly.[2] In response, the World Health Organization (WHO) declared TB a global emergency. By 2020, there were advances in the war against HIV-associated TB, but an estimated 215,000 deaths occurred that year alone. Unfortunately, the COVID-19 pandemic further diminished these gains as multiple TB-related services were disrupted. [3]

Clinical tuberculosis diseases range from asymptomatic latent infection (LTBI) to severe illness, also called TB. Clinicians diagnose latent infection through targeted testing with a purified protein derivative test (PPD) or Interferon Gamma release assays (IGRA). Immunosuppression can compromise the sensitivity of these tests. For this reason, the "cut off" for a positive PPD test is lowered to 5mm of induration in a person with HIV.[4] Many experts prefer to use IGRAs because the positive and negative controls afford recognition of a test compromised by insufficient immune responses. Patients with no additional risk factors with latent tuberculosis infection have a 10% risk of progression to active tuberculosis diseases. People with HIV (PWH) experience a 10% per year risk of reactivation.

PWH are approximately 26 times more likely to develop active tuberculosis if infected. HIV immunosuppression and HIV stage 3 (AIDS) dramatically increase the virulence of TB infection leading to more aggressive and earlier disease manifestations. Conversely, effective antiretroviral therapy (ART) can partially mitigate the risk of active tuberculosis by 50%-80%. However, the risks relative to HIV uninfected patients remain elevated even in those who have good CD4 counts (>700 cells/mL) on ART. The immune dysregulation caused by HIV infection leads to ineffective clearance of the bacilli by macrophages, failure of cytokine production, and inability to clear the infection, leading to rapid progression of TB infection to disease or reactivation of latent tuberculosis infection.[5]

Finding and treating all latent tuberculosis is imperative to end this dual pandemic. Current guidelines stress all people living with HIV should be screened for tuberculosis regardless of risk factors.[5] More frequent screening is needed if the clinician identifies specific risk factors. Anyone found to have a positive screening and no suspicion of active TB disease (no signs or symptoms such as prolonged cough, fever, weight loss, night sweats, negative physical exam, or negative chest x-ray) should receive treatment for latent tuberculosis. Currently, the recommended treatments for LTBI are 12 once-weekly doses of isoniazid and rifapentine (3HP) supported with directly observed therapy, or four months of rifampin daily, or three months of daily isoniazid and rifampin. If taken as prescribed, the cure rates are greater than 90%, illustrating the need to support adherence.[6]

The treatments of LTBI are highly effective but are sometimes challenging for PWH because of medication interactions. If unfavorable drug interactions are present, an older treatment regimen of nine months of daily isoniazid is favored. Isoniazid is a highly efficacious regimen but is limited by potential decreased adherence over nine months.[7] All current HIV medications can be used with isoniazid, and the patient should receive prophylactic B6 to prevent neuropathy.

Rifapentine

The 3HP regimen can be administered without dose adjustments to patients receiving efavirenz, twice-daily

raltegravir, abacavir, tenofovir disoproxil fumarate, lamivudine, or emtricitabine. Use is contraindicated with all other NNRTIs, including etravirine and rilpivirine. Using etravirine and rilpivirine in some single-tablet regimens and long acting injectables requires extra caution when reviewing interactions. Dolutegravir (DTG) may also be used if resistance is not suspected (i.e., patients receiving twice daily DTG therapy). Integrase inhibitors are currently the most popular HIV treatment regimens. Unfortunately, bictegravir, cabotegravir, and elvitegravir are contraindicated due to a significant decrease in the antiretroviral concentrations driven by rifapentine. It is similarly contraindicated with protease inhibitors (PI) as their concentration is dramatically reduced and not overcome by boosting. Maraviroc, fostemsavir, and lenacapavir are not recommended.[6]

Rifampin

Rifampin containing regimens have the most complex drug interactions. Clinicians reviewed these regimens for drug interactions before initiation. Rifampin lowers the levels of all PIs by more than 75%; therefore, rifampin cannot be used to treat TB in a PWH on a PI-based regimen. Efavirenz is the only NNRTI that can be co-administered without dose adjustments; its use is contraindicated with all other NNRTIs, including etravirine and intramuscular or oral rilpivirine. Tenofovir disoproxil fumarate, abacavir, lamivudine, or emtricitabine are considered safe. Dolutegravir may also be used, but only if resistance is not suspected. When used with rifampin, the dolutegravir dose must be doubled to 50mg twice daily. Bictegravir, cabotegravir, and elvitegravir are contraindicated due to a significant decrease in antiretroviral concentrations.[6]

