Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

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Antiretroviral Therapy to Prevent Sexual Transmission of HIV (Treatment as Prevention) (Last updated December 18, 2019; last reviewed December 18, 2019)

Panel's Recommendations

- All persons with HIV should be informed that maintaining a plasma HIV RNA (viral load) of <200 copies/mL, including any measurable value below this threshold value, with antiretroviral therapy (ART) prevents sexual transmission of HIV to their partners. Patients may recognize this concept as Undetectable = Untransmittable or U=U **(AII)**.
- Persons with HIV who are starting ART should use another form of prevention with sexual partners (e.g., condoms, pre-exposure prophylaxis [PrEP] for the HIV-negative sexual partner, sexual abstinence) for at least the first 6 months of treatment and until a viral load of <200 copies/mL has been documented **(AII)**. Many experts would recommend confirming sustained suppression before assuming that there is no further risk of sexual HIV transmission **(AIII)**.
- When the viral load is ≥200 copies/mL, additional methods are needed to prevent transmission of HIV to sexual partners until resuppression to <200 copies/mL has been confirmed **(AIII)**.
- Persons with HIV who intend to rely upon ART for prevention need to maintain high levels of ART adherence **(AIII)**. They should be informed that transmission is possible during periods of poor adherence or treatment interruption **(AIII)**.
- At each visit for HIV care, clinicians should assess adherence to ART and counsel patients regarding the importance of ART to their own health as well as its role in preventing sexual HIV transmission **(AIII)**.
- Providers should inform patients that maintaining a viral load of <200 copies/mL does not prevent acquisition or transmission of other sexually transmitted infections (STIs) **(AII)**.
- Providers should also routinely screen all sexually active persons with HIV for STIs, both for their own health and to prevent transmission of STIs to others **(AIII)**.

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

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

Antiretroviral therapy (ART) not only reduces morbidity and mortality for persons with HIV but has now been definitively shown to prevent sexual transmission of the virus when the plasma HIV RNA (viral load) is consistently suppressed to <200 copies/mL, which includes any measurable viral load that is lower than this threshold value. Providers who manage patients with HIV need to be aware of the data supporting treatment as prevention (TasP, which persons with HIV may recognize as Undetectable = Untransmittable or U=U), its implications, and how to operationalize this prevention strategy in clinical practice. For persons with HIV who intend to rely on TasP for HIV prevention, providers should make an individualized assessment of the person's risk tolerance, personal health, history of maintaining viral suppression on treatment, and access to health care services and ART, as well as other factors that may affect their ability to maintain a high level of adherence to ART.

Evidence that Viral Load Suppression Prevents Sexual HIV Transmission

Suppressing the HIV viral load to <200 copies/mL with ART prevents sexual transmission of HIV. Observational data collected in the early 1990s from heterosexual couples demonstrated that sexual transmission from untreated persons with HIV was rare at viral loads of <1,000 copies/mL to 1,500 copies/mL and that the risk of transmission increased in dose-response fashion with increasing viral load.[1,2] Additional reports[3-7] and a meta-analysis[8] supported the observation that sexual HIV transmission risk in heterosexual persons was correlated with plasma viral load, and transmission was infrequent below the lowest limits of quantification for the viral load assays used at the time.

The first prospective clinical trial designed specifically to address this question was HPTN 052,

which randomized people with HIV who were in mixed HIV status couples (previously referred to as serodiscordant couples) to initiate ART early or to delay initiation. Initial results from this study were reported in 2011,[9] with final results reported in 2016.[10] The 2016 analysis reported that no phylogenetically linked sexual transmissions of HIV occurred among 1,763 couples who were followed a median of 5.5 years while the person with HIV was on ART and had a viral load <400 copies/mL for at least 6 months. Notably, four phylogenetically linked infections occurred within the 90 days after the partner with HIV had started ART and was presumably not yet virally suppressed, and four others occurred after the partner with HIV had experienced virologic failure. There were also a number of transmission events that were not phylogenetically linked, indicating acquisition from someone other than the enrolled study index partner.[11] HPTN 052 was conducted almost exclusively among heterosexual couples that lived in Africa and Asia and did not track the number or type of sexual exposures. In addition, ART was used as an adjunct to a comprehensive prevention package that provided condoms and encouraged condom use, as well as frequent testing for HIV and other sexually transmitted infections (STIs).

