Guidance for Sandyford staff on HIV pre-exposure prophylaxis (PrEP)

What's new:

Ensure a **confirmed negative HIV test** before giving PrEP

Individualised assessment of **renal risk** at **baseline** should reduce number of people needing routine urinalysis

Definition of '**undetectable viral load'** for transmission risk is specified as **<200 copies/mL**

Routine follow-up is at **3mths** except in very specific situations

Summary flowchart

1 Introduction

1.1 Who is this guidance for?

This guidance is for staff working in specialist sexual health services in NHSGGC.
With the support of this guidance, clinicians working in Sandyford Sexual and Reproductive Health Services will be able to

- Understand what PrEP is, who might benefit and who will not be likely to benefit
- Be able to provide accurate information to individuals requesting PrEP
- Be able to apply NHS funded PrEP eligibility criteria and discuss this with individuals
- Be able to provide baseline testing prior to starting PrEP
- Understand the monitoring required and participate in management of individuals taking PrEP medication

1.2 What is HIV PrEP?

PrEP stands for Pre-Exposure Prophylaxis and is the name given to medicines that can be taken by someone who is HIV negative to reduce their risk of becoming infected with HIV.
PrEP is one of several ways of reducing sexual transmission of HIV (such as condom use or changes in behaviour). PrEP medication should therefore be considered as just one component of wider interventions to prevent HIV transmission in those at highest risk. The evidence base for the use of PrEP is included in Appendix 3

PrEP medication has been available on NHS prescription in Scotland since July 2017. It is indicated for HIV negative adults aged 16 years and over who are at high and ongoing risk for HIV infection.

Please see these useful links for background:

http://www.steveretsonproject.org.uk/information-for-men/safer-sex/prep-faqs-1/

www.prep.scot

2 Eligibility and exclusion criteria

2.1 Universal criteria

Before being assessed for eligibility for NHS-funded PrEP, the individual must satisfy **all** of the following universal criteria**:**

1. Be aged **16 years or over**
2. Have a **negative HIV test** (test used should be appropriate for window period)
3. Be able to and agree to attend for **regular 3 monthly review** including for monitoring, sexual health care and support, and to collect prescriptions
4. Be willing to **stop** NHS-funded PrEP if eligibility criteria are no longer met
5. Be **ordinarily resident** in Scotland

2.2 Eligibility criteria

If all of the above universal criteria are met for NHS funded PrEP, the client may be assessed for **clinical eligibility** for PrEP.

An individual is eligible for PrEP if <u>one or more</u> of the following apply:

1. Current sexual partners, irrespective of gender, of people who are **HIV positive** and with a **detectable viral load**.
2. MSM & transgender women with a documented **bacterial rectal STI** in the last **12** months
3. MSM & transgender women reporting **condomless penetrative anal sex** with **two or more** partners in the last 12 months and likely to do so again in the next 3 months
4. Individuals, irrespective of gender, at an **equivalent high risk of HIV** acquisition, as agreed with another specialist clinician

MSM includes trans men with male partners

For individuals from other health boards out-with GG&C, their home health board will be cross-charged for drug costs.

2.3 Exclusion criteria

PrEP should not be used:

- If the individual is **already HIV-positive**
- You suspect **HIV seroconversion**
- In monogamous serodiscordant couples where the HIV positive partner is on **treatment** and has a **viral load reliably below 200 copies/mL** and a good expectation of maintaining this
- Significant **renal impairment** (eGFR<60 ml/min) or known **osteoporosis**
- In individuals who are **hepatitis B surface antigen** positive (i.e. current infection). For these clients tenofovir disoproxil may be used for suppression of their hepatitis so should be prescribed in co-ordination with their local hepatology centre

2.4 Can people get PrEP from non-NHS sources?

- Some people choose to buy PrEP online at a cost of around £40-50 for each month's supply. Information on how to do this is in the i-base guide http://i-base.info/uk-guide-to-prep/
- It is legal for a patient to purchase and import 3 months of generic drug via the internet for personal use
- The website www.iwantprepnow.co.uk has been set up by community advocates to provide information about PrEP and links to sellers.
- Clients may want to purchase PrEP online if they do not meet the current eligibility criteria but would like to use this prevention. They should be offered monitoring through specialist sexual health services, with the monitoring schedule outlined below.

3 Prescribing PrEP and Managing Patients on PrEP

3.1 What do I do when someone wants to start PrEP?

3.1.1 When someone enquires by phone or via the website:

- Direct client to sources of information about eligibility and background to PrEP such as www.prep.scot or https://www.sandyford.org/sexual-health-information/sexual-health/hiv-prevention-testing/prep/
- Offer appointment for test express for pre-PrEP testing including STI & BBV testing, urinalysis and U&Es
- Offer appropriate appointment according to current operational guidance for eligibility assessment and supply for when results will be available

3.1.2 When someone attends the clinic to discuss first prescription of NHS PrEP:

Clearly **document** in the clinical notes:

- Formal assessment of eligibility and indication for NHS Scotland funded PrEP with documentation as either 1, 2, 3 or 4 to correlate with above eligibility criteria. If not eligible please clearly document this in the notes and STISS code *(see section Appendix 2 p 17).*
- Last serum HIV test date and result. **Clients should have a documented negative HIV test in the last 4 weeks before starting PrEP.**
- Most recent likely HIV risk. If high risk of exposure <72 h then consider PEPSE (see Sandyford PEPSE guideline) at this point
- Routine sexual health and testing history
- Hepatitis B testing and vaccination history unless already completed on NaSH
- Full medical history focussing on risk factors for and history of osteoporosis and renal disease. Risk factors for chronic kidney disease (CKD) include: age >40 years, diabetes, hypertension and ischaemic heart disease
- All other medications including over the counter medication, focussing especially on medication associated with renal impairment
- Any recreational drug use

  - Discussion of other risk reduction methods and motivational interviewing if this has not already occurred within this episode of care.

