

Post Exposure Prophylaxis after Sexual Exposure to HIV

*If you require information on **occupational** exposure to blood borne viruses, including HIV, please refer to the NHSGGC board protocol which can be downloaded from www.nhsggc.org.uk/phpu.*

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SUMMARY

1. The recommended first-line PEPSE regimen is now **tenofovir disoproxil 245mg/ emtricitabine 200mg** with **raltegravir 1200mg od** for **28 days**.
2. Final HIV testing is recommended at a minimum of **45 days** after the PEPSE course is completed (i.e. a minimum of 73 days (10.5 weeks) after exposure for a 28 day course). For sexual exposures this can be performed at 12 weeks to align with syphilis testing.
3. **Population viraemia** rather than source seroprevalence is used to determine risk as the majority of people living with HIV in the UK are aware of their status and on effective antiretroviral therapy
4. Receptive vaginal sex with partner of unknown HIV status from high risk group – PEPSE is now ‘generally **not recommended**’.
5. Insertive vaginal sex with a partner of unknown HIV status from high risk group – PEPSE is now ‘**not recommended**’.
6. Human bite – PEPSE is now ‘generally **not recommended**’.
7. The decision to administer PEPSE should be based on **risk of HIV transmission** and not to manage a state of acute anxiety following a sexual exposure
8. Due to current HIV outbreak in PWID in GGC (10.8% prevalence) sexual exposure from PWIDS in Glasgow should be considered **higher risk**

Practice Points

- Everyone presenting for PEPSE should be assessed for PrEP eligibility and offered direct continuation onto PrEP
- If the person’s baseline HIV test is positive, PEPSE should be **continued** until review by the HIV service
- **Most PEPSE supply is now in 30-day sealed bottles. Prescribe the 30-day supply on NaSH, but ask the person to discard the last two days**

Rationale for PEPSE

Pathogenesis studies indicate that there may be a window of opportunity to prevent HIV infection by inhibiting viral replication after an exposure. Once HIV crosses a mucosal barrier it may take up to 72 hours before HIV can be detected within regional lymph nodes and up to five days before HIV can be detected in blood. Initiation of antiretroviral therapy (ART) has been shown to reduce spread and replication of virus in all tissues if initiated quickly after inoculation in an animal model.

When To Prescribe PEPSE following Sexual Exposure

- PEPSE should only be started within **72 hours** of exposure and ideally within 24 hours and be continued for 28 days.

The risk of HIV transmission following a sexual exposure depends on:

- The type of sexual exposure
- HIV viral load of the index
- Susceptibility of the recipient if the sexual partner is not virologically suppressed e.g. genital ulcer disease

Estimated prevalence of people with detectable HIV viraemia in adults over 15-74 years in UK 2018

		Estimated number of people with detectable virus*	Estimated population size	Rate per 1000
Gay and bisexual men	England	12,000	518,050	23.0
	London	5,000	155880	32.1
	Elsewhere	7,000	361090	20.9
Heterosexual men	Black African	1,900	331950	5.8
	Non-black African	3,840	19,563,630	0.2
Heterosexual women	Black African	3,240	373330	8.7
	Non-Black African	2,530	20,308,360	0.1
PWID	All	700	104,470	6.7
	Men	400	77,340	5.3
	Women	300	26,710	11.5

Based on PHE 2018 data

Number of diagnosed persons are based on HARS (HIV & AIDS Reporting System).

Estimates of the undiagnosed from MPES (Multi-Parameter Evidence Synthesis) using the upper bound of the estimates to be conservative.

*Viral load undetectable is defined as <200 copies/ml and above this figure is considered detectable and 'transmissible'.

Assumptions made that all persons living with undiagnosed HIV have detectable (transmissible) virus. Also added to this, is the number persons living with diagnosed HIV who did not have evidence of undetectability in 2018 (either because of treatment failure, not started ART, not retained in care, missing viral load measurement).