Tenofovir Alafenamide

Previously, guidelines did not recommend using tenofovir alafenamide (TAF) with any rifamycin because of decreased tenofovir concentrations. However, recent data demonstrate high intracellular tenofovir levels despite using rifampin or rifapentine. TAF's antiviral effect depends on the intracellular drug concentration, so coadministration should not adversely affect it[8] This is a significant benefit as TAF has become a workhorse in ARV coformulation.

Medication Interactions

Medication interactions similarly influence the treatment of active tuberculosis disease in the setting of HIV. Multiple studies have confirmed the importance of aggressively treating tuberculosis while not delaying the initiation of HIV therapy. Ideally, HIV treatment should begin as soon as tolerance to the anti-tuberculosis drugs is confirmed. The lower the CD4 count, the more urgent is ART initiation.[9] Drug susceptible tuberculosis is treated with a three or four drug "cocktail" for a two-month "intensive phase" followed by four to seven months of two drugs in continuation. The initial drugs should include isoniazid, rifamycin, pyrazinamide, and ethambutol. Isoniazid, pyrazinamide, and ethambutol have no significant interactions with antiretroviral drugs. This article outlined the myriad interactions with rifamycins. Despite these challenges with the use of rifamycin, it is essential for successful TB treatment and allows for a shortened length of therapy. PWH should be treated with a rifamycin unless the TB isolate is resistant, even if that means altering their HIV treatment.[6]

Fortunately, rifabutin is an available alternative to rifampin that maintains *M. tuberculosis* killing with fewer, albeit not entirely, drug-drug interactions. The usual rifabutin dose is 300mg daily and can be used with dolutegravir and raltegravir. Oral rilpivirine may need an increased dose to 50mg daily, and intramuscular rilpivirine is not recommended. Rifabutin at a lower dose of 150 mg daily can be used with ritonavir boosted PIs. It cannot be used with cobicistat boosted antiretrovirals. The dose of rifabutin must be increased if used with efavirenz. Rifabutin is not recommended with bictegravir or cabotegravir IM.[6] As with the addition of any new medication, it may be advisable to reassess HIV viral load to ensure that suppression is maintained.

Conclusion

The treatment of HIV and tuberculosis coinfection is complex but vital to the health and well-being of our patients. Through the diligent diagnosis and treatment of all TB infections, we can improve the health of our patients and communities. Multiple TB information resources and expert consultation are available to guide individualized therapy.

References

1. CDC. History of World TB Day. https://www.cdc.gov/tb/worldtbday/history.htm#:~:text=TB%20in%20humans%20can%20be,China%20(2%2C300%20years%20ago) Accessed May 9, 2023
2. Canetti C, Riccardi, N, Martini M, Villa S, Di Biagio A, Codecasa L, Castagna A, Ilaria B, Gazzaniga V, Besozzi G. HIV and tuberculosis: A historical perspective on conflicts and challenges, (2020); 122 https://doi.org/10.1016/j.tube.2020.101921
3. WHO. Tuberculosis. https://www.who.int/health-topics/tuberculosis#tab=tab_1 Accessed May 8, 2023
4. https://www.cdc.gov/tb/publications/factsheets/testing/skintesting.pdf
5. smail, H., Riou, C., du Bruyn, E., Lai, R. P.-J., Harley, Y. X. R., Meintjes, G., … Wilkinson, R. J. (2018). *The Immune Response to Mycobacterium tuberculosis in HIV-1-Coinfected Persons. Annual Review of Immunology,* 36(1), 603–638. doi:10.1146/annurev-immunol-042617-053420
6. HIV.gov. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/mycobacterium-0?view=full. Accessed May 8, 2023.
7. CDC. Managing Drug Interactions in the Treatment of HIV-Related Tuberculosis. https://www.cdc.gov/tb/publications/guidelines/tb_hiv_drugs/recommendations04.htm. Accessed May 8, 2023.
8. Badowski M & Shah R. Managing Drug Interactions in HIV and TB Coinfection Is Complex. *Pharmacy Times* 2022;11 (2).
9. Torok, ME, & Farrar, JJ, (2011). When to Start Antiretroviral Therapy in HIV-Associated Tuberculosis. *N Engl J Med* 2011; 365:1538-1540. DOI: 10.1056/NEJMe1109546

CROI 2023 update

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It is challenging to summarize a gigantic meeting in one page, but I'll try to concisely give my take-home messages for practical patient care. As usual, this year's conference was rich with new data but richer in emotions since we had three years of in-person interruption due to the COVID-19 pandemic. Attendees seemed excited to be able to finally reconnect in person and assess the damage of the pandemic on the goal of HIV elimination.