- **Offer** appointment with sexual health adviser to discuss risk reduction and other support. This may include information and support for those involved in chemsex if appropriate, and/or referral to SRP Choices

- **Assess** if patient has a significant medical history (e.g diabetes, hypertension, kidney problems, heart disease) or is on medication likely to impair renal function or if you are unsure whether the person is eligible. If so then please ask for advice from a senior GUM clinician. Sometimes it will be necessary to book the patient into GUM complex clinic for discussion of initiation of PrEP.

Some common medicines associated with renal impairment
ACE inhibitors (eg lisonopril)
Angiotensin receptor blockers (eg candesartan, losartan)
Diuretics (bendroflumethazide)
NSAIDs (such as ibuprofen, naproxen) or COX II inhibitors

3.1.2 What information do people need about starting PrEP?

People need to understand:

- PrEP medication
  - how it works
  - indications and limitations
  - how to take their medication
  - effectiveness
  - risks and benefits
  - need for adherence
  - common side effects
  - the risk of interactions with other medication
- The need for 3-monthly HIV and STI testing and monitoring of kidney function at appropriate intervals
- The symptoms of seroconversion and when and how to seek an urgent HIV test
- Importance of considering other risk reduction practices, such as condom use
- Benefits of informing GP to improve prescribing safety

Supply a patient information leaflet (PIL) or text information from www.prep.scot or ibase http://www.steveretsonproject.org.uk/media/3624/prep-in-scotland-2nd-ed-final.pdf via NaSH SMS.

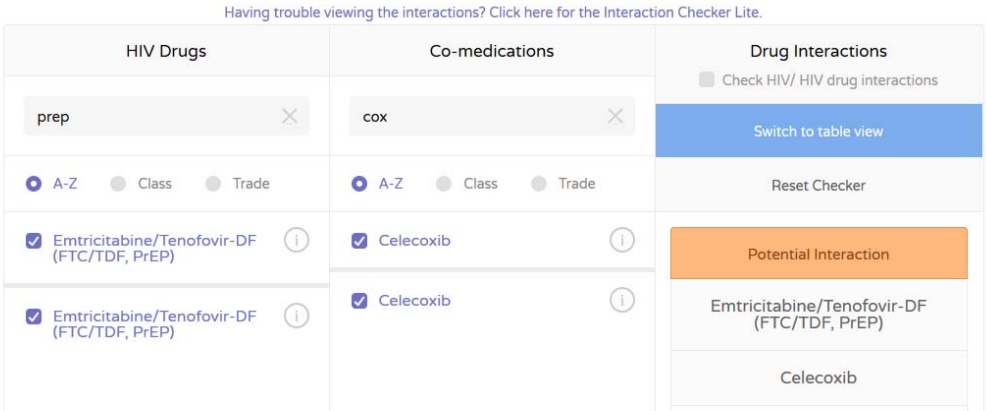
3.1.3 What drugs might interact with PrEP medication?

All staff should check ECS via clinical portal for accurate medication list if any doubt at all about other medications.

Potential drug-drug interactions must be checked at http://www.hiv-druginteractions.org/

The main concern is of additive renal toxicity.

The Liverpool interaction website has a specific entry for PrEP:



3.1.4 What tests do people need before starting PrEP?

The purpose of baseline testing is

i) to **rule out HIV** before starting PrEP to avoid risk of HIV drug resistance

ii) to rule out risk of **hepatitis B reactivation**

iii) to assess **risk of renal impairment** and decide on appropriate frequency of renal monitoring

iv) to rule out **co-existent STIs** include HCV which are known to be more common in those seeking PrEP.

v) in women, to **exclude pregnancy** risk

Test	**Indication**
Syphilis	All
HIV 4th generation*	All
Hep B core Ab	If Hep B status unknown
Hep C Ag	All MSM
Vulvo vaginal NAAT	All females
Urine NAAT	All males
Rectal NAAT	All MSM
Pharyngeal NAAT	All MSM
Urinalysis	All
Pregnancy test	Females where appropriate
U&E	All
uPCR	If urinalysis protein 1+ or more

Do not do LFTs at baseline for PrEP assessment

3.1.5 How do I assess renal risk?

Good renal function is indicated by a healthy filtration rate (eGFR) and absence of any urinary protein or blood (assessed by dipstick and sometimes urine biochemistry).

- eGFR should be calculated using the **CKD-EPI equation**: see **Appendix 6** for instructions
- eGFR must be **>60 ml/min** for PrEP to be prescribed.
- eGFR **between 60 and 90 ml/min** indicates possible **early renal impairment** and patients will need more frequent renal testing. The lab do NOT do this calculation for us.
- If patients are under the age of 18 you need a different equation due to lower muscle mass. Please use: http://labtestsonline.org.uk/understanding/analytes/gfr/tab/test/ or http://nephron.com/bedside_peds_nic.cgi

What do I do if the urinalysis is positive?