- The risk of HIV transmission per exposure from someone known to have HIV and not taking suppressive anti-retroviral therapy (ART) is :-

Type of exposure	Estimated risk of HIV transmission per exposure from an HIV-positive individual who is NOT on suppressive ART*
Receptive anal intercourse	1 in 90
Receptive anal intercourse with ejaculation	1 in 65
Receptive anal intercourse no ejaculation	1 in 170
Insertive anal intercourse	1 in 666
Insertive anal intercourse not circumcised	1 in 161
Insertive anal intercourse and circumcised	1 in 909
Receptive vaginal intercourse	1 in 1000
Insertive vaginal intercourse	1 in 1,219
Semen splash to eye	<1 in 10,000
Receptive oral sex (giving fellatio)	< 1 in 10,000
Insertive oral sex (receiving fellatio)	< 1 in 10,000
Mucocutaneous	1 in 1000
Blood transfusion (one unit)	1 in 1
Needlestick injury	1 in 333
Sharing injecting equipment (includes chemsex)	1 in 149
Human bite	< 1 in 10,000

*These figures are estimates that have been deduced from cohort and modelling studies

Calculating the risk of HIV transmission from a single exposure

$$\begin{aligned}
 &\text{Risk of HIV transmission} = \\
 &\text{risk that source has HIV infection and has a detectable viral load} \\
 &\quad \times \\
 &\text{risk per exposure}
 \end{aligned}$$

Example

e.g. a man presents for PEPSE after unprotected anal sex with ejaculation with man of unknown HIV status living in London.

Risk of HIV transmission =

Risk of detectable viral load.....32 per 1000 (*last column, first table*)

Risk of exposure.....1 in 65

Combined risk = $32/1000 \times 1/65 = 1 \text{ in } 2031$ or around 0.05%

There are other factors which may also further increase risk of HIV transmission in Box 1.

Box 1: Factors increasing the risk of HIV transmission if the index case is HIV-positive and NOT ON ART:

1. A high plasma HIV viral load (VL) in the index case – with each \log_{10} increase in plasma HIV RNA the per-act risk of transmission is increased 2.9 fold [95% confidence interval (CI) 2.2-3.8] (75). This may be particularly relevant during primary HIV infection (62).
2. Breaches in the mucosal barrier such as mouth or genital ulcer disease and anal or vaginal trauma following sexual assault or first intercourse (76, 77).
3. Menstruation or other bleeding – theoretical risk only
4. Pregnancy or postpartum – per-act probability of HIV acquisition higher in late pregnancy (adjusted relative risk [aRR] 2.82, $p=0.01$) and the postpartum period (aRR, 3.97, $p=0.01$) as compared to that during the non-pregnant period.(78)
5. Sexually transmitted infections in HIV positive individuals not on ART (79, 80) or HIV negative individuals with genital ulcer disease (81).

There is no evidence of the exact risk threshold at which PEPSE is indicated. Previous guidance suggested that if the risk of HIV transmission is $>1/1000$ then PEPSE is recommended, between $1/1000$ and $1/10,000$ PEPSE should be considered and $<1/10,000$ PEPSE is not recommended. These thresholds were not evidence-based so have been removed but there is recognition they may assist services in making decisions on a case-by-case basis. In this guidance it is now used:-

- **Recommended:** the benefits of PEPSE are likely to outweigh the risks, PEPSE should be given unless there is a clear reason not to.
- **Consider:** the risk of HIV transmission is low, the risk / benefit balance of PEPSE is less clear. The risk should be assessed on a case by case basis taking into consideration factors shown in footnotes c and d in below table.
- **Generally not recommended:** the risk of HIV transmission is very low, the potential toxicity and inconvenience of PEPSE is likely to outweigh the benefit

unless there is a clear specific extenuating factor which increases the risk. We anticipate PEPSE should very rarely be given when the risk has been assessed and discussed. The risk here is generally $<1/10,000$ but specific factors may increase the risk to $>1/10,000$.

- **Not recommended:** the risk of HIV transmission is negligible and PEPSE should not be given.

If there is uncertainty over whether PEPSE should be given discuss with the GUM Dr of the day urgently

Particular situations

Adolescents- The risk calculation/assessments for an adolescent following sexual or occupational exposure should be the same as those for an adult. A decision on whether to offer PEPSE should be made in the same way. The decision about whether to complete the decision-making process and/or provide PEPSE with or without involvement of the parent or guardian should be made in the context of UK laws and judgements about autonomy in healthcare decision-making, and balanced against protecting young people from harm.

