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Australasian Society for HIV, Viral Hepatitis
and Sexual Health Medicine

A guide for clinicians to discuss

U = U

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Overview

ASHM has developed this guide to inform clinicians and other healthcare service providers of the latest scientific developments in how antiretroviral treatment (ART) for people living with HIV prevents onward sexual transmission of HIV to their partners. This guide provides a summary of the evidence, explores important implications, and provides suggestions for legal and psychosocial referrals.

With the release over recent years of findings from three key studies looking at how effectively ART prevents sexual transmission of HIV, it is now clear that for people who take ART daily as prescribed and achieve and maintain an undetectable viral load there is effectively no risk¹ of sexually transmitting the virus to an HIV-negative partner.

This is a major advance, not only for what it means about the central role played by people with HIV in ending new HIV infections, but also because of the major, consequent psychological significance for people living with HIV. An understanding of these recent findings can help reduce the fear and prejudice that underpin HIV-related stigma.

Some commentaries state that an undetectable viral load needs to be sustained over at least six months. This is an overly-conservative reading of the evidence. As long as the individual has an undetectable viral load and the clinician is confident that the patient can maintain adherence to their ART regimen, there is no minimum (six month) period over which this must occur.

Intensive professional support may be needed to help some individuals with an undetectable viral load maintain treatment adherence. This will be particularly the case for individuals with limited health literacy, language and/or cognitive abilities. Engaging support services or carers for some individuals may be of benefit. For details of such services see *Psychosocial support* in the section *Issues to consider*. Clinical monitoring of viral load is an essential element in this monitoring - see the *Viral load testing* paragraph in the section *Definitions*.

The Prevention Access Campaign's Undetectable = Untransmittable (U=U) - including the 2016 U=U consensus statement (<https://www.preventionaccess.org/consensus>) - is a public-facing campaign led by prominent community, clinical and research advocates to raise awareness of the new evidence that supports the assertion that a person on ART, who has an undetectable viral load and continues with effective treatment, has effectively no risk of sexually transmitting the virus to an HIV-negative partner.

The main purpose of the Undetectable = Untransmittable campaign is to disseminate accurate and unambiguous information to people with HIV and those at risk, and also challenge HIV-related organisations in government, civil-society and the private sector, to promote awareness and understanding of U=U. Clinicians may find that some patients have encountered this messaging prior to engaging in clinical care, and thus require professional support to understand what it means.

1. It is recognised that there are different phraseologies to describe the risk of HIV transmission in these circumstances. In epidemiology, even when a zero risk is described it is also reported with a confidence interval which includes non-zero values. At the same time, the resounding evidence from the three key studies shows no linked transmission from people with sustained undetectable viral load. Therefore, this guide uses the phraseology that there is “effectively no risk” of sexually transmitting the virus to an HIV-negative partner, a phraseology also adopted by the US CDC.

Terminology

Undetectable viral load

The amount of virus in the blood is known as 'viral load'. An undetectable viral load means that the amount of virus in the blood is below the limit of detection of the viral load test or 'assay'. An undetectable viral load means that ART has been effective in suppressing viral replication; it does not mean HIV is no longer present but that it is present in such low amounts that CD4 cells and the immune system generally experience little damage. Viral load is the most important indicator of initial and sustained response to ART and should be measured in all HIV-infected patients at entry into care, at initiation of therapy, and on a regular basis thereafter (ASHM, 2014).

Viral load testing

Viral load testing is the preferred method of monitoring HIV disease and determining the effectiveness of ART (WHO, 2017). Viral load tests are used to determine the amount of virus in the blood, usually expressed as the number of HIV copies per millilitre (ml) of blood (e.g. 2,500 copies/ml). There are a number of different types of viral load tests, with most sensitive enough to detect viral loads above 20-500 copies/ml, depending on the assay being used. Most viral load tests used in Australia and New Zealand have a lower limit of detection of HIV virus between 20-75 copies/ml (Lab Tests Online, 2017), while most low and middle-income countries use viral load assays with a limit of detection of 500 copies/ml (ICASO, 2017). Regardless, the clinical evidence suggests there is no significant difference in terms of transmission risk once someone has a viral load below the limit of detection, irrespective of the sensitivity of assay.