Undoubtedly the biggest disappointment was doxycycline post-exposure prophylaxis failure to protect cisgender women in Kenya from sexually transmitted infections, mainly chlamydia trachomatis and Neisseria gonorrhea (Stewart J., et al., Abstract 121LB.).

There was a lot of excitement regarding long-acting agents, the most notable presentations were the following:

1-Long-Acting Cabotegravir + Rilpivirine (LA CAB + RPV) in a Safety Net Clinic Population in San Francisco described the proof of concept of a directly observed therapy in 133 persons living with HIV (PWH) followed at the Ward 86 HIV Clinic with a high prevalence of drug use, mental health disorders, and unstable housing. At the median point of 33 days, 55 out of 57 participants previously without virologic suppression achieved virologic suppression. The authors concluded that starting LA CAB + RPV demonstrated highly successful

virologic outcomes in a population of PWH with high adherence barriers. The overall virologic failure rate of 1.5% in this population with and without virologic suppression at baseline was similar to the 1.4% rate in phase III trials of PWH who were switched to LA CAB + RPV while virologically suppressed (Gandhi, Abstract 518).

2-SOLAR (Switch Onto Long-Acting Regimen) 12-Month Results – This study was a randomized switch trial of LA CAB + RPV vs. oral Biktarvy® (B/F/TAF). The results showed that patients stable on B/F/TAF who have Integrase inhibitors (INI) as their first regimen have a low risk of virologic failure (VF) if they switch to LA CAB + RPV. Still, VF is often associated with HIV resistance to NNRTI and INI (Ramgopal MN, CROI 2023, Abs. 191).

3-Another exciting phase 2b study with 20 patients evaluated the effectiveness of a LA regimen of injectable Lenacapavir in combination with two broadly neutralizing antibodies (bNAbs), GS-5423 and GS-2872, which found that with one exception, all participants remained virally suppressed at week 26. The one virologic failure at week 16 achieved virological suppression when they resumed their baseline oral ART (Eron J, CROI 2023, Abs. 193).

A notable switch study of Biktarvy® to Doravirine 100 mg + Islatravir 0.75mg (DOR/ISL) caught the attention of conference participants because of the FDA hold on Islatravir development at high dose due to lymphopenia. This was a large blind, randomized trial of patients without a diagnosis of Hepatitis B, no prior virologic failure, and no known resistance to DOR, currently receiving Biktarvy® with VL<50 c/ml for at least three months. Out of the 641 participants, 321 were randomized to DOR/ISL. There was only one virologic failure at week 48 with no evidence of resistance to DOR or ISL. In conclusion, this one pill combination was virologically non-inferior to Biktarvy,® however, the mean CD4 changes at week 48 was - 19.7cell/mm3 for DOR/ISL, and + 40.5cell/mm3 for those who continued Biktarvy® (Mills AM, CROI 2023, Abs. 197). The currently designed naïve and switch phase 3 trials of ISL will be using 0.25 mg/day.

One of the multiple weight change-related abstracts was a follow-up of the ADVANCE study. This study of ART-naïve patients with three arms demonstrated higher weight gain in the Dolutegravir (DTG) + TAF/FTC arm compared to DTG+TDF/FTC, while patients in the third arm who received Efavirenz (EFV) + TDF/FTC gained the least weight. After 192 weeks, all participants were switched to open-label TDF/3TC/DTG, and 52 weeks later, those who switched from TAF/FTC + DTG had significant reductions in weight, total cholesterol, LDL, triglycerides, fasting glucose, and HbA1C; those who switched from TDF/FTC/EFV had a significant rise in weight and reductions in total cholesterol, LDL, triglycerides, fasting glucose and HbA1C (Bosch B, CROI 2023, Abs. 671).