- If there is protein on urinalysis at baseline (i.e. + or more) urine for uPCR (urinary protein creatinine ratio) should be sent to biochemistry.
- If urinalysis shows **protein +** only please discuss with a member of the GUM senior team before PrEP is started. In most cases, PrEP will be started, with a uPCR sent and patient should be added to 'SC GUM results virtual' list so that uPCR result can be checked and acted on if necessary.
- If urinalysis shows **protein ++** or **+++,** this needs further investigations. Please check BP, send uPCR, enquire about medical history and add to GUM virtual review. Do not start PrEP in this situation.
- Renal toxicity and other health issues can also manifest as dipstick-positive blood or glucose so if these are present, ask for senior advice.

3.1.6 What do I do about starting PrEP on the day of presentation?

- In specific circumstances of high immediate risk PrEP may be started only after a negative blood-based point-of-care test after careful discussion of the risk/benefits and only if a blood-based plasma test is also taken and there are no symptoms suggestive of seroconversion.

3.1.7 What are the main side effects of PrEP?

- Most people taking TDF/FTC will not experience any major side effects
- Mild nausea, stool disturbance, bloating and headache are reported by fewer than 10% and usually stop within the first month
- The most serious side effect is the potential for renal toxicity, particularly in those aged over 40 and/or with pre-existing kidney issues
- Additional care is also needed if there is reduced bone density (osteoporosis or osteopenia)

3.2 How should people take PrEP?

- The evidence base is for use of Truvada® (branded tenofovir disoproxil fumarate 300mg + emtricitabine 200mg) but bioequivalent generic regimes are now used

PrEP can be taken in a couple of ways:

- Daily dosing
- event based dosing (EBD) – the evidence base for this only applies to MSM

Daily and event-based PrEP showed similar efficacy in MSM so either may be offered to MSM.

1. **Daily dosing** – for anal or vaginal sex
    - o One dose is taken every day, ideally at the same time every day, regardless of sexual activity.
    - o Protection is achieved after 7 days for insertive or receptive vaginal sex.
    - o If a double dose is taken as the initial dose (followed by daily dosing) then protection is achieved for anal sex after 2 hours of initial dose.
    - o If PrEP is discontinued this should be at least 48 hours (2 doses) after last anal sex and 7 days (7 doses) after vaginal sex.

2. **Event-based dosing** – **for anal sex only** (Figure 3)
    - o Single sex act of condomless anal sex:
        - loading dose of 2 tablets of TDF/FTC 2-24 hours before sex
        - 1 tablet 24 hours (22-26 hours) after the first dose
        - another tablet 48 hours (46-50 hours) after the first dose
    - o Multiple sex acts of condomless anal sex:
        - Loading dose of 2 tablets of TDF/FTC 2-24 hours before first sex
        - 1 tablet daily for all days involving an act of condomless anal sex and the two days following the last episode of condomless anal sex.
    - o If restarting EBD within 7 days of the last dose, the loading dose can be 1 tablet instead of 2

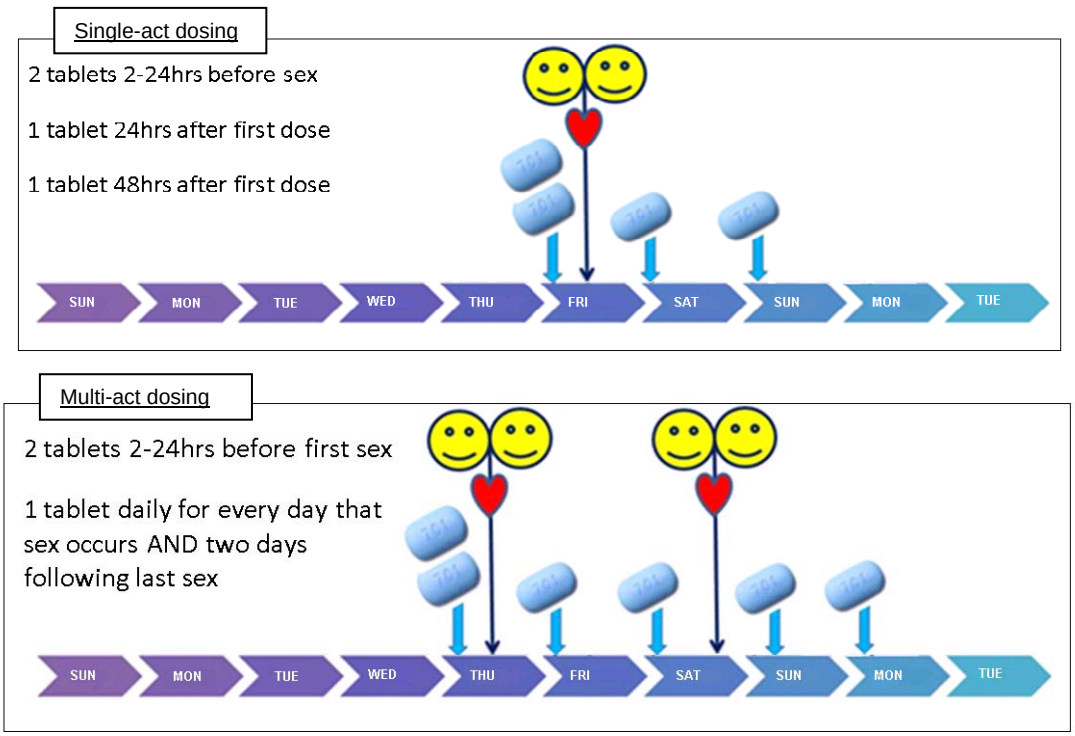


Figure 3: Event based dosing (

- The number of tablets prescribed at the first visit should be:
    - **30 doses**
        - for those within the window period for HIV testing when starting PrEP
    - **90 doses**
        - for those with a negative HIV fourth generation test outwith the window period
        - no symptoms of recent seroconversion
        - no abnormalities expected on baseline testing.

