HIV PEP - Sexual exposure recommendations – Evidence to decision

Recommendations are numbered based on the sequence in which they appear in section 4.2 of the EMI guidelines.

Recommendation 1

Recommended	GRADE: 1C[1]
Please see the sexual exposures algorithm. HIV PEP is **recommended** following sexual exposure where there is a significant risk of HIV transmission. For HIV PEP recommendations by type of exposure and source status, please see table 7 *HIV PEP recommendations by type of exposure and source status*. [1, 22-34].	

[1] Strong recommendation, low certainty evidence.

Evidence to decision

Benefits and harms

There are a number of different scenarios where HIV PEP is either recommended or not recommended following sexual exposure. Where HIV PEP is recommended, the benefits of administering HIV PEP outweigh the risks. Effective treatment confers significant individual benefit and reduces the risk of onward transmission.

Where HIV PEP should be considered, other extenuating factors that influence decision-making including more detailed knowledge of local HIV prevalence within the index case population should be considered (please refer to Table *5 Baseline and follow up testing* for further information).

Certainty of the Evidence	Low

Heterosexual exposures

Overall the estimated risk of transmission of HIV (in the setting of uncontrolled HIV infection), per condomless coital act, for receptive vaginal sex and insertive vaginal sex is 1 in 1000 and 1 in 1219 respectively [1]. Correct use of a condom reduces the risk of transmission by 93%-100% [22; 23]. According to a 2020 systematic review that examined HIV transmission risk in serodiscordant partners with or without ART or condom use, there is a lower risk of transmission associated with vaginal sex compared with anal sex [24]. Circumcision has been shown to significantly reduce HIV acquisition in heterosexual males in high prevalence settings [25]. The risk of transmission is greater during the initial two and a half months of infection [26; 27]. The cumulative incidence of transmission of HIV to females in couples who practice condomless anal intercourse is reported to be 27.8%, compared to 11.7% transmission to females who do not report anal intercourse [22]. A systematic review and meta-analysis [28] of published longitudinal studies provides new knowledge on a key HIV acquisition risk among women who have sex with men. Overall, HIV incidence was approximately twice as high (pooled crude RR = 1.56, pooled adjusted RR = 2.23) among women reporting receptive anal intercourse (RAI) than women reporting receptive vaginal intercourse (RVI) only. Since women do not typically practice RAI in all sex acts, the results of the pooled estimate is consistent with current evidence suggesting that HIV risk per URAI (unprotected receptive anal intercourse) act is up to 10–20 times higher than per URVI (unprotected receptive vaginal intercourse) act.

Gay, bisexual and other men who have sex with men (gbMSM)
Overall the risk of transmission of HIV, per condomless coital act in serodiscordant partners where the individual living with HIV has a detectable viral load is 1 in 90 for receptive anal sex and 1 in 666 for insertive anal sex [1]. An Australian cohort study has estimated the per coital risk of HIV to be lower in circumcised gbMSM (0.11, 95% CI 0.02 - 0.24) versus uncircumcised gbMSM (0.62, 95% CI 0.07 - 1.68) [29]. Thus, receptive UAI with ejaculation was found to be approximately twice as risky as receptive UAI with withdrawal or insertive UAI for uncircumcised men and over 10-times as risky as insertive UAI for circumcised men. Transmission is very unlikely if the source of the exposure is on effective antiretroviral treatment and has a very low or undetectable viral load [30; 31].

Orogenital exposures
The risk associated with oral sex or other orogenital contact cannot be accurately predicted, and is considered low, but not zero [30; 32]. A cohort study demonstrated that after an estimated total of over 19,000 condomless orogenital exposures with a partner living with HIV, no HIV seroconversion occurred [33]. A modelling study from 1999 also estimated an upper limit risk of 4/10,000 [34].

For further information, please see Table 9 *Risk of HIV transmission per exposure where source is known to be living with HIV and not on ART* and Table 10 *Estimated risk of HIV transmission by type of exposure where source HIV status is unknown.*

Values and preferences
There are certain factors that increase the risk of HIV transmission following a high-risk sexual exposure. Where a decision is made by a health professional to prescribe HIV PEP, it is likely that most patients in this situation would want the recommended course of action and only a small proportion would not.

