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U=U Guidance for Implementation in Clinical Settings

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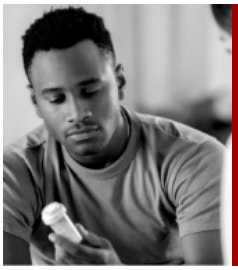

U=U Guidance for Implementation in Clinical Settings

What is U=U?

People who achieve and maintain an undetectable HIV viral load do not sexually transmit HIV.

This scientific finding, called "Undetectable = Untransmittable," or "U=U," has been promoted as a health equity initiative by the Prevention Access Campaign since 2016 and has been endorsed by the U.S. Centers for Disease Control and Prevention, the New York City Health Department, the New York State Department of Health (NYSDOH), and many other health departments and experts. U=U asserts that individuals who keep their viral load below the level of assay detection (typically HIV RNA <20 copies/mL) do not pass HIV through sex. Leading scientists recently lent their support to U=U, assessing the evidence base as "scientifically sound" [Eisinger, et al. 2019].

As emphasized in the NYSDOH U=U Policy Statement and detailed in the accompanying FAQ, the U=U concept is a "driving force to accelerate the achievement of New York State's Ending the Epidemic goals." Specifically, U=U aligns with numerous efforts to dismantle HIV-related stigma and improve the health, well-being, and self-esteem of all people living with HIV, particularly by removing fear from their sexual and romantic relationships and combating the isolation they may experience. The statement further elaborates: "Endorsing U=U opens a new and hopeful chapter in New York State's HIV epidemic, creating unprecedented opportunities for New Yorkers living with HIV and the institutions that serve them."

Evidence Base Supporting U=U

Evidence from the last 3 decades has established that adherence to HIV antiretroviral therapy (ART) suppresses viral replication, improves the health of people with HIV, and reduces the risk of sexual transmission. These data have accumulated from observational cohort studies as well as ecological studies correlating incidence and viral suppression rates in communities. (See **Glossary**, below.)

Recently, an "overwhelming body of evidence has emerged" that *durable* viral suppression (HIV RNA <200 copies/mL) can eliminate the risk of sexual HIV transmission [Eisinger, et al. 2019]. The HPTN 052 randomized clinical trial and 3 observational cohort studies, PARTNER, PARTNER 2, and Opposites Attract, evaluated the effect of viral suppression in preventing HIV transmission [Cohen, et al. 2016; Rodger, et al. 2016; Bavinton, et al. 2018; Rodger, et al. 2019]. The studies followed thousands of male and heterosexual couples in which one partner had HIV and the other did not (i.e., serodiscordant couples) and documented no genetically linked HIV transmissions when the partner with HIV was taking ART and was virally suppressed. In the PARTNER and Opposites Attract studies, anal sex without condoms was reported over 88,000 times among serodiscordant couples of men who have sex with men, and vaginal or anal sex without condoms was reported 36,000 times among heterosexual serodiscordant couples—all without any linked transmissions.

These studies provide robust evidence that individuals *do not* sexually transmit HIV if they are virally suppressed (HIV RNA <200 copies/mL) or have an undetectable viral load (typically HIV RNA <20 copies/mL).

Glossary

Viral load suppression: When a person with HIV has a measured quantitative HIV RNA viral load <200 copies/mL of blood.

Undetectable viral load: When an HIV viral load is below the level of detection on a specific assay, typically HIV RNA <20 copies/mL but as high as 50 copies/mL.

Durably undetectable: When a person has maintained an undetectable viral load for at least 6 months—indicating that their HIV is at a stable, undetectable level and that they will not pass HIV through sex if they continue to adhere to treatment.

Untransmittable: The finding—established by various clinical trials and observational studies—that people who maintain an undetectable viral load have so little HIV in their blood and other secretions that they have "effectively no risk" of passing HIV to others through sex.

Application to Clinical Practice

The concept of U=U is grounded in the following principles [Eisinger, et al. 2019]:

Adherence: For HIV treatment to provide maximum benefit, it is essential that ART is taken as prescribed; the goal is to achieve an undetectable viral load. Achieving an undetectable viral load can require ART for up to 6 months. Once an undetectable viral load is achieved, continued adherence to ART is required to ensure that the virus remains suppressed so it is not transmitted through sex.

Because *maintaining* an undetectable viral load is foundational to the U=U strategy and may be functionally challenging for many individuals with HIV, it is recommended that consistent adherence to ART is demonstrated before relying on U=U as a sole, effective HIV prevention strategy. Consistent adherence may be confirmed with:

- Two consecutive undetectable viral load test results separated by at least several weeks; *or*
- More conservatively, a full 6-month period during which all viral load test results are durably undetectable.

