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SEXUAL HEALTH FOR ALL

Burnett Foundation Aotearoa

PrEP and PEP Guidelines for Aotearoa New Zealand

The 2023 New Zealand Sexual Health Society (NZSHS) *PrEP and PEP Guidelines for Aotearoa New Zealand* were produced by NZSHS in collaboration with Burnett Foundation Aotearoa, with funding from Te Whatu Ora.

These guidelines are an adaptation and update of the 2021 ASHM (formerly the Australasian Society of HIV, Viral Hepatitis and Sexual Health Medicine) PrEP Guidelines Update for New Zealand, which was initially adapted to the NZ context from the 2018 ASHM PrEP Guidelines. The PEP section is a new addition to these guidelines and is an adaptation and update of the ASHM Australian National Guidelines for post-exposure prophylaxis after non-occupational and occupational exposure to HIV (second edition). The *PrEP and PEP Guidelines for Aotearoa New Zealand* panel acknowledges the work of ASHM and the authors in the previous versions that these guidelines are adapted from.

ASHM has not been involved in the 2023 update of the NZSHS PrEP and PEP Guidelines for Aotearoa New Zealand.

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Contents

1. Introduction

Availability and uptake of human immunodeficiency virus (HIV) pre- and post-exposure prophylaxis (PrEP and PEP) among people at high risk of acquisition have the potential to significantly reduce HIV transmission in Aotearoa New Zealand (NZ) and globally.

Combination HIV prevention involves the simultaneous use of complementary behavioural, biomedical and structural prevention strategies, which address the specific but diverse needs of populations at risk of HIV infection.[1] Combination HIV prevention includes, but is not limited to, condom promotion and distribution, harm reduction, education, antiretroviral therapy for those living with HIV, interventions to reduce stigma and discrimination, PrEP, PEP and access to sexual and reproductive healthcare services, including screening and treatment of sexually transmitted infections (STIs).

When used with optimal medication adherence, PrEP is a highly effective HIV-prevention strategy for people at elevated risk of HIV infection,[2-12] and is now recommended as standard care in clinical guidelines globally.[13-16]

People not receiving PrEP who seek care within 72 hours after a sexual, injection-related or occupational HIV exposure should be evaluated for the need for PEP (see Chapter 9: HIV post-exposure prophylaxis), with the option of transitioning to PrEP thereafter for those with ongoing risk.

PrEP is an essential part of the *National HIV Action Plan for Aotearoa New Zealand 2023-2030*,[17] which has the aim of eliminating HIV transmission within NZ. The HIV Action Plan supports the UNAIDS target of 95% of people who are at risk of HIV using combination prevention.[18]

There are limited data about PrEP use in Māori in Aotearoa New Zealand. Available data are presented in this guideline; however, further research by Kaupapa Māori methodologically trained Māori researchers is urgently needed. Inequities in healthcare are not acceptable, and it is critical that inequities in PrEP and PEP provision are eliminated.

Co-formulated tenofovir disoproxil and emtricitabine (TD* and FTC) has been funded for use as PrEP by the NZ Pharmaceutical Management Agency (PHARMAC) since March 2018, with a widening of access criteria in July 2022. Access and prescribing criteria for PHARMAC-funded PEP were also widened in July 2022.[19] PHARMAC-funded PrEP and PEP can be prescribed by any relevant prescriber including (but not limited to) general practitioners, nurse practitioners, and sexual health physicians. People who are ineligible for publicly funded healthcare (e.g., temporary migrants) can purchase PrEP or PEP from a pharmacy with a private script (starting at approximately $30 per monthly supply, 2023).

These New Zealand Sexual Health Society (NZSHS) *PrEP and PEP Guidelines for Aotearoa New Zealand* are an adaptation and update of the 2021 ASHM (formerly Australasian Society of HIV, Viral Hepatitis and Sexual Health Medicine) *PrEP Guidelines Update for New Zealand*, which was initially adapted to the NZ context from the 2018 *ASHM PrEP Guidelines*. The PEP section (see Chapter 9) is a new addition to these guidelines, and is adapted from the ASHM *Australian Post-*

Exposure Prophylaxis (PEP) for HIV Guidelines.[20] ASHM has not been involved in the 2023 update of the NZSHS PrEP and PEP Guidelines for Aotearoa New Zealand.

The recommendations in these guidelines are designed to:

- support the safe prescribing of PrEP and PEP for people at elevated risk of HIV infection
- assist clinicians in their evaluation and HIV risk assessment of patients who are seeking PrEP or PEP
- assist clinicians in educating their patients about the role that PrEP and PEP can play alongside other prevention tools such as condoms
- assist clinicians in initiating their patients on PrEP or PEP by providing information on dosing schedules
- assist clinicians in the monitoring of patients on PrEP or PEP, including testing requirements and management of side-effects and toxicity
- assist clinicians to be aware of more complex situations such as the use of PrEP or PEP in pregnancy and in chronic hepatitis B infection
- assist clinicians in transitioning patients from PEP to PrEP, where elevated risk of HIV infection is likely to be ongoing
- assist clinicians in understanding how to safely cease PrEP.

These guidelines are intended for use by:

- clinicians who provide care to people at elevated risk of acquiring HIV infection
- peer workers
- counsellors and people performing HIV testing, including point-of-care testing
- health programme policymakers
- health consumers and others with an interest in HIV PrEP.

People not receiving PrEP who seek care within 72 hours after a sexual, injection-related or occupational HIV exposure should be evaluated for the need for PEP (see Chapter 9: HIV post-exposure prophylaxis).

PrEP should be recommended by clinicians as an important HIV-prevention strategy for people at elevated risk for HIV (see Chapter 4: Suitability for PrEP).

PrEP and PEP should be provided as part of a wider suite of sexual health and STI prevention strategies that include continued promotion of condoms to prevent HIV and other STIs, timely and more frequent HIV testing, immediate access to HIV treatment on diagnosis and comprehensive STI screening.

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2. PrEP safety and efficacy

For a full review of PrEP safety and efficacy, please see the *Pre-exposure prophylaxis for the prevention of HIV Infection in the United States – 2017 update* starting from page 16: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

For a review of efficacy of PrEP 2-1-1, please see the World Health Organization's 2019 update, *What's the 2+1+1? Event-driven oral pre-exposure prophylaxis to prevent HIV for men who have sex with men: Update to WHO's recommendation on oral PrEP*, starting from page 6:

https://apps.who.int/iris/bitstream/handle/10665/325955/WHO-CDS-HIV-19.8-eng.pdf?ua=1

3. Indications for PrEP in Aotearoa New Zealand

HIV epidemiology in Aotearoa New Zealand

In 2021, there were 112 people (93 men and 19 women) notified with HIV in Aotearoa New Zealand, of whom 39 had been previously diagnosed overseas.[1]

Aotearoa New Zealand has a concentrated HIV epidemic; in 2021, 67% of those newly diagnosed with HIV with a known mode of transmission were men who have sex with men (MSM), 28% acquired HIV heterosexually, and 3% acquired HIV through unsafe injecting drug use (IDU) practice.[1] Overall in NZ, MSM are estimated to be 348 times more likely to be living with diagnosed HIV than heterosexual men and women.[2] This trend has continued since 1996 when enhanced surveillance began.[3] A 2011 study of undiagnosed HIV in a community sample of MSM in Auckland found an undiagnosed HIV prevalence of 1.3% overall, or 1 in 5 (21%) of those living with HIV.[4] Preliminary data from a 2022 study suggests the proportion undiagnosed is now likely to be lower.[5]

There are limited local data on transgender and non-binary people and HIV in Aotearoa New Zealand;[1] however, incidence appears to be low in contrast to many other areas of the world. The most vulnerable parts of the transgender and non-binary community in NZ are likely to be people whose sexual networks include MSM.

Globally, sex workers are disproportionately affected by HIV; however, rates in NZ are very low. A study of HIV prevalence in sexual health clinics over a 12-month period in 2005-2006 found no HIV cases, diagnosed or undiagnosed, among current sex workers.[6] Among 358 sex workers attending an Auckland Sexual Health Service outreach clinic between 2018-2020, only one person (on treatment and undetectable) was living with HIV.[7]

Since 2007, there have been no children known to be born with perinatally acquired HIV in NZ.[1]

Aotearoa New Zealand recorded the highest number of new HIV diagnoses ever in 2016. Since then, HIV notifications have decreased significantly, largely driven by a sharp decline in the number of MSM who acquired HIV locally. This may be due to the combination prevention measures of condom use, access to PrEP, and early testing and treatment, as well as the impacts of the COVID-19 pandemic. The number of NZ-acquired HIV diagnoses through heterosexual contact remains low.[1] HIV transmission via IDU is rare in NZ.[8]

Approximately one third (36%) of new HIV diagnoses among MSM between 2011 and 2020 were late presentations (CD4 count < 350 cells/μL),[9] living a median 4 years with unrecognised infection.[10] This proportion has improved since the period 2005-2010 (when it was 41%)[10] and is consistent with proportions recorded in Europe, UK and Australia.[9] Late diagnosis is more common among people with heterosexually acquired HIV, in whom over half (55%) of cases between 2011 and 2020 had a CD4 count below 350 cells/μL at the time of diagnosis.[9]

Among Māori, the majority of HIV diagnoses occur among Māori MSM (some of whom identify as Takatāpui).[1] Evidence from 2011 suggests Māori MSM have the same prevalence of HIV as other NZ MSM, although proportionately less of that is diagnosed.[4] HIV diagnosis in this group may therefore occur later, supported by surveillance data showing Māori MSM being more likely than

European MSM to present with advanced HIV disease (CD4 < 200 cells/μL).[9] While cases in European MSM have declined sharply since 2016, cases in non-European ethnicities, including Māori, have declined less steeply.[12]

HIV risk categories

Data from the Sydney-based Health in Men (HIM) study[13] have provided useful evidence of subpopulations at greatest HIV risk, on the assumption that Aotearoa New Zealand and Australia have a broadly similar HIV epidemic profile.

Table 3.1 summarises the main factors associated with an increased risk of HIV acquisition among gay and bisexually identified men in the HIM study.[13] Although the HIM study collected data from 2001 to 2007 and HIV notification trends have changed since then, the same factors are likely to remain relevant to HIV transmission and its prevention today. These factors were validated as eligibility criteria in an analysis of data from the Victorian PrEPX study[14] and continue to guide PrEP prescribing throughout Australia and NZ.

Table 3.1 Factors associated with elevated risk of HIV acquisition among men who have sex with men in the Health in Men (HIM) study, Australia, 2001–2007[13]

Risk factor	HIV incidence per 100 person years (95% CI)	
All gay and bisexual men regardless of behavioural practices	0.78	(0.59–1.02)
A regular sexual partner of an HIV-positive man with whom condoms were not consistently used in the last 6 months	5.36	(2.78–10.25)
At least one episode of receptive, unprotected anal intercourse with any casual male partner with HIV infection or a male partner of unknown HIV status during the last 6 months	2.31	(1.48–3.63)
Rectal gonorrhoea diagnosis in last 6 months	7.01	(2.26–21.74)
Rectal chlamydia diagnosis in last 6 months	3.57	(1.34–9.52)
Methamphetamine use in last 6 months	1.89	(1.25–2.84)
More than one episode of anal intercourse during the last 3 months when proper condom use was not achieved (e.g., condoms slipped off or broke)	1.30	(0.95–1.77)
A regular sexual partner of CLAI or having at least one episode of insertive CLAI where the serostatus of partner is not known or is HIV-positive	0.94	(0.35–2.52)
In uncircumcised men having at least one episode of insertive CLAI where the serostatus of partner is not known or is HIV-positive	1.73	(0.43–6.90)
In circumcised men (comparison group, low risk, PrEP not recommended)	0.65	(0.16–2.61)

Notes: The HIM study uses the terminology 'gay and bisexual men'; this guideline uses 'MSM' to focus on behaviour rather than identity. CI: confidence interval; CLAI: condomless anal intercourse; HIV: human immunodeficiency virus; PrEP: pre-exposure prophylaxis.

Of note, due to the specifics of data collection for the HIM study, not all indicators were available to support each individual eligibility criterion for PrEP. Some indicators were collected in different forms or had a different denominator or reference period. Most importantly, the HIV viral load of HIV-positive regular partners is now known to have a significant impact on HIV transmission,[15-17]

and data on the HIV viral load of the source partners were not collected in the HIM study. Early and sustained antiretroviral treatment that leads to viral suppression (sometimes referred to as undetectable or undetectable viral load) benefits the health of people living with HIV, reduces stigma and prevents the sexual transmission of HIV. People who take antiretroviral therapy for HIV daily as prescribed, and who achieve and maintain an undetectable viral load, cannot sexually transmit the virus to an HIV-negative partner. This is known as U=U (undetectable = untransmissible).[18]

Infectious syphilis was uncommon in the HIM cohort and was not associated with HIV transmission; however, its incidence has increased greatly since 2007 in Australia and NZ. Syphilis is associated with an increased risk of HIV among MSM globally,[19, 20] and is therefore included in the PrEP suitability assessment. Drug use is another important factor that influences sexual behaviour and HIV risk acquisition and that has emerged since the HIM study. Methamphetamine use has been associated with increased risk of HIV infection in high-income countries internationally.[21] In New Zealand, MSM who reported any drug use, polydrug use, or specifically cannabis, alkyl nitrites (poppers) or methamphetamine use, also reported significantly elevated rates of sexual partnering, unprotected sex with casual male partners or STI diagnoses.[22]

Combination HIV prevention

The HIV and sexual health sector in NZ has been an early adopter and advocate of PrEP, resulting in its public funding on 1 March 2018 for people at highest risk of acquiring HIV. Access criteria were widened in July 2022, with PrEP being funded for those considered to be at elevated risk of HIV exposure, where PrEP is clinically appropriate.

Box 3.1 Goals from the National HIV Action Plan for Aotearoa New Zealand 2023-2030

Goal	Objectives
• Reduced number of new locally acquired HIV infections	Increase knowledge and understanding of new infections and behaviours driving HIV transmission, and increasing uptake of combination prevention. This includes meeting the UNAIDS target of 95% of people who are at risk of HIV using combination prevention.
• Improved Māori health and wellbeing in relation to HIV by delivering on Tiriti o Waitangi obligations	Equity for Māori across outcomes for HIV.
• Decreased mortality and negative consequences of HIV on health and wellbeing	Ensuring people living with HIV are diagnosed early, have timely access to treatment and are able to access suitable support services.
• Decreased experiences of stigma and discrimination for people living with HIV	Ensure that people have a better understanding of HIV and that we have better regulatory frameworks and practices that help reduce stigma and discrimination experienced by people living with HIV. Address the intersecting types of stigma and discrimination experienced by different communities living with HIV.
• Equity in relation to all HIV goals and objectives	Focus efforts on populations that are more likely to experience HIV transmission, delayed diagnosis, poor clinical outcomes, and complex and layered stigma and discrimination

PrEP is an essential part of the *National HIV Action Plan for Aotearoa New Zealand 2023-2030*,[23] which has the aim of eliminating HIV transmission within NZ, and the vision that all people living with HIV have healthy lives free from stigma and discrimination (see Box 3.1). In order to realise these objectives, clear goals have been set. These goals have been informed by the *UNAIDS Global AIDS Strategy 2021-2026*,[24] the 2021 *UN Political Declaration on HIV and AIDS*,[25] and the *Aotearoa New Zealand Sexually Transmitted and Blood Borne Infection Strategy 2023-2030*.[26]

The HIV Action Plan supports the UNAIDS target of 95% of people who are at risk of HIV using combination prevention. Currently, uptake in Aotearoa New Zealand falls short of this target. It is estimated that at least 5847 individuals meet the criteria for PrEP.[27] However, according to community dispensing data from 2021, only 1648 individuals (one-quarter of those eligible) had their PrEP prescriptions initiated or renewed in the previous 3 months, indicating continuous PrEP use.[28] According to 2021 PHARMAC data, Māori account for 9.5% of PrEP dispensing, with 3.8% in Pacific Peoples.[28]

Data from the 'Flux' study[29] showed that among a 2018/19 cohort of Aotearoa New Zealand MSM reporting casual sex, 27.4% consistently used condoms for anal sex, 22.7% used PrEP, 6.2% reported living with HIV and relying on undetectable viral load as a method of HIV prevention and 31.8% of the study participants reported condomless anal sex and no PrEP use.[29]

PrEP in NZ is seen as part of a wider suite of sexual health and STI prevention strategies. Our most at-risk communities suffer from (1) an ongoing epidemic of syphilis (including a resurgence of congenital syphilis cases); (2) high rates of gonorrhoea; and (3) stubbornly high chlamydia rates.[30] The sexual and mental health (including drug and alcohol addiction) of our gender and sexually diverse minorities remain poor. Free access to quality blood borne virus and sexual health care remains problematic for Māori, Pasifika, regional and remote areas, recent immigrants and other culturally and linguistically diverse communities. Transgender and non-binary people face barriers accessing services such as gender-affirming surgery and, in some areas, gender-affirming hormonal therapy or mental health support.

An enduring and effective public health response to HIV and STIs in Aotearoa New Zealand will require high rates of condom use for sex among MSM and other affected communities. Care should be taken to position PrEP as a universal prevention strategy for all. Both condoms and PrEP are highly effective in preventing HIV, with condoms also providing broad protection against other STIs.

