



PROUD Results Key Messages and Q&A
to be used as a supplement to
PROUD key messages, Q&A and further HIV PrEP trial information
(v2.0, 23rd February 2015)

The following key messages and Q&As have been developed to help study personnel and study representatives respond to enquiries from external audiences about the PROUD study results.

Contents

PROUD STUDY RESULTS	2
CLINICAL RESULTS	7
COST EFFECTIVENESS	8
POLICY	9
PROUD PILOT STUDY	11
OTHER AT RISK POPULATIONS	13
IPERGAY STUDY RESULTS	14

PROUD STUDY RESULTS

Key messages:

- PrEP was highly effective in the PROUD study which mimicked the real-world setting as much as possible.
- The PROUD study attracted a population who we would wish to offer PrEP to, as they were at risk of catching HIV.
- HIV incidence in the population who came forward to access PrEP was much higher than we expected, based on sexual health clinic data, despite extensive use of PEP among participants in the deferred group.
- Our concerns that PrEP effectiveness may be compromised in the real-world setting were completely unfounded.
- Participants incorporated PrEP into existing risk reduction strategies, which continued to include condom use.
- STIs were common in the study and there was no difference in the number of men diagnosed with STIs between those on PrEP and those not on PrEP.
- The sexual health clinics that took part in the PROUD study were able to integrate PrEP into their routine HIV risk reduction package.

1. What was the HIV incidence in the study?

There were 23 HIV infections during the study. Among participants randomised to receive PrEP immediately, we observed three infections with 243 person-years of follow-up giving a HIV incidence of 1.2 per 100 person-years. Among participants randomised to the deferred group, we observed 20 infections with 222 person-years of follow-up giving a HIV incidence of 9 per 100 person-years. The difference in HIV incidence between the two groups was 7.8 per 100 person-years (90% CI 4.3-11.3).

2. Was the HIV incidence observed in the study expected?

The national HIV incidence reported for men who have sex with men attending sexual health clinics in 2012 was estimated at 1.34 cases per 100 person years, derived from avidity assay data. We anticipated attracting a higher risk population and therefore expected to observe a HIV incidence of approximately 2.5 per 100 person years. . The HIV incidence of 9 in the deferred group is shockingly high. It is roughly seven times higher than the national average for MSM in sexual health clinics and more than three times higher than we expected to observe among a higher risk population in the study. The fact that the HIV incidence in the deferred group was so much higher in the PROUD study, demonstrates that the offer of PrEP attracted people, who would most benefit from it.

3. How effective was Truvada in the PROUD study?

Truvada reduced the risk of HIV by 86% when comparing participants randomised to the immediate PrEP group to participants randomised to the deferred group. This was a statistically

significant level of protection ($p=0.0002$) with a 90% confidence interval ranging from 64% to 96%. This is the highest reported effect size from a randomised controlled trial of PrEP to date.

NB: PrEP trials to date have reported the 95% confidence interval which in PROUD, for comparison, ranges from 58% to 97%. We report the 90% confidence interval in order to have 95% confidence around the lower bound of the reduction in risk of HIV.

4. Was the effectiveness of Truvada observed in the study expected?

The reduction in HIV was much greater than we expected. There has only been one previous PrEP trial in gay men (iPrEX) which was placebo-controlled, and this observed a 44% reduction in HIV, with a 95% confidence interval of 15% to 63%. In PROUD, we expected to observe an effect size within the upper range of the iPrEX confidence interval.

5. What does the PROUD data tell us about effectiveness that we didn't know from iPrEX?

The iPrEX study was a placebo controlled trial which reported 44% effectiveness across the study population. Based on drug level testing in iPrEX, it appears that approximately 54% of participants were taking PrEP regularly. Therefore the 44% level of effectiveness was achieved with less than perfect adherence. An analysis of the iPrEX data limited to participants who had detectable drug in their blood, suggested Truvada could reduce HIV by as much as 92% if taken frequently. In iPrEX, as well as the other placebo-controlled PrEP trials conducted to date, participants attended monthly clinic visits and were well supported to adhere to daily pill taking. Similarly, because they did not know if the investigational product was effective or if they were on a placebo, there was little reason to expect a change in sexual risk behaviour.

The concern in the UK was whether Truvada would be effective enough in a real world setting without access to such frequent and well-resourced support. The PROUD study results show that when integrated into existing sexual health services with quarterly visits and routine standards of care, adherence was sufficiently high to achieve 86% effectiveness across the whole study population, and this level of effectiveness was not compromised by changes in sexual risk behaviour. This is important evidence to understand the potential impact of PrEP in the real-world setting.

6. What data were used to estimate the effectiveness of Truvada?

In total, 96% of participants contributed some time to the main analysis of effectiveness. We included HIV test results data from the first HIV test at enrolment to the earliest of one of the following three time-points:

- (1) the HIV test at the end of the first year of follow-up when participants were either in the immediate PrEP or deferred groups;
- (2) the HIV test when participants on the deferred arm attended their first visit at which PrEP was prescribed;
- (3) the first HIV positive test.