If an individual stops or is inconsistent in taking ART, that person may no longer have an undetectable viral load or may be at high risk of recrudescent viremia. In this scenario, transmission is possible; a patient must be undetectable in order for U=U to be an effective HIV prevention strategy.

Monitoring: Per NYS guidelines, viral load testing should be performed every 4 months after an individual achieves an undetectable viral load. If viral suppression and stable immunologic status are maintained for >1 year, then viral load testing can be extended to every 6 months in select patients thereafter.

Best Practices

- **Adherence:** U=U assumes that an individual is adherent to HIV treatment and is consistently taking antiretroviral medications as prescribed, which is the only way to maintain an undetectable viral load. Suspension of ART adherence or intermittent adherence may lead to a viral rebound, negating the effectiveness of U=U as a stand-alone HIV prevention strategy. Care providers should carefully address all likely barriers to adherence, which may include poverty, housing instability, and other key social factors, and offer all available adherence supports, referrals for assistance, and other interventions, along with HIV prevention strategies that do not rely on viral suppression. (See NYSDOH *Retention and Adherence Programs in Medical Settings*.)
- **Viral load monitoring:** Care providers should follow existing NYS guidelines for monitoring viral load in patients on treatment.
- **Screening and treatment for sexually transmitted infections (STIs) other than HIV:** The emergence of effective alternatives to condoms to prevent HIV—including pre-exposure prophylaxis (PrEP) and HIV treatment—may reduce condom use and may require more careful monitoring of other STIs, including at extragenital sites.
  - Care providers should already be encouraging all patients to get tested for STIs; using U=U as a strategy to prevent HIV transmission provides an additional opportunity to remind patients of the importance of regular screening for other STIs. (See the NYSDOH AI STI screening guidelines.)
  - Care providers should consider offering STI screening every 3 months for all individuals with HIV who rely on U=U as a sole strategy to prevent the sexual transmission of HIV; this is the same screening frequency recommended for those taking PrEP.

Special Topics

- **Virologic "Blips" and U=U:** Patients on previously suppressive ART with newly detectable viral loads may be experiencing low-level transient viremia ("blips") and not virologic failure. By definition, a virologic blip occurs when a patient's HIV is undetectable on a viral load test, is at a low but detectable result on a repeat viral load test (usually HIV RNA of 20 to 200 copies/mL, or reports of detected HIV RNA <30 copies/mL, but can be higher), then is again measured at an undetectable level shortly thereafter.

Virologic blips likely occurred in individuals participating in HPTN 052, PARTNER, PARTNER 2, and Opposites Attract; still, there was no transmission from people whose measured HIV viral load was consistently suppressed. This demonstrates that people with HIV whose tested viral load levels remain undetectable do not sexually transmit HIV, even if they have temporarily detectable but low levels of HIV during virologic blips while adherent to their medications.

- **HIV RNA in genital secretions and U=U:** In research studies, 8% to 16% of semen samples from men with HIV had detectable virus despite undetectable HIV RNA in blood plasma [Sheth, et al. 2009; Kantor, et al. 2014]. A similar dynamic holds for residual virus in vaginal secretions [Olesen, et al. 2016]. There is no evidence that detectable virus in genital secretions while plasma viral load is undetectable is associated with transmission. Detectable virus in genital secretions likely occurred in HPTN 052, PARTNER, PARTNER 2, and Opposites Attract; however, there was no transmission from people whose measured HIV load was consistently suppressed.
- **U=U and HIV transmission through breastfeeding:** Studies demonstrate that ART *greatly reduces* the risk of HIV transmission from individuals who breastfeed their babies [Gartland, et al. 2013]. However, research *has not* established that people whose HIV is undetectable do not transmit HIV during breastfeeding.
- **U=U and HIV transmission through sharing of injection drug equipment:** Studies demonstrate that ART *greatly reduces* the risk of HIV transmission through sharing of injection drug use equipment [Wood, et al. 2009]. However, research *has not* established that people with an undetectable HIV viral load do not transmit HIV through needle sharing.
- **U=U and needlestick injuries:** Research has not established that people with an undetectable HIV viral load do not transmit HIV to people who are stuck by a needle containing their blood. HIV post-exposure prophylaxis (PEP) may be indicated.