Like other biomedical interventions, PrEP risks privileging those with higher health literacy and access. Although Aotearoa New Zealand's healthcare system has funded PrEP for people at elevated risk of HIV, there are still barriers: not all regions have easily accessible free sexual healthcare; temporary migrants are often excluded from publicly funded healthcare; and many PrEP-seeking MSM report discomfort requesting PrEP from a clinician.[31] Other barriers include insufficient knowledge about PrEP and PEP among communities at risk of HIV, difficulty finding prescribers willing to offer PrEP (especially in rural areas), the need to disclose sensitive information to the prescriber, and stigma. In addition, there are acknowledged barriers to accessing culturally safe healthcare for Māori within Aotearoa New Zealand which impacts on access to PrEP and uptake. To be an effective public health intervention, PrEP must be delivered as part of a comprehensive sexual healthcare package that is accessible regardless of ethnicity, location, income, age, literacy, culture or migrant status.

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4. Suitability for PrEP

Pre-exposure prophylaxis (PrEP) is publicly funded by PHARMAC. All general practitioners and other relevant prescribers can prescribe PrEP using the PHARMAC special authority form.

No specialist training is required to prescribe PrEP; however, it is recommended that the available resources and training guidance[1] are reviewed by those unfamiliar with PrEP prescribing.

PrEP is funded in Aotearoa New Zealand for HIV-negative individuals who are at elevated risk of HIV exposure, where use of PrEP is clinically appropriate.

Men who have sex with men (MSM) are 348 times more likely to be diagnosed with HIV in Aotearoa New Zealand than the heterosexual community.[2] MSM, trans and non-binary people who share sexual networks with MSM should be assessed to determine whether PrEP is appropriate for them. PrEP is generally not indicated for cisgender heterosexual people in Aotearoa New Zealand due to the low risk of HIV acquisition; however, there are situations where PrEP use is appropriate (see Box 4.1).

Doctors and nurse practitioners who are not comfortable prescribing PrEP to people at elevated risk of HIV acquisition should refer the patient immediately to a colleague, or another service that does provide PrEP.

People requesting PrEP who are not eligible for publicly funded healthcare should still be assessed to determine if they would benefit from PrEP and these people then have the option of self-funding. The cost is approximately NZ$30 (2023) for a one-month supply; however, it must be acknowledged that the associated costs of the required laboratory testing and consultations will significantly add to this.

It should also be highlighted that sexual history-taking is a necessary and routine part of medical practice, and when this process identifies that a patient may be at elevated risk of HIV, clinicians should proactively offer these patients PrEP. Furthermore, clinicians are encouraged to raise PrEP as an HIV prevention strategy with patients whom they perceive to be at elevated risk of HIV infection, even if the purpose of the patient's visit is not related to sexual health, sexually transmitted infections (STIs) or drug use.

These PrEP guidelines recommend daily PrEP for all people at elevated risk of HIV infection. In addition, it is recommended that event-driven PrEP (also known as on-demand PrEP or PrEP 2-1-1) may be considered as an alternative option for certain populations[3] (see Chapter 6: Providing PrEP).

PrEP providers need to obtain a thorough sexual and drug-use history at baseline to determine a person's suitability for PrEP and to review their ongoing need for PrEP at each 3-monthly clinical review. It is important to acknowledge that a person's behaviour may change over time, and that a person may wish to continue PrEP even if their current HIV acquisition risk is not high. In addition, people may feel reluctant to disclose their HIV risk to their healthcare provider due to societal stigma.

These guidelines acknowledge that PrEP should be recommended as an HIV prevention strategy for people who have been at risk of HIV infection during the previous 3 months and who foresee having similar risks in the next 3 months. PrEP is also recommended for people who have not been at risk of HIV infection during the previous 3 months, but whose circumstances have changed, and they foresee HIV risk occurring in the next 3 months.

Please note that people who are eligible for PrEP based on their sexual behaviour may be simultaneously eligible for PrEP based on their injecting and other drug-use behaviour and vice versa.

The following suitability criteria can be used to help structure a discussion with a patient about their sexual health and behaviour. Guidance on how to initiate and guide a discussion about a person's sexual and drug-using behaviour in primary practice is available.[4]

There may be other situations where PrEP use is indicated, and clinicians who have limited experience with prescribing PrEP are encouraged to discuss with a PrEP-experienced clinician those patients whose PrEP suitability is unclear.

Box 4.1 PrEP suitability criteria for men (cis or trans) who have sex with men, and trans women and non-binary people who share sexual networks with MSM*

HIV risk in the previous 3 months and/or the future 3 months

The clinician should offer PrEP if the patient describes a history of any of the following HIV acquisition risks in the previous 3 months, and/or if the patient forsees that there are likely to be similar risks in the next 3 months:

- Condomless anal or vaginal intercourse with a regular HIV-positive partner who is either not on treatment, or who is on treatment but has a detectable HIV viral load >200 copies/ml
- Condomless anal or vaginal intercourse with any casual or non-exclusive MSM partner
- One or more episodes of rectal gonorrhoea, rectal chlamydia or infectious syphilis
- One or more episodes of anal intercourse where a condom slipped off or broke, where the HIV serostatus of the partner was not known, or where the partner was HIV-positive and not on treatment or had a detectable viral load >200 copies/ml
- When a person presents with concerns of deteriorating mental health and the possibility of increased HIV acquisition risk behaviour in this setting
- When a person presents with a history of intermittent binge drinking of alcohol or recreational drug use (especially methamphetamine use) and has concerns about their HIV acquisition risk behaviour in this setting

The clinician could also consider prescribing PrEP in the following circumstances:

- When an HIV-serodiscordant couple experience undue suffering and anxiety about inter-couple HIV transmission despite the positive partner being virologically suppressed on treatment
- When a person reports being so anxious about HIV infection that it may prevent them from having regular HIV testing or engaging in any form of anal sex.

Notes: *Cis: gender identity or expression matches the sex assigned at birth. *Trans: gender expression or identity differs from sex assigned at birth.

Only a small proportion of participants in PrEP studies have been transgender (trans) or non-binary people.[5-7] As a result, limited data are available for these populations. Incorrect assumptions can be made about trans and non-binary people and their sexual practices, as they may practise vaginal or neovaginal and anal intercourse, both insertive and receptive.

Trans and non-binary people who are at elevated risk of acquiring HIV on the basis of their sexual history, or future anticipated risk, are eligible to access PrEP. It is essential for clinicians to take a sexual history using appropriate and sensitive language to assess risk. The Aotearoa New Zealand STI Management Guidelines for use in Primary Care provide useful guidance for clinicians.[4]

Box 4.2 PrEP suitability criteria for heterosexual people

HIV risk in the previous 3 months and/or the future 3 months

The clinician should offer PrEP if the patient describes a history of any of the following HIV acquisition risks in the previous 3 months, and/or if the patient foresees that there are likely to be similar risks in the next 3 months:

- At least one episode of condomless intercourse (insertive or receptive) with a regular HIV-positive partner who is either not on treatment, or who is on treatment with a detectable viral load >200 copies/ml
- Condomless intercourse with any casual MSM partner of unknown HIV status
- Overseas travel to a high HIV-prevalence country, and condomless sex with partners of unknown HIV status.

The clinician could also consider prescribing PrEP in the following circumstance:

- When an HIV-serodiscordant couple experience undue suffering and anxiety about inter-couple HIV transmission despite the positive partner being virologically suppressed on treatment.

PrEP suitability criteria for people who inject drugs

HIV transmission via injecting drug use is rare in NZ.[8] In the first instance, people who inject drugs should be advised of and provided with options for using sterile needles, syringes and other injecting equipment, and offered opioid substitution therapy for those who use opioids. People who inject drugs can be referred to local needle and syringe programmes, including the New Zealand Needle Exchange Programme. Patients disclosing injecting drug use should also be offered other harm reduction resources, including information about overdose prevention and anonymous drug-checking services, especially if accessing drugs from an illicit supply.

Because people who inject drugs are susceptible to a range of infections and injuries, PrEP and other HIV-prevention interventions should be integrated into prevention and clinical care services for hepatitis A, B and C infection and other infectious diseases, and overdose prevention. These interventions include screening for hepatitis A, B and C viruses and providing vaccination for hepatitis A and B where clinically indicated, as well as screening for injection-related injuries and infections including abscesses, septicaemia and endocarditis.[9]

The NZ PrEP and PEP Guidelines panel is cognisant of the concerns of the International Network of People who Use Drugs. The network cautions against prioritising PrEP at the expense of other proven interventions as the prime HIV-prevention strategy for people who inject drugs, and emphasises that access to harm-reduction services remains a critical component of HIV prevention in people who inject drugs.[10] This approach is particularly relevant in Australia and NZ where sterile needle and syringe coverage is high and HIV prevalence and incidence among people who inject drugs remains low and stable.[11,12]

A recent systematic review of HIV-treatment adherence among people who inject drugs in the USA and Canada, undertaken to inform potential PrEP adherence interventions for people who inject drugs, found that younger age, female sex, homelessness and incarceration were obstacles to HIV treatment adherence.[13] By comparison, self-sufficiency, use of opioid substitution therapy

and high quality patient-provider relationships were facilitators of adherence.[13] Self-reports from HIV-negative people who inject drugs were that HIV–related stigma in social networks, negative experiences with healthcare providers, lack of money, homelessness and the criminal justice system were likely barriers to PrEP access.[14] These factors should be considered when providing support to people commencing PrEP when they are at risk of HIV through injecting drug use.

In people whose sexual partners include injecting drug users, PrEP should be considered, taking into account the risks and benefits, as well as patient preference. If other risk factors for HIV acquisition are present, PrEP should be offered accordingly.

Box 4.3 PrEP suitability criteria for people who inject drugs

HIV risk in the previous 3 months and/or the future 3 months

The clinician should offer PrEP if the patient describes a history of any of the following HIV acquisition risks in the previous 3 months, and/or foresees that there are likely to be similar risks in the next 3 months:

- Shared injecting equipment with an HIV-positive person or with MSM of unknown HIV status.

NB: Some people who inject drugs may also be at elevated risk for HIV acquisition through sexual behaviour.

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5. Clinical assessment before starting PrEP

All patients whose sexual or drug injecting history indicates the recommendation or consideration of PrEP, and who are interested in taking PrEP, must undergo laboratory testing. The tests identify those for whom this intervention would be harmful, or for whom it could present specific health risks that would require close monitoring.

HIV testing

For patients' safety, those with acute or chronic HIV infection should be identified through taking a medical history and HIV testing. A negative HIV test result must be documented at the time the patient is evaluated for PrEP, as the daily or event-driven tenofovir disoproxil* and emtricitabine (TD*/FTC) combination alone is insufficient for treatment of acute or chronic HIV infection.

HIV testing must be repeated every 3 months when patients attend for a prescription refill. This requirement for quarterly visits should be explained to patients during the initial discussion about whether PrEP is appropriate for them.

A fourth-generation HIV antibody and p24 antigen venous blood test should be used and should be performed within 14 days of the patient's being evaluated for PrEP. If there is no recent HIV test result, clinicians can prescribe PrEP on the same day as an HIV test and advise patients to start PrEP once informed the test is negative.

Rapid, point-of-care tests (PoCT) should not be used alone to screen for HIV infection when considering PrEP because they are less sensitive than blood tests. Failure to detect very early HIV infection by rapid testing in the PrEP context has been reported.[1] These tests include rapid home-based HIV testing kits which are available in NZ. However, a rapid PoCT can be used for the same-day initiation of PrEP, providing that a venous blood test for a fourth generation HIV antibody and antigen test is obtained and tested simultaneously. A PoCT can exclude potential PrEP users who are found to be HIV-positive, and any reactive PoCT should be confirmed by conventional laboratory testing in line with the New Zealand HIV Testing Guidelines.[2] Clinicians should not accept patient-reported HIV test results, including home-based HIV test results, or documented anonymous test results. Any positive HIV antibody test result must be managed according to local health pathways.

A course of post-exposure prophylaxis (PEP) may be required before transitioning to PrEP (see Chapter 9) if a patient has had a recent high-risk exposure (within 72 hours).

The window period for fourth-generation serological HIV testing is 45 days.[3] PrEP use in people with primary HIV infection (defined as the period following HIV acquisition in which the virus spreads throughout the body, the viral reservoir is established, and seroconversion occurs) may delay detection of infection, prolong seroconversion, and lead to the development of resistance mutations.[4] However, PrEP start should not be delayed in patients likely to be at ongoing elevated risk of HIV infection, who have had a recent high-risk exposure outside the 72-hour window for the commencement of PEP. Primary HIV infection at the time of starting PrEP is rare in NZ. People who would benefit from PrEP may never be outside the window period for testing. Delaying

starting PrEP in this situation would mean withholding an effective method of HIV prevention from those who would benefit most. Patients who have had a recent high-risk exposure outside the 72-hour window for the commencement of PEP should be assessed for PrEP, and closely monitored for seroconversion with an additional fourth-generation HIV blood test 1 month after starting, before reverting to standard PrEP monitoring. HIV viral load and HIV proviral DNA tests are not routinely recommended to screen for early HIV infection.

Acute HIV infection should be considered in people at high risk of HIV who may have had recent exposure to HIV (e.g., no condom or a condom broke during sex with an HIV-positive partner not on treatment, or a casual partner of men who have sex with men; recent injecting drug use with shared injecting equipment with MSM, or person known to be HIV-positive).

In a prospective study of 2226 people at high risk of HIV infection who underwent twice-weekly HIV nucleic acid testing, 50 people were evaluated for their clinical signs and symptoms during acute HIV infection. Symptoms and signs occurred in 94% of participants with acute HIV infection, just before and around the time of peak HIV viraemia.[5] The most common symptoms were fever, headache and malaise, while the most common signs were related to the head, eyes, ears, nose, throat, tachycardia and lymphadenopathy (Table 5.1).

Table 5.1 Symptoms and abnormalities associated with primary or acute HIV infection, overall and by region.[3]

Symptoms and abnormalities	Africa (*n* = 31)		Thailand (*n* = *17*)		Overall (*n* = 48)	
	n	%	*n*	%	*n*	%
Symptom						
Fever	18	55	7	41	25	50
Headache	17	52	6	35	23	46
Feeling of illness	14	42	5	29	19	38
Coughing	10	30	9	53.5	19	38
Abnormality						
HEENT[a]	6	18	16	94	22	44
Lymphadenopathy[b]	9	9	16	94	19	38
Tachycardia	11	33	5	29	16	32

Notes: a. Head, ears, eyes, nose and throat. b. A condition or disease affecting the lymph glands of the body resulting in lymph nodes that are abnormal in size, consistency or number.

Initiation of TD*/FTC PrEP in people with undiagnosed primary or acute (symptomatic) HIV infection has been associated with the development of resistance to TD*/FTC, mostly commonly to the FTC component.[6-9]

People who present with signs or symptoms consistent with acute HIV infection should not be commenced on PrEP until HIV infection has been excluded.

Patients with indeterminate HIV test results at baseline should not be started on PrEP. They should be assessed for early HIV infection and discussed with local infectious diseases or sexual health specialists as indicated. Such patients can only be started on PrEP if and when HIV infection is excluded.

Concerns about TD* or FTC resistance

PrEP is highly effective at preventing HIV acquisition, and the overall risk of developing resistance mutations to tenofovir or emtricitabine during PrEP use is very low.[10] Resistance mutations are predominately acquired through unrecognised primary HIV infection at the time of starting PrEP, or through suboptimal PrEP adherence.[10,11]

In those with unrecognised HIV infection at the time of starting PrEP, the development of resistance mutations has been observed in up to 45.8% of cases,[12] most commonly emtricitabine-specific mutations (M184V/I), which can potentially occur within days.[13] Resistance mutations for TDF are rare,[12] consistent with the higher genetic barrier to TDF compared with FTC.[14] Suboptimal PrEP adherence increases seroconversion rates; however, the emergence of resistance among these patients is less common because drug selection pressure is low. Only 4.9% of patients who had a primary HIV infection while using PrEP developed drug-related resistance, predominantly emtricitabine-specific mutations.[12]

Much evidence related to the development of resistance is from clinical trials and case studies. The prevalence of drug-resistant HIV strains must be monitored globally as PrEP use is scaled-up; however, mathematical modelling indicates that the number of HIV-1 infections that would be averted by PrEP greatly exceeds the number of drug-resistant infections that could occur.[15] People with emtricitabine-specific mutations (M184V/I) alone generally achieve viral suppression when rapidly linked to care and initiated on antiretroviral therapy.[13,16]

Assessment of renal function at baseline

In HIV-positive patients, the use of TD* was reviewed in a meta-analysis and was associated with a statistically significant loss of renal function, with the effect being judged as clinically modest.[17] TD* use was not associated with increased risk of fractures, hypophosphataemia or severe proteinuria.[17] Rarely, proximal renal tubular dysfunction (including Fanconi syndrome) may occur with TD* use.[17-19]

Overall, TD* use in PrEP studies has not been associated with significant clinical renal problems.[20-22] The Iniciativa Profilaxis Pre-Exposición (iPrEx) study showed a small but statistically significant mean decline in creatinine clearance (CrCL) from baseline but the decline in CrCL was reversible with PrEP cessation.[20] Factors associated with a decline in estimated glomerular filtration rate (eGFR) include commencement of PrEP at age 40 years or over, a baseline eGFR below 90 mL/min/1.73m^2, and good adherence.[22] **There are no data for people using PrEP who have an eGFR below 60 mL/min/1.73m^2; therefore starting PrEP in people whose eGFR is well established to be below 60 mL/min/1.73m^2 is not recommended**. However, see comments below on managing people who are found to newly have an eGFR around 60 mL/min/1.73m^2 at baseline testing.