HIV Status of Index-

Index partner is of unknown HIV status- proactive attempts should be made to determine the status but without delaying starting PEPSE

Index partner known to be HIV positive- attempts should be made at earliest opportunity to determine HIV viral load, resistance profile where relevant and treatment history of the index. PEPSE is not recommended if the index partner is on ART and has had an undetectable viral load for at least 6 months (at the time of last measurement and within the last 6 months) and with good reported adherence. Individuals should still be encouraged to undergo a formal PEPSE assessment and verification of index partner's HIV details even when they believe the partner has an undetectable HIV viral load.

If there are any doubts about the ART history, the index partner's adherence to ART or the viral load, then PEPSE should be given following condomless receptive anal intercourse

In the setting where the individual is known to be HIV-positive and known not to be on suppressive ART, the risk per exposure can be calculated by multiplying the number 1 and the risk per exposure. ie

Risk of HIV transmission = risk that source is HIV positive with a detectable HIV viral load X risk per exposure = 1 x risk per exposure

eg, if a man presents for PEPSE following condomless receptive anal intercourse with ejaculation with an HIV-positive male partner who is not on ART:

Risk of HIV transmission = $1 \times 1/65 = 1/65 = 0.015$ (or 1.5%)

Following insertive vaginal intercourse with an HIV-positive partner not on ART, PEPSE should be 'considered' rather than routinely 'recommended' as the risk is $1/1219$. Again, presence of additional factors in Box 1 should be reviewed and clinician discretion applied.

Sexual assault - There is concern (though no published evidence) that transmission of HIV is likely to be increased as a result of any trauma following aggravated sexual intercourse (anal or vaginal). Clinicians may therefore consider recommending PEPSE more readily in such situations, particularly if the assailant is from a high prevalence group. If the assailant is from a low prevalence group in the UK, after the balance of risks and benefits are discussed with the patient, it is likely PEPSE provision will generally not be indicated.

People engaged in transactional sex - HIV prevalence can vary significantly. In male sex workers can be around 14%. In women in Western Europe prevalence can be <math><1\%</math> but can be between 2.5-8% from Eastern Europe. In Glasgow injecting drug use is associated with higher prevalence of HIV, this should be considered particularly amongst street sex workers, homeless women or those already known to inject drugs.