Food Insecurity in Older Adults with HIV

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The U.S. Department of Agriculture defines food insecurity as "a lack of access to enough food for every person in a household to live an active, healthy life".[1] The United Nations defines it more specifically as "the limited or uncertain availability of nutritionally adequate, safe foods or the inability to acquire personally acceptable foods in socially acceptable ways."[2] Regardless of the definition, food insecurity is distinct from hunger, defined as an "individual-level physiological condition that may result from food insecurity" because of prolonged involuntary lack of food.[1] According to the nonprofit organization Feeding America, 34 million Americans experience food insecurity, including an estimated 775,000 New Jersey residents.

Food insecurity appears to be more common among people with HIV (PWH) in the U.S. compared with the general population. Up to 25%-80% of PWH may be food insecure compared with 14% of the general population.[3] While beyond the scope of this article, globally, the intersection of HIV and food insecurity is an enormous problem in sub-Saharan Africa and other resource-limited regions of the world with a high prevalence of HIV.[4]

Why is food insecurity more common among PWH, and what are the implications? Food insecurity is associated with behaviors linked to increased rates of HIV transmission, including injection drug use and transactional sex.[5] Furthermore, some of the factors associated with food insecurity intersect with demographic groups that are disproportionally affected by HIV; these factors include poverty, other chronic diseases, and systemic racism. Often, PWH who experience food insecurity have decreased access to HIV care and treatment.[6] Food insecurity is also associated with decreased adherence to antiretroviral therapy and clinic appointments, lower CD4 cell counts, and lower rates of virologic suppression.[6-8] Other consequences of food insecurity among PWH are worse physical health status, increased use of acute medical care, and increased mortality.[9-11]

Lack of access to nutritionally adequate food can cause weight loss and poor nutritional status. Food insecurity may contribute to obesity and diabetes when people consume less expensive, energy-dense foods, such as meals from fast food restaurants. While data on PWH are not yet available, we know that food insecurity contributes to metabolic and cardiovascular disease and mortality in the general population.[12] Women with HIV who experience food insecurity have higher markers of inflammation, even after accounting for HIV suppression, which raises concern about increased cardiovascular risk.[13]

Older PWH are particularly vulnerable to food insecurity and its consequences. One of the first studies to address this, conducted at the University of California San Francisco Silver Project, was a demonstration project focused on PWH aged 50 and older.[14] Among 230 participants (89% men), 15% had low food security, and 17% had very low food security, defined as food insecurity with hunger. The authors estimated that these rates were three to four times the general population's rate. They also found that food insecurity was associated with risky alcohol or drug use, being sedentary, having depressive symptoms, and being dependent on

instrumental activities of daily living, meaning that the individual could not perform some complex tasks such as shopping, managing medications, and housework without assistance.

Our research group at Weill Cornell Medicine in New York recently investigated food insecurity in a study of 162 PWH age 55 and older, one-third of whom were women and half of whom were Black.[15] We found that 36% experienced food insecurity within the prior year, and as expected, financial insecurity was more common in the food-insecure group. Surprisingly, only 16% of those with food insecurity reported using a meal or nutrition program, a rate similar to those without food insecurity. Food insecurity was associated with depression and several key functional limitations, including the ability to shop, walk across a small room, and handle money. There was also a trend for food insecurity to be associated with frailty, defined as a state of increased vulnerability resulting from an aging-associated decline in reserve,[16] As commonly done, we assessed frailty using the Fried frailty phenotype based on low grip strength, low energy, slowed walking speed, low physical activity, or unintentional weight loss.[17]

San Francisco and New York data support the importance of screening PWH –especially older adults- for food insecurity. One simple method is the two question Food Insecurity Screener (see box). Once identified, providers can refer patients with food insecurity to community-based resources, such as food pantries, congregate meal programs, or meal delivery programs. Older PWH can access nutrition assistance through County Area Agencies on Aging, State Aging and Disability Resource Centers, and the Agency for Community Living's Eldercare Locator (https://eldercare.acl.gov/ or 1-800-677-1116) sponsored by the U.S. Administration on Aging.

Food Insecurity Screener[18]

This two-item screening tool, based on the U.S. Household Food Security Survey, is a validated screening tool in healthcare settings.[19]

"I'm going to read you two statements that people have made about their food situation.

For each statement, please tell me whether the statement was often true, sometimes true, or never true for your household in the last 12 months."