Three prospective observational studies—PARTNER 1,[12] PARTNER 2,[13] and Opposites Attract[14]—provided data from more diverse populations of mixed HIV status couples in which condomless sex was common. Clinical follow-up in these studies closely mimicked that of routine clinical care. Conducted in 14 European countries (PARTNER 1 and PARTNER 2) as well as Australia, Thailand, and Brazil (Opposites Attract), the investigators followed 548 heterosexual and 1,481 male-male mixed HIV status couples that engaged in 144,631 episodes of condomless vaginal or anal sex while the partner with HIV had a suppressed viral load on ART, defined as <200 copies/mL. In these studies, no phylogenetically linked transmissions were observed; however, as in HPTN 052, there were numerous non-phylogenetically linked transmissions attributed to partners outside the enrolled study couple relationship.

Integrating the Principles of Treatment as Prevention into Clinical Care

The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends that providers inform all persons with HIV that maintaining an HIV viral load <200 copies/mL with ART prevents sexual transmission of HIV **(AII)**. This information may help motivate patients and help relieve stigma that can be a barrier to getting tested and entering into care, starting and remaining adherent to ART, and ultimately achieving and maintaining a viral load <200 copies/mL.[15] Although PARTNER 1, PARTNER 2, and Opposites Attract were designed to follow patients in the study as they would be typically be followed in clinical care for HIV, the participants reported high levels of ART adherence at study entry and many reported at least 1 year of condomless sex with an established sexual partner without transmission. As the principles of TasP are integrated into the clinical management of people with HIV who are on ART, implementation research will be critical to maximize the effectiveness of TasP in practice.

Frequency of Viral Load Assessment

The Panel has issued recommendations for viral load monitoring to manage the health of persons with HIV (see Plasma HIV-1 RNA (Viral Load) and CD4 Count Monitoring). However, current data are insufficient to determine whether these recommendations represent the optimal monitoring schedule for the purpose of preventing sexual transmission of HIV. In the PARTNER studies and Opposites Attract, viral loads were generally assessed every 3 to 6 months during study follow-up, usually during the course of regular HIV care. Pending further data, the Panel recommends no change to the existing recommendations for monitoring viral load (see Plasma HIV-1 RNA (Viral Load) and CD4 Count Monitoring) **(BII)**.

Time to Adequate Suppression after Starting Antiretroviral Therapy

A subgroup analysis from the Partners PrEP Study provided data regarding the risk of HIV transmission during and after the first 6 months on ART for the partner with HIV.[16] This analysis included 1,573 heterosexual East African couples in which the partners without HIV were randomized to the placebo arm

of the Partners PrEP Study and were tested monthly for HIV while the viral load of the partner with HIV was assessed every 6 months. Three phylogenetically linked infections were diagnosed in the 6 months prior to the first follow-up visit for the partners with HIV. The observed incidence rate of 1.79 per 100 person-years during this initial 6-month period after the partner with HIV started ART was slightly less than the 2.08 per person-years incidence rate observed in couples in which the person with HIV was not receiving ART. Viral suppression in this study was defined as <40 copies/mL, and the three infections were diagnosed at 0 days, 56 days, and 149 days after the partner with HIV started ART. After the partners with HIV had been taking ART for ≥6 months, no further transmissions were observed.

At this time, the Panel recommends that persons with HIV who are starting ART use another form of prevention with sexual partners for at least the first 6 months of treatment and until a viral load of <200 copies/mL has been documented **(AII)**. Many experts would recommend confirming sustained suppression before assuming that there is no further risk of sexual transmission of HIV **(AIII)**.

Adherence to Antiretroviral Therapy

Adherence to ART is paramount for persons who intend to prevent HIV transmission by achieving and maintaining a suppressed viral load. Viral rebound typically occurs within days to weeks after ART cessation and has been observed as early as 3 to 6 days after stopping treatment.[17-29] The minimum level of adherence that is required to prevent sexual transmission has not been determined and may vary depending on the ART regimen. In the key studies that defined the efficacy of TasP, adherence levels prior to study entry and during follow-up were very high. In clinical practice, most people who start ART will achieve a viral load <200 copies/mL within 6 months, but once this viral load is achieved, maintaining viral suppression can be a challenge, especially for those who have difficulty accessing ART and other HIV care. The Centers for Disease Control and Prevention (CDC) estimates that during 2015, 60% of persons with HIV and 78% of persons engaged in clinical care had viral loads <200 copies/mL at their most recent assessment.[30] Observational cohort data have demonstrated that within the first year of starting ART, up to 10% of persons with HIV can experience loss of viral suppression; however, the likelihood of maintaining a suppressed viral load generally improves over time. After a few years, 5% or fewer of persons on ART may experience loss of viral suppression.[31,32]

The Panel recommends that persons with HIV who intend to rely upon TasP be made aware of the need for high levels of ART adherence **(AIII)**. The Panel further recommends that adherence be assessed and counseling be provided at each visit for HIV care to reinforce the importance of adherence for the individual's health as well as its role in preventing HIV transmission **(AIII)**. Patients should be informed that transmission is possible during periods of poor adherence or treatment interruption **(AIII)**.