In patients on a stable, suppressive ART regimen, viral load testing should be repeated every 3 to 4 months, or as clinically indicated, to confirm continuous viral suppression. Clinicians may extend the interval to 6 months for adherent patients whose viral load continues to be suppressed and whose clinical and immunologic status is stable (ASHM, 2014).

Significant increases in viral load, which are rare if the individual is adherent, likely means that a change in ART regimen is required. The frequency of viral load testing may need to be individualised if clinical circumstances change. For example, testing more than 3 monthly may be indicated for individuals who have reported, or are at risk of, reduced adherence.

Viral blips

A viral blip is where after virologic suppression, there is an isolated detectable HIV RNA level that is followed by a return to virologic suppression. Blips are not usually associated with subsequent virologic failure (Lima, Harrigan & Montaner, 2009). Viral load blips are not uncommon and the only instances of linked HIV transmission have been seen in circumstances where virological suppression was not achieved after initiating ART, or at confirmed virological failure on ART. There is no evidence that viral blips pose an increased risk of HIV transmission.

Virological failure

Some individuals who initiate ART will not reach an undetectable viral load, also known as virological failure. Factors that can contribute to virological failure include drug resistance, drug toxicity, and poor treatment adherence (ASHM, 2014). To be able to establish this, viral load testing should be undertaken.

What is Undetectable = Untransmittable?

Undetectable = Untransmittable, often shortened to U=U, is the health promotion campaign to promote understanding of the updated clinical findings that demonstrate if someone is on ART and has a sustained undetectable viral load, there is effectively no risk of sexually transmitting the virus to an HIV-negative partner. According to the Prevention Access Campaign (2017), the U=U message is an unprecedented opportunity to transform the lives of millions of people living with, and affected by, HIV and to radically transform the field. It argues that message of U=U has the potential to:

- Improve the lives of people with HIV by dramatically reducing the shame and fear of sexual transmission, and opening up possibilities for conceiving children without alternative means of insemination
- Dismantle HIV stigma at community, clinical, and personal levels
- Encourage people living with HIV to start and stay on treatment, which keeps them and their partners healthy
- Strengthen advocacy efforts for universal access to treatment, care, and diagnostics to save lives and bring us closer to ending the epidemic.

More information on the scientific evidence in support of the U=U message is in the next section of this guide.

Support for U=U

There is wide-spread support for the message of U=U across the HIV sector, including from government bureaucracies, international HIV organisations, medical organisations and community advocates (Prevention Access Campaign, 2017). Leading international organisations who support the science of the U=U campaign include:

- Centers for Disease Control and Prevention (US CDC)
- British HIV Association (BHIVA)
- International AIDS Society (IAS)
- Joint United Nations Programme on HIV and AIDS (UNAIDS)
- International Council of AIDS Service Organisations (ICASO)
- NAM Aidsmap

Leading Australasian organisations who have signed the U=U Consensus Statement include:

- Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM)
- Australian Federation of AIDS Organisations (AFAO)
- Australian Research Centre in Sex, Health and Society (ARCSHS) at La Trobe University
- Body Positive, New Zealand
- National Association of People with HIV Australia (NAPWHA)

A full list of U=U Community Partners is available at www.preventionaccess.org/map.

Current science

What is the evidence?

Three major studies published in recent years provide robust support for the assertion that if someone takes ART daily, as prescribed, and achieves and maintains an undetectable viral load there is effectively no risk of sexually transmitting the virus to an HIV-negative partner. The three studies, explained here in further detail, are the HPTN-052 study, the PARTNER study and the Opposites Attract study.

HPTN-052 study (Cohen et al, 2016)

From 2005, 1763 serodiscordant couples (including heterosexual and same-sex male couples) from nine countries were enrolled. The HIV positive partner was randomised to early or delayed antiretroviral treatment (ART). The 2011 interim analysis reported that 39 HIV-negative partners had acquired HIV and that 28 of these were phylogenetically linked (HIV acquired from their partner). Of the 28, only one occurred in the early treatment group (viral load not yet undetectable). All subjects were then offered HIV treatment and underwent follow up until 2015. The final data published in September 2016 reported 78 new infections, of which 72 were phylogenetically linked to a source partner. 46 were linked to the HIV-positive partner in the study and eight occurred after the positive partner commenced antiretroviral therapy. Of these final eight, four occurred before virological suppression was achieved, while the remaining four occurred in the context of treatment failure. In summary, no participants with an undetectable viral load transmitted HIV to their sexual partner during the study.