Data from the iPrEx open-label extension (iPrEx-OLE) study found a significant increase in both urine alpha-1 microglobulin, a urine marker of impaired tubular reabsorption, and proteinuria after 6 months of TD*/FTC exposure, suggesting that subclinical tubular injury occurs on PrEP.[23]

There are limited data regarding whether event-driven versus daily PrEP reduces the likelihood of renal toxicity. However, in the Intervention Préventive de l'Exposition aux Risques avec et pour les Gays (IPERGAY) study, no significant decline was observed in the mean slope of eGFR in the TD*/FTC versus placebo arms over a median of 9.4 months follow-up,[24] suggesting that event-

driven PrEP may not influence renal function. In the Alternative Dosing to Augment PrEP Pill Taking (ADAPT) study, a creatinine elevation was observed in 9% of 178 participants evaluated, but creatinine elevation did not differ between participants in the daily, time-driven and event-driven PrEP study arms (p = .05).[25]

Recent data from the DISCOVER study, where MSM and transgender women at risk of HIV were randomised to TDF/FTC versus tenofovir alafenamide (TAF)/FTC, reported a significant difference in change in eGFR and tubular proteins during the study favouring TAF/FTC.[26] More broadly, the DISCOVER study found that TAF/FTC was non-inferior to TDF/FTC in terms of preventing HIV infection;[26] however, TAF/FTC has not been licensed yet in NZ for use as PrEP.

For all patients considered for PrEP, their risk factors for chronic kidney disease should be assessed at baseline. These risk factors include diabetes, hypertension, smoking, concurrent medications and a known history of renal impairment or history of kidney injury or structural abnormality. Measurements of baseline serum creatinine, eGFR, the urine protein: creatinine ratio (PCR) and blood pressure should also be taken. The Cockcroft–Gault formula for estimating creatinine clearance (CrCl) is regarded as the ideal way to measure the eGFR. However, for most practitioners, this is not practical. Instead, it is reasonable to measure the patient's renal function using the eGFR as reported by the laboratories.

For people who are found to newly have an eGFR around 60 mL/min/1.73m^2 at baseline, the eGFR should be repeated within 7 days because clinical situations occur when the eGFR may be unreliable, e.g., recent consumption of cooked meat. In this setting, the clinician should ask the individual to fast or avoid a cooked meat meal within 4 hours of repeat eGFR testing. Exceptional dietary intake, e.g., vegetarian diet, high protein diet, creatinine supplements, and extremes of body size (e.g., high muscle mass) may underestimate eGFR. Being underweight or having low muscle mass may overestimate eGFR.

If after repeat testing a person's eGFR remains just below or just above 60 mL/min/1.73m^2, it is recommended that the clinician speak to a specialist in PrEP as these patients may still be able to commence PrEP with close monitoring. Of note, in this setting, event-driven PrEP may be a suitable option if criteria are met (see Chapter 6).

These guidelines recommend that creatinine, eGFR and urinary PCR measurements for each person are evaluated at baseline. The eGFR should be repeated 3 months after commencing PrEP and 6-monthly thereafter. More intensive monitoring may be warranted in the following people:

- those over the age of 40 years
- those with a baseline eGFR of less than 90 mL/min/1.73 m^2
- those with other comorbidities (e.g., hypertension, diabetes)
- those taking nephrotoxic drugs.

A minority of people may experience a decline in eGFR; further investigations and consideration of a referral to a specialist renal service are recommended when there is sustained decrease in eGFR of 25% or more or a sustained decrease in eGFR of 15 mL/ min/1.73 m^2.[27]

Assessment and management of sexually transmitted infections at baseline

People at risk for HIV infection are also at high risk for STIs. Clinicians should screen for STIs (specifically gonorrhoea, chlamydia and infectious syphilis) using the standard-of-care tests and procedures, and manage any detected STI as recommended by the Aotearoa New Zealand STI Management Guidelines for use in Primary Care.[28] Importantly, the presence of an STI at baseline should not delay the commencement of PrEP. Of note, in the NZPrEP study it was reported that 18% of study participants tested positive for rectal chlamydia or gonorrhoea at baseline.[29]

Patients starting on PrEP should be informed about:

- prevention of STI acquisition and transmission
- combining condom and PrEP use for the prevention of STIs
- frequency of STI testing
- signs and symptoms of STIs.

Patients should be encouraged to present for testing and treatment whenever signs or symptoms of STIs appear.

Assessment of hepatitis A, B and C status

People being assessed for PrEP can also be at risk of acquiring hepatitis A (HAV), hepatitis B virus (HBV)[30] and hepatitis C virus (HCV) infection.[31] HBV and HCV infection status should be documented by screening serology when PrEP is initiated. Screening for hepatitis A immunity should be offered; however, it is not funded for this indication in NZ, and is not mandatory when initiating PrEP.

Vaccination against HBV is recommended (but not funded) for adults at risk of sexual exposure, including MSM, as well as current or recent injecting drug users.[32] People identified at baseline as having undiagnosed chronic hepatitis B should be referred to the Hepatitis Foundation of New Zealand, with assessment as per local health pathways. Those with chronic hepatitis B infection who would like to commence PrEP should be managed in conjunction with a specialist, and should only be offered daily PrEP and not event-driven PrEP. They should also be counselled on the importance of strict adherence to PrEP to prevent both a flare in their hepatitis B infection and the development of hepatitis B resistance to TD*/FTC.

People identified at baseline with undiagnosed hepatitis C infection should be managed as per local health pathways. Effective treatment for Hepatitis C is available. A diagnosis of hepatitis B or hepatitis C is not an obstacle to HIV PrEP initiation.

Hepatitis A vaccination is recommended (but not funded) for men who have sex with men, and should be considered for injecting drug users.[32] Hepatitis A serology is not mandatory before vaccination. There is no harm in vaccinating an already immune person; however, some groups with a higher probability of prior infection may wish to avoid the expense of vaccination if found not to be immune.

Assessment of bone health

Low bone mineral density (BMD) was observed at baseline in approximately 10% of people receiving TD*/FTC for PrEP in the iPrEx study.[33] People should be counselled about the effects of TD* on BMD and counselled to decrease alcohol and cigarette use, to undertake weight-bearing exercise and ensure their diet provides adequate amounts of calcium and vitamin D.[34] A clinician may suspect that a person is vitamin D deficient and may wish to test their vitamin D levels. There is no evidence that over-the-counter vitamin D supplements reduce tenofovir-related BMD changes.

A small but statistically significant decline in BMD was observed by week 24 in participants of the iPrEX study. The decline in BMD correlated directly with levels of intracellular TD*-DP and was found to be reversible once PrEP was ceased.[35]

There are no data available on whether event-driven PrEP is less likely to cause a decline in BMD.

Recent data from the DISCOVER study found that TAF/FTC versus TDF/FTC was associated with less decline in BMD.[26]

A person with a history of osteoporosis will require careful monitoring while on PrEP. If the clinician suspects that a person may have osteoporosis, they may recommend BMD testing. In those people over the age of 40 years thought to be at risk of having reduced BMD, a FRAX® tool to evaluate fracture risk can be used to assess the need for dual-energy X-ray absorptiometry (DXA) scanning. For further information see https://www.sheffield.ac.uk/FRAX/tool.aspx?country=31.

Assessment for pregnancy in people of childbearing potential

The risk of HIV transmission to women increases by over two-fold when they are pregnant.[36] As reviewed recently, current evidence suggests that PrEP can be used safely during pregnancy and breastfeeding.[37]

See *Chapter 8: Special clinical considerations* for further information about PrEP use in pregnancy and breastfeeding.

The NZ PrEP and PEP Guidelines panel will continue to monitor the safety of TD*/FTC PrEP regimens when used during pregnancy and breastfeeding.

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6. Providing PrEP

Goals of PrEP

The ultimate goal of human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP) is to reduce the acquisition of HIV infection and its resultant morbidity, mortality and associated cost to people and society. Therefore, clinicians initiating PrEP should:

- prescribe medication regimens that are proven safe and effective for HIV-negative people who are suitable for PrEP to reduce their risk of HIV acquisition. Only co-formulated tenofovir and emtricitabine (TD*/FTC) is licensed in Aotearoa New Zealand for use as PrEP and is the only regimen that should be used.
- educate patients about the medications and the dosing regimen to optimise safe medication use.
- provide counselling on sexually transmitted infections (STIs) and their prevention including the use of condoms.
- provide medication-adherence support and counselling to help patients achieve and maintain protective levels of medication.
- provide HIV risk-reduction support and offer harm reduction including referrals to help patients minimise their risk of acquiring HIV, viral hepatitis B and C and STIs.
- provide effective contraception to people who are taking PrEP who do not wish to become pregnant.
- monitor patients on a quarterly basis to screen for HIV infection, STIs and toxicity and to determine whether PrEP remains indicated.

PrEP licensing in New Zealand

Co-formulated tenofovir disoproxil* and emtricitabine (TD*/FTC) is registered by the NZ Medicines and Medical Devices Safety Authority, Medsafe, for daily use and is subsidised by the NZ Pharmaceutical Management Agency, PHARMAC.

Daily PrEP

Daily PrEP is the most commonly prescribed PrEP regimen in NZ. Daily use of TD*/FTC is highly efficacious at preventing HIV transmission in the setting of high medication adherence.[1,2,3,4,5] A detailed review of these and other studies that have demonstrated the efficacy and effectiveness of daily PrEP is beyond the scope of these guidelines. For more information, see *Chapter 2: PrEP safety and efficacy*.

The NZ PrEP and PEP Guidelines panel recommends that daily TD*/FTC should be offered to all populations at elevated risk of HIV infection.

Event-driven PrEP

Event-driven PrEP involves taking 2 tablets of TD*/FTC 2–24 hours before a potential sexual exposure to HIV, followed by a third tablet 24 hours after the first dose and a fourth tablet 48 hours after the first dose. This regimen is referred to as 2 + 1 + 1 dosing of PrEP.[6] If sex continues

for several days, people take one tablet of TD*/FTC daily until the last sex act, following which one dose 24 hours later and again at 48 hours are taken after the last episode of sex.

Evidence in support of event-driven PrEP dosing

Data on the efficacy of non-daily PrEP dosing are available for cisgender MSM. Very few transgender women have been evaluated in randomised controlled trials of event-driven PrEP;[7-9] nor have such trials been undertaken in cisgender women, transgender men, non-binary people, or in people whose principal HIV exposure risk is injecting drug use. Pharmacological studies in cisgender women suggest that event-driven PrEP does not provide adequate tissue levels of PrEP to provide high levels of HIV protection; therefore, event-driven PrEP should not be recommended for cisgender women.

Data on how efficacious event-driven PrEP is for MSM in reducing HIV transmission came initially from the randomised, placebo-controlled trial, IPERGAY (Intervention Préventive de l'Exposition aux Risques avec et pour les Gays).[10] This study evaluated the efficacy of event-driven PrEP comprising 2 tablets of TDF/ FTC (versus placebo) taken 2–24 hours before potential sexual exposure to HIV, followed by a third tablet 24 hours after the first dose and a fourth tablet 48 hours after the first dose. If multiple episodes of sex occurred, the participants were advised to continue to take one tablet daily until the last sex act then take the 2 final doses, 24 hours apart. If sexual activity was resumed within a week, a single rather than a double dose before sex was recommended. If sexual activity resumed more than a week later, the loading dose schedule (2 tablets) was recommenced. The incidence of HIV was high in the placebo group (6.6 per 100 person-years) and a risk reduction in the TDF-FTC group of 86% [95% confidence interval (CI), 40 to 98; $p = .002$] was observed.[10]

Demonstration studies have been undertaken to determine how effective event-driven PrEP is when used in community settings. In an open-label extension study of the IPERGAY study, an HIV risk reduction of 97% (95% CI, 81–100) with event-driven PrEP was reported in 361 participants with a median follow-up of 18 months.[8] In a study of 1069 people commencing PrEP in a single clinic in France, four HIV infections were diagnosed over 486 years of person follow-up.[7] In the French ANRS Prévenir study, of 3049 participants, 50.5% took daily PrEP and 49.5% took event-driven PrEP, with some shifting between regimens occurring within the study.[9] The median number of partners in the 3 months before PrEP commencement was 12 (interquartile range [IQR] 6-25) in the daily group and 10 (IQR 5-15) in the event-driven group ($p < .0001$). The median number of condomless sex events in the previous 4 weeks was 2 (0 to 8) and 2 (0 to 4) in the daily and event-driven participants, respectively ($p < .0001$). Follow-up in the daily and event-driven groups was 2713 years and 2723 years, respectively. The HIV-1 incidence was 3 in both study groups with an incidence of 1.1 per 1000 person-years for each group (95% CI 0.2-3.2).

The efficacy of event-driven PrEP in people who use it infrequently

To address the question of whether event-driven PrEP is efficacious for people using it infrequently, the IPERGAY study team undertook a post-hoc analysis of IPERGAY study participants who reported relatively infrequent sex.[11] Overall, IPERGAY participants reported using a median of 15 PrEP tablets per month. The post-hoc study looked at the follow-up time between two consecutive visits during which participants in the placebo and active study arms used less than 15 tablets per month and reported they used PrEP 'systematically or often' during sexual intercourse. During these periods of lower PrEP use, participants had a median of 5 episodes of sex per month (IQR 2-10) and used a median of 9.5 tablets per month (IQR 6-13). Six HIV infections occurred in the placebo arm (incidence: 9.2 per 100 person-years, total follow-up time:

64.9 person-years) and 0 in the TDF/FTC arm (incidence: 0 per 100 person-years, total follow-up time: 68.9 person years; p = .013). The relative reduction of HIV incidence in the treatment group was 100% (95% CI, 39-100). The study investigators concluded that an event-driven PrEP strategy remains highly effective in MSM even when they have infrequent sex.[11]

Notably, of concern to the NZ PrEP and PEP Guidelines panel were the wide 95% confidence intervals of the relative risk reduction in this group of IPERGAY participants practising infrequent sex.[11] However, the data from the Prévenir study described above are reassuring in terms of the efficacy of less frequent use of event-driven PrEP.[9]

Toxicity and event-driven PrEP

There are few data available to determine whether event-driven PrEP offers less toxicity. In the IPERGAY study, no significant decline in the mean slope of estimated glomerular filtration rate (eGFR) in the TD*/FTC versus placebo arms was observed over a median of 9.4 months follow-up.[12] In the HIV Prevention Trials Network (HPTN) study 067, the Alternative Dosing to Augment PrEP Pill Taking (ADAPT) study, 9% of 178 participants at one study site had creatinine elevation, but this was not significantly different between participants in the daily, time-driven and event-driven PrEP study arms (p = .05).[13] In the Prévenir study,[9] the incidence of serious adverse events was low and similar with both daily and on-demand dosing regimens. The incidence of drug-related adverse events was low overall, but was significantly lower among participants using daily PrEP than in those using on-demand PrEP (5·93 events per 100 person-years *vs* 7·42 events per 100 person-years; incidence rate ratio 0·80, 95% CI 0·65–0·99). This difference was mainly driven by a higher rate of gastrointestinal adverse events in participants using on-demand PrEP than in those using daily PrEP, as most drug-related adverse events were gastrointestinal events. This was thought to be possibly due to the starting and stopping of PrEP with the on-demand regimen. There was no difference in the incidence of grade 1 creatinine plasma concentration increase, or in the proportion of participants with eGFR of less than 70 mL/min or less than 50 mL/min between PrEP dosing regimens.

Preference for event-driven versus daily PrEP

In the Prévenir study, in which MSM were offered the choice of daily or event-driven PrEP, approximately half of the participants opted for each regimen.[9] In a report from the PRELUDE study from New South Wales, Australia, one third of participants enrolling in the study expressed a preference for non-daily PrEP.[14] Similarly, in the AM PrEP implementation study (the Netherlands), 27% of men opted to take event-driven PrEP.[15] In the PrEP in NSW Transition Study,[16] PrEP-experienced gay and bisexual men were asked about interest in and preference for different PrEP modalities. This study found 42.8% of participants had interest in event-driven PrEP and 21.8% indicated it was their preference. Higher interest and preference for non-daily PrEP was associated with being concerned about side-effects and perceived difficulties with daily adherence.