	Index HIV positive		Index of unknown HIV status	
	HIV VL unknown or detectable	HIV VL undetectable	From high prevalence country / risk-group (e.g. MSM) ^a	From low prevalence country / group
SEXUAL EXPOSURES				
Receptive anal sex	Recommend	Not recommended ^b <i>Provided on ART >6 months with undetectable HIV VL within the last 6 months & good adherence</i>	Recommend	Not recommended
Insertive anal sex	Recommend	Not recommended	Consider ^{c,d}	Not recommended
Receptive vaginal sex	Recommend	Not recommended	Generally not recommended ^{c,d}	Not recommended
Insertive vaginal sex	Consider ^c	Not recommended	Not recommended	Not recommended
Fellatio with ejaculation	Not recommended	Not recommended	Not recommended	Not recommended
Fellatio without ejaculation	Not recommended	Not recommended	Not recommended	Not recommended
Splash of semen into eye	Not recommended	Not recommended	Not recommended	Not recommended
Cunnilingus	Not recommended	Not recommended	Not recommended	Not recommended
OCCUPATIONAL AND OTHER EXPOSURES				
Sharing of injecting equipment	Recommended	Not recommended	Generally not recommended ^e	Not recommended
Sharps injury	Recommended	Not recommended	Generally not recommended ^{e,f}	Not recommended
Mucosal splash injury	Recommended	Not recommended	Generally not recommended ^e	Not recommended
Human bite	Generally not recommended ^e	Not recommended	Not recommended	Not recommended
Needlestick from a discarded needle in the community			Not recommended	Not recommended
<p>Recommended: the benefits of PEP are likely to outweigh the risks, PEP should be given unless there is a clear reason not to.</p> <p>Consider: the risk of HIV transmission is low, the risk / benefit balance of PEP is less clear. The risk should be assessed on a case by case basis taking into consideration factors shown in footnotes c and d below.</p> <p>Generally not recommended: the risk of HIV transmission is very low, the potential toxicity and inconvenience of PEP is likely to outweigh the benefit unless there is a clear specific extenuating factor which increases the risk (see footnotes c, d, e, f below). We anticipate PEP should very rarely be given when the risk has been assessed and discussed (section 6.1.2 and 6.2.1.2)</p> <p>Not recommended: the risk of HIV transmission is negligible and PEP should not be given</p>				
<p>^a High prevalence countries or risk-groups are those where there is a significant likelihood of the index case individual being HIV-positive. Within the UK at present, this is likely to be MSM, IDUs from high-risk countries (see d below) and individuals who have immigrated to the UK from areas of high HIV prevalence, particularly sub-Saharan Africa (high prevalence is >1%). HIV prevalence country specific HIV prevalence can be found at https://aidsinfo.unaids.org</p>				
<p>^b The index case 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) with good reported adherence. Where there is any uncertainty about HIV VL results or adherence to ART then PEP should be given after condomless anal intercourse with an HIV-positive person. The viral load threshold considered 'undetectable' in the PARTNER 1 and 2 and HPTN052 studies was <200 copies/ml.</p>				
<p>^c Factors that influence decision-making in <u>all exposures</u>: More detailed knowledge of local HIV prevalence within index case population ^a</p>				
<p>^d Factors that may influence decision-making include in <u>sexual exposures</u>:</p> <ol style="list-style-type: none"> 1. Breaches in the mucosal barrier such as genital ulcer disease and anal or vaginal trauma following sexual assault or first intercourse 2. Multiple episodes of exposure within a short period of time e.g. group sex 3. Sexually transmitted infection in either partner 				
<p>^e HIV prevalence amongst IDUs varies considerably depending on whether there is a local outbreak and country of origin and is particularly high in IDUs from Eastern Europe and central Asia. Region-specific estimates can be found in the UNAIDS Gap Report http://www.unaids.org/sites/default/files/media_asset/05_Peoplewhoinjectdrugs.pdf.</p>				
<p>^f Factors that may influence decision-making include in <u>occupational exposures</u>: Deep trauma or bolus of blood injected</p>				

What to Prescribe for PEPSE

tenofovir disoproxil 245mg/emtricitabine 200mg ONE tablet
with
raltegravir 600 mg TWO tablets (1200mg total) once daily
for 28 days.

or

tenofovir disoproxil 245mg/emtricitabine 200mg ONE tablet
with
raltegravir 400mg ONE tablet twice a day
for 28 days

Pack size

We generally use 30-day bottles for stability reasons – raltegravir once daily only comes in this size. In this case please **prescribe the full 30-day supply on NaSH** and then ask the person to **discard the last two days**.

A smaller supply of 7-day pre-packs with twice-daily raltegravir can be used where there is significant uncertainty about whether PEP will continue and the person is being re-assessed. These packs are also used to start PEPSE in emergency locations

If someone attends having had a starter pack it is generally easier to switch them to once daily raltegravir and give a 30-day continuation supply with instruction to discard the extra tablets once they have completed a total of 28 days treatment. Agree a 'stop date' or transition date to PrEP

Please make sure people are absolutely clear about the number of tablets to take especially if switching from twice-daily to once-daily raltegravir

How to Take

- Tenofovir/ emtricitabine- Take with or just after food or a meal.
- Raltegravir- It does not matter if you take these tablets before or after food or on an empty stomach

Special Considerations

Concern about HIV resistance

If there is concern about exposure to someone with established antiretroviral drug resistance please discuss with the GUM Dr of the Day.

Pregnancy

Take a contraceptive history and request a baseline pregnancy test if needed in women of childbearing age considering PEPSE. Pregnancy and breastfeeding should not alter the decision to start PEPSE.

For women who are at risk of pregnancy, we recommend use of the standard first-line PEPSE regimen ie OD raltegravir if available, BD if not

For women who are pregnant, raltegravir 400mg twice daily is preferred as the third agent. Where accessing raltegravir 400mg might cause delay it is recommend using raltegravir 600mg twice daily (this differs from labelling on the 30 day pack) and switching at the earliest opportunity.