7. How many participants enrolled in the study?

From November 2012 to April 2014, 544 participants joined the study at 13 sexual health clinics in England. In total, 275 were randomised to the group who received PrEP immediately and 269 to the group who were to receive PrEP after a deferred period of 12 months.

8. Could couples enrol and how were they randomised?

Participants with regular sexual partners who also met eligibility requirements were encouraged to enrol at the same time and both partners were randomly allocated to the same study group, minimizing the possibility of PrEP being shared. In total, 19 participants enrolled with a partner and were randomized to the same study group.

9. How many participants contributed follow-up time to the study?

In total, 523 (96%) of 544 participants enrolled, contributed to the follow-up time. Three were positive for p24Ag at enrolment and 18 did not have any HIV tests in follow-up that we have been able to trace at the enrolling clinic or other PROUD clinics.

10. How many person-years of follow-up were collected for the HIV analysis?

For the HIV result, we calculated the person-years of follow-up contributed by all 523 participants who returned to the clinic, and this added up to 465 person-years. We expected 504 person-years if everyone had attended the study visits perfectly according to the study protocol.

11. Were person-years of follow-up similar between the study groups?

Follow-up time was similar in the two groups with 94% (243/259 person-years) for the immediate PrEP group and 90% (222/245) for the deferred group. However, participants in the immediate group attended the quarterly visits more consistently than participants in the deferred group.

12. Why did participants randomised to receive PrEP acquire HIV?

Three participants in the immediate PrEP group acquired HIV. We suspect that one participant may have been sero-converting when he joined the study and the other two participants may not have been using PrEP at the time of their sero-conversions. Details of each infection are as follows:

- One participant tested HIV negative at enrolment but positive in the first 4 weeks of the study. We cannot rule out the possibility that he was sero-converting at the time of joining the study, and this was possible based on risks taken the week before he enrolled.
- Another participant was HIV negative at enrolment and diagnosed with HIV at another clinic 14 months later. His only prescription for PrEP was at enrolment. We cannot confirm whether he was sero-converting at the time of joining the study, sero-converted during the study while using PrEP, or sero-converted during the study while not using PrEP.
- The third participant was HIV negative up to three months after joining the study, when he received his last prescription for PrEP. He did not attend the clinic again. At 12 months, he was admitted to a different hospital with a sero-conversion illness, indicating recent infection acquired during the study. He told the hospital staff that he had not taken any PrEP for months.

13. When were the participants randomised to the deferred group diagnosed with HIV?

In the deferred group, six participants were diagnosed with HIV at their first study visit after enrolment so we cannot rule out the possibility they caught HIV before enrolling. In fact, we know that one participant was RNA PCR positive as the clinic had a stored specimen which they were able to go back and test. Nonetheless, he is included as he meets the statistical analysis plan definition of negative at baseline (p24Ag negative). Fourteen deferred participants were diagnosed with HIV after at least one HIV negative test result at a follow up visit, so even if everyone whose first test in the study was positive is discounted there is still a profound difference between the groups with 1 infection in the immediate (second participant described above) and 14 in the deferred.

14. How have you measured adherence in the study?

At each clinic visit (scheduled at month 1, 3, 6, 9, and 12 in the first year), participants in the immediate group were prescribed sufficient bottles of pills to last slightly beyond the next scheduled visit. For this analysis, we have estimated adherence based on pill prescribed, whereby the total number of pills dispensed to all participants is divided by the total number of accumulated days of follow-up.

We aimed to collect self-reported adherence data using an online daily diary and monthly questionnaire, but less than half the participants completed the data regularly and therefore it was not completed consistently enough to use for the main data analysis. We are also collecting adherence data using MEMS caps in a sub-group of up to 50 participants. We will conduct sub-group analyses with these data in due course.

15. What was the adherence in the study?

On average, the 275 participants randomised to the immediate group, were prescribed enough tablets to have taken a tablet on 88% of the days they were in the study. Of all the participants in the immediate group, 156 (56%) were prescribed enough tablets to have taken a tablet on 100% of days they were in the study. Fourteen (5%) participants met our definition of 'never started PrEP' (clinic reported as never started, 0 prescribed after enrolment, 0 visits after enrolment).

16. How much Post-Exposure Prophylaxis (PEP) was used by participants in the study?

At enrolment, 184 (34%) participants reported using PEP for sexual exposure (PEPSE) in the last year, 71 (13%) reported use more than once. This is higher PEP use than seen in the general MSM GUM population. During the study, 12 (5%) participants in the immediate group were prescribed PEP (14 prescriptions – generally related to a risk of exposure during low/no PrEP adherence) and 85 (31%) participants in the deferred group (total of 174 prescriptions). The high rates of PEP use among participants in the deferred group makes the high HIV incidence in this group even more shocking.