Counseling Individuals With HIV About U=U

Care providers should inform all patients of the following: "People who keep their HIV viral load at an undetectable level by consistently taking HIV medications will not pass HIV to others through sex."

Sharing this message with *all* patients can help accomplish the following:

- Diminish stigma associated with having HIV.
- Reduce barriers to HIV testing and treatment.
- Increase interest in starting and staying on ART.
- Improve self-esteem by removing the fear of being contagious.
- Support healthy sexuality regardless of HIV status.
- Reduce sex partners' concerns.

Providing this message is important regardless of the patient's current sexual activity, as many people living with HIV maintain celibacy because of the fear and anticipatory guilt of potentially transmitting HIV.

Encourage patients newly diagnosed with HIV and those previously diagnosed but not taking ART to immediately start (or restart) treatment.

Explain that doing so will help them avoid damage to their body and immune system and will prevent transmission of HIV to their sex partners.

- The importance of ART should be framed primarily in terms of helping the individual with HIV maintain personal health. Prevention of transmission is a secondary, fortuitous effect of HIV self-care.
- Evidence is emerging that initiation of ART as soon as possible after diagnosis, even on the same day as diagnosis or at the first clinic visit, improves long-term outcomes, such as virologic suppression and engagement in care at 12 months [Ford, et al. 2018]. Extensive support is available to people living with HIV for adherence to treatment and engagement in care.

Provide the following information about U=U to patients (proposed script):

- *Keeping your HIV undetectable helps you live a long and healthy life.*
- *To get your HIV to an undetectable level and to keep it undetectable, take antiretroviral medicines as prescribed.*
- *It may take up to 6 months of taking HIV treatment medicines to bring your HIV down to an undetectable level.*

- *If your HIV is undetectable and you are taking your medications as prescribed, you can be sure you will not pass HIV through sex.*
- *People who keep their HIV at an undetectable level will not pass HIV to others through sex.*
- *If you stop taking HIV medicines, your HIV can rebound to a detectable level within 1 to 2 weeks and you may pass HIV to your sex partners.*
- *Keeping your HIV at an undetectable level helps you safely conceive a child with your partner.*

Counsel patients to share information about the research on U=U as follows (proposed language in italics):

- *In 4 recent research studies that involved thousands of couples, no one who was on HIV treatment and whose HIV was undetectable passed HIV to their HIV-negative sex partner.*

Advise patients that they can share the following personal information with current or potential sex partners:

- When they last had a viral load test and if their viral load was undetectable.
- **Note:** Individuals should tell partners that their HIV is undetectable only if they have taken HIV medicines consistently since their last test with an undetectable viral load.

Care providers should encourage all sexually active patients and their partners, particularly those who do not use condoms consistently, to get tested regularly for bacterial STIs.

- Regular testing and prompt treatment can reduce transmission of bacterial STIs among individuals and throughout the population.
- It is also important to inform patients that common STIs may be asymptomatic.

Counseling Couples About U=U

Care providers should counsel *all* patients on strategies to maintain a healthy, fulfilling, and worry-free sex life, including the use of HIV treatment, condoms, PrEP, and emergency PEP.

Counseling for couples in which one partner has HIV can include the following:

- **HIV treatment:** Couples may decide that ART and an undetectable viral load for the partner with HIV provides sufficient protection against HIV transmission.
- **PrEP:** PrEP is a safe and effective daily pill that prevents HIV infection. The partner without HIV may decide to take PrEP if they:
  - Are unsure that their partner's HIV viral load is undetectable, especially if their partner has only recently started ART.
  - Have more than 1 sex partner.
  - Feel more secure with the added perception of protection provided by PrEP. (See the NYSDOH AI guideline *PrEP to Prevent HIV Acquisition* for more information.)
- **PEP:** After a possible HIV exposure (e.g., if a sex partner with HIV has not consistently taken ART or is not virally suppressed), the immediate initiation of emergency PEP can prevent HIV infection. (See the NYSDOH AI guideline *PEP for Non-Occupational Exposure to HIV* guideline for more information.)
- **Condom use:** Condoms protect against other STIs, such as gonorrhea, chlamydia, and syphilis, and help prevent pregnancy.

Counsel patients to find a prevention strategy that works for them.

- If an individual who does not have HIV is unsure if their partner has an undetectable level of virus or is anxious about acquiring HIV, care providers should encourage that person to choose a prevention strategy that works for them, whether that is use of PrEP, emergency PEP, condoms, or a combination of these strategies.
- Care providers should emphasize that no one should ever be compelled to have sex without condoms.

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