Adherence can be especially challenging for certain groups of patients, such as adolescents and young adults, homeless persons, persons with active substance use disorder, and persons who are involved with the criminal justice system. Recommendations to help manage and maximize ART adherence can be found in Adherence to the Continuum of Care. Persons for whom there is concern about adherence also merit counseling on how to properly use other prevention methods, especially barrier methods that prevent STIs.

Managing Transient Viremia, or "Blips"

Highly adherent patients may experience intermittent or transient viremia, commonly termed "viral blips." Blips are defined in the context of effective treatment as a single, measurable HIV RNA level, typically <200 copies/mL, that is followed by a return to a viral load below the limit of detection or quantification. With contemporary ART regimens, about 10% of persons per year who are adherent to ART may experience a blip.[33-35] Most blips likely represent normal biological fluctuation (i.e., variation around a mean undetectable viral load) or laboratory artifact and not inadequate adherence.[36-38] Persistent viremia ≥200 copies/mL has been associated with increasing risk of virologic failure[33,39] that, in the context of TasP, can lead to increased risk of sexual transmission.[10] The PARTNER studies and Opposites Attract excluded observation time when the viral load of

the participant with HIV was ≥200 copies/mL. The frequency of blips <200 copies/mL was not reported in Opposites Attract; however, in PARTNER 1 and PARTNER 2, transient elevations in viral loads above the limit of detection (50 copies/mL in these studies) but <200 copies/ml were observed for 6% and 4% of the total follow-up time, respectively, during which time no phylogenetically linked infections were observed.

One of the clinical challenges with blips is that they can only be defined retrospectively once the viral load has returned to a suppressed value. The Panel recommends that when the viral load is ≥200 copies/mL, persons with HIV and their sexual partners should use another form of prevention (e.g., condoms, pre-exposure prophylaxis for sexual partners without HIV, sexual abstinence) to protect against HIV transmission until a viral load <200 copies/mL is achieved **(AII)**. This recommendation applies both to persons who are starting ART (as noted earlier) and to those who have been taking ART and have achieved viral suppression but develop viral loads ≥200 copies/mL.

In cases where a patient achieves resuppression to <200 copies/mL after a detectable viral load ≥200 copies/mL, or when a patient with a viral load <200 copies/mL switches regimens (e.g., for regimen simplification or to avoid certain side effects), providers should check the viral load per recommendations in Plasma HIV-1 RNA (Viral Load) and CD4 Count Monitoring and Optimizing Antiretroviral Therapy in the Setting of Virologic Suppression **(AIII)**. There are presently no data to guide how long, if at all, a person might need to continue to use another form of prevention in these two circumstances. Individualized assessment is recommended based on the length and quality of adherence and time with viral load <200 copies/mL preceding the viral load ≥200 copies/mL.

Effect of Sexually Transmitted Infections on Treatment as Prevention

The presence of STIs in a person with HIV does not appear to meaningfully alter the risk of sexual transmission when the person's viral load is <200 copies/mL. The PARTNER studies and the Opposites Attract study regularly assessed participants for STIs, which were diagnosed in 6% of heterosexual participants and 13% to 27% of men who have sex with men. Although the authors of the studies noted that their findings could not rule out the possibility that STIs in participants with viral loads <200 copies/mL might affect the risk of HIV transmission, when viewed collectively, these data suggest that any effect is very small, since STIs were common and no linked infections were observed. The Panel recommends that patients using TasP be informed that maintaining a viral load of <200 copies/mL does not prevent acquisition or transmission of other STIs, and that it is not substitute for condoms or behavioral modifications **(AII)**. Providers should also routinely screen all sexually active persons with HIV for STIs, both for their own health and to prevent transmission of STIs to others **(AIII)**. Refer to CDC's Sexually Transmitted Diseases Treatment Guidelines for details.