Women should be counselled that antiretrovirals used for PEPSE are unlicensed in pregnancy and that their risks/ benefits must be carefully discussed

Women who are breastfeeding must be counselled regarding the transfer of antiretrovirals to the infant via the breastmilk. For full details see BASHH/ BHIVA full PEPSE guidance

Renal dysfunction

In patients with other comorbidities such as significant renal dysfunction (eGFR <50ml/min) this should be discussed with a GU Dr of the Day as alternatives may be needed.

Drug interactions

For detailed information see [Liverpool HIV Interactions \(hiv-druginteractions.org\)](http://liverpool.hiv-druginteractions.org). Pharmacists based at the Brownlee can also be contacted for advice Mon- Fri 9-5 on 53383

Antacids and multivitamins (products containing metal cations e.g. magnesium / aluminium, which can chelate and reduce the absorption of integrases) should be avoided where possible during PEPSE with once daily raltegravir. An alternative non-interacting medication should be used or non-essential mineral supplements stopped. BD raltegravir could be considered but metal cation containing medicines must be separated by at least 4 hours from twice daily

Swallowing difficulty

Tenofovir/ emtricitabine, can be dissolved in 100 ml of water or orange juice and taken immediately.

Side Effects

Raltegravir with tenofovir disoproxil/emtricitabine as a PEPSE regimen is generally well tolerated and routine provision of anti-emetics and anti-diarrhoeals is not recommended. If patient experiences significant side effects discuss with GU Dr of the Day

Starting PEPSE

Once risk assessment completed if PEPSE is felt appropriate the following assessment should be done

- Items to discuss with individual commencing PEPSE:
 - The rationale for PEPSE
 - The lack of conclusive data for the efficacy of PEPSE
 - Start PEPSE as soon as possible and importance of adherence to optimise efficacy
 - The potential side-effects of PEPSE
 - Drug interactions including over the counter drugs such as multivitamins/ antacids/ iron
 - Take full medical and sexual history including and drug use/ chems
 - Emergency contraception (if appropriate)
 - Seek urgent medical attention if they develop symptoms of possible seroconversion
 - The arrangement for follow up appointments
 - Verbal consent and HIV test (4th generation test)
 - The need to continue PEPSE for 28 days if the baseline result is negative
 - The need to have a follow-up HIV test a minimum of 45 days after completion of the PEPSE course – this is a minimum of 10.5 weeks post-exposure if the 28 days course is completed
 - The need to use condoms until the follow-up HIV testing is negative
 - Coping strategies, assessment of vulnerabilities and social support
 - For patients with ongoing concerns of sexual risk-taking, appropriate advice and/or signposting should be provided such as PrEP, counselling, addictions services etc
 - **If patient is going to continue on PrEP after PEPSE follow PrEP after PEPSE pathway on the CEG PrEP protocol.**

5 a) Baseline Investigations

	Baseline	2 weeks	12 weeks	6 months
HIV test	Yes- mark as urgent		Yes *	
Gonorrhoea, Chlamydia, Syphilis	all	Only CT/GC could be deferred to later date to reduce appointments	STS. Only add CT/GC if new risks	
UE	yes	Only if abnormal at baseline		
LFT	yes	Only if abnormal at baseline		
Pregnancy test	If appropriate	If appropriate		
Hepatitis B	Immunocompetent adults who have completed Hep B vaccination and responded (ie HBsAb >10 IU at any time) no baseline or follow up Hep B testing is required If they are not as above check Hep B Core antibody and HBsAB and see vaccination info below		If unvaccinated or HBsAb <10 IU at the time of exposure: Hep B Core Ab	Only advised if HBsAb remains <10 IU at 12-weeks: Hep B Core Ab
Hepatitis C PCR	yes		For high risk exposure e.g. HCV+ index,	

*HIV testing can be done a minimum 45 days after completion of the PEPSE course (see BHIVA HIV testing guidelines for further information). If the 28-day PEPSE course is completed this is 73 days (~10.5 weeks) post-exposure. For sexual exposure, to align with syphilis follow-up testing at week 12, the HIV test can be done at the same visit.