The choice of PrEP schedule: daily versus event-driven PrEP

Daily PrEP is suitable for all people who are at elevated risk of HIV. Event-driven PrEP can be considered as an alternative option for people at elevated risk of HIV, who were assigned male at birth, and who are not taking exogenous oestradiol-based hormones (see Table 6.1). This covers cis men, trans women and non-binary people assigned male at birth *who are not using exogenous oestrogen*, and is regardless of gender of sexual partners. In these individuals, event-driven PrEP can be used in cases where daily PrEP is not acceptable, sex is infrequent and a person feels they

can plan ahead for sex at least 2 hours in advance. Other reasons that people may choose or merit event-driven PrEP include concerns about side-effects from daily PrEP, poor kidney function (however, see toxicity section above) or financial constraints. **Of note, event-driven PrEP is contraindicated in people with chronic hepatitis B infection.**

Table 6.1 Suitability for daily vs event-driven PrEP for sexual exposure, based on gender and use of exogenous oestrogen

People	Daily PrEP	Event-driven PrEP
Cisgender men	Yes	Yes*
Cisgender women	Yes	No
Trans men	Yes	No
Trans women using exogenous oestrogen	Yes	No
Trans women who are NOT using exogenous oestrogen	Yes	Yes*
Non-binary people assigned male at birth, using exogenous oestrogen	Yes	No
Non-binary people assigned male at birth, who are NOT using exogenous oestrogen	Yes	Yes*
Non-binary people assigned female at birth	Yes	No

Notes: * Where a person expresses a preference for event-driven PrEP, sex is infrequent and a person feels they can plan ahead for sex at least 2 hours in advance. Event-driven PrEP is contraindicated in people with chronic hepatitis B infection.

Daily PrEP would be preferential for those people who prefer daily PrEP, who cannot predict when sex will occur, who cannot delay sex for more than 2 hours and for those whose potential exposure to HIV occurs more than twice a week. Daily PrEP is the only suitable regimen for people with chronic hepatitis B infection to maintain virological suppression, prevent drug resistance and hepatitis flares.

The NZ PrEP and PEP Guidelines panel recommends that caution be used in recommending event-driven versus daily PrEP to adolescent MSM because there have been no trials of event-driven PrEP in adolescent MSM and because adherence rates to daily PrEP have been consistently low in studies of adolescent MSM.[17,18]

Evaluation of the need for ongoing PrEP

Along with encouraging safer sex practices and safer injecting techniques, as needed, clinicians should support their patients to decide when to commence PrEP and when to discontinue its use.

The duration of PrEP use will depend on whether the person's risk of HIV continues over time. PrEP should only be prescribed to those patients who are able to adhere to a regimen that has been shown to be efficacious and who express a willingness to do so.

Adherence to PrEP should be assessed at each follow-up visit. PrEP users who disclose that they have had suboptimal adherence, but who are willing and suitable to continue on PrEP, should be offered additional adherence education (see Chapter 10: Improving medication adherence, including offering referral to peer-based support services). If a PrEP user repeatedly reports adherence that is sufficiently suboptimal to compromise both PrEP's efficacy (i.e., fewer than 4 tablets per week when taking a daily regimen) and the patient's safety, the clinician should stop prescribing PrEP. See also *Chapter 9: HIV post-exposure prophylaxis* for the course of action to follow if a patient is not adherent to PrEP and has had a risk of exposure in the last 72 hours.

PrEP script duration including extension of PrEP scripts

The initial and ongoing prescriptions should offer a 90-day medication supply. Reasonable attempts should be made to avoid multiple patient visits when initiating PrEP. A prescription can be provided on the same day as the baseline HIV test is ordered as long as the patient is advised not to fill the script until confirmed to be HIV-negative and the Special Authority is approved. Another option is to send the script to the patient or pharmacy once the Special Authority is approved.

PrEP prescriptions should cover no more than 90 days of TD*/FTC supply at a time. People who use event-driven PrEP should also present for HIV and STI testing on a quarterly basis, even if they do not need a prescription refill at that time.

Laboratory and clinical schedule at baseline and follow-up

The recommended schedule of testing and follow-up of people on PrEP is outlined in Table 7.1 in *Chapter 7: Clinical follow-up and monitoring*.

Indicated medication

The medications proven safe and effective and currently approved by Medsafe for PrEP in healthy adults at elevated risk of acquiring HIV infection are the fixed-dose combination of TD* and FTC in a single daily dose.

Long-acting injectable cabotegravir (CAB-LA) is an additional prevention choice for people at elevated risk of HIV infection, but is not available in NZ and is therefore not covered within these guidelines.

What not to use for PrEP

There have been some overseas reports of HIV seroconversion in MSM taking unprescribed antiretroviral medication for PrEP.[19]

DO NOT use any other HIV antiretroviral medications, either in place of or in addition to TD* or FTC.

Do not provide PrEP as expedited partner therapy (i.e., do not prescribe for a person who is not in your care).

PrEP dosing schedule

A daily PrEP regimen involves the person taking a single daily tablet at approximately the same time each day. Taking the tablet some hours earlier or later than usual will not adversely influence the levels of the drug. If the person forgets to take a tablet for one day, there is no need to take 2 tablets the next day.

The event-driven PrEP regimen involves the person taking a loading dose of PrEP where 2 tablets of PrEP are taken together as early as 24 hours before sex, or as late as 2 hours before sex. After sex, another PrEP tablet is taken 24 hours after the loading dose and then a final PrEP tablet is taken 48 hours after the loading dose. People who have more than one episode of at-risk sex over a period of days should keep taking a single PrEP tablet every day that they are having sex

until the last day that at-risk sex occurs, then they should take a single daily PrEP tablet for 2 days after the last at-risk sex act.

PrEP medication side-effects

Patients taking PrEP should be informed of TD*/FTC side-effects experienced by participants in PrEP trials. These include headache, nausea, flatulence and the potential for renal injury or hepatotoxicity. In these trials, side-effects were uncommon and usually resolved within the first month of taking PrEP (known as 'start-up syndrome'). Clinicians should discuss the use of over-the-counter medications for headache, nausea and flatulence should they occur. Patients should also be counselled about symptoms that indicate a need for urgent evaluation (e.g., those suggesting possible acute renal injury or acute HIV infection). See *Chapter 5: Clinical assessment before starting PrEP* for a review of the signs and symptoms of acute HIV infection.

PrEP medication drug interactions

In addition to the safety data obtained in PrEP clinical trials, data on drug-drug interactions and longer-term toxicities have been obtained by studying the component drugs individually for their use in treatment of people with HIV infection. Studies have also been performed in small numbers of healthy adults without HIV infection.

FTC and TD* are primarily excreted by the kidneys by a combination of glomerular filtration and active tubular secretion. Since both drugs are primarily eliminated by the kidneys, co-administration of TD*/FTC with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of TD*, FTC and other renally eliminated drugs,[20] including (but not limited to) cidofovir, aciclovir, valaciclovir, ganciclovir, valganciclovir, aminoglycosides and high-dose or multiple non-steroidal anti-inflammatory drugs.

Cocaine, methamphetamine and alcohol use are not known to influence the concentrations of PrEP drugs, but use of these drugs may have an effect on the person's ability to maintain full adherence to PrEP.

The University of Liverpool has a freely available HIV Drug Interactions Checker https://www.hiv-druginteractions.org which should be used when prescribing PrEP or PEP.

Time to achieving and maintaining protection

The pharmacokinetics of TD* and FTC vary by tissue.[21] Current evidence suggests that for both rectal and vaginal exposure, high protection is achieved after 7 days of daily dosing.[22] People with a vagina need to maintain high adherence to daily dosing of TD*/FTC to maintain adequate drug levels in vaginal and cervical tissues.[22] Very limited data are available about intracellular drug concentrations in penile tissues susceptible to HIV infection to inform considerations of protection for insertive sex partners. Limited data exist for transgender and non-binary people therefore extra attention to daily dosing is recommended.

- WHO[23] recommends that individuals eligible for event-driven PrEP can start PrEP by taking two doses 2–24 hours prior to potential exposure, regardless of whether they intend to use an oral daily or event-driven PrEP dosing regimen, and continue to take one dose per day until two days after the day of the last potential sexual exposure.
- All other individuals should start daily PrEP by taking one dose per day for 7 days prior to potential exposure to HIV and can stop taking daily PrEP 7 days after the last potential

exposure.

PrEP and travel

PrEP can play an important role in preventing HIV infection in people travelling outside of NZ, along with other measures to reduce HIV and STIs.[24] If a patient eligible for event-driven PrEP wants to take daily PrEP while on an overseas trip, they can commence 2 tablets on the day of departure and cease PrEP once it is no longer needed (see section below on ceasing PrEP). Alternatively, the patient can take a double-dose 2-24 hours before sex and then use the event-driven regimen outlined above during the overseas trip. Other populations including those who inject drugs, cisgender women, trans and non-binary people assigned female at birth, and trans and non-binary people using exogenous oestradiol, who want to take PrEP while on an overseas trip should commence PrEP 7 days before their departure.

PEP use and PrEP

If a person is not taking PrEP but presents within 72 hours of a potential HIV exposure, they should be assessed for post-exposure prophylaxis (PEP) as a matter of urgency and should be offered PEP immediately according to current PEP Guidelines (see Chapter 9) if appropriate. If HIV acquisition risk is likely to continue into the future, PrEP should be offered.

Discontinuing PrEP

Clinicians should regularly advise people using PrEP about how to discontinue PrEP. The need for PrEP may end when a partner with HIV achieves sustained HIV viral suppression after at least 6 months of antiretroviral therapy, when a patient enters a mutually monogamous relationship with a seroconcordant partner, or when other social circumstances change.

There is now substantial clinical evidence that cisgender MSM can safely cease event-driven PrEP by taking a dose of PrEP 24 and 48 hours after their last at-risk sexual exposure.[7-9] Recently, WHO recommended that individuals eligible for event-driven PrEP can continue to take one dose per day until two days after the day of the last potential sexual exposure, regardless of whether they are taking daily or event-driven PrEP.[23]

All other individuals can stop taking daily PrEP 7 days after the last potential exposure.[23]

Upon discontinuation for any reason, the following should be documented in the health record:

- HIV status at the time of discontinuation
- Reasons for PrEP discontinuation
- Recent medication adherence and reported sexual risk behaviour.

Recommencing PrEP

Clinicians should advise any patient who has discontinued PrEP on how to safely recommence PrEP if their risk for HIV infection increases again in the future (see Chapter 4: Suitability for PrEP). Clinicians should advise that if and when a patient decides to recommence PrEP, they must first have repeat HIV testing in case they have acquired HIV infection during the time that they were not taking PrEP. All other baseline clinical and laboratory evaluations need to be repeated also when a patient recommences PrEP and quarterly visits for PrEP scripts and ongoing evaluations must follow thereafter.

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7. Clinical follow-up and monitoring

Recommended schedule of testing and follow-up for people on PrEP

Once pre-exposure prophylaxis (PrEP) is initiated, patients should return for follow-up every 3 months. Clinicians may wish to see patients more frequently in the period after PrEP initiation (e.g., 1 month after initiation) to:

- assess and re-confirm HIV-negative test status in patients with a recent pre-PrEP HIV exposure
- assess side-effects
- monitor renal function in patients at particular renal risk
- assess adherence
- answer questions.

Box 7.1 and Table 7.1 set out the recommended schedule of testing and follow-up for people who are prescribed PrEP.

Box 7.1 PrEP follow-up procedures

PrEP follow-up procedures
At least every 3 months:
• Repeat HIV testing and assess for signs or symptoms of acute infection to document that patients are still HIV-negative. Rapid point-of-care tests (PoCTs) are not recommended for monitoring patients receiving PrEP.
• Test for sexually transmitted infections (STIs). This involves NAAT tests for chlamydia and *Neisseria gonorrhoea* as per Aotearoa New Zealand STI Management Guidelines for use in Primary Care (www.sti.guidelines.org.nz), and a blood test for syphilis serology.[1] The patient should also be tested for Hepatitis B unless known to be immune.
• Assess side-effects, PrEP adherence and ongoing PrEP suitability.
• Respond to questions and provide any new information about PrEP use.
• Provide support for medication adherence and risk-reduction behaviours.
In addition:
• Repeat pregnancy testing for people at risk.
• Test for hepatitis C virus (HCV) in people who inject drugs who report continued sharing of injecting equipment and men who have sex with men (MSM) with elevated risk of HCV acquisition (e.g., sexual practices that predispose to anal trauma).
At least every 6 months:
• Monitor estimated glomerular filtration rate (eGFR), creatinine and urine PCR.
• If the patient has risk factors for renal impairment (e.g., hypertension, diabetes, nephrotoxic medications, age >40, eGFR <90), renal function may require more frequent monitoring (see Chapter 5: Clinical assessment before starting PrEP).
At least every 12 months:
• Test for hepatitis C.

Table 7.1 Laboratory evaluation & clinical follow-up of people who are prescribed PrEP, including event-driven PrEP

Test	Baseline (Week 0)	About 30 days after initiating PrEP*	90 days after initiating PrEP	Every subsequent 90 days on PrEP	Other frequency
HIV testing and assessment for signs or symptoms of acute infection	**Y**	**Y** Retest HIV if any doubt about window period for baseline HIV test. Can be done by giving client a lab form to do this and does not require a visit	**Y**	**Y**	**N**
Assess side-effects	**N**	**Y**	**Y**	**Y**	**N**
Hepatitis B serology Vaccinate if non-immune	**Y**	**N**	**Y** (if not immune)	**Y** (if not immune)	**Y** If patient required hep B vaccine at baseline, confirm immune response to vaccination 1 month after last vaccine dose
Hepatitis C serology	**Y**	**N**	**N**	**N**	**Y** Every 12 months, or more frequently if ongoing risk e.g., non-sterile injecting drug use and MSM with sexual practices that predispose to anal trauma
Liver function tests	**Y**	**N**	**N**	**N**	**N**
STI (i.e., syphilis, gonorrhoea, chlamydia) as per www.sti.guidelines.org.nz[1]	**Y**	**N**	**Y**	**Y**	**Y -** Test if presents with symptoms in between PrEP visits
eGFR at 3 months and then every 6 months	**Y**	**N**	**Y**	**N**	**Y -** At least every 6 months or according to risk of chronic kidney disease
Urine protein:creatinine ratio (PCR) baseline	**Y**	**N**	**Y**	**N**	**Y** Every 6 months
Pregnancy test (for people who may become pregnant)	**Y**	**Y**	**Y**	**Y**	**N**

Notes: * 30-day follow-up recommended if recent HIV risk before starting PrEP.

Y: yes, N: no. eGFR: estimated glomerular filtration rate. STI: sexually transmitted infection. MSM: men who have sex with men. Hepatitis A serology/vaccination are not prerequisites for PrEP, and are not funded for this indication in NZ, however could be offered at the baseline visit.

Testing for HIV

HIV testing should be repeated every 3 months using a fourth generation HIV antibody and antigen test via a venous blood draw. Rapid point-of-care tests, including home testing HIV diagnostic kits, should not be used for monitoring patients receiving PrEP.

A patient's ongoing HIV risk and adherence to PrEP should be assessed when the patient presents for their quarterly clinical review (see Chapter 10: Improving medication adherence). Patients should be familiar from their baseline visit with the requirement for quarterly clinical reviews to obtain ongoing PrEP prescriptions.

A positive HIV test result

Any positive HIV test result should be managed urgently by appropriate counselling and referral to an HIV specialist. Assistance can be sought via telephone from a local infectious diseases or sexual health physician. It is very important for the clinician to recognise that HIV acquisition in a person who is using PrEP is a highly significant event and that the initial emphasis should be on supporting the person rather than focusing on how the infection occurred. If a patient is diagnosed with HIV infection while taking PrEP, their current health and wellbeing should be the chief immediate priority as opposed to enquiries about their adherence to PrEP.

Acute HIV infection should be suspected in people at risk for HIV who were not taking PrEP at the time that they were recently exposed to HIV (e.g., no condom, or a condom broke during sex with an HIV-positive partner who was not on antiretroviral treatment, or has a detectable HIV viral load; condomless anal sex with a casual partner; recent injecting drug use with shared injecting equipment with an HIV-positive partner). Also, infection with tenofovir disoproxil* (TD*)- or emtricitabine (FTC)-resistant HIV is possible; however, it is very uncommon while on PrEP, with only a few cases reported internationally.[2] Therefore, in addition to sexual behaviour and injecting drug use, clinicians should elicit a history of any signs and symptoms of viral infection during the preceding month, including the day of PrEP evaluation. See Table 5.1 in *Chapter 5: Clinical assessment before starting PrEP* for clinical symptoms and abnormalities of acute (primary) HIV infection.

Indeterminate HIV test results in the first 3 months on PrEP

There is a potential for PrEP to delay or attenuate seroconversion in people who may have been exposed to HIV just before starting PrEP, or who acquire HIV infection while taking PrEP (e.g., due to poor adherence or transmitted drug-resistant virus).[3-5] There is not a broad international agreement on how to manage these patients. Patients who have an indeterminate HIV test result while on PrEP (particularly those with repeated indeterminate test results) should be closely monitored in conjunction with an HIV specialist and in consultation with a clinical microbiologist who should be informed that the patient is taking PrEP.

The NZ PrEP and PEP Guidelines panel will continue to monitor this issue with a view to providing further guidance.