Treatment as Prevention Applies Only to Sexual Transmission of HIV

Available clinical data only support the use of TasP to prevent sexual HIV transmission in patients with viral loads <200 copies/mL. The effectiveness of this strategy to prevent transmission from blood exposure (e.g., through nonsterile drug injection) has not been determined. In addition, while suppression of maternal viral load substantially reduces the risk of perinatal transmission and transmission through breastfeeding, it does not eliminate these risks, and transmission has occurred via breastfeeding despite continuous viral suppression (refer to the Perinatal Guidelines for details).

References

1. Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N Engl J Med*. 2000;342(13):921-929. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10738050.

2. Tovanabutra S, Robison V, Wongtrakul J, et al. Male viral load and heterosexual transmission of HIV-1 subtype E in

northern Thailand. *J Acquir Immune Defic Syndr*. 2002;29(3):275-283. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11873077.

3. Apondi R, Bunnell R, Ekwaru JP, et al. Sexual behavior and HIV transmission risk of Ugandan adults taking antiretroviral therapy: 3 year follow-up. *AIDS*. 2011;25(10):1317-1327. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21522005.

4. Castilla J, Del Romero J, Hernando V, Marincovich B, Garcia S, Rodriguez C. Effectiveness of highly active antiretroviral therapy in reducing heterosexual transmission of HIV. *J Acquir Immune Defic Syndr*. 2005;40(1):96-101. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16123689.

5. Del Romero J, Castilla J, Hernando V, Rodriguez C, Garcia S. Combined antiretroviral treatment and heterosexual transmission of HIV-1: cross sectional and prospective cohort study. *BMJ*. 2010;340:c2205. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20472675.

6. Melo MG, Santos BR, De Cassia Lira R, et al. Sexual transmission of HIV-1 among serodiscordant couples in Porto Alegre, southern Brazil. *Sex Transm Dis*. 2008;35(11):912-915. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18607309.

7. Reynolds SJ, Makumbi F, Nakigozi G, et al. HIV-1 transmission among HIV-1 discordant couples before and after the introduction of antiretroviral therapy. *AIDS*. 2011;25(4):473-477. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21160416.

8. Attia S, Egger M, Muller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS*. 2009;23(11):1397-1404. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19381076.

9. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011;365(6):493-505. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21767103.

10. Cohen MS, Chen YQ, McCauley M, et al. Antiretroviral therapy for the prevention of HIV-1 transmission. *N Engl J Med*. 2016;375(9):830-839. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27424812.

11. Eshleman SH, Hudelson SE, Redd AD, et al. Treatment as prevention: characterization of partner infections in the HIV prevention trials network 052 trial. *J Acquir Immune Defic Syndr*. 2017;74(1):112-116. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27532476.

12. Rodger AJ, Cambiano V, Bruun T, et al. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *JAMA*. 2016;316(2):171-181. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27404185.

13. Rodger AJ, Cambiano V, Bruun T, et al. Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. *Lancet*. 2019;393(10189):2428-2438. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31056293.

14. Bavinton BR, Pinto AN, Phanuphak N, et al. Viral suppression and HIV transmission in serodiscordant male couples: an international, prospective, observational, cohort study. *Lancet HIV*. 2018;5(8):e438-e447. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30025681.

15. Calabrese SK, Mayer KH. Providers should discuss U=U with all patients living with HIV. *Lancet HIV*. 2019;6(4):e211-e213. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30772420.

16. Mujugira A, Celum C, Coombs RW, et al. HIV transmission risk persists during the first 6 months of antiretroviral therapy. *J Acquir Immune Defic Syndr*. 2016;72(5):579-584. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27070123.

17. Harrigan PR, Whaley M, Montaner JS. Rate of HIV-1 RNA rebound upon stopping antiretroviral therapy. *AIDS*. 1999;13(8):F59-62. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10371167.

18. Davey RT, Jr., Bhat N, Yoder C, et al. HIV-1 and T cell dynamics after interruption of highly active antiretroviral therapy (HAART) in patients with a history of sustained viral suppression. *Proc Natl Acad Sci USA*. 1999;96(26):15109-15114. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10611346.

19. Garcia F, Plana M, Ortiz GM, et al. The virological and immunological consequences of structured treatment interruptions in chronic HIV-1 infection. *AIDS*. 2001;15(9):F29-40. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11416735.

20. Skiest DJ, Morrow P, Allen B, et al. It is safe to stop antiretroviral therapy in patients with preantiretroviral CD4 cell counts >250 cells/microL. *J Acquir Immune Defic Syndr*. 2004;37(3):1351-1357. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15483464.