PARTNER study (Rodger et al, 2016)

Published in July 2016, the PARTNER study observed 1166 heterosexual and same-sex male HIV serodiscordant couples from 14 European countries with more than 58,000 episodes of condomless anal/vaginal intercourse. 11 HIV-negative partners acquired HIV but there were no linked transmissions.

Opposites Attract study (Bavinton et al, in press)

The Opposites Attract study followed 358 serodiscordant male couples from Australia, Thailand and Brazil from early 2012 to December 2016. 343 couples attended at least one follow-up visit by the end of the study and participated in the study for an average time of just over 18 months. A total of 591 couple-years of follow-up were included in the analysis. There were 16,889 acts of condomless anal intercourse, in which over 12,000 were when the HIV-negative partner was not taking Pre-Exposure Prophylaxis (PrEP). Three new HIV infections occurred but there were no linked transmissions.

Summary

Between the PARTNER study and the Opposites Attract study, there have now been a combined 39,162 reported episodes of condomless anal sex in male couples when the HIV-positive partner had an undetectable viral load and the HIV-negative partner was not taking PrEP.

These studies provide robust evidence that if people take ART daily as prescribed, and achieve and maintain an undetectable viral load, there is effectively no risk of sexually transmitting the virus to an HIV-negative partner. The findings of these studies underpin the rationale for the Undetectable = Untransmittable campaign.

🔑 Implications

The implications of U=U are highly significant. For so long, being HIV positive has carried stigma, stemming largely from the person with HIV being perceived as a risk to others. This negative characterisation, which has been around since the beginning of the epidemic, has also been internalised by some people with HIV.

The message of U=U is an unprecedented opportunity to transform the lives of people with, and affected by, HIV. An understanding of U=U can go a long way to alleviating HIV transmission-related anxiety. It can empower people with HIV to be comfortable in the totality of who they are and have a greater confidence to pursue a full sex life.

Clinicians are likely the first professionals with whom a newly-diagnosed person will be able to safely speak. Amidst the understandable fear and concern they may experience, the message of U=U is crucial. This will be particularly so if it gives people with HIV the confidence to disclose their status. It can help substantially address any already existing HIV-related stigma. It can also serve as a significant additional incentive to consider starting ART.

Condoms have been and remain a crucial prevention measure for HIV and some other STIs. People with HIV and those at risk should be informed that correct and consistent condom use provides a high level of protection from HIV and a number of STIs. We acknowledge though, that condoms have not been, nor are perceived to be, fool-proof. This is due to a range of factors including the use of alcohol and other drugs and unequal power dynamics when negotiating sex, leading to condom failure (e.g incorrect usage, condom-breakage), or reduced condom effectiveness from inconsistent usage. Over time this has been estimated to result in condom effectiveness ranging from 70-90%, compared to non-use (Johnson et al, 2018; Smith et al, 2015).

It is understood that among gay and bisexual men with HIV, there has been an ongoing awareness of the fallibility of condoms. This has caused some anxiety around transmitting HIV to their partners, leading to mental distress.

Issues to consider

What about those who do not have a sustained undetectable viral load?

There are a range of factors that will affect whether an individual will have an undetectable viral load (and be able to sustain it). Some people who have access to treatment may choose not to be treated or may not be ready to start. Others who start treatment may have challenges with adherence for a variety of reasons such as stigma, mental health challenges, substance use issues, unstable housing, difficulty affording medications, drug resistance, and/or intolerable side effects (CDC, 2016).

It is very important to explain clearly to all patients that in order not to sexually transmit HIV, a person with HIV must have an undetectable viral load and remain treatment adherent. More intensive support from the clinician will likely be needed for individuals with cognitive issues, limited health literacy, and differences in language and cultural norms.

In order to assist people who may have limited health literacy, language and/or cognitive abilities, consideration should be given to whether a support person or carer should attend services with the individual. A list of HIV peer-support organisations and AIDS councils can be found at the end of this document, if the individual does not already have their own support person.

For people with HIV who do not have a suppressed viral load, there remains other highly effective options including condoms and PrEP, which can be used individually or in combination to prevent HIV transmission.