1. "We worried whether our food would run out before we got money to buy more."
2. "The food that we bought just didn't last, and we didn't have money to get more

A response of "often true" or "sometimes true" to either question equals a positive screen for food insecurity.

References

1. U.S. Department of Agriculture (USDA). https://www.ers.usda.gov/topics/food-nutrition-assistance/food-security-in-the-u-s/definitions-of-food-security/ Accessed January 28, 2023.
2. Nutrition and HIV/AIDS. Statement by the Administrative Committee on Coordination, Sub-Committee on Nutrition at its 28th Session Nairobi, Kenya: 2001. https://www.unscn.org/files/Annual_Sessions/28th_SCN_Session/28th_session_REPORT.pdf Accessed February 27, 2023.
3. Feldman MB, Alexy ER, Thomas JA, Gambone GF, Irvine MK. The Association Between Food Insufficiency and HIV Treatment Outcomes in a Longitudinal Analysis of HIV-Infected Individuals in New York City. *J Acquir Immune Defic Syndr.* Jul 1 2015;69(3):329-37.
4. The Lancet H. The syndemic threat of food insecurity and HIV. *Lancet HIV.* Feb 2020;7(2):e75.
5. Strike C, Rudzinski K, Patterson J, Millson M. Frequent food insecurity among injection drug users: correlates and concerns. *BMC Public Health*. Dec 8 2012;12:1058.
6. Young S, Wheeler AC, McCoy SI, Weiser SD. A review of the role of food insecurity in adherence to care and treatment among adult and pediatric populations living with HIV and AIDS. *AIDS and behavior*. 2014;18 Suppl 5(05):S505-S515.
7. Kalichman SC, Cherry C, Amaral C, et al. Health and treatment implications of food insufficiency among people living with HIV/AIDS, Atlanta, Georgia. *J Urban Health*. Jul 2010;87(4):631-41.
8. Weiser SD, Yuan C, Guzman D, et al. Food insecurity and HIV clinical outcomes in a longitudinal study of urban homeless and marginally housed HIV-infected individuals. *Aids*. Nov 28 2013;27(18):2953-8.
9. Anema A, Chan K, Chen Y, Weiser S, Montaner JS, Hogg RS. Relationship between food insecurity and mortality among HIV-positive injection drug users receiving antiretroviral therapy in British Columbia, Canada. *PLoS One*. 2013;8(5):e61277.
10. Weiser SD, Bangsberg DR, Kegeles S, Ragland K, Kushel MB, Frongillo EA. Food Insecurity Among Homeless and Marginally Housed Individuals Living with HIV/AIDS in San Francisco. *AIDS and Behavior*. 2009/10/01 2009;13(5):841-848.
11. Weiser SD, Hatcher A, Frongillo EA, et al. Food insecurity is associated with greater acute care utilization among HIV-infected homeless and marginally housed individuals in San Francisco. *J Gen Intern Med.* Jan 2013;28(1):91-8.
12. Sun Y, Liu B, Rong S, et al. Food Insecurity Is Associated With Cardiovascular and All-Cause Mortality Among Adults in the United States. *J Am Heart Assoc.* Oct 20 2020;9(19):e014629.
13. Leddy AM, Roque A, Sheira LA, et al. Food Insecurity Is Associated With Inflammation Among Women Living With HIV. *J Infect Dis.* Jan 9 2019;219(3):429-436.
14. Hessol NA, Zepf R, Zobell E, Weiser SD, John MD. Food Insecurity and Aging Outcomes in Older Adults Living with HIV. *AIDS Behav.* Dec 2017;21(12):3506-3514.
15. Bhatia S, Johnston CD, Derry-Vick H, et al. Food Insecurity Is Associated with Key Functional Limitations and Depressive Symptoms in Older People Living with HIV. *AIDS Patient Care STDS*. 2022:375-378. vol. 10.
16. Xue QL. The frailty syndrome: definition and natural history. *Clin Geriatr Med.* Feb 2011;27(1):1-15.
17. Fried LP, Tangen CM, Walston J, et al. frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci* Med Sci. Mar 2001;56(3):M146-56.
18. Feeding America. https://www.feedingamerica.org/hunger-in-america/food-insecurity Accessed January 28, 2023.
19. Hager ER, Quigg AM, Black MM, et al. Development and validity of a 2-item screen to identify families at risk for food insecurity. *Pediatrics.* Jul 2010;126(1):e26-32.