21. Pogany K, van Valkengoed IG, Prins JM, et al. Effects of active treatment discontinuation in patients with a CD4+ T-cell nadir greater than 350 cells/mm3: 48-week Treatment Interruption in Early Starters Netherlands Study (TRIESTAN). *J Acquir Immune Defic Syndr*. 2007;44(4):395-400. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17195761.

22. Steingrover R, Pogany K, Fernandez Garcia E, et al. HIV-1 viral rebound dynamics after a single treatment interruption depends on time of initiation of highly active antiretroviral therapy. *AIDS*. 2008;22(13):1583-1588. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18670217.

23. Hamlyn E, Ewings FM, Porter K, et al. Plasma HIV viral rebound following protocol-indicated cessation of ART commenced in primary and chronic HIV infection. *PLoS One*. 2012;7(8):e43754. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22952756.

24. Rothenberger MK, Keele BF, Wietgrefe SW, et al. Large number of rebounding/founder HIV variants emerge from multifocal infection in lymphatic tissues after treatment interruption. *Proc Natl Acad Sci USA*. 2015;112(10):E1126-1134. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25713386.

25. Hurst J, Hoffmann M, Pace M, et al. Immunological biomarkers predict HIV-1 viral rebound after treatment interruption. *Nat Commun*. 2015;6:8495. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26449164.

26. Li JZ, Etemad B, Ahmed H, et al. The size of the expressed HIV reservoir predicts timing of viral rebound after treatment interruption. *AIDS*. 2016;30(3):343-353. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26588174.

27. Calin R, Hamimi C, Lambert-Niclot S, et al. Treatment interruption in chronically HIV-infected patients with an ultralow HIV reservoir. *AIDS*. 2016;30(5):761-769. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26730568.

28. Colby DJ, Trautmann L, Pinyakorn S, et al. Rapid HIV RNA rebound after antiretroviral treatment interruption in persons durably suppressed in Fiebig I acute HIV infection. *Nat Med*. 2018;24(7):923-926. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29892063.

29. Namazi G, Fajnzylber JM, Aga E, et al. The control of HIV after antiretroviral medication pause (CHAMP) study: posttreatment controllers identified from 14 clinical studies. *J Infect Dis*. 2018;218(12):1954-1963. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30085241.

30. Centers for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2016. HIV Surveillance Supplemental Report. 2018;23(4). Available at: https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-supplemental-report-vol-23-4.pdf.

31. O'Connor J, Smith C, Lampe FC, et al. Durability of viral suppression with first-line antiretroviral therapy in patients with HIV in the UK: an observational cohort study. *Lancet HIV*. 2017;4(7):e295-e302. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28479492.

32. Marks G, Patel U, Stirratt MJ, et al. Single viral load measurements overestimate stable viral suppression among HIV patients in care: clinical and public health implications. *J Acquir Immune Defic Syndr*. 2016;73(2):205-212. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27105049.

33. Grennan JT, Loutfy MR, Su D, et al. Magnitude of virologic blips is associated with a higher risk for virologic rebound in HIV-infected individuals: a recurrent events analysis. *J Infect Dis*. 2012;205(8):1230-1238. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22438396.

34. Sorstedt E, Nilsson S, Blaxhult A, et al. Viral blips during suppressive antiretroviral treatment are associated with high baseline HIV-1 RNA levels. *BMC Infect Dis*. 2016;16:305. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27329293.

35. Warren AM, Cheng AC, Watson K, Lewin SR, Hoy JF. Outcomes following detection of low level plasma HIV RNA in

HIV-infected patients previously virologically suppressed on antiretroviral therapy: a retrospective observational study. *Sex Health*. 2017;14(3):238-243. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28445685.

36. Nettles RE, Kieffer TL. Update on HIV-1 viral load blips. *Curr Opin HIV AIDS*. 2006;1(2):157-161. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19372801.

37. Lee PK, Kieffer TL, Siliciano RF, Nettles RE. HIV-1 viral load blips are of limited clinical significance. *J Antimicrob Chemother*. 2006;57(5):803-805. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16533823.

38. Miller LG, Golin CE, Liu H, et al. No evidence of an association between transient HIV viremia ("Blips") and lower adherence to the antiretroviral medication regimen. *J Infect Dis*. 2004;189(8):1487-1496. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15073687.

39. Young J, Rickenbach M, Calmy A, et al. Transient detectable viremia and the risk of viral rebound in patients from the Swiss HIV Cohort Study. *BMC Infect Dis*. 2015;15:382. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26392270.