Guidelines on the use of pre-exposure prophylaxis (PrEP)

Michael Brady
King's College Hospital, London

Alison Rodger
University College London

On behalf of the BHIVA/BASHH PrEP guideline writing committee

Disclosures

I have received honoraria for speaking engagements from Gilead Sciences

Guideline writing group

David Asboe	Consultant HIV and Sexual Health, Chelsea and Westminster NHS Foundation Trust
Valentina Cambiano	Lecturer in Infectious Disease Modelling and Biostatistics, University College London
Dan Clutterbuck	Consultant HIV and Sexual Health, NHS Lothian,
Monica Desai	Consultant Epidemiologist, Public Health England
Nigel Field	Senior Lecturer, University College London
Justin Harbottle	Programme Officer, Terrence Higgins Trust
Zahra Jamal	Policy and Research Officer, NAZ
Sheena McCormack	Professor of Clinical Epidemiology, MRC Clinical Trials Unit at UCL
Adrian Palfreeman	Consultant HIV and Sexual Health, University Hospitals of Leicester NHS Trust
Mags Portman	Consultant HIV and Sexual Health, Mortimer Market Centre
Killian Quinn	Consultant HIV and Sexual Health, King’s College Hospital, London
Melinda Tenant-Flowers	Retired Consultant in HIV and Sexual Health Medicine, King’s College Hospital, London
Ed Wilkins	Consultant in Infectious Diseases, North Manchester General Hospital
Ingrid Young	Chancellor's Fellow, Usher Institute, University of Edinburgh

Community Consultation

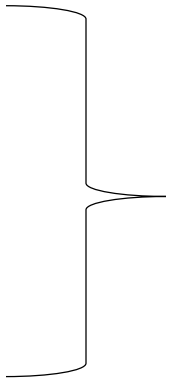
- Yusef Azad (NAT)
- Takudzwa Mukiwa (THT)
- Will Nutland (Prepster)
- Greg Owen (I Want PrEP Now)
- Michelle Ross (CliniQ)
- Sophie Strachan (Sophia Forum)
- Marc Thompson (Prepster/Black Out UK)
- George Valiotis (HIV Scotland)

Guidelines: Structure

Section 1-3: Objectives, Methods, Summary Recommendations

Section 4: Detailed evidence review:

- Efficacy
- Adherence
- Safety
- Risk behaviour
- Timelines for starting and stopping PrEP



I. MSM
II. Heterosexual
III. People who inject drugs
IV. Trans people
V. Young people

Sections 5-7: Practical guidance to support:

- Risk assessment
- Starting PrEP and stopping PrEP
- On-going management and monitoring

Section 8. Buying generic PrEP

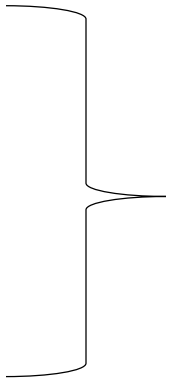
Section 9. Cost effectiveness of PrEP in high income countries

Guidelines: Structure

Section 1-3: Objectives, Methods, Summary Recommendations

Section 4: Detailed evidence review:

- Efficacy
- Adherence
- Safety
- Risk behaviour
- Timelines for starting and stopping PrEP



I. MSM
II. Heterosexual
III. People who inject drugs
IV. Trans people
V. Young people

Sections 5-7: Practical guidance to support:

- **Risk assessment**
- **Starting PrEP and stopping PrEP**
- **On-going management and monitoring**

Section 8. Buying generic PrEP

Section 9. Cost effectiveness of PrEP in high income countries

Section 5: Eligibility - Recommendations

We recommend that

- PrEP with daily or on-demand oral TD-FTC is offered to MSM, and daily oral TD-FTC is offered to trans women, at elevated risk of HIV acquisition through recent (6 months) and on-going condomless anal sex. (1A)
- PrEP with daily oral TD-FTC is offered to HIV-negative people having condomless sex with partners who are HIV positive, unless the partner has been on ART for at least 6 months and their plasma viral load is <200 copies/mL. (1A)