A recent high-risk exposure (within 72 hours)

A course of post-exposure prophylaxis (PEP) may be required if a patient had a recent high-risk exposure (within 72 hours), and PrEP adherence was suboptimal. PEP may need to consist of a

three-drug regimen, depending on the nature of the exposure. See *Chapter 9: HIV post-exposure prophylaxis* for management of such cases.

Monitoring of renal function

Renal function should be monitored at 3 months and 6-monthly thereafter. More intensive monitoring may be warranted in certain populations (see also 'Assessment of renal function at baseline' in Chapter 5: Clinical assessment before starting PrEP):

- those over the age of 40 years
- those with a baseline eGFR of less than 90 mL/min/1.73 m^2
- those with other comorbidities (e.g., hypertension, diabetes)
- those taking nephrotoxic drugs.

A small decline in eGFR while using PrEP is not uncommon; further investigations and consideration of a referral to a specialist renal service are recommended when there is sustained decrease in eGFR of 25% or more or a sustained decrease in eGFR of 15 mL/ min/1.73 m^2. Exceptional dietary intake (e.g., vegetarian diet, high protein diet), creatinine supplements, and extremes of body size (e.g., high muscle mass) may underestimate eGFR.

PrEP is contraindicated if eGFR <60 mL/min/1.73m^2. The management of people with high and ongoing risk of HIV infection, but whose eGFR has declined below or around 60 mL/min/1.73 m^2 since commencing TD*/FTC, is challenging. This situation typically requires consultation with a physician who is expert in PrEP. Cessation of TD*/FTC for 1 month may restore eGFR to above 60 mL/min/1.73 m^2, following which TD*/FTC may be recommenced with cautious monitoring. In these circumstances, consideration should be given to using event-driven TD*/FTC, although there are no data to show that this will stabilise the eGFR above 60 mL/min/1.73 m^2.

Testing for STIs

As PrEP-users are at increased risk for STIs,[6] clinicians should screen for STIs (specifically gonorrhoea, chlamydia and infectious syphilis) every 3 months using the standard-of-care tests and procedures, and manage any detected STI as recommended by the Aotearoa New Zealand STI Management Guidelines for use in Primary Care.[1] Partner notification should be undertaken using the most appropriate available resources.

It is important to note that for MSM, STI tests must include a first void urine (vaginal swab if relevant), throat swab and anal swab for chlamydia and gonorrhoea.

At each follow-up visit, patients taking PrEP should be reminded about:

- prevention of STI acquisition and transmission
- the need for quarterly STI testing
- the need to present for testing and treatment whenever signs or symptoms of an STI appear.

The presence of an STI at follow-up testing does not prevent the ongoing prescription of PrEP.

Hepatitis B and hepatitis C virus infections

Hepatitis B virus

For people who are hepatitis B virus (HBV) non-immune at baseline, clinicians should provide hepatitis B vaccination and confirm their immune response 1 month after the last vaccine dose.

For people who state that they have been vaccinated for hepatitis B at baseline, clinicians should test for hepatitis B surface antibody; if their hepatitis B surface antibody is below 10 IU/mL, they should be vaccinated with one dose of hepatitis B vaccine and their hepatitis B surface antibody titre should be checked 1 month later. If their titre does not rise above 10 IU/mL, their hepatitis B vaccination should then be completed.

Both TD* and FTC are active against HBV.[7] If people living with chronic HBV infection stop taking these medications, severe hepatic flares can occur.[7] Patients with chronic HBV need to be counselled regarding the risks of poor adherence and the risks of self-ceasing PrEP medication. Advice should be sought from a liver specialist before commencing PrEP, for patients who are known to have chronic HBV. A person taking PrEP who has chronic HBV infection should be assessed by a clinician experienced in the management of hepatitis B before ceasing PrEP. If PrEP is discontinued, close monitoring is strongly advised.

Only daily PrEP should be offered to people with chronic HBV. For additional guidance about the management of PrEP in people with chronic hepatitis B, see *Chapter 8: Special clinical considerations*.

Hepatitis C virus

In contrast to hepatitis B, the risk of sexual transmission of hepatitis C virus (HCV) has been considered low. However, HCV infection thought to be sexually transmitted began to emerge in predominantly HIV-positive MSM in the early 2000s.[8-12] Subsequent studies suggest that sexual transmission of HCV also occurs in HIV-negative MSM eligible for or using PrEP.[13-15] The incidence of HCV infection is lower in countries with widespread uptake of HCV direct-acting antiviral therapy.[14,16] HCV infection is associated with high-risk sexual behaviour, including receptive condomless anal intercourse, unprotected fisting, sharing of toys, chemsex and group sex, as well as an association with recent STIs.[8, 17-18]

All people who inject drugs should be monitored for hepatitis C virus (HCV), as should MSM, trans and non-binary people who engage in sexual contact that may predispose to anal trauma.

In those using PrEP, HCV should be tested at least annually, and more frequently if necessary, following sexual history-taking and review of injecting practices.[19]

Managing side-effects

Patients taking PrEP should be assessed for side-effects associated with TD*/FTC use, most importantly those suggesting possible acute renal injury. A review of symptoms experienced in the iPrEx (Iniciativa Profilaxis Pre-Exposición) study showed that potential PrEP-associated symptoms peaked at 1 month, when 39% of participants reported symptoms, compared with 22% at baseline. Gastrointestinal symptoms occurred in a median of 28% of participants across study sites (range 11–70%) and non-gastrointestinal symptoms occurred in a median of 24% of participants (range 3–59%). The odds of gastrointestinal symptoms were higher in those with evidence of high adherence to PrEP. By 3 months, symptoms had returned to pre-PrEP levels.[20]

Bodybuilding increases muscle mass, which may result in increased creatinine levels in blood. When evaluating and managing PrEP-users with creatinine clearance changes, clinicians should take into consideration the history of steroid, protein, creatine powder use (which also increases blood creatinine levels) and bodybuilding. A wash-out period of 14 days cessation of creatine before renal function assessment may be recommended.

The NZ PrEP and PEP Guidelines panel will monitor evidence in this area and update the guidelines as appropriate.

Optional assessments

Therapeutic drug monitoring

Initial demonstration projects in Australia conducted therapeutic drug monitoring as part of research protocols to evaluate medication adherence and HIV seroconversions among study participants. Their results revealed a high correlation between self-reports of tablet taking and blood concentrations of TD* and FTC, and high adherence to PrEP (over 90%).[21,22] In NZ there are no clinical laboratories that quantify TD*/FTC concentrations in plasma, cells or urine for therapeutic drug monitoring in the setting of PrEP. Therapeutic drug monitoring is likely to be used primarily for research and possibly for evaluations of people who acquire HIV infection while taking PrEP.

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8. Special clinical considerations

This chapter provides information about relevant patient groups in Aotearoa New Zealand, including Māori, people ineligible for publicly funded healthcare, transgender people, those who are pregnant, people who have chronic HBV or renal failure, and adolescent minors.

Māori

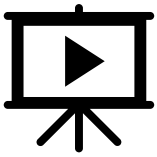
Māori health inequities are extensive and exist across multiple health indicators. These include the social determinants of health, access to health and healthcare, the quality of healthcare provision, and, in turn, the health outcomes Māori experience compared with the rest of the population.[1] Inequities in healthcare are not acceptable, and it is critical that inequities in PrEP and PEP provision are eliminated.

A study of unrecognised HIV in 2011 found Māori MSM had the same HIV prevalence as non-Māori MSM, although proportionately less of that was diagnosed.[2] Additionally, community studies suggest Māori MSM are less likely to have ever tested for HIV,[3] and may engage in more condomless casual sex.[4] MSM of Māori, Pacific, Asian and the combined group of MELAA (Middle Eastern, Latin American and African) ethnicities were more likely to present late, and to have advanced HIV disease (except for MELAA), compared to those of European ethnicity.[5]

There are limited data about pre-exposure prophylaxis (PrEP) use among Māori men who have sex with men (MSM). An Auckland demonstration project of early PrEP adopters found that at enrolment, Māori reported similar rates of condomless receptive anal intercourse and rectal sexually transmitted infections (STIs) as that of Europeans.[6] The 12-month follow-up data from this demonstration project showed proportionately lower study retention and medication adherence among Māori/Pacific participants, compared with non-Māori/Pacific participants.[7] These results are consistent with US findings on minority groups where Black MSM also had poorer engagement with PrEP services.[8] An evaluation of the *Ending HIV* campaign by Burnett Foundation Aotearoa found Māori MSM less likely than non-Māori MSM to self-report PrEP use in the previous 6 months.[9] Overall, the data imply that PrEP is needed by Māori MSM, but they will face proportionately greater barriers accessing PrEP when delivered through existing health services.

The Aotearoa Statement on closing the gap on STIs and blood borne viruses (BBVs) among indigenous peoples of Australasia (www.nzshs.org/events/the-aotearoa-statement) is an important framework to use to plan responses to Māori sexual health needs. This statement recommends that interventions will be most effective when led by or co-designed with Māori. Furthermore, all tangata whenua (people of the land) are entitled to equitable access to the healthcare that meets their needs. To optimise HIV prevention and PrEP use, clinicians need to actively ensure they are providing culturally safe care for their Māori patients. This prerequisite starts with understanding any unconscious biases and acknowledging that different health outcomes for Māori cannot be explained by genetics or behaviour but are in fact the result of structural barriers and socio-cultural factors stemming from colonisation and racism.[10] This understanding should inform a clinician's approach to providing care for Māori patients (see Box 8.1).

Box 8.1 Useful resources



Developing Māori Health Equity Capability among Health Professionals from 'competence' to 'safety'

Professor Papaarangi Reid, Associate Professor Rhys Jones and Associate Professor Elana Curtis

Dealing with Diversity, The Profession and in Practice

Professor Papaarangi Reid

Cultural Safety Training Plan for Vocational Medicine in Aotearoa[11]

A plan for cultural safety training that can be used by medical colleges in the development of their own cultural safety training programmes for registrars and fellows.

Clinicians should initiate conversations with Māori MSM to discuss PrEP, and whether they would benefit from its use. Clinicians should not hesitate, where more convenient for the patient, and with the patient's consent, to refer to a public sexual health clinic that offers free services and comprehensive care.

Clinicians should be sensitive when taking a sexual behaviour history, bearing in mind that Māori MSM, like other MSM, may not feel comfortable discussing sexual history. If Māori MSM request PrEP without disclosing full sexual history, clinicians should acknowledge that the conversation might be uncomfortable for the patient and manage the situation rather than simply declining PrEP. Laboratory evaluations should not delay the provision of a script for PrEP; scripts can be provided on the first visit with laboratory results followed up separately. To maximise retention, services should be designed to be easily accessible and minimise the need for multiple visits.

There are large ethnic disparities in chronic hepatitis B virus (HBV) infection. Recent data suggest that 6% of Māori, 7% of Pasifika and 8-9% of people with Chinese or South Asian ethnicity have chronic HBV compared to less than 1% of those with European or Indian ethnicity.[12] Given the higher rates of chronic HBV infection among Māori, clinicians caring for Māori MSM must carefully follow these PrEP guidelines and screen for HBV and, as required, provide HBV vaccinations. Note that people with chronic HBV should only be offered daily PrEP to maintain sustained virological suppression of HBV.

People ineligible for publicly funded PrEP, including newly arrived migrant MSM

Little is known about PrEP use among migrant MSM newly arrived in NZ. The overall number of MSM reported to have HIV infection in NZ has declined since the peak in 2016. In 2022, 35 (44%) of 80 MSM notified with HIV in NZ had previously been diagnosed overseas. Nine of the 45 MSM first diagnosed in NZ were reported to have acquired HIV overseas, which was similar to the number in the previous 2 years, but a decline from the annual average of 26 over the 5 years from 2015 to 2019. Of the 45 MSM diagnosed in NZ in 2022, 19 (42%) were European, 13 (29%) Asian, six (13%) Māori, four (9%) Latin American or African ethnicity and three (7%) were Pacific Peoples. For three (7%) men, although diagnosed in NZ, their usual place of residence was overseas.[13] Of the 45 MSM diagnosed in NZ in 2022, 34 were NZ citizens or permanent residents, 6 were international students or temporary workers, and the migration status of 5 was unknown.[14]

People who come to NZ to study or work (with a work visa of less than 2 years' duration) are in most cases ineligible for publicly funded healthcare.[15] International students are often required to have overseas student health insurance; however, the coverage for sexual health needs is typically limited. Additionally, some students are reluctant to use their private health cover for sexual health testing, prevention and treatment because of concerns about privacy or a prospective immigration process.

People who are ineligible for publicly funded healthcare can pay the full, unsubsidised amount for a private script for PrEP (around NZ$30 per month depending on pharmacy mark-up, 2023); however, the costs for medical appointments and laboratory testing can be prohibitive. Clinicians should be aware of the most cost-effective options available in their regions, and direct patients to these accordingly.

More information can be found in *Chapter 12: How to access PrEP in Aotearoa New Zealand*.

Transgender women

Globally, transgender women have a high prevalence of HIV infection compared to cisgender men and women.[16] Transgender women have represented less than 1% of study participants in PrEP trials[17] and face additional barriers to accessing PrEP compared with MSM, requiring differentiated PrEP implementation strategies.[18]

There are limited local data on transgender and non-binary people and HIV in Aotearoa New Zealand;[13] however, incidence appears to be low in contrast to many other areas of the world. The most vulnerable parts of the transgender and non-binary community in NZ are likely to be people whose sexual networks include MSM.

The Iniciativa Profilaxis Pre-Exposición (iPrEX) clinical trial enrolled the highest number of transgender women to date and found that, compared to MSM, transgender women were more likely to report transactional sex, condomless anal intercourse and more recent sexual partners.[19] In iPrEX, no HIV infections were observed in transgender women whose blood levels were compatible with taking 4 or more doses of PrEP weekly. However, using stratified analyses, PrEP did not provide a benefit for transgender women in the iPrEX study (hazard ratio 1.1, 95% CI: 0.5 to 2.7) compared to the overall 44% reduced HIV incidence in the active study arm.[19]

A recent retrospective analysis of the iPrEX study sought to determine whether the differential efficacy of PrEP in MSM versus transgender women was a result of different baseline clinical and behavioural factors that could make PrEP less efficacious in transgender women.[20] The authors found that baseline characteristics between MSM and transgender women explained almost 100% of the difference in PrEP's efficacy during the iPrEX study. However, the authors were not able to comment on whether the use of gender-affirming hormone therapy may have contributed to PrEP's being less effective in the transgender women study participants.[20]

Oestrogen, which is used as part of gender-affirming hormone therapy, increases the activity of 5'-nucleotidase enzymes and can decrease the active metabolites of tenofovir and emtricitabine, or increase the nucleotides that compete against the active metabolites of tenofovir and emtricitabine within cells. Therefore, oestrogen could plausibly reduce cellular levels of tenofovir and emtricitabine in transgender women, making PrEP less efficacious. There have been some small studies in transgender women taking gender-affirming hormone therapy and PrEP. One study of 20 Thai transgender women commencing gender-affirming hormone therapy and PrEP

showed a 12% reduction in plasma tenofovir levels in the presence of gender-affirming hormone therapy,[21] although PrEP did not reduce oestrogen levels.

In another study, 32% lower levels of plasma tenofovir were observed in eight transgender women taking gender-affirming hormone therapy compared to eight cisgender men; plasma emtricitabine was also significantly lower in the transgender study participants.[22] These findings are not consistent; a 2022 Brazilian study suggested that PK parameters of tenofovir and emtricitabine for daily oral PrEP are not significantly affected by oestradiol-based feminising hormone therapy.[23] A study of 24 transgender women using oestradiol-based hormone therapy showed that TDF concentrations in dried blood spots after 4 weeks of directly observed daily TD*/FTC PrEP use were comparable to those in cisgender men.[24] A further study compared the rectal tissue levels of the active metabolites of tenofovir and emtricitabine in 4 HIV-positive transgender women taking gender-affirming hormone therapy versus 4 HIV-positive post-menopausal cisgender women. This study reported that there was a significantly lower ratio of the active metabolite of tenofovir diphosphate to its competing nucleotide dATP in the rectal tissue of the transgender versus cisgender participants.[25] However, this study did not find a decrease in the ratio of the active metabolite emtricitabine triphosphate to its competing nucleotide, dCTP.

While PrEP does not appear to impact on gender-affirming hormone levels, lower PrEP levels have been associated with feminising hormone therapy in some studies. This is not thought to impact on the efficacy of daily PrEP; however, raises concerns about the potential efficacy of event-driven PrEP in this population. Event-driven PrEP is therefore not currently recommended for trans women using gender-affirming hormone therapy, as more data are required.

To help support transgender women to optimise their PrEP use and adherence, it is recommended that health practitioners provide gender-affirming care.[24] Such clinical care includes appropriate use of preferred pronouns and names, safe access to bathrooms of choice and access to gender-affirming hormone therapy and surgery.[26]

Transgender men

There are very few data regarding PrEP knowledge, acceptability and use in transgender men. In a 2017 study of 181 transgender youth from the USA, of 42 people identifying as transgender men (23.2%), only 16 had ever used HIV prevention services and none had ever used PrEP.[27] Transgender men were significantly less likely to have ever used PrEP than transgender women.[27]

To optimise HIV prevention and PrEP use, clinicians caring for transgender men need to actively raise PrEP as an HIV prevention option for them and take a sensitive and detailed sexual behaviour history. Gender-affirming care should be provided to transgender men by health practitioners (see Box 8.2).