Individuals who appear unable to self-manage their medication adherence or use of other prevention options such as condoms, should be provided with intensive, ongoing clinical and peer support. If this does not lead to sustained treatment adherence nor the use of other preventive measures, and the clinician believes that the individual may be placing others at risk of HIV, it may be appropriate for the clinician to contact the local health department or in New Zealand, the local Public Health Unit. As a last resort, the clinician may wish to confer with the relevant state/territory health department contact responsible for overseeing the National Guidelines for the Management of People with HIV Who Place Others at Risk (POAR Guidelines). The POAR guidelines are available at <http://www.health.gov.au/internet/main/publishing.nsf/content/phd-hiv-guideline-at-risk>.

PrEP

Some partners of people with HIV who have a sustained undetectable viral load may express a wish to be prescribed PrEP due to anxiety about HIV transmission. This is unnecessary from a clinical point of view, with the ASHM PrEP clinical guidelines (2017) stating that, “individuals are not considered to be a high or medium risk of HIV acquisition (and thus eligible for PrEP) if the person they have had sexual contact with has an undetectable viral load”.

However, other issues may need to be explored such as anxiety around sex with their positive partner, or sexual partners outside of the relationship. In such circumstances, a clinician may decide to offer PrEP.

PEP

According to the Australian National Guidelines for Post-Exposure Prophylaxis after Non-Occupational and Occupational Exposure to HIV, “PEP is no longer routinely recommended for non-occupational exposure when an HIV-positive source has an undetectable viral load” (ASHM, 2016).

Disclosure in the context of U=U

Having an undetectable viral load for a sustained period and continuing to take ART means the individual is not putting their sexual partner at risk of HIV. However, it is important to discuss the pluses and minuses of a person with HIV disclosing their status to their partner. A partner may become upset if they learn about the individual’s status after sexual interaction, while on the other hand it could cause unnecessary interpersonal consequences even when there is effectively no risk of transmission.

There is no longer a legal requirement in any Australian state or territory, or New Zealand, to disclose HIV positive status before sex. However, there continue to be cases in both Australia and New Zealand of people with HIV being charged with exposing or transmitting HIV. So, it may be necessary for individuals to consider disclosing their status even when there is effectively no risk of transmission. For further information regarding legal advice, see ‘Legal Advice for Individuals’ below. For further information on HIV and the law, refer to the ASHM 2017 Consensus Statement available at <https://www.ashm.org.au/products/product/HIV%20Consensus>.

STIs

Condoms can help prevent HIV transmission as well as other STIs and pregnancy. Clinicians should also promote regular STI testing, as this is crucial in reducing morbidity and onward transmission. Men who have sex with men who have HIV should have a full STI screen up to four times a year (STIGMA, 2014).

Combination prevention

The choice of HIV prevention method may be different depending upon a person's sexual practices, circumstances and relationships. For instance, if someone is having sex with multiple partners or is in a non-monogamous relationship, they might consider using condoms to prevent other STIs.

Psychosocial support

Newly-diagnosed individuals may wish to speak with peers for psycho-social support. Positive organisations around the country can be found at <http://napwha.org.au/networks-members/plhiv-organisations>. There are some peer-support groups for individuals from particular communities, including Aboriginal and Torres Strait Islanders and women. Support from other HIV sector organisations, including AIDS councils, may also be of use and can be accessed at <https://www.afao.org.au/about-afao/members>.

Legal advice for individuals

In Australia, laws that affect people living with HIV vary across states and territories. If the patient has legal questions regarding their own circumstances, it is strongly recommended that you refer them for legal advice. The HIV/AIDS Legal Service is best equipped to assist and can be contacted on 02 9206 2060 or by email at halc@halc.org.au. While they are a NSW-based community legal centre, they do take enquiries from people residing interstate.

Legal obligations for clinicians

The courts are yet to examine the scenario in which an individual accused of exposing others to HIV or transmission of HIV, uses undetectable viral load as a defence against the allegation; on the grounds that they were uninfected. Where evidence is adduced that the individual's clinician advised them that they could have condomless sex with effectively no risk of transmission of HIV due to maintaining an undetectable viral load, the court would consider whether the clinician acted reasonably and would likely have regard to what is the accepted standard of care. With the development of this guide, there is now evidence-based, peer advice supporting clinicians' choice to promote the benefits of the U=U message. This will likely be considered an authoritative source of what is best practice. It is recommended that clinicians record in their clinical notes the content of any discussion about risk.

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