We suggest that

- PrEP with daily oral TD-FTC (or TDF alone if FTC contraindicated) should be offered on a case-by-case basis to heterosexual men and women with current factors that may put them at increased risk of HIV acquisition (2B)

Good Practice Point

- Consider PrEP with daily oral TD-FTC on a case-by-case basis in people with current factors other than condomless anal sex that may put them at increased risk of HIV acquisition

Section 5: Eligibility - Recommendations

We recommend that

- PrEP with daily or on-demand oral TD-FTC is offered to MSM, and daily oral TD-FTC is offered to trans women, at elevated risk of HIV acquisition through recent (6 months) and on-going condomless anal sex. (1A)
- PrEP with daily oral TD-FTC is offered to HIV-negative people having condomless sex with partners who are HIV positive, unless the partner has been on ART for at least 6 months and their plasma viral load is <200 copies/mL. (1A)

We suggest that

- PrEP with daily oral TD-FTC (or TDF alone if FTC contraindicated) should be offered on a case-by-case basis to heterosexual men and women with *current factors that may put them at increased risk of HIV acquisition (2B)*

Good Practice Point

- Consider PrEP with daily oral TD-FTC on a case-by-case basis in people with *current factors other than condomless anal sex that may put them at increased risk of HIV acquisition*

Section 5: Eligibility – Good Practice Point

Consider PrEP with daily oral TD-FTC on a case-by-case basis in people with current factors other than condomless anal sex that may put them at increased risk of HIV acquisition

Consider PrEP on a case-by-case basis

PrEP may be offered on a case-by-case basis to HIV-negative individuals considered at increased risk of HIV acquisition through a **combination of factors** that may include the following:

Population-level indicators

- Heterosexual black African men and women
- Recent migrants to the UK
- Transgender women
- People who inject drugs
- People who report sex work or transactional sex

Clinical indicators

- Rectal bacterial STI in the previous year
- Bacterial STI or HCV in the previous year
- Post-exposure prophylaxis following sexual exposure (PEPSE) in the previous year; particularly where repeated courses have been used

Sexual behaviour/sexual-network indicators

- High-risk sexual behaviour: reporting condomless sex with partners of unknown HIV status, and particularly where this is condomless anal sex or with multiple partners
- Condomless sex with partners from a population group or country with high HIV prevalence (see UNAID definitions [1])
- Condomless sex with sexual partners who may fit the criteria of 'high risk of HIV' detailed above
- Engages in chemsex or group sex
- Reports anticipated future high-risk sexual behaviour
- Condomless vaginal sex should only considered high risk where other contextual factors or vulnerabilities are present

Drug use

- Sharing injecting equipment
- Injecting in an unsafe setting
- No access to needle and syringe programmes or opioid substitution therapy

Sexual health autonomy

Other factors that *may* affect sexual health autonomy

- Inability to negotiate and/or use condoms (or employ other HIV prevention methods) with sexual partners
- Coercive and/or violent power dynamics in relationships (e.g. intimate partner/domestic violence)
- Precarious housing or homelessness, and/or other factors that may affect material circumstances
- Risk of sexual exploitation and trafficking

PrEP Impact Study: eligibility criteria

1. Men (cisgender and transgender) and transgender women who:
   - Have sex with men
   - Have had a negative HIV test in the preceding year
   - Report condomless intercourse (excluding oral) in the previous 3 months
   - Are likely to have condomless intercourse in the next 3 months.
2. HIV negative partners of an HIV positive person when:
   - The HIV positive partner is not known to be virally suppressed
   - Condomless intercourse (excluding oral) is anticipated before treatment of the HIV positive partner takes effect
3. ***HIV negative persons who are clinically assessed and considered to be at similar high risk of HIV acquisition as those with a serodiscordant partner who is not known to be virally suppressed***