Box 8.2 Useful resources for gender-affirming care

Useful resources for gender-affirming care

Social stigmatisation and discrimination, including within the healthcare system, is a barrier to accessing health services and contributes to adverse outcomes. Transgender people have the right to respectful health care.[28]

Clinicians should take steps to create a welcoming environment for their trans and gender-diverse patients. This approach includes considering the clinical environment, using the right language, asking the right questions and sensitively recording medical notes. Some helpful resources for clinicians are:

- Professional Association for Transgender Health Aotearoa https://patha.nz
- Pride in Health https://prideinhealth.org.nz
- Trans Hub www.transhub.org.au/clinicians
- Gender Minorities Aotearoa https://genderminorities.com/database/medical-surgical/providers/
- Primary Care Gender Affirming Hormone Therapy Initiation Guidelines https://patha.nz.resources/Documents/Primary-Care-GAHT-Guidelines_Web_29-Mar.pdf.
- Rainbow Mental Health http://rainbowmentalhealth.nz/
- Trans and gender diverse language guide https://www.acon.org.au/wp-content/uploads/2019/07/TGD_Language-Guide.pdf

People taking PrEP during conception, pregnancy and breastfeeding whose partners are not virologically suppressed

Conception in serodiscordant couples

People without HIV infection who have sexual partners with documented HIV infection are at risk of HIV acquisition during natural attempts to conceive (i.e., without a condom) if their HIV-positive partner has a detectable or variably detectable plasma viral load. Providers should discuss with their patients the available information about the potential risks and benefits of PrEP in these circumstances.[29] For people wanting to conceive where their HIV-positive partner is stably virologically suppressed on combination antiretroviral therapy (cART), PrEP can still be offered to the patient if they express concerns about the risk of acquiring HIV in this setting. In this case, the patient may need to self-fund PrEP.

Pregnancy

The risk of acquiring HIV increases by approximately two-fold during pregnancy.[30] In addition, if HIV infection is acquired during pregnancy, there is a higher risk of HIV transmission to the infant than if the pregnancy occurred during chronic HIV infection because the HIV viral load is much higher during acute HIV infection.

The current evidence suggests that PrEP can be used safely during pregnancy and breastfeeding.[31]

The use of TD*-containing regimens by HIV-positive cis-women throughout pregnancy has not been associated with adverse pregnancy outcomes, but lowered bone mineral density (BMD) has been observed in the first month of life in newborns exposed to TD* in utero,[32] as has a lower length and head circumference at 1 year of age.[33]

A systematic review of 26 studies involving TDF and FTC exposure during pregnancy did not identify safety concerns that would limit the use of PrEP in pregnant or lactating women at

continuing risk of HIV acquisition.[34] An additional systematic review in 2020 looked at five completed studies, with data from 1042 TDF/FTC PrEP-exposed pregnancies.[35] One study found that PrEP-exposed infants had slightly lower adjusted mean z-scores for length and head circumference at 1 month of age; however, they were comparable to PrEP-unexposed infants in these measurements 1 year after birth.[36] The remainder of the studies did not observe differences in pregnancy or perinatal outcomes associated with TDF/FTC exposure.

The World Health Organization has included PrEP as an HIV-prevention strategy during pregnancy[37] and a number of other jurisdictions recommend PrEP for safe conception and for use during pregnancy and breastfeeding.[38]

Some people with HIV-positive partners may prefer to continue PrEP while pregnant, due to the increased risk of acquisition of HIV if their partners are not virologically suppressed during pregnancy.[38]

Providers should discuss with their patients available information on potential adverse pregnancy outcomes when beginning or continuing PrEP during pregnancy so that they can make an informed decision. TD*/FTC is classified as category B3 by the NZ Medicines and Medical Devices Safety Authority, Medsafe.[39]

The consensus of the NZ PrEP and PEP Guidelines panel is that PrEP may be continued during pregnancy in people at risk for HIV acquisition.

Breastfeeding

Although experience with PrEP during breastfeeding is lacking, there is substantial experience with the use of TD*/FTC during the breastfeeding period by HIV-positive cis-women taking TD*/FTC-based antiretroviral therapy. TD* and FTC are secreted in breast milk, although at much lower concentrations (0.03% and 2%, respectively) than the levels achieved with the doses recommended for the treatment of infants with HIV infection.[40] In the PrEP setting, a study evaluating antiretroviral excretion in breast milk and infant absorption suggests PrEP can be safely used during breastfeeding with minimal infant drug exposure.[41]

If a person acquires HIV infection while breastfeeding, the risk of transmission to the infant is higher than in an established infection, because of high viral load soon after seroconversion. Therefore, PrEP can be continued during breastfeeding in people at risk of HIV acquisition.

Patients with chronic active HBV infection

Both TD* and FTC are active against HIV and hepatitis B virus (HBV) infections. They may prevent the development of significant liver disease by suppressing HBV replication. Only TD*, however, is currently approved for this use in NZ. Therefore, ongoing treatment with TD*/FTC may be especially indicated in people with active HBV infection who are also at risk of HIV acquisition.

Of note, there are two case reports of patients who were receiving TD* for treatment of hepatitis B and who acquired HIV infection.[42] Plasma levels of tenofovir and prescription refills suggested that the patients' medication adherence was good. It is recommended that people with established hepatitis B infection who require treatment for hepatitis B infection receive combined TD*/FTC and have ongoing monitoring for HIV, PrEP and hepatitis B infection.

All people who test positive for hepatitis B surface antigen (HBsAg) should be evaluated by a clinician experienced in the treatment of HBV infection. For clinicians without this experience, co-management with an infectious diseases or liver specialist is recommended.

People living with chronic HBV infection should be tested for HBV DNA by the use of a quantitative assay to determine the level of HBV replication before PrEP is prescribed, and at regular intervals (e.g., every 3–6 months) while taking PrEP.[43] TD* presents a very high barrier to the development of HBV resistance. However, it is important to reinforce the need for consistent adherence to the daily doses of TD*/FTC to prevent re-activation of HBV infection with the attendant risk of hepatic injury, and to minimise the possible risk of developing TD*-resistant HBV infection.[44] For these reasons, event-driven PrEP is contraindicated in patients with chronic hepatitis B infection.

If PrEP is no longer needed to prevent HIV infection in a patient with chronic hepatitis B, a separate determination should be made about whether the patient requires ongoing treatment for HBV infection. Acute flares resulting from the re-activation of HBV infection have been seen in those with and without HIV infection after stopping TD* and other medications used to treat HBV infection. When people living with chronic hepatitis B elect to discontinue PrEP, they should first be evaluated by a clinician experienced in the management of HBV infection to ascertain their need for ongoing HBV treatment, and to monitor for any hepatic flares that occur if PrEP is ceased.

Patients with chronic renal failure

Patients without HIV infection and with established chronic renal failure, e.g., with estimated glomerular filtration rate (eGFR) that is consistently less than 60 mL/min/1.73 m^2 should not be prescribed PrEP. The only PrEP regimen proven effective to date and available in NZ is TD*/FTC, which is not indicated for those with chronic renal failure.[39] However, if a patient with chronic renal failure is at substantial risk of HIV, their condition should be discussed with specialists in the management of HIV and renal disease.

Adolescent minors

As a part of primary health care, HIV screening should be discussed with all adolescents who are sexually active or have a history of injecting drug use. Parental or guardian involvement in an adolescent's healthcare is often desirable but is sometimes contraindicated for the safety of the adolescent, and can compromise full disclosure.

Clinicians should carefully consider the data discussed below on the safety and efficacy of daily PrEP taken by persons under 18 years of age, including the possibility of bone mineral density loss, and other toxicities among youth who are still growing. Data are also available about the safety of TD*/FTC when used in treatment regimens for young people with HIV infection.[45] The clinician and the patient may conclude that the short-term, proximal risk of acquiring HIV infection greatly outweighs any short-term, or as yet undetermined, long-term risk of PrEP toxicity. Clinicians are encouraged to seek expert advice in complex situations.

Adherence to PrEP in adolescents may be suboptimal: a PrEP demonstration programme involving daily PrEP use for 18- to 22-year-old HIV-negative MSM reported that tenofovir diphosphate intracellular levels, a marker of cumulative TD* adherence, were consistent with good adherence peaking at 56% at 1 month, but declining thereafter.[46] In another open-label, 48-week

study of 78 adolescent MSM commencing PrEP, Project PrEPare, highly protective levels of PrEP were observed in 54% of adolescents at week 4 but declined thereafter.[47] Following this finding that PrEP levels declined markedly in these adolescent participants after the week 4 visit, the authors recommended that adolescents should be offered more frequent clinical monitoring to enhance their PrEP adherence.

The NZ PrEP and PEP Guidelines panel endorses this approach and encourages clinicians to work with adolescents taking PrEP to develop strategies to optimise adherence.

In the Project PrEPare study, there was no observed elevation in serum creatinine levels and significant increases were observed in bone mineral density for the spine, hip and total body between baseline and week 48. However, there was a slight but statistically significant decline in the total body z-score during this time, suggesting that bone growth may have been suboptimal in the study participants.[47] Although not observed in this study, higher levels of PrEP adherence as measured by red blood cells levels of tenofovir diphosphate have been associated with lower hip bone mineral density in adolescents.[48] Further research is needed to determine whether there is a long-term increased risk of bone fractures in young MSM who have had PrEP.

Globally until recently, regulatory approval of Truvada [tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC)] PrEP was limited to adults over 18 years of age. However, on 15 May 2018, the US Food and Drug Administration (FDA), based on data from the Project PrEPare study discussed above, expanded its approval of Truvada as PrEP against HIV to include adolescents at-risk, weighing at least 35kg.

PrEP use for prevention of HIV in adolescents has not been approved by Medsafe.[39] However, clinicians are able to prescribe PrEP off-label for adolescents. In this setting, a decision to prescribe PrEP for a person under 18 years of age should be made at the discretion of the prescriber and on the advice of a specialist. The prescriber is responsible for obtaining and documenting informed consent from their patient. Informed consent should take into account the risks and benefits of that treatment versus other available treatments or no treatment at all, based on the individual circumstances.

Adolescents may obtain publicly funded PrEP with an off-label prescription, provided they meet the PHARMAC criteria.

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9. HIV post-exposure prophylaxis

The criteria for post-exposure prophylaxis (PEP) prescribing were widened in Aotearoa New Zealand in July 2022. PEP can now be prescribed by any relevant prescriber, including general practitioners and nurse practitioners.

This chapter outlines the management of individuals who have been exposed (or suspect they have been exposed) to HIV in non-occupational and occupational settings. It is adapted from the Australian *National Guidelines on post-exposure prophylaxis after non-occupational and occupational exposure to HIV (2nd ed.)*.[1]

There are currently no data from randomised controlled trials on the use of post-exposure prophylaxis (PEP) and evidence for use has been extrapolated from animal data, perinatal transmission, occupational exposure and small prospective studies of PEP regimens in HIV-negative men. Accordingly, assumptions are made about the direction of management.

People not receiving human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP) who seek care within 72 hours after an isolated sexual, injection-related or occupational HIV exposure should be evaluated for the need for post-exposure prophylaxis (PEP). PEP may also be considered where a person receiving PrEP reports poor adherence and seeks care within 72 hours after an HIV exposure.

The clinician should take a history to differentiate isolated exposures from ongoing exposure. If potential HIV exposure is likely to be ongoing, the client should be offered transition to PrEP after completion of the 28-day PEP course.

Before you begin

The experience of presenting for PEP can be stressful in itself. Research has documented cases where people stated they did not re-present for PEP due to a previous negative experience and then later seroconverted.[2] Therefore, it is important that clinicians respond to each presentation in a non-judgemental way, using non-stigmatising language, and facilitating whānau support where requested.

To be effective, initiation of PEP needs to occur within 72 hours of the exposure; however, the earlier the better and within 24 hours is recommended. It is therefore important that PEP is easily accessible to those who need it. PEP has traditionally been available from sexual health clinics and emergency departments. With widening of prescribing criteria, PEP can now be prescribed by GPs and other relevant practitioners, increasing the options available for a patient. Training for staff should include the necessity to triage, assess and treat these patients with the appropriate priority.

Assessment of the risk of HIV transmission

The risk of HIV transmission through a single exposure is determined by:

- The nature of the exposure with its estimated risk (Table 9.1)
- The risk that the source is HIV-positive, if their status is unknown (Table 9.2)
- Factors associated with the source and exposed individuals.

Risk of HIV transmission

= *risk per exposure* **x** *risk of source being HIV-positive*

Many factors modify the risk of HIV transmission and should be considered in the risk assessment.

Viral load (VL):

- Higher plasma VL is associated with increased risk of HIV transmission.[3]
- People who take antiretroviral therapy for HIV daily as prescribed, and who have achieved and maintained an undetectable viral load for at least 6 months, cannot sexually transmit the virus to an HIV-negative partner. This is known as U=U (undetectable = untransmissible).[4] An undetectable viral load is likely to significantly reduce the risk of percutaneous transmission; however, the risk of *percutaneous* transmission with an undetectable viral load has not been studied, so U=U only applies for *sexual* exposures.
- Undetectable viral load is defined in these guidelines as less than 200 copies/mL.

Other factors that increase the risk of HIV transmission:

- a sexually transmitted infection (STI) in the source or exposed individual, especially genital ulcer disease and symptomatic gonococcal infections
- source ejaculation during receptive anal or vaginal intercourse
- a breach in genital mucosal integrity (e.g., trauma, genital piercing or genital tract infection)
- a breach in oral mucosal integrity when performing oral sex
- penetrating, percutaneous injuries with a hollow bore needle, direct intravenous or intra-arterial injection with a needle or syringe containing HIV-infected blood
- the uncircumcised status of the HIV-negative exposed individual practising insertive anal intercourse (IAI) or insertive vaginal intercourse (IVI).

PEP is recommended where the risk of transmission can be calculated to be greater than 1/1000. Exposed persons who meet this threshold should be informed of their risk and recommended PEP. Exposed persons who have a risk of between 1/1000 and 1/10,000 may wish to consider PEP, particularly if there are additional circumstances suggesting increased risk or if the risk is close to 1/1000. Most exposed persons who present requesting PEP will fall into this category of risk.

Exposed persons with a risk of transmission less than 1/10,000 should be informed that their risk is low and advised that the harms of PEP outweigh the potential benefits. Hence, PEP is not recommended for them and should not be offered. **Where individuals have multiple exposures within 72 hours a cumulative risk should be considered.**

Immediate management of an individual with known or suspected exposure to HIV

- After oral exposure, spit out blood/body fluids and rinse mouth with water.
- Wash wounds and skin sites that have been in contact with blood or body fluids with soap and water.
- Irrigate mucous membranes and eyes (remove contact lenses) with water or saline.
- Do not inject antiseptics or disinfectants into wounds.
- Do not douche the vagina or rectum after sexual exposure.

Clinical assessment

In making a clinical assessment, health practitioners should consider the gender, culture, language and literacy level of the patient, and their intellectual capacity. The following details should be discussed and documented in the patient's history.

1. Information about the exposure

- Date and time of exposure
- Type of exposure, including blood or body fluids involved, trauma, first aid measures applied and any contributory factors.

Table 9.1 Exposure and transmission risk/exposure with known HIV-positive source who is NOT on antiretroviral treatment

Type of exposure with known HIV-positive source who is NOT on antiretroviral treatment	Estimated risk of HIV transmission/exposure*
Receptive anal intercourse (RAI) – ejaculation	1/70[5]
– withdrawal	1/155[5]
Shared needles and other injecting equipment	1/158[6]
Insertive anal intercourse (IAI) uncircumcised	1/160[5]
Insertive anal intercourse (IAI) circumcised	1/900[5]
Receptive vaginal intercourse (RVI) **	1/1250[7]
Insertive vaginal intercourse (IVI)	1/2500[7]
Receptive or insertive oral intercourse	Unable to estimate risk – extremely low (<1/10,000)[8]
Needlestick injury (NSI) or other sharps exposure	1/440[6]
Mucous membrane and non-intact skin exposure †	< 1/1000

Notes: All sexual risk estimations are for condomless sexual contact. It is assumed that a similar risk is incurred when a condom fails.

* These estimates do not take into account source viral load.

** While not quantifiable, the risk is likely to be higher in trans and non-binary individuals using testosterone, due to atrophic changes of the vaginal epithelium. The risk of HIV transmission for receptive vaginal intercourse in individuals with a neovagina is unknown, and is likely to be affected by surgical construction method.

† Human bites are extremely low risk.

2. Information about the exposed person

- Most recent HIV test and result
- Potential exposures within the last 3 months (or earlier if last HIV test longer than 3 months ago)
- Previous use of PEP or PrEP
- Evaluation of current STIs
- Pregnancy risk, contraception and lactation (consider emergency contraception)
- Medical history, in particular Hepatitis B (HBV) and Hepatitis C (HCV) infection, renal disease, psychiatric history
- Medication history, including drug allergies
- Drug and alcohol history.

If potential HIV exposure is likely to be ongoing, the client should be offered transition to PrEP after completion of the 28-day PEP course.