17. Were pharmacokinetic samples tested during the study?

The main reason for collecting PK samples was to confirm that participants who reported taking their PrEP really were. We had no reason to think that participants would tell us they were not

taking PrEP when they actually were. We knew from previous studies that volunteers sometimes feel obliged to tell clinic staff they are taking pills when they are not. As such, we planned to collect PK samples from participants who reported taking 4 or more tablets in the week before sample collection. We collected two additional samples to test drug levels in a participant in the immediate group who sero-converted and a participant in the deferred group who accessed Truvada elsewhere (*details below*). We collected samples from a small number of clinics as not all clinics taking part in PROUD were able to process the PK samples. Results of all 59 samples tested were consistent with participant reports of adherence.

Details of the two additional samples that we collected in a sero-converter and deferred participant are below in case required:

- One participant in the immediate group had a positive HIV result soon after joining the study when he had taken 15 doses of Truvada. He stopped Truvada as advised and returned for the PK sample 5 days after stopping when drug was detected.
- One participant in the deferred group reported acquiring a generic version of Truvada from elsewhere. The clinician collected a PK sample which confirmed presence of the drug.

18. Was there any evidence of participants in the deferred group using PrEP from elsewhere?

Based on discussions in the clinic, 12 in-depth interviews with participants in the deferred group, and anecdotal feedback, PrEP use among participants in the deferred group appears to have been rare, which is supported by the study results. At least two participants in the deferred group reported acquiring Truvada from elsewhere, and in one case the clinician collected a PK sample which confirmed presence of the drug.

19. Was there evidence of changes in sexual behaviour?

Questionnaires about sexual behaviour in the previous 90 days were completed and returned by 534 participants at baseline (271 in the immediate group vs 263 in the deferred group) and by 406 participants at 1 year (212 vs 194). Total number of different anal sex partners varied widely at the two time points, and we detected no significant difference between groups at 1 year.

However, a larger proportion of participants allocated to immediate PrEP than allocated to deferred PrEP reported receptive anal sex with ten or more partners without a condom (21% vs 12%).

Overall, our concerns that PrEP effectiveness may be compromised in the real-world setting were unfounded. The reported differences in behaviour between the two groups did not undermine the effectiveness of PrEP not impact on STI infections.

20. Did the study collect data on sexual behaviour more frequently than at enrolment and the 12 month study visit?

We aimed to collect sexual behaviour data using an online daily diary and monthly questionnaire, but less than half the participants completed the data and therefore it was not completed consistently enough to use for the main data analysis. We will conduct sub-group analyses with these data in due course.

21. Was there any evidence of an increase in STIs?

The number of STIs diagnosed at enrolment and during the study was very high. However, there were no statistically significant differences in STIs between the study groups.

- There were a slightly higher proportion of participants diagnosed with any STI during follow-up among participants randomised to receive PrEP immediately (57%) compared to the deferred group (50%).

NB: Any STI includes syphilis, rectal, urethral, oral gonorrhoea and chlamydia.

- Looking solely at rectal gonorrhoea and chlamydia, as STIs indicative of condomless sex, the difference was slight at 35% among participants randomised to receive PrEP immediately compared to 32% in the deferred group.

These results were based on fewer screenings for STIs in the deferred group reflecting the fact that participants in the deferred group attended fewer quarterly clinic visits. For instance, there were 974 screenings for rectal gonorrhoea in the immediate group compared to 749 in the deferred group. This means that we may have underestimated STI infections in the deferred group during the study.

CLINICAL RESULTS

Key messages:

- The PROUD study results are in line with previous evidence showing Truvada to be safe and well-tolerated with minimal concerns about resistance.

22. Where there any safety concerns?

Consistent with previous studies, Truvada was shown to be safe and well-tolerated in the PROUD study. Side effects were infrequent, mild and transient. A small number of individuals required closer than annual renal monitoring; these were older participants with co-morbidities on other medication.

23. Was there any evidence of resistance?

Three participants developed minority M184I or M184V mutations (emtracitabine associated). It appears that all three participants were seroconverting when they initiated PrEP. No K65R mutations (tenofovir associated) were observed. The numbers seen are small, but the PROUD study results are in line with previous evidence showing minimal concerns about resistance. The mutations seen so far should not have an impact on the success of antiretroviral treatment if treatment guidelines are followed.

24. Where there any adverse events?

There were very few interruptions of PrEP due to adverse reactions considered related to Truvada. Only 21 (8%) participants interrupted PrEP use due to an adverse reaction and 20 of these subsequently restarted PrEP.

COST EFFECTIVENESS

Key messages:

- The PROUD study results will inform two ongoing cost-effectiveness analyses being conducted by PHE and UCL designed to evaluate under which conditions, if any, the offer of PrEP will be cost-effective in the UK.

25. Is there evidence to show that Truvada PrEP will be cost-effective in the UK?

Modelling and cost effectiveness analysis is on-going in order to evaluate under which conditions, if any, the offer of PrEP will be cost-effective in the UK. The analyses will be considered by the PrEP Policy sub-group (see policy section) who are considering the case for the NHS to fund PrEP provision and for local authorities to provide it through Sexual Health clinics.

26. How will cost-effectiveness be measured in