Mary Jo Hoyt: Celebrating the life of a nursing leader who impacted the care of women and children affected by HIV

Andrea Norberg, DNP, MS, RN Executive Director François Xavier Bagnoud Center
Deborah Storm, PhD, RN Director for Research and Evaluation François Xavier Bagnoud Center (retired 2016)

Mary Jo Hoyt, the former Director for Capacity Development at the François Xavier Bagnoud Center (FXB Center), Rutgers School of Nursing, sadly, and unexpectedly, died on November 7, 2022 at St. Luke's Hospital in Kansas City. We had the great fortune to work with Mary Jo at FXB Center and are honored to share with our readership how her work contributed to advancing HIV prevention and care at multiple levels, with a focus on women and children affected by HIV. In life, Mary Jo would have discouraged this tribute, but we are compelled to tell some of her professional story as she is truly among the unsung heroes of HIV prevention and care.

Mary Jo's career as a nurse and family nurse practitioner involved in HIV care encompassed a range of diverse experiences beginning in 1990 as a staff nurse at the Bailey House Center for People Living with AIDS and in 1993 becoming the Director of the Women's Health Program within the Section of HIV Medicine at St. Vincent's Hospital in New York. Saint Vincent's Hospital and Bailey House were among the first clinics and supportive housing resource centers for persons with HIV on the East Coast. Mary Jo was a pioneer committed to both patient care and early nursing leadership. She was active in the Association of Nurses in AIDS Care (ANAC) and was president of ANAC in 1993-1994.

In 1999, Mary Jo relocated to New Jersey where she became the Research Program Manager for the Pediatric AIDS Clinical Trials Unit (PACTU) at New Jersey Medical School, Division of Pediatric Allergy, Immunology, and Infectious Diseases (then University of Medicine and Dentistry of New Jersey) in Newark under the direction of Dr. James Oleske. In this role, she was a key part of the team implementing clinical trials that over time have revolutionized the care and outcomes of treatment for children living with HIV and the prevention of perinatal HIV transmission.

Mary Jo transitioned to a position at FXB Center in 2003 to manage the Global Education and Training Program for the International Maternal, Pediatric and Adolescent Clinical Trials (IMPAACT) Group. This training program helped to support the implementation of pediatric and perinatal HIV clinical trial protocols in newly established research settings in sub-Saharan Africa. Mary Jo understood the crucial importance of translating research into practice. From 2007-2011, she directed the FXB Center's Global HIV Program, providing technical assistance and training related to prevention of perinatal transmission in several countries with funding from the President's Emergency Plan

for AIDS Relief (PEPFAR). She was remarkably effective leading FXB Center personnel and working with partners in Tanzania, Botswana, and other countries developing national clinical guidelines and curricula that were instrumental to these countries' abilities to advance clinical services for perinatal HIV prevention and improve the care and clinical outcomes of women and children affected by HIV.

Beginning in 2011 as the FXB Center Director for Education and Capacity Development, Mary Jo focused on projects funded by the Centers for Disease Control and Prevention (CDC) to implement a national framework and comprehensive services to eliminate perinatal HIV transmission in the United States (U.S.). As principal investigator for this program at FXB, she worked with CDC to bring multidisciplinary experts together and create resources to implement the newest recommendations and interventions that have now reduced the rate of perinatal HIV transmission to 1% or less in the U.S. She worked actively to promote and participate in collaborations with colleagues across the country that resulted in the development of publications addressing preconception care, HIV preexposure prophylaxis, perinatal HIV service coordination, and other topics with an emphasis on dissemination into practice.

Mary Jo was able to bridge divides and bring people together for common purposes. She was a strong, kind leader who provided mentorship to many. It brings a smile recalling how she was able to marshal staff and resources to get things done. Although most of our time was work-focused, we enjoyed the times we were able to have a cup of coffee or a meal and share information about our lives, families, home renovations, etc. After Mary Jo left FXB Center in 2018 to return home to Kansas City, MO, we remained in touch intermittently or heard news though others. However, learning of her death prompted us to reflect that while she was no longer with us, she was not forgotten and the impact of her work lives on.