3.3. Communication with GP (and other healthcare providers)

As we are providing long-term medication that may cause additive renal toxicity it is preferable that we contact the patient's GP on initiation of PrEP and after each annual review. In the case of complex co-morbidity it may be appropriate to communicate with other care providers.

A template can be found under 'GP PrEP' in NaSH document library. Please Q these letters to Suzanne Hughes, Medical Secretary who will send these letters out.

4. What follow up do people need?

4. 1 Follow up schedule

These follow up arrangements may be amended for operational reasons

For non medically-complicated MSM patients please book into the **SRP clinic** at **3 months**.

Medically complicated patients are best followed in the **GUM complex clinic**.

Tailored arrangements are needed for heterosexual men and women especially partners of those living with HIV.

Give 3 months of PrEP except in the following situations:

Face-to-face review at 1 month:

- Risk of significant exposure in the 4 weeks prior to the baseline HIV test
- High likelihood of medical complexity such as likely drug-drug interactions or intolerance

4.2 What to discuss at follow-up

- Reason for continuing PrEP and check meets criteria for prescribing
- New co-medications or illnesses
- Regimen followed and any adherence challenges
- HIV risk-reduction advice
- Recreational drug use, alcohol and whether other support is needed

4.3 What investigations do people need while taking PrEP?

Every 3 months:

Test	Indication
Syphilis	All
HIV 4th generation	All
Vulvovaginal NAAT	All females
Urine NAAT	All males
Rectal NAAT	All MSM
Pharyngeal NAAT	All MSM
Pregnancy test	Females if appropriate
HCV Ag	If risk history suggests

Every 6 months in addition if renal risk*

UE	
Urinalysis	
uPCR	If urinalysis protein 1+ or more

***** *age >40, eGFR <90 ml/min at baseline, renal concern drugs, co-morbidities can be 3 monthly if significant concern*

Every year in addition

Hep C Ag	All
Hep B cAb	If not known to be immune

Renal monitoring

Monitoring for renal toxicity is now guided by assessment of risk at baseline and patient age.

- Calculate baseline eGFR using CKD-EPI if this has not already been done as per Appendix 6
- **Normal renal function** is when eGFR >90 ml/min, no proteinuria at baseline and no renal risks (age <40):
    - Annual UE only. No need for dipstick testing.
- **Early CKD:** eGFR 60 to 90 ml/min and/or proteinuria at baseline or **renal risk** (age >40, medication associated with renal impairment, hypertension, diabetes)
    - UE plus urinalysis every 6 months or more frequently if eGFR <75 ml/min.
- **Stage 3 CKD** (eGFR <60 ml/min) PrEP should only be considered on a case-by-case basis. If eGFR is <60 ml/min do not supply further PrEP and seek specialist help.

4.4 What else to do at follow-up

- Supply 90 days of medication or a suitable amount if Event-Based Dosing
- Arrange an acceptable follow-up ensuring that supply will last
- Code eligibility on the STISS coding page for that episode

4.5 When should I ask for help with PrEP prescribing and monitoring?

Contact senior GUM team for specialist advice in the following situations:

- PrEP initiation or continuation in those with abnormal tests (including + or more of protein on dipstick urinalysis)
- Immediate management of
  - people with known/suspected exposure to HIV and incorrect use of PrEP
  - people with symptoms suggestive of HIV infection
  - people on PrEP found to have HIV infection should be seen ideally the same day to consider intensification of PrEP to full high barrier antiretroviral regimen pending resistance testing
- Any concerns about your patient or questions you can't answer

4.5. When should people stop PrEP?

Continuing eligibility, willingness and ability to adhere to treatment should be assessed and documented at each visit

- Discontinue *NHS funded* PrEP if
  - Universal criteria are no longer all met
  - None of the eligibility criteria apply
  - Any exclusion criteria are met
  - Discontinue PrEP if unacceptable side effects or toxicities
- Ideally, PrEP should not be discontinued for at least 2 doses or 48 hours following last episode of risk (anal sex) or 7 days (vaginal sex),

If a patient is no longer eligible for NHS funded PrEP, but wishes to continue on self-funded PrEP they should still attend the PrEP clinic for monitoring

Who should professionals and the public phone for advice?