Recommendation 2

NOT recommended	GRADE: 1A[2]

HIV PEP is **NOT recommended** if the index partner has been on ART for at least 6 months with an undetectable plasma HIV viral load (at the time of last measurement and within the last 6 months) AND with good reported adherence.

For HIV PEP recommendations by type of exposure and source status, please see table 7 *HIV PEP recommendations by type of exposure and source status*.

[2] Strong recommendation against, high certainty evidence.

Evidence to decision

Benefits and harms

The risk of HIV transmission is negligible and HIV PEP should not be administered because the potential toxicity and inconvenience of administering HIV PEP is likely to outweigh the benefit.

Certainty of the Evidence	High

Studies have confirmed that individuals on suppressive ART cannot transmit HIV sexually regardless of sexual orientation [35-40]. Transmission is eliminated if the source of the exposure is on effective antiretroviral treatment that is, has been on ART for at least 6 months with an undetectable plasma HIV viral load (at the time of last measurement and within the last 6 months) and with good reported adherence [30, 40].

A randomised controlled trial (RCT) (HPTN-052) conducted in 2011 [40] recruited serodifferent heterosexual couples randomised to early or delayed (CD4 guided) ART with 8509 person-years follow-up in the HIV-negative partners. The results showed that early ART resulted in a 93% lower risk of within couples transmission (hazard ratio 0.07; 95% CI, 0.02 to 0.22). Although there were eight phylogenetically linked transmissions in the early ART arm, four occurred in the initial period of ART prior to viral suppression and four were later (> 3 years), when the index cases had treatment failure and had evidence of detectable viral load. Significantly there were documented transmission while the index case was virologically suppressed (HIV-VL <200 copies/ml) [41].

The PARTNER study was a prospective observational study carried out at 75 sites in 14 European countries. The first phase of this study (PARTNER 1) recruited both gay and heterosexual serodifferent couples (partner living with HIV taking suppressive ART) who reported condomless sex between 2010 and 2014. The results highlighted no phylogenetically linked transmission were found in 888 serodifferent couples (340 gay and 548 heterosexual couples) [30]. In PARTNER 1, the upper 95% confidence limit for transmission rate for gbMSM was 0.84/100 couple-years of follow-up (CYFU) and therefore, the second phase of this study (PARTNER 2) [42] recruited and followed up gbMSM couples only from 2014-2018 [30; 42]. The results showed that there were zero phylogenetically linked within-couple transmissions, reducing the upper 95% confidence limit to 0.23/100 CYFU. The results of both studies provide a similar level of evidence on viral suppression and HIV transmission risk for gbMSM to that previously generated for heterosexual couples and suggests that the risk of HIV transmission in gbMSM couples through condomless sex when HIV viral load is suppressed is effectively zero [42]. A further systematic review [24] of published systematic reviews and meta-analyses conducted in 2020, concluded that ART and condom use were found to result in a significant reduction in the risk of sexual transmission of HIV in both homosexual and heterosexual populations. ART was associated with a 52%

reduction in transmission risk compared to no ART, with a relative risk of 0.48 (95% CI 0.439–0.525). ART with suppressed viral loads was associated with a minimal risk of transmission, with a median time at risk of 0.00 person-years (95% CI 0.00–0.00 person-years). The study also found that a lower risk of transmission was associated with vaginal sex compared to anal sex, early ART compared to late ART, and ART compared to no ART.

For further information, please see Table 9 *Risk of HIV transmission per exposure where source is known to be living with HIV and not on ART* and Table 10 *Estimated risk of HIV transmission by type of exposure where source HIV status is unknown.*

Values and preferences

Most patients in this situation would want to receive the recommended course of action and only a small proportion would not. The evidence supporting this recommendation is of high quality, indicating the benefits of not prescribing HIV PEP outweigh the risks and further research is unlikely to change our confidence in the estimate of benefit.