If a patient is known to be HBV- or HCV-positive, advice from a liver, sexual health or infectious diseases specialist should be sought before PEP is commenced.

3. Information about the source person

- HIV status if known
- Demographics factors, e.g., gender, country of origin

It is useful to contact the source to establish exposure risk. In practice, this is often not possible in cases of non-occupational exposure. **Provision of PEP should not be delayed while attempting to obtain this information.**

If the source cannot be contacted, or chooses not to disclose their HIV status or have an HIV test, the seroprevalence data (see Table 9.2) will assist in determining the need for PEP.

If the source is contactable:

- If the source discloses they are HIV-positive, consent should be gained to seek treatment details from their doctor. It is useful to know if they are on treatment or not, and if their viral load is undetectable, as well as any known drug resistance.
- If the source is taking PrEP (pre-exposure prophylaxis), PEP is generally not required. Decisions to prescribe PEP should still be considered on a case-by-case basis due to potential for non-adherence of the source.
- Check hepatitis B and C status of source, and current STIs.

Table 9.2 HIV prevalence in Aotearoa New Zealand

Source population group*	Prevalence (per 1000)
Heterosexual men **	1.2 (0.12%)[9]
Heterosexual women **	1.4 (0.14%)[9]
Men who have sex with men (MSM)	65 (6.5%)[10]
MSM at sex-on-site venues	105 (10.5%)[10]
Injecting drug users:	
· Needle exchange attendees	~10 (~1%)[11]
· MSM (past/recent injecting drug use)	(14.0/24.2%)[12]

Notes: *Data are for cisgender (not transgender) population groups. There are limited local data on transgender and non-binary people and HIV in Aotearoa New Zealand;[13] however, incidence appears to be low in contrast to many other areas of the world. The most vulnerable parts of the transgender and non-binary community in NZ are likely to be people whose sexual networks include MSM.

** Based on data from sexual health clinic attendees, which is likely to be an over-estimate of the prevalence in the general population. As a comparison, the prevalence of HIV in NZ blood donors is 2.6/100,000 population.[14]

Globally, sex workers are disproportionately affected by HIV; however, rates in NZ are very low. A study of HIV prevalence in sexual health clinics over a 12-month period in 2005-2006 found no HIV cases, diagnosed or undiagnosed, among current sex workers.[10] Among 358 sex workers attending an Auckland Sexual Health Service outreach clinic between 2018-2020, only one person (on treatment and undetectable) was living with HIV.[15]

The majority of people living with HIV in NZ are aware of their diagnosis, and most are using antiretroviral therapy. Most of those using antiretroviral therapy are undetectable.[16] People who take antiretroviral therapy for HIV daily as prescribed, and who have achieved and maintained an undetectable viral load for at least 6 months, cannot sexually transmit the virus to an HIV-negative partner (U=U).[4]

An undetectable viral load is likely to significantly reduce the risk of percutaneous transmission; however, the risk of *percutaneous* transmission with an undetectable viral load has not been studied, so U=U only applies for *sexual* exposures.

HIV seroprevalence in overseas populations: The seroprevalence overseas varies widely, with a High Prevalence Country (HPC) being defined as having a prevalence of >1% in the general population. However, variance is not only between countries but also in different risk groups. The highest global seroprevalence is in Eswatini (26.8%), with a prevalence of 60.8% among sex workers in that country.[17] For seroprevalence for individual countries, go to https://www.cia.gov/the-world-factbook/about/archives/2021/field/hiv-aids-adult-prevalence-rate/country-comparison.

4. PEP recommendations

PEP consists of a 28-day course of antiretroviral therapy, either two-drug or three-drug treatment, as recommended in Table 9.3.

Two-drug regimen:

Co-formulated Tenofovir disoproxil* 245mg with emtricitabine 200mg (One tablet once daily)

Three-drug regimen:

Co-formulated Tenofovir disoproxil* 245mg with emtricitabine 200mg (One tablet once daily)

PLUS

Dolutegravir 50mg (once daily)

There is no direct evidence to support the greater or lesser efficacy of three- over two-drug preventative regimens. The main factor affecting efficacy appears to be starting PEP as early as possible after exposure (ideally within 24 hours). Any possible benefit conferred by the addition of a third drug must also take into account potential side-effects, toxicity, adherence and cost-effectiveness.

Situations where there is uncertainty or complexity, such as known or suspected antiretroviral resistance in the source, pregnancy, renal impairment, drug interactions, breastfeeding or chronic hepatitis B or C, should be discussed with an infectious diseases or sexual health physician.

If potential HIV exposure is likely to be ongoing, the client should be offered transition to PrEP after completion of the 28-day PEP course, assuming that the HIV test remains negative.

Where PEP is recommended, it should be prescribed and started as soon as possible after the exposure *and within 72 hours (ideally within 24 hours)*

Occupational HIV transmission is rare. There has only been one confirmed case of occupational HIV transmission in the United States since 1999[19] and no cases in the UK over the same time period.[20] This may be due to a number of factors, including change in practices to reduce the risk of needlestick injury and a greater proportion of patients on treatment with undetectable viral load.

Table 9.3 PEP recommendations

NB: Decisions to follow these recommendations must be based on the professional judgment of the clinician and consideration of individual patient circumstances.

	Source known HIV-positive		Source of unknown HIV status	
	HIV VL unknown or detectable	HIV VL undetectable	Source known to be MSM or from high-prevalence country[18]	Source from other (low-prevalence) population
Sexual exposure				
Receptive anal sex	3 drug	Not recommended	2 drug	Not recommended
Insertive anal sex uncircumcised	3 drug	Not recommended	Consider 2 drug	Not recommended
Insertive anal sex circumcised	3 drug	Not recommended	Consider 2 drug	Not recommended
Receptive vaginal sex	3 drug	Not recommended	Consider 2 drug[a]	Not recommended
Insertive vaginal sex	3 drug	Not recommended	Not recommended	Not recommended
Fellatio	Not recommended[b]	Not recommended	Not recommended	Not recommended
Cunnilingus	Not recommended	Not recommended	Not recommended	Not recommended
Semen splash into eye	Not recommended	Not recommended	Not recommended	Not recommended
Occupational and other exposures				
Shared injecting equipment	3 drug	3 drug[c]	Consider 3 drug	Not recommended
Occupational needle-stick injury	3 drug	3 drug[c]	Generally not recommended[d]	Not recommended
Mucosal exposure/ splash injury to infectious fluids	3 drug	Generally not recommended[e]	Generally not recommended	Not recommended
Human bite	Not recommended[f]	Not recommended	Not recommended	Not recommended
Needle-stick injury from a discarded needle in community			Not recommended	Not recommended

Notes: PEP is not recommended for any exposure when the source is from a low-prevalence population or where the source is taking HIV pre-exposure prophylaxis (PrEP). Decisions to prescribe PEP when source is using PrEP can still be considered on a case-by-case basis due to potential for non-adherence of the source.

a. Where the source is from a high-risk group and normally resides outside NZ, the risk may be greater. Other factors that may influence decision-making include breaches in the mucosal barrier, multiple exposures within the previous 72 hours, STI in either partner. Where there is doubt, PEP should be given.
b. PEP may be recommended for receptive oral intercourse with ejaculation if the exposed person has a breach in their oral mucous membrane.
c. The risk of transmission is likely to be low, but in the absence of evidence to support U=U in the setting of a percutaneous exposure, the authors support offering PEP in this situation.
d. In the occupational setting, the source is usually able to be identified and tested for HIV, and PEP is usually only prescribed or continued for those who have definitely been exposed to HIV. If the source is unable to be tested immediately, the exposed healthcare worker should be commenced on PEP without waiting for the results if the source is at high risk of being HIV-positive. If the source is unable to be identified or tested, then the risk of the source being HIV-positive must be assessed from any epidemiological or other information available. The use of PEP should be decided on a case-by-case basis, and it is recommended that an expert is always consulted in this situation. It is reasonable to always offer PEP to a healthcare worker who has had a significant exposure to a source who is HIV-positive, even if the source has an undetectable HIV viral load.
e. Very low risk of transmission; however, 2 drug PEP could be considered for an occupational exposure based on the professional judgment of the clinician and consideration of individual patient circumstances.
f. PEP could be considered for patients who fulfil ALL of the three following criteria: a) the biter's saliva was visibly contaminated with blood; b) the biter is known or suspected to have a plasma HIV viral load >1000 copies/ml; and c) the bite has resulted in severe and/or deep tissue injuries.

5. PEP discussion

The currently recommended PEP regimens are well tolerated, with minimal side-effects, drug–drug interactions, dosing requirements and pill burden. Alternative regimens may be recommended following discussion with a specialist, depending on the medical history of the exposed person, or source information concerning antiretroviral treatment history and the results of past HIV resistance testing.

Clinicians must inform patients who are prescribed PEP about the following:

- PEP must be commenced within 72 hours of exposure (ideally within 24 hours)
- PEP provides high levels of protection but does not prevent 100% of infections
- the importance of adherence
- HIV seroconversion signs and symptoms (see Table 9.4)
- the potential adverse effects of treatment and possible drug interactions (see Table 9.5)
- measures for preventing re-exposure to HIV
- baseline and follow-up HIV testing (see Table 9.6).

HIV-related stigma and discrimination unfortunately still exist in many settings. Effective treatment for HIV is available and funded for anyone living with HIV in Aotearoa New Zealand, regardless of residency status. With early treatment and care, people living with HIV can expect a life expectancy similar to a person without HIV. Failure to diagnose HIV can result in serious illness and onward transmission to others.

Table 9.4 Signs and symptoms of HIV seroconversion

Signs and symptoms of HIV seroconversion	
• May be asymptomatic	• Headache
• Fever	• Lymphadenopathy
• Sore throat	• Myalgia
• Fatigue	• Rash

Patients should adopt risk-reduction practices until their seronegative status is confirmed at follow-up. This includes safer sexual and injecting behaviour as well as preventing exposing others to their body fluids through other means such as accidents or body tissue donation. People with child-bearing potential should be counselled about pregnancy, the risk of vertical transmission, contraception, and offered emergency contraception if indicated.

If potential HIV exposure is likely to be ongoing, the client should be offered transition to PrEP immediately after completion of the 28-day PEP course, assuming their HIV serology remains negative.

6. Prescribing PEP

Patients should receive a prescription for the complete course, and should have follow-up arranged with a specialist PEP provider or the patient's GP. Medication packs should be available if delays in accessing PEP from a pharmacy are likely, for example after-hours or in rural locations. It is helpful for services to be aware of pharmacies in the area which stock PEP, particularly those which are open after hours.

Medication interactions should be checked using the Liverpool HIV Drug Interactions Checker https://www.hiv-druginteractions.org/checker

PEP requires a special authority for funding.

Table 9.5 Specific medications and cautions

Medication	Comments and cautions
Tenofovir/emtricitabine	• Once-daily dosing. • Well tolerated. • Mild GI side-effects not uncommon at initiation and are expected to settle within 1-2 weeks. • Tenofovir can impact renal function; however, the risks are very low with a 28-day course, in a person who is otherwise well with no renal risk factors. • Use with caution or avoid in renal disease. Tenofovir should not be used if eGFR <50. • Use zidovudine/lamivudine where tenofovir is directly contraindicated and seek expert advice. Zidovudine/lamivudine requires BD dosing, and has frequent side-effects, so is not recommended as a first line agent.
Dolutegravir	• Once-daily dosing. • Well tolerated when used in PEP with high rates of adherence and regimen completion rates. **Drugs that are contraindicated**: • Dofetilide (not available in Aotearoa New Zealand) **Drugs that should be used with caution**: • Phenytoin, phenobarbital, rifampicin, St John's Wort, carbamazepine - increase dolutegravir dose to 50mg BD or stop St John's Wort. • Antacids containing polyvalent cations e.g., Mg or Al – use at least 2 hours before or 6 hours after the dolutegravir dose. • Products containing calcium or iron – use at least 2 hours before or 6 hours after the dolutegravir dose OR dose concomitantly with food. • Metformin – increase monitoring of glycaemic control, adjustment in metformin dose may be required. Medication interactions should be checked using the Liverpool HIV Drug Interactions Checker - https://www.hiv-druginteractions.org/checker

Non-occupational exposure:
PEP can be prescribed by any relevant prescriber in Aotearoa New Zealand, including general practitioners and nurse prescribers.

The PHARMAC criteria for funded PEP are BOTH:

1. Treatment course to be initiated within 72 hours post exposure; and
2. Any of the following:
    i. Patient has had condomless anal intercourse or receptive vaginal intercourse with a known HIV-positive person with an unknown or detectable viral load greater than 200 copies per ml; or
    ii. Patient has shared intravenous injecting equipment with a known HIV-positive person; or
    iii. Patient had had non-consensual intercourse and the clinician considers that the risk assessment indicates prophylaxis is required; or
    iv. Patient has had condomless anal intercourse with a person from a high HIV prevalence country or risk group whose HIV status is unknown.

Exposed persons with appropriate risk who do not meet the PHARMAC criteria can be offered self-funded PEP, which costs approximately NZ$30 for a course of 2-drug PEP, or approximately NZ$1345 for a course of 3-drug PEP, depending on pharmacy mark-up (2023).

Occupational exposure:
PEP for an occupational exposure must be prescribed by a named HIV prescriber (usually an infectious diseases or sexual health specialist).

The PHARMAC criterion for funded PEP is:

- The patient has percutaneous exposure to blood known to be HIV-positive.

7. Laboratory assessment and follow up

After potential exposure to HIV, individuals should have baseline and follow-up testing for HIV and other infections (depending on mode of exposure).

PEP should be initiated immediately, and must not be delayed while awaiting the results of baseline testing. Where possible, the results should be followed up within 24 hours of the specimen being collected.

Individuals found to be HIV-positive or indeterminate on baseline testing, or during follow-up, require immediate referral to an HIV specialist.

Table 9.6 Laboratory monitoring of individuals who are prescribed PEP

Test	Baseline (Week 0)	Week 4-6	Month 3
HIV serology	x	x	x
Syphilis	x	x	x
Hepatitis B*	x		x
Hepatitis C	x		x
FBC, LFT, Creat, eGFR	x		
STI testing †	x	x	x
Pregnancy test^	x	x	

Notes: * Individuals with evidence of previous immunity to hepatitis B (HBsAb positive) will require no further follow-up. Patients who have already commenced PEP whose baseline serology is consistent with chronic/active hepatitis B should have LFTs +/- viral load monitored. Advice from a specialist in the management of viral hepatitis should be sought.

† As per Aotearoa New Zealand STI Management Guidelines for use in Primary Care.

^ If clinically indicated.

Management of possible exposure to other conditions

Hepatitis B

All individuals presenting for PEP are assessed for the possibility of hepatitis B exposure. Individuals with evidence of previous immunity to hepatitis B (HBsAb positive) will require no further follow-up. Non-immune individuals should be offered immunisation (unfunded indication) and follow-up. Non-immune individuals exposed to a source who is known to have chronic hepatitis B (HBsAg positive) should be managed as per the *Communicable Disease Control Manual* https://www.tewhatuora.govt.nz/publications/communicable-disease-control-manual/

Sexually transmitted infections

Individuals presenting for non-occupational PEP require appropriate targeted screening for chlamydia, gonorrhoea and syphilis. If symptoms of STI are present, further tests, empiric treatment and follow-up are required. For further advice see the Aotearoa New Zealand STI Management Guidelines for use in Primary Care at www.sti.guidelines.org.nz.

Hepatitis C

Individuals who are potentially at risk of hepatitis C infection (e.g., people who have shared needles and other injecting equipment, or who have had a needlestick injury, or men who have sex with men that have engaged in condomless anal sex) require baseline and follow-up testing for hepatitis C. Effective treatment for hepatitis C is available – refer to HealthPathways.

Pregnancy and breastfeeding

All people who have the potential to be pregnant at the time of presentation for PEP should be offered pregnancy testing. Emergency contraception is offered to people presenting for PEP within 72 hours, who are at risk of pregnancy. Follow-up pregnancy tests should be offered at 3-4 weeks post-exposure where indicated. Specialist advice should be sought urgently for people who require PEP and are pregnant or breastfeeding.

Tetanus

Individuals who sustain wounds or abrasions should have their tetanus status assessed and be offered immunisation as indicated.

Additional clinical management issues

1. Individuals at risk of HIV acquisition who decline PEP

Education about risk reduction (including PrEP) and HIV seroconversion should be provided. It is important that the patient remains engaged with a health service to ensure follow-up testing over the following 3 months.

2. Individuals at negligible risk of HIV transmission who request PEP

This response may relate to anxiety and fear about an apparently negligible exposure or to undisclosed more serious risk behaviours.

It is important that the clinician takes a supportive approach and documents all advice given, including if PEP was not recommended. Early follow-up and a low threshold for psychological referral is recommended.

3. Individuals who re-present for PEP

People who present for repeat PEP should be supported, with each presentation assessed on its merits in a non-judgemental manner.

Repeat presentation(s) and extension of PEP courses warrant careful assessment of the context of risk behaviour and should prompt consideration for PrEP, referral to mental health, risk-reduction counselling and/or AOD services. Safer sex information should be an integral part of the consultation.