Information is available at https://www.sandyford.org/sexual-health-information/sexual-health/hiv-prevention-testing/prep/ with links to FAQs and other documents and www.prep.scot http://www.steveretsonproject.org.uk/media/3624/prep-in-scotland-2nd-ed-final.pdf

Professional helpline: 0141 211 8646

Sexual health advisers: 0141 211 8639

5 References

HIV Scotland Short Life Working Group (2017). *PrEP in Scotland Report* Available at: http://www.hivscotland.com/our-work/prep-in-scotland/ [accessed 12/12/2018]

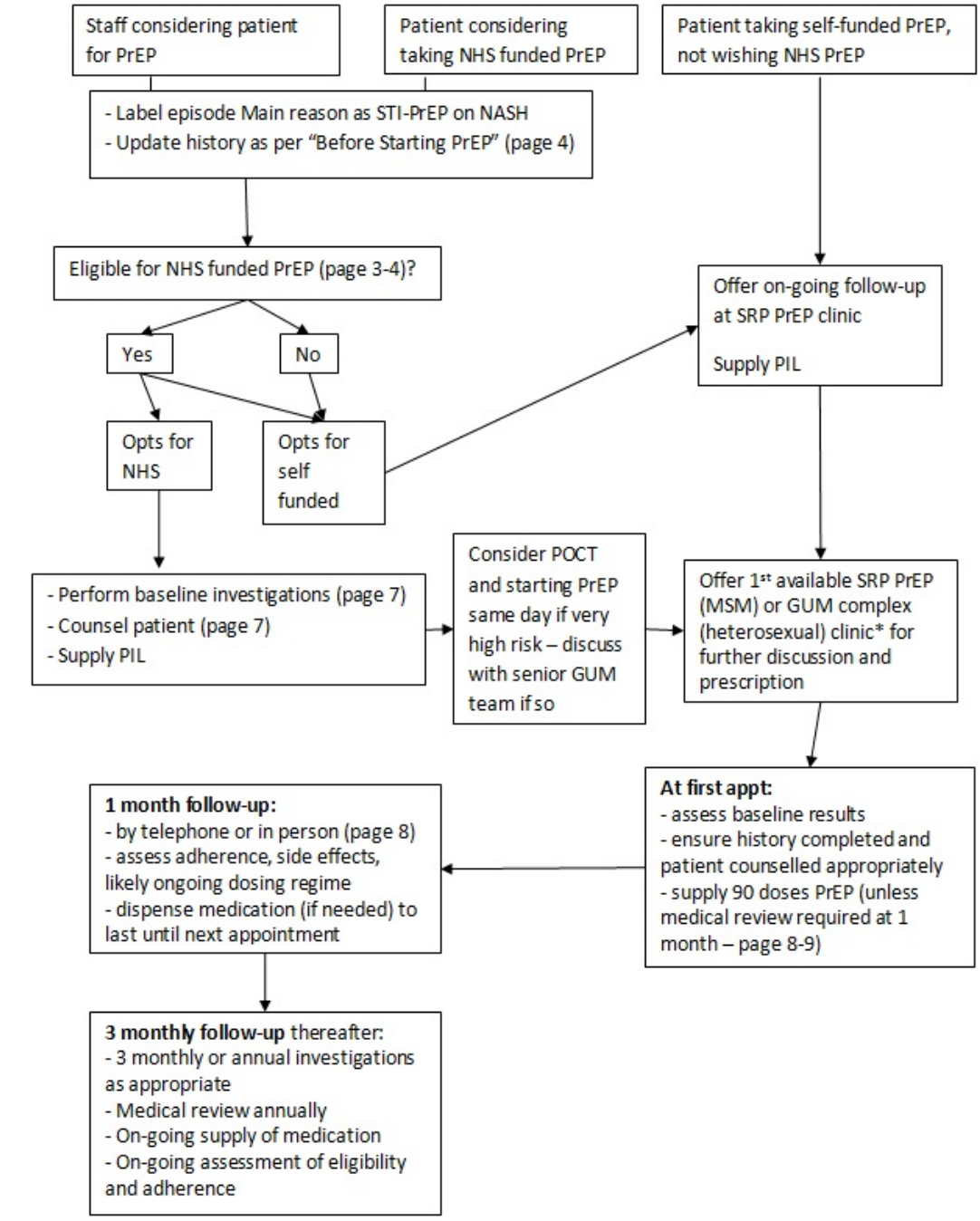
British HIV Association and British Association of Sexual Health and HIV. *BHIVA/BASHH guidelines on the use of HIV pre-exposure prophylaxis (PrEP) 2018*
Available at: https://www.bhiva.org/PrEP-guidelines [accessed 12/12/2018]

NSW Ministry of Health. *Pre-Exposure Prophylaxis of HIV with Antiretroviral Medications,* Expanded PrEP Implementation in Communities in *New South Wales* (EPIC-NSW). Available at: http://www1.health.nsw.gov.au/pds/ActivePDSDocuments/GL2016_011.pdf [accessed 12/12/2018]

McCormack S *et al*; Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial Lancet 2016; 387: 53–60

Molina JM et al. On-Demand Pre-exposure Prophylaxis in Men at High Risk for HIV-1 Infection. N Engl J Med 2015; 373:2237-2246

Appendix 1: Management Summary Flowchart



Appendix 2: PrEP Coding

STISS Coding (figure2) is required for all clients who are identified as eligible for PrEP (**even if they decline**) and must be performed at each clinic visit (see below for flow chart). This is important for the national monitoring of the success of the PrEP programme and helps plan services.

If PrEP advice or monitoring is the main focus of the consultation, use NaSH to record "STI-PrEP" as the Main Reason for attending (figure 1):

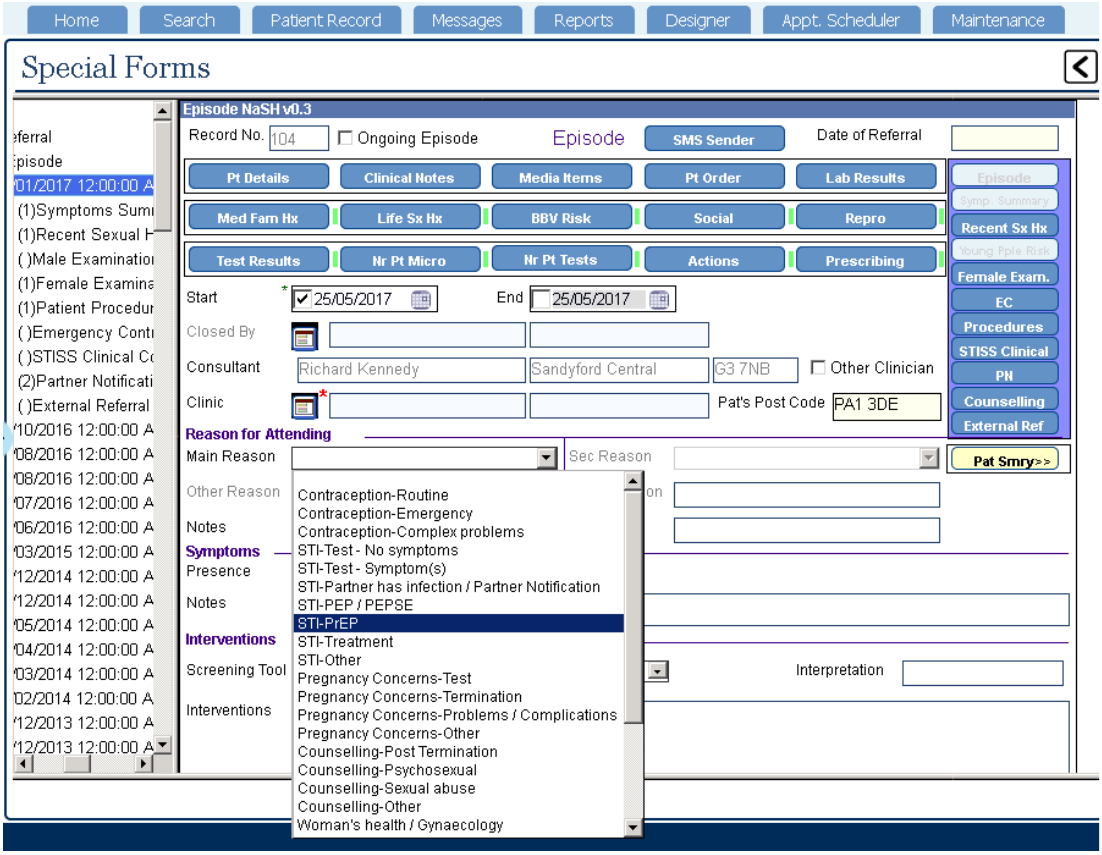


Figure 1: Episode reason

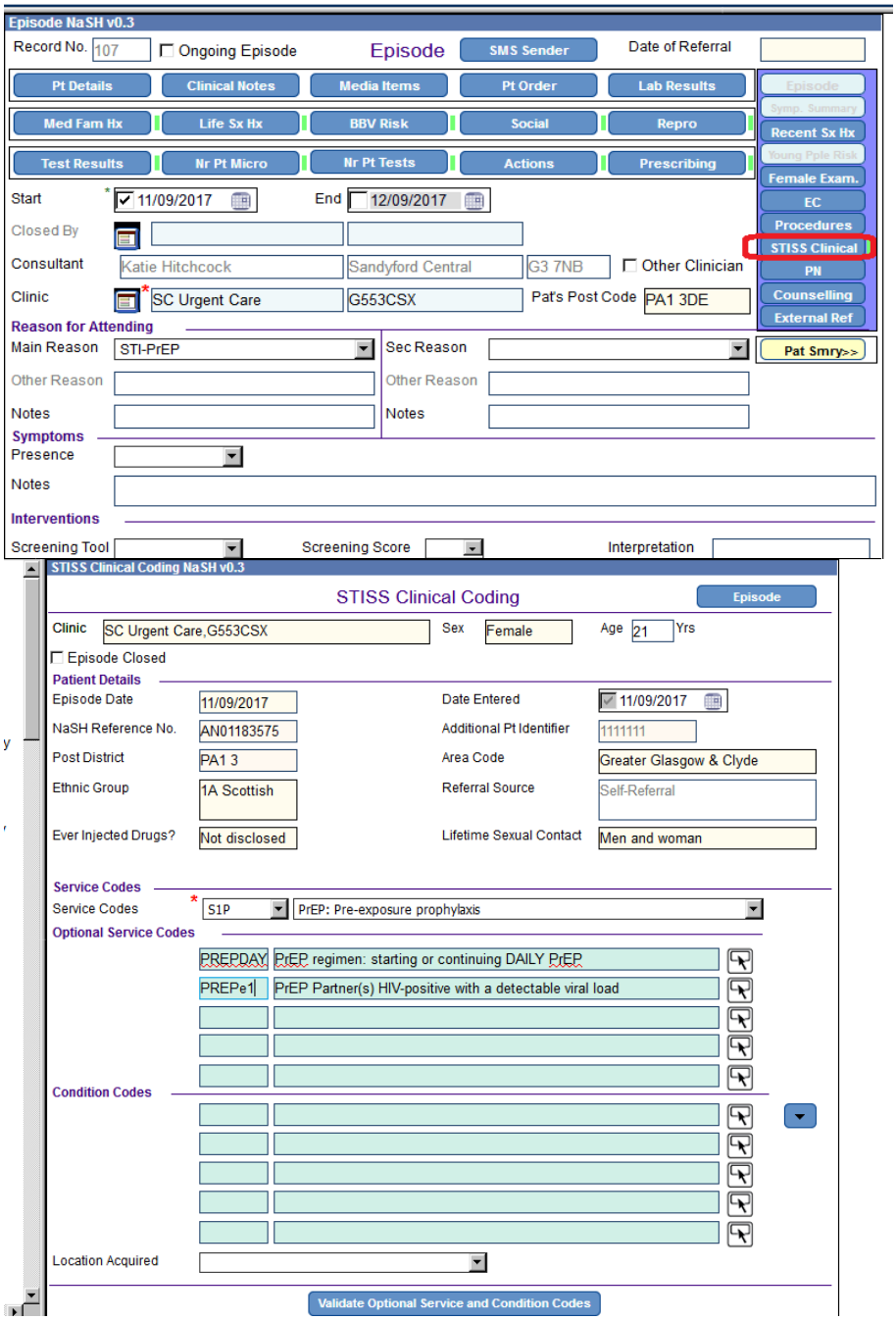
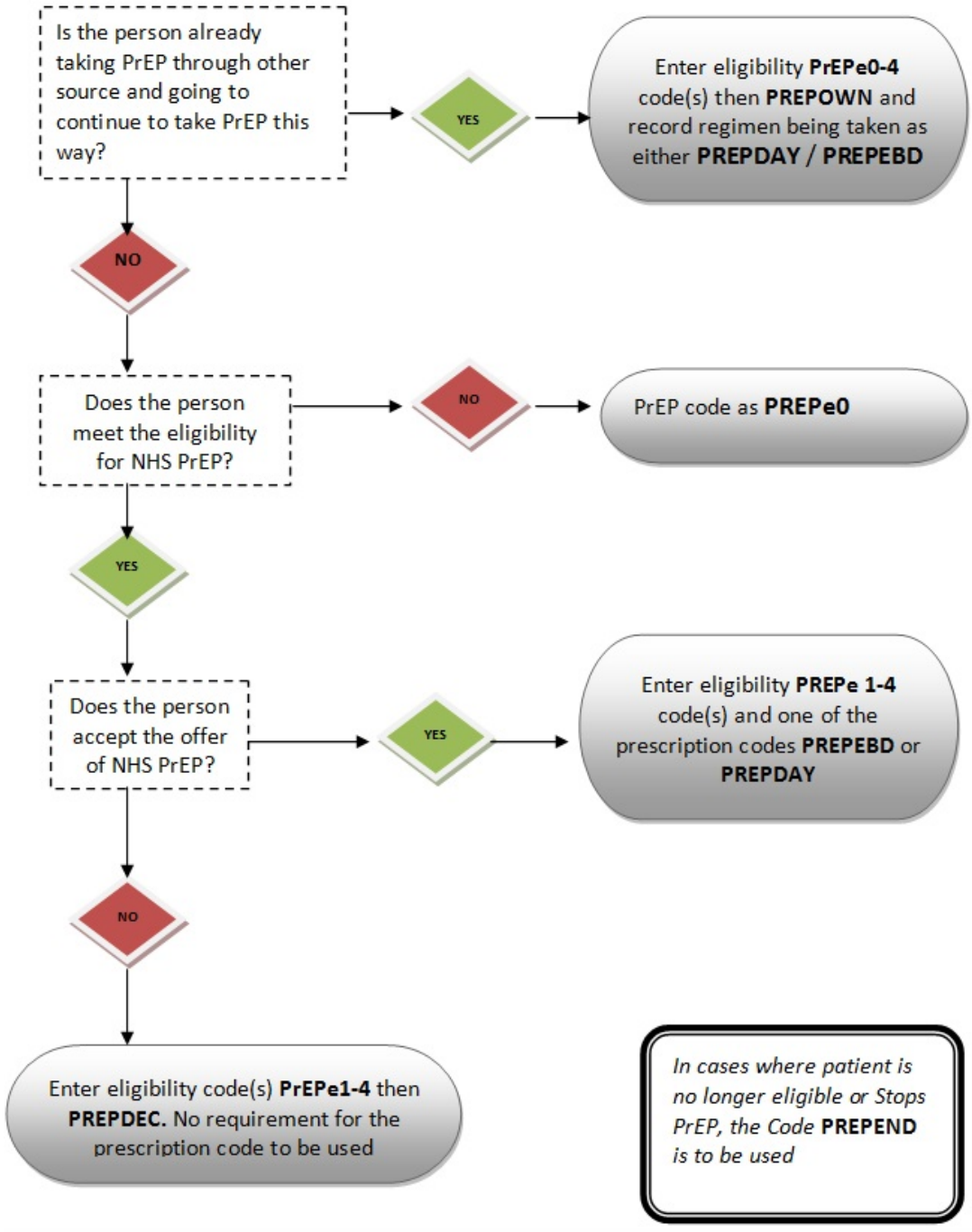


Figure 2: STISS coding

This flowchart shows coding in practice.



Appendix 3: Evidence base for PrEP use

In 2015 two studies (PROUD, UK and iPERGAY, France) reported efficacy in men who have sex with men (MSM) of 86%. Efficacy is linked to levels of adherence. These studies are felt to be most comparable to predicted PrEP use in Scotland.

- These studies used a combination of 2 oral antiretroviral drugs: tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC). The brand name for these medications combined into a single pill is “Truvada®”. Several generic versions of TDX/FTC exist (a common example being “Tenvir-EM”) and can be sourced at individuals’ own expense for short term use through online pharmacies.
- Medications that are “bioequivalent” to TDF (such as tenofovir disoproxil succinate) may be used in place of TDF for PrEP, although have not been specifically studied. NHS Scotland has procured these for use in the national PrEP programme.
- Other types of PrEP have been studied (including alternative antiretrovirals and non-tablet formulations), but are not licensed for use in Scotland
- The safety profile of Truvada® use for HIV negative individuals reports adverse reactions in 2% in those using PrEP and some rare but serious side effects (see details below).

The 2018 BHIVA/ BASHH guideline for PrEP use fully discusses the evidence base on pp 15-51 of the guideline.

Appendix 4: Abbreviations

- CKD: chronic kidney disease: reduction in filtration or evidence of glomerular or tubular damage
- CT – Chlamydia trachomatis
- eGFR: estimated glomerular filtration rate
- FTC - emtricitabine
- GC – Neisseria gonorrhoeae
- GG&C – NHS Greater Glasgow and Clyde
- HIV PrEP – PrEP stands for “pre-exposure prophylaxis”. In this context, HIV PrEP refers to medication taken before sex to prevent infection with HIV. The terms PrEP and HIV PrEP are used interchangeably in this document.
- MSM – men who have sex with men (the term MSM used in this document includes transmen having male sexual partners)
- NAAT – Nucleic acid amplification test
- NHS – the term in this document refers to NHS Scotland
- PEP – In this document PEP refers to Post Exposure Prophylaxis of HIV
- PIL – patient information leaflet
- POC – point of care test for HIV
- TDX - tenofovir disoproxil (the X stands for the range of salts)
- Terms females and males include trans- and cis- of each
- U&E – urea and electrolytes
- uPCR – urinary protein creatinine ratio

Appendix 5: 2018 BASHH/BHIVA Flowchart

BHIVA/BASHH guidelines on the use of PrEP

Flow chart

Wanting to start PrEP

First visit assessment and documentation

- Reasons for seeking PrEP
- Medical history relevant to TD-FTC including bone and renal health, concomitant medications
- Risk assessment and eligibility for PrEP
- Consideration of acute HIV infection and eligibility for PEPSE
- Details of HIV/STI screens last 12 months
- Timing of condomless sex acts last 6 months
- If MSM: discussion of both regimens (daily and on demand)
- Reasons adherence is important before and after risk of exposure
- Potential toxicities and how to manage
- Risks and benefits of online purchase and community websites with information about online purchase if required
- Results HIV/STI screen
- Decision to start and time to start
- Recommended follow-up at 1 or 3 months after starting PrEP for HIV/STI screen, adherence check and serum creatinine and eGFR
- Code using GUMCAD codes (See Appendix 1)

Baseline testing

- HIV testing using combined HIV antigen/antibody test (plus POCT if same day initiation is preferable)
- STI screen
- Screen for HBV and HCV testing for those at risk
- Serum creatinine, eGFR and urinalysis
- Pregnancy testing if indicated

Quarterly visit documentation

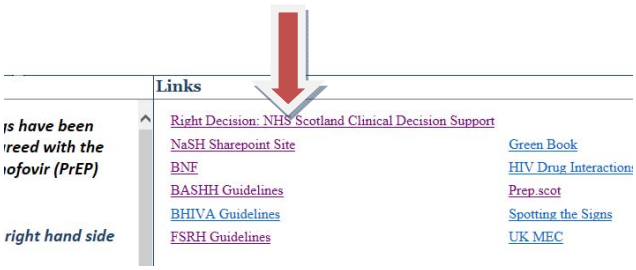
- Reason for continuing PrEP
- Regimen followed and reasons for non-adherence including adverse events
- Support provided for medication adherence
- HIV risk-reduction advice
- Recreational drug or alcohol use with referral to support services, if required
- Results HIV/STI screen (including HCV testing in MSM, trans women and other at-risk groups)
- Prescription for 90 days
- Arrange follow-up for 3 months
- Code using GUMCAD codes (Appendix 1)

Monitoring

- Result of HIV testing using a combined antigen/antibody test
- Results of STI screen (including HCV testing in MSM, trans women and other at-risk groups)
- Serum creatinine and eGFR annually if >90 mL/min/1.73 m^2 and aged <40 years, more frequently if <90 mL/min/1.73 m^2 or >40 years or other risk factors for renal disease.

Appendix 6: How to calculate eGFR by CKD-EPI

Quickest way to access calculators is via the Right Decision platform
Search 'CKD-EPI' and 'calculator' and select the BMJ Best Practice calculator
Remember to set the units to 'mcmol/L'
Once open the calculator sits in a tab on the browser next to NaSH and can be left open



Opens in a new tab: search ' CKD-EPI'