- Follow up testing can be done in grab kit appointments, if it is not possible to book these appointments on the day the patient could be added to the SHA virtual diary to be reminded to book
- Consider referral to Choices counselling to help with risk reduction or drugs/ alcohol services as appropriate

Hepatitis B Vaccination

For those that present with unclear vaccination status and do not have documented HBs Ab >10IU they should be offered a booster/ first dose of vaccine. For those who it is felt have had a higher risk of exposure to Hepatitis B they should be vaccinated for hepatitis B +/- hepatitis B immunoglobulin if index is known to be HBsAg positive. If MSM and not vaccinated previously for Hepatitis A give dual vaccine

Hepatitis B schedule- see Hepatitis Protocol

Hepatitis C

Hepatitis C is rarely transmissible through penile-vaginal intercourse or oral sex so baseline and follow-up hepatitis C testing is only indicated in MSM who have had condomless anal sex (further details in BASHH guidelines), PWID and occupational exposures.

Other Sexual Health Considerations

- **Baseline CT/GC/ syphilis testing** should be performed and repeated at end of window periods. (15-17% of PEPSE recipients had an STI at baseline and 4-5% were diagnosed with an STI 2/52 post exposure)
- **Emergency contraception-** should be offered where indicated
- **Vaccines-** MSM should be opportunistically offered vaccinations for Hepatitis A and HPV where indicated in addition to Hepatitis B
- **PrEP Follow up-** Individuals presenting for PEPSE who may be at ongoing risk of HIV should be booked into a PrEP follow up appointment prior to completing PEPSE. See PrEP CEG flow chart of initiating PrEP after PEPSE pathway. For these patients they would have HIV testing 4 weeks after PEPSE was initiated.

Special Scenarios

Chronic Hepatitis B Infection

Baseline hepatitis B virus (HBV) testing of Hepatitis B core antibody should be undertaken in those of unknown HBV status, and vaccination (and HBIG, depending on risk of exposure) initiated in those who are not known to be immune whilst awaiting results.

If someone is known to have Hepatitis B prior to starting PEPSE this should be discussed with the GU doctor of the day

Individuals found to have new Hepatitis B infection at baseline can still have PEPSE but should be discussed with GU doctor of the day

Use of PEPSE in Populations using PrEP

Decisions about the need for PEPSE in the setting of people on PrEP but with less than optimal PrEP adherence depends on length of time since the last dose of PrEP and the site of exposure.

Anal sex: If the only exposure has been through anal sex -for people on daily PrEP, where fewer than 4 pills have been taken in the last 7 days, or for people on event-based PrEP and PrEP has not been taken as recommended PEPSE is indicated.

Vaginal sex: Where the potential HIV exposure is through vaginal sex and PrEP adherence has been suboptimal, PEPSE should be considered if more than 48 hours have elapsed since last dosing or if fewer than six tablets have been taken within the previous 7 days.

Frontal or neovaginal sex: Where the potential exposure to HIV is through frontal sex in trans men or through neovaginal sex in trans women, then PEPSE should be considered if more than 48 hours have elapsed since last dosing or if fewer than six tablets have been taken within the previous 7 days.

When to stop PEPSE due to missed doses

In general if more than 48 hours has elapsed since the last dose of PEPSE it should be discontinued and consideration given as to when follow up HIV testing should be done and if patient needs PrEP going forwards.

Advice to Patients-

What if I miss my dose?

- If you forget to take a dose, take it as soon as you remember it.
- However, if it is time for your next dose, skip the missed dose and go back to your regular schedule.
- Do not take a double dose to make up for a forgotten dose.
- If more than 48 hours has elapsed since the last dose then discontinue PEPSE.

Seroconversion During PEPSE

Individuals experiencing a skin rash or flu-like illness while or after taking PEPSE should be advised to attend for urgent review to exclude an HIV seroconversion.

Anyone found to be HIV positive after PEPSE has been started should be discussed urgently with the GU doctor of the day.

Anyone found to be HIV positive at baseline should be managed as standard for new HIV diagnosis

Further high risk exposures while on PEPSE

In the event of a further high-risk sexual exposure during the last two days of the PEPSE course, PEPSE should be continued until 48 hours after the last high-risk exposure for anal sex or until 7 days after the last high-risk exposure for vaginal/frontal sex.

If they have not already been referred for ongoing PrEP after PEPSE this should be discussed again with them