4. Individuals who are on PrEP

If an individual is presenting to start PrEP and they have had a possible exposure within the last 72 hours, they should be offered PEP and can then be transitioned to PrEP immediately after completion of the 28-day PEP course, assuming their HIV serology remains negative.

See Table 9.7 for guidance on switching from PrEP to PEP. If switching from PrEP to PEP occurs in an emergency department, expert advice should be sought and the individual referred back to their PrEP prescriber as a matter of urgency.

Table 9.7 Switching from PrEP to PEP

Risk event	Adherence to PrEP	Recommendations
Requires 3-drug PEP	At least 4 doses in the week of the risk event	Continue PrEP
Requires 3-drug PEP	PrEP 2-1-1 taken appropriately	Consider risk reduction counselling
Requires 2-drug PEP	< 4 doses in the week of the risk event(s)	Transition to 3-drug PEP if last risk event is within the 72-hour PEP window. Thoroughly assess context of adherence difficulty and intervene.

5. Transitioning from PEP to PrEP

Ideally, HIV status should be confirmed as negative at 12 weeks post-PEP if transitioning from PEP to PrEP. However, individuals at risk may never be out of the serological testing window and PrEP initiation may be a matter of urgency. Individuals should be tested for HIV at the end of their PEP course, and transitioned immediately onto PrEP if their test remains negative.

6. Renal disease

All patients having PEP should be assessed for renal impairment. Tenofovir should not be used if creatinine clearance is less than 50mL/min (60mL/min for PrEP). Zidovudine with lamivudine with both doses adjusted to degree of renal function is recommended as a 2-drug regimen with a third agent as indicated.

7. Gender identity and history

It is important to not make assumptions about an individual's gender identity, sexual orientation, anatomy, the type of sex they may have (e.g., anal, vaginal/'*front hole*') or the level of risk associated with that sex (e.g., a trans man having condomless receptive sex with a cisgender man could be at high risk regardless of whether that sex is anal or vaginal). The need for PEP should be assessed based on the type of exposure determined during the clinical assessment. It may be beneficial to use open-ended questions to allow people to choose what information they disclose about the types of sexual interaction in which they engage.

8. Individuals who have been sexually assaulted

Those who present due to sexual assault should be assessed for their need for PEP as early as possible after the event. This is usually best done in a specialist sexual assault centre (where specialist counselling and forensic testing can also occur). However, PEP, if indicated, should not be delayed pending referral. Cisgender male-to-male or transgender sexual assault clients should always be offered PEP if penile-anal penetration has occurred. There are no data on HIV prevalence for convicted sexual assailants in NZ; however, overall prevalence of HIV in NZ correctional facilities is <0.1%.[21] Given that the risk of exposure is low, PEP is generally not recommended following heterosexual sexual assault; however, the decision to prescribe PEP should be made on a case-by-case basis. Factors such as multiple assailants, penile-anal penetration, trauma or an assailant who is from a high prevalence country may increase the exposure risk. Emergency contraception should always be offered for people at risk of pregnancy in this situation.

9. Children

The management of children requiring PEP is beyond the scope of this guideline. Children at potential risk of HIV exposure should be discussed with relevant paediatric services.

10. Prisoners and detainees

People living in correctional or detention facilities who are potentially exposed to HIV sexually, through injecting drug use or other means require assessment for PEP as soon as possible after exposure. HIV prevalence in NZ correctional facilities is <0.1%.[21] Timely disclosure of exposure is obviously a limiting factor in these circumstances. The provision of assessment and treatment in correctional facilities should be available across all jurisdictions.

11. Individuals who commenced PEP overseas

Those who started PEP while overseas may have been prescribed antiretroviral drugs which are not available or recommended in Aotearoa New Zealand. Frequently, they may not have had all of the recommended baseline tests and STI/BBV evaluations recommended in Table 9.6. These should be completed as soon as possible and the individual should complete the PEP course using a NZ-recommended PEP regimen. This can cause some anxiety to the patient and should be carefully explained and the individual reassured.

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10. Improving medication adherence

Medication adherence is critical to achieving the maximum prevention benefit of pre-exposure prophylaxis (PrEP) and reducing the risk of selecting for a drug-resistant virus in the event of HIV acquisition.[1,2]

In randomised, blinded, placebo-controlled trials of PrEP, adherence varied[2] and was lower among cisgender women in some studies,[3,4] in transgender women[5] and young PrEP users.[6-8] PrEP adherence has generally been higher in more recent trials, open-label extensions and demonstration projects, particularly among men who have sex with men (MSM). These better adherence rates have been due to increasing knowledge about PrEP's efficacy and differing motivations for taking PrEP.[1,9,10]

Common reasons for non-adherence may include a perceived low risk of acquiring HIV,[3,11,12] start-up symptoms[12-15] and concerns regarding long-term side-effects,[11,12,16] factors of daily life such as medication management,[12,17] perceived and enacted stigma due to being eligible for PrEP[12] and lack of social support from partners, family and friends.[12] Common challenges to PrEP adherence, particularly for MSM, are party drug and alcohol use.[17] Party drug use (at the event level) is known to increase the likelihood of missing a dose on the same as well as the next day, thus potentially affecting the efficacy of event-driven PrEP.[18] People with mental health disorders are also more likely to self-discontinue the use of PrEP.[19] Studies of adolescent MSM using PrEP have shown that approximately 55% of participants have evidence of high adherence at week 4, but adherence declines markedly after the first month.[7,8]

Patient education and adherence counselling focused on medication self-management are needed to support ongoing daily PrEP use (Box 10.1).

Box 10.1 Key components of medication-adherence counselling

Improving medication adherence

Provide simple explanations and education on the following issues:

- Relationship of adherence to the efficacy of PrEP
- Medication dosage and schedule
- Management of common side-effects
- Signs and symptoms of acute HIV infection and recommended actions

Support adherence:

- Tailor daily dose taking to patient's daily routine (e.g., with tooth brushing, before bed)
- Identify reminders and devices (e.g., apps, beepers, alarms) to minimise forgotten doses
- Identify and address potential barriers to adherence.

Monitor medication adherence in a non-judgemental manner:

- Normalise occasional missed doses while ensuring patient understands importance of daily dosing for optimal protection
- Reinforce success
- Identify factors interfering with adherence and plan with patient to address these factors
- Assess side-effects and provide advice on how to manage them.

Various approaches can be used to effectively support medication adherence.[20] These include:

- educating patients about the medications
- helping patients anticipate and manage side-effects
- helping patients establish dosing routines that fit with their work and social schedules
- providing reminder systems and tools such as pill boxes and electronic reminders
- addressing substance abuse or mental-health needs that may impede adherence
- arranging more frequent clinic visits for adolescents to enhance their adherence
- facilitating whānau, social and peer support.

When initiating a PrEP regimen, clinicians need to educate patients about medication schedules (for daily or event-driven PrEP, that is, the use of PrEP before and after potential HIV exposures), how to commence taking PrEP and how to cease taking PrEP and what to do if they experience problems such as side-effects or missed doses. See *Chapter 6: Providing PrEP* regarding specific recommendations about dealing with missed doses.

Medication adherence should be discussed at each visit when the PrEP script is provided, to identify barriers to optimal PrEP adherence and develop appropriate management plans.

Evidence that different dosing strategies can be effective provides an opportunity to offer flexibility, choice and convenience to patients who are benefiting from PrEP. Event-driven PrEP is an option for certain populations (see Chapter 6: Providing PrEP), and has been endorsed in guidance from the World Health Organization.[21] Event-driven PrEP could be considered for certain populations when taking daily medication is not acceptable, sex is infrequent and a person feels they can plan their sexual activity. If patients choose to take event-driven PrEP, their behaviour and PrEP pill use patterns should be discussed at each visit, to help determine if they should perhaps switch to daily PrEP.

Side-effects can lead to non-adherence. Clinicians should inform patients about the most common side-effects and should work with patients to develop a specific plan for handling them, including the use of specific over-the-counter medications that can mitigate symptoms.

In the context of discussing PrEP adherence, patients should be reminded about the need to be tested for HIV and sexually transmitted infections (STIs) every 3 months or earlier if required, due to perceived risks or symptoms.

The importance of using condoms to prevent STIs, or to help prevent HIV if PrEP adherence has been suboptimal should be discussed with patients. To improve adherence and effectiveness of PrEP, patients should also be informed about how to stop taking PrEP and re-start it, so that they are prepared for these changes. See chapter 6. Providing PrEP regarding specific recommendations on starting and ceasing PrEP.

Clinicians may wish to explore and address other potential barriers to optimise PrEP use such as misconceptions about PrEP, behavioural factors (e.g., substance use), depression, partner violence and unstable housing. To improve adherence to their PrEP medication, some patients may benefit from referral to mental health or social services, or peer-based support services provided by various organisations (e.g., services provided by Burnett Foundation Aotearoa, Body Positive, Positive Women Inc, New Zealand Sex Workers Collective).

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11. Behavioural strategies to reduce risk

In the era of HIV, PrEP and treatment as prevention, behavioural methods of risk reduction—including condom use, clean injecting equipment, HIV serosorting, strategic positioning, and negotiated safe practices with sexual partners—retain their importance in preventing HIV transmission.

However, some vulnerable people may be unable to effectively negotiate use of these prevention strategies, especially condoms, with their regular or casual partners. The initiation of PrEP is straightforward, but on occasion it may be appropriate to refer some particularly vulnerable people with complex needs to health professionals with expertise in HIV prevention and sexual health.

PrEP's efficacy relates directly to the patient's adherence to PrEP medication not to whether the patient is using condoms in tandem with PrEP.[1,2] People using PrEP should be supported with ongoing information about the role that condoms and other practices play in preventing HIV when PrEP adherence is suboptimal as well as the role that condoms play in sexually transmitted infection (STI) prevention.

Provide feedback on HIV risk factors identified during sexual and substance use history-taking:

- Elicit barriers to, and facilitators of, consistent condom use and other safer sex and substance use practices.
- Elicit barriers to, and facilitators of, reducing injecting drug use.
- Discuss with patients the barriers to, and facilitators of, evidence-based drug treatment where indicated and requested.

Support risk-reduction efforts:

- Help patients identify one or two feasible, acceptable, incremental steps toward risk reduction.
- Identify and address anticipated barriers to accomplishing planned actions to reduce risk.

Monitor medication adherence in a non-judgemental manner:

- Acknowledge the effort required for behavioural change.
- Reinforce success.

If not fully successful, assess factors interfering with completion of planned actions and help patient identify the next steps.

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12. How to access PrEP in Aotearoa New Zealand

There are 3 ways to access HIV pre-exposure prophylaxis (PrEP) in Aotearoa New Zealand.

1. Publicly funded PrEP
For people eligible for publicly funded healthcare, PrEP will be funded for those at elevated risk of HIV acquisition (requires special authority). Any relevant prescriber can write a script for PrEP which can be taken to any pharmacy for dispensing.

2. Private script for supply from pharmacy
Any doctor can write a private script for PrEP. Patients can have this script dispensed at a community pharmacy. Depending on pharmacy mark-up, each bottle of 30 pills will cost approximately NZD$30 (2023). This option is generally used by people who are not eligible for publicly funded healthcare.

3. Through personal importation
There are multiple overseas suppliers who will supply PrEP for import into NZ at a range of costs. Given the current low cost of PrEP available within NZ, it is generally no longer cost-effective to import the drug from overseas. For those where the cost remains prohibitive, Burnett Foundation Aotearoa has partnered with an overseas pharmacy to support a scheme that provides PrEP at no cost to those who have a prescription. See Burnett Foundation Aotearoa website for more information.

Tips for clinicians:

- Personal importation is legal, but not routine. It is recommended that patients are asked to sign a consent form acknowledging that they understand and accept the risks of importing generic PrEP from overseas. New Zealand's Medical Protection society has developed a patient consent form specifically for importing PrEP. You can contact them on 0800 225 5677 to obtain a copy of the form.
- Add "I am aware that this is to be imported from overseas" to the script to help prevent the shipment being delayed at the border.

13. Models of PrEP delivery

Since 1 March 2018, combination tenofovir disoproxil* and emtricitabine (TD*/FTC) for HIV PrEP has been publicly funded by PHARMAC, and can now be initiated by any relevant prescriber, including GPs and nurse practitioners.

Making PrEP easily accessible for all who would benefit requires clinicians to be aware of, and be competent and comfortable with, prescribing PrEP. The role of medical providers in primary care is instrumental to optimising PrEP access and use.

Below is a list of PrEP resources designed for clinicians to upskill their knowledge and skills in the provision of PrEP:

- Burnett Foundation Aotearoa PrEP information for clinicians: https://www.burnettfoundation.org.nz/prep-information-for-clinicians/ - includes free online modules aimed for NZ-based primary care clinicians on PrEP prescribing, and related topics
- Goodfellow Unit
- Burnett Foundation Aotearoa PrEP information for patients: https://www.burnettfoundation.org.nz/learn/staying-safe/prep/

The prescription and provision of PrEP clinical and laboratory monitoring are straightforward for GPs and other clinicians. However, some providers who are less experienced in serving populations at elevated risk of HIV and/or other sexually transmitted infections (e.g., men who have sex with men, transgender and non-binary people who share sexual networks with MSM, Māori and Pasifika, people who have sex overseas in places of high HIV prevalence, people whose partners are at high risk for HIV and STIs, and people who inject drugs) may wish to consider establishing relationships with specialist colleagues experienced in HIV and sexual health medicine. HIV clinics and sexual health clinics can provide information and support if required.

When starting PrEP services, providers should also establish:

1. Appropriate referral pathways to ensure that specific needs of PrEP users are adequately provided for (e.g., regular HIV and STI testing, the management of chronic hepatitis B infection, treatment of hepatitis C and possible abnormal liver and kidney function – see *Chapter 5: Clinical assessment before starting PrEP* for more details.

2. Communication with local pharmacies to ensure uninterrupted refills of PrEP scripts. Some community pharmacies do not keep the medication in reserve and would have to order it in. Same-day order and delivery might not always be possible. Other pharmacies with higher client load requiring HIV medications will have PrEP medication in reserve. Many pharmacies also offer a delivery service. It is ideal for PrEP-users to get their scripts renewed and filled before they completely run out of medication.

An important approach to successful PrEP implementation is to engage representatives from HIV community-based organisations working with relevant populations in the delivery of PrEP. Community-based organisations such as Burnett Foundation Aotearoa and Body Positive can assist with PrEP promotion and education and, depending on their capacity, may also be able to assist with behavioural screening and adherence support. Similarly, support from community-

based Māori and Pasifika rainbow organisations, as well as other organisations working with culturally diverse communities is essential to ensuring equitable PrEP uptake.

When embarking on PrEP prescribing, providers should also consider the capacity of their practices to accommodate new patients and maintain follow-up every 3 months while taking PrEP. Several approaches may be helpful in dealing with these changes to practice:

- Careful planning of clinic appointments to allow sufficient space for PrEP initiation and regular follow-up visits.
- Where resources allow, automating most steps in the patient pathway, to reduce the patient registration-to-PrEP prescription time.
- Task shifting including having clinical nurse specialists, or trained nurses with clinician supervision, in charge of PrEP-related services where possible.
- Developing systems and procedures for recording and monitoring PrEP use.

Clinical practices that are planning to build up their PrEP patient population can consider developing a customised communications plan for PrEP demand creation, including media channels and communication strategies which will be used to drive local PrEP awareness and use, with input from relevant local community-based organisations and sexual health services.

Lastly, if for relevant reasons a medical practitioner or clinic setting is not prescribing PrEP, provision should be made for people seeking PrEP or who are identified as likely to benefit from PrEP, to be efficiently directed to a local PrEP provider.

Glossary

AIDS acquired immunodeficiency syndrome

ART antiretroviral therapy

ASHM Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine

BBV blood borne virus

BMD bone mineral density

Cisgender A term used to describe people whose gender aligns in an expected way with the sex assigned to them at birth, for example a man who was assigned as male at birth.

eCrCl estimated creatinine clearance rate

eGFR estimated glomerular filtration rate

FTC emtricitabine

HBV hepatitis B virus

HCV hepatitis C virus

HIV human immunodeficiency virus

IDU injecting drug use

iPrEx Pre-exposure Prophylaxis Initiative

Medsafe New Zealand Medicines and Medical Devices Safety Authority

MSM men who have sex with men

Non-binary A term some transgender people use to describe that their gender identity does not comfortably fit into a binary category of man/boy or woman/girl.

NZ New Zealand

NSP needle and syringe programme

OST opioid substitution therapy

PCR protein:creatinine ratio

PEP post-exposure prophylaxis

PHARMAC NZ Pharmaceutical Management Agency

PrEP pre-exposure prophylaxis

PoCT point-of-care test

STI sexually transmitted infection

TD* tenofovir disoproxil maleate or fumarate or phosphate

Transgender A term used to describe people whose gender does not align in an expected way with the sex assigned to them at birth. Transgender people can have a binary gender identity (for instance, man or woman) or non-binary gender identity.

UVL undetectable viral load

WHO World Health Organization

NZSHS
THE NEW ZEALAND SEXUAL HEALTH SOCIETY INCORPORATED
SEXUAL HEALTH FOR ALL

Burnett Foundation
Aotearoa