We also learned things about Mary Jo that we hadn't known. The initial phase of her career took her from Kansas City to Central and South America where she provided nursing care in poverty-stricken areas of St. Lucia and Venezuela. In Venezuela, she provided medical care to people living in unimaginable poverty. Without resources and with very little physician support, she tended to the many sick and dying people that she encountered. She once carried a severely malnourished baby—in a box on her head—across a riverbed that had filled with raging flood water caused by heavy rain. That sounds just like the Mary Jo that we knew and further illustrates the impact that she had on the people and communities she served.

Mary Jo's life ended too soon, but her memory lives on. May she rest in peace.

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Rutgers François-Xavier Bagnoud Center SCHOOL OF NURSING

New Jersey HIV Links Planning Committee

Division of HIV, STD, and TB Services
- Jihad Slim, MD, Medical Director
- Chelsea Betlow Director Program Innovation & Strategic Initiatives
- Nahid Suleiman, PhD, Ryan White Part B Program Manager
- Amelia M. Hamarman, MSEd, MS, STD/STD-HIV Services

- Darcel M. Reyes, PhD, ANP-BC
- Michelle Thompson, Program Manager

New Jersey Department of Health–Division of HIV, STD, and TB Services (NJDOH-DHSTS) (609) 984-5874 • www.state.nj.us/health/hivstbtb

- NJ HIV/AIDS statistical reports, regulations, forms, and links to HIV care, prevention programs, and training
- New Jersey rapid testing site: www.njhiv1.org
- New Jersey AIDS/STD Hotline: (800) 624-2377

François-Xavier Bagnoud (FXB) Center, School of Nursing, Rutgers, The State University of New Jersey (973) 972-5644 • Fax: (973) 972-0397 • http://www.fxbcenter.org/about.html

- HIV/AIDS conferences, training
- Free online continuing education (CE) credits for healthcare professionals
- HIV/AIDS MEDICAL UPDATE SERIES: with funding from NJDOH-DHSTS
- Free on-site HIV medical education for healthcare sites. **Contact** Michelle Thompson at (973) 972-1293 or ccthomps@sn.rutgers.edu

François-Xavier Bagnoud Center, School of Nursing,
Rutgers, The State University of New Jersey
65 Bergen Street, 8th floor, Newark, NJ 07101-1709

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NJDOH-DHSTS The New Jersey AIDS Drug Distribution Program (ADDP) and Social Media for Agencies, Centers and Academic Institutions http://hpcpsdi.rutgers.edu/training/main.php

HIV/AIDS Training & Information Resources

AIDS Education and Training Center (AETC) Program

- National Coordinating Resource Center: www.aidsetc.org
- Northeast/Caribbean AETC: www.necaaetc.org
- National Clinician Consultation Center: http://www.nccc.ucsf.edu/
  HIV Warmline: (800) 933-3413
  Post-Exposure Prophylaxis Hotline/PEPline: (888) 448-4911
  Perinatal HIV Hotline: (888) 448-8765
  Pre-Exposure Prophylaxis Hotline (PrEPline): 888-HIV-PREP
  Substance Use Warmline: (855) 300-3595
  Hepatitis C Warmline: 844-437-4636

HIVinfo: a service of the US Department of Health and Human Services, offers access to the latest, federally approved HIV/AIDS medical practice guidelines, HIV treatment and prevention clinical trials, and other research information. www.hivinfo.nih.gov

US National Institutes of Health: a registry and results database of publicly and privately supported clinical studies conducted around the world. http://clinicaltrials.gov

US Centers for Disease Control and Prevention (CDC): http://www.cdc.gov/hiv/default.html

Health Resources and Services Administration (HRSA): http://www.hrsa.gov

FDA MedWatch: (800) FDA-1088; Subscribe to **e-bulletin:** www.fda.gov/medwatch/elist.htm

Center for Quality Improvement and Innovation: no-cost, technical assistance for Ryan White funded grantees to improve the quality of HIV care nationwide. www.cqii.org

TargetHIV Center: technical assistance and training resources for the Ryan White HIV/AIDS Program community. https://targethiv.org

New Jersey HIVLinks Mailing List.

If you would like to be added to our mailing list, please contact Michelle Thompson at ccthomps@sn.rutgers.edu. To be deleted from the mailing list, please contact *FXBCenter@sn.rutgers.edu*. Current and past issues of NJ HIVLinks can be found at FXBCenter.org.