PrEP and renal function

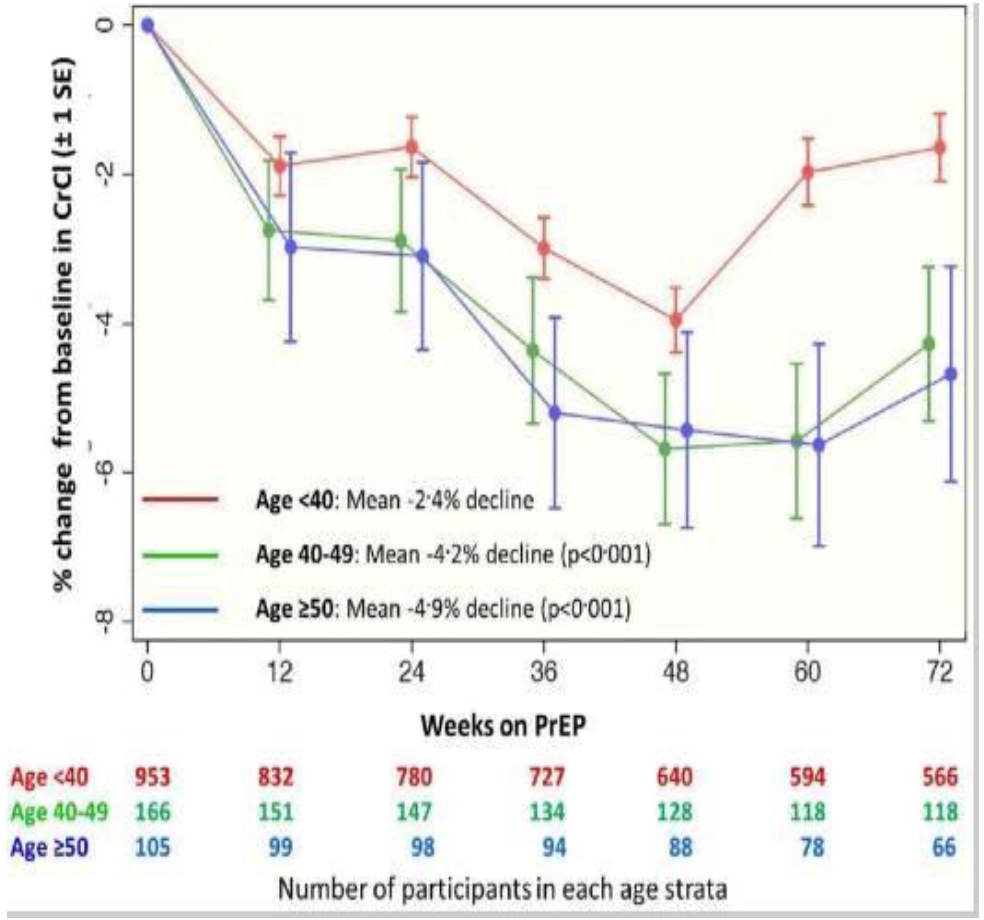
- In iPrEX, proteinuria by dipstick was detected regularly (12% dipsticks), but there was no between group difference in the proportion of participants ever positive for proteinuria[1]
- PPV of proteinuria in predicting creatinine elevation was poor at 0.7%
- In Partners PrEP[2] the overall mean decline for those receiving PrEP compared to placebo was estimated to be 2–3mL/min/1.73 m2 ($p \leq 0.01$).
- No difference in proportion of participants with a confirmed >25% decline in eGFR from baseline by 12 and 24 months between PrEP and placebo arms
- No difference in markers of tubulopathy between the TDF-FTC and placebo group over a median of 2 years' follow-up

1. Grant RM, Lama JR, Anderson PL et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med 2010; 363 : 2587–2599
2. Baeten JM, Donnell D, Ndase P et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med 2012; 367 : 399–410

PrEP, renal monitoring and age

- In iPrEx-OLE the probability of CrCl falling to ≤60 mL/min was more likely when participants started PrEP at older ages (>40 years) or with a starting CrCl ≤90 mL/min
- No participants under 40 years of age experienced a CrCl drop to ≤60 mL/min

- Being aged >40 years or with a lower baseline creatinine clearance (≤90 mL/min) at PrEP initiation independently associated with a risk of CrCl falling ≤60 mL/min.
- CrCl fell to ≤60 ml/min in 9 individuals (0.1%). All 9 of the drops occurred in participants who started PrEP at CrCl <90ml/min and 8/9 occurred in participants starting PrEP ≥50 years of age



Gandhi *et al.* Age, baseline kidney function, and medication exposure are associated with declines in creatinine clearance on PrEP: an observational cohort study

PrEP and renal function - recommendations

Section 6 – Baseline Assessment

•We recommend that baseline renal function is assessed with a serum creatinine, eGFR and urinalysis but PrEP can be commenced while waiting for the results. (1A)

•We suggest that the eGFR for individuals starting TDF is >60 mL/min/1.73 m2. (2A)

• We suggest that individuals with eGFR <60 mL/min/1.73 m2 should be started on PrEP only on a case-by-case basis and after a full assessment and discussion with the patient of the risk and benefits and obtaining specialist renal advice (2B).

Section 7 - Monitoring on PrEP

•If eGFR >90 mL/min/1.73 m2 at baseline (and follow up) and the person is aged <40 years then annual eGFR should be conducted. (1A)

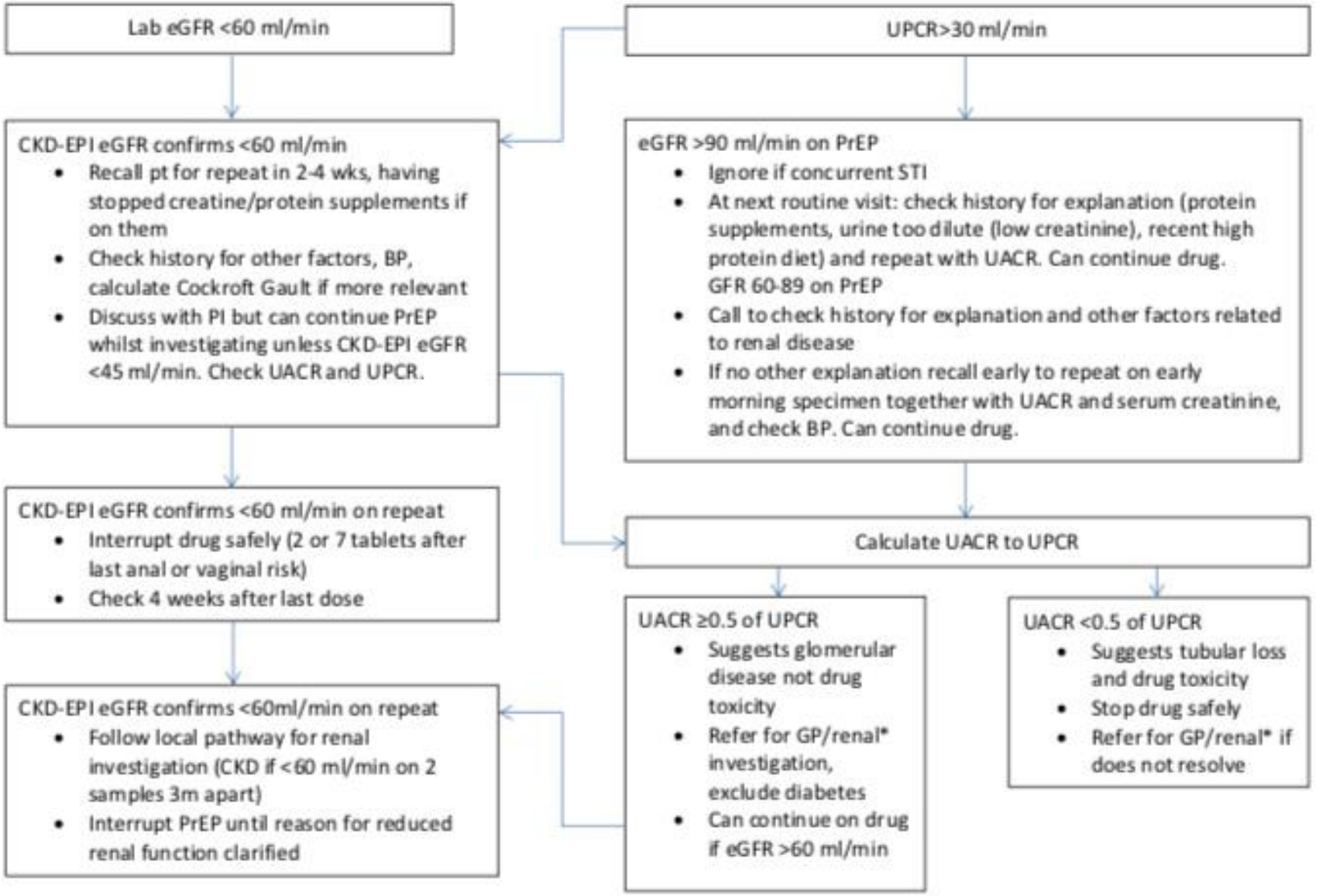
•If eGFR 60–90 mL/min/1.73 m2, aged >40 years or concomitant risk factors for renal impairment, more frequent monitoring of renal function at physician discretion is recommended, but should be at least 6 monthly. (2B)

•If eGFR <60 mL/min/1.73 m2, the risks and benefits of continuing PrEP should be assessed on a case-bycase basis. Specialist renal input should be obtained to determine further investigations and frequency of monitoring. (1C)

PrEP Impact – renal monitoring

Plan for managing renal parameters_v1.1_17042019

Fig 1 Algorithm for managing abnormal renal parameters (*depending on local pathways & patient preference)



Recommendations: Timelines for starting and stopping PrEP

- We recommend that, if the risk of HIV acquisition is through anal sex, PrEP can be started with a double dose of TD-FTC taken 2–24 hours before sex and continued daily until 48 hours after the last sexual risk. (1B)
- We recommend that if the risk of HIV acquisition is through vaginal sex, PrEP should be started as a daily regimen 7 days ahead of the likely risk and continued daily for 7 days after the last sexual risk. (1C)

- We recommend that if PrEP for anal sex has been interrupted and it is less than 7 days since the last TD-FTC dose then PrEP can be re-started with a single dose of TD-FTC. (1B)

Section 8: Generics / online

- The MHRA advise it is legal to buy up to 3 months medicines from outside the EU for personal use.

- Supported by advice from GMC, Medical Defence Unions and Imperial College Ethics Committee
  - Duty of Care
  - Good Medical Practice

- Two UK studies have demonstrated generic TD-FTC purchased online contains real drug[1,2]

1. Wang X, Nwokolo N *et al.* InterPrEP: internet-based pre-exposure prophylaxis (PrEP) with generic tenofovir DF/emtricitabine (TDF/FTC) in London: analysis of pharmacokinetics, safety and outcomes. *HIV Med* 2017; 19: 1–6
2. Wang X, Nutland W *et al.* Quantification of tenofovir disoproxil fumarate and emtricitabine in generic pre-exposure prophylaxis tablets obtained from the internet. *International Journal of STD & AIDS*. https://doi.org/10.1177/0956462419841144

Section 7: Generics - Good Practice Points

- Clinicians should discuss PrEP, including buying online with those deemed to be at high risk for HIV.
- Clinicians should sign post to IWantPrEPnow if unable to access PrEP on the NHS.
- The discussion of sourcing PrEP online needs to be fully informed including risks and benefits.
- Clinicians should ensure that people buying generic PrEP are taking medication that is labelled as containing both tenofovir and FTC and are taking PrEP correctly.
- Generic PrEP users should be advised to have regular STI (including HCV if at risk) and HIV tests and renal monitoring in line with the monitoring schedule in this guideline.
- Clinicians should offer full support, including renal monitoring, to patients who are taking PrEP sourced online.
- Therapeutic drug monitoring is not required for those taking generic PrEP.

Mags Portman

(27th May 1974 – 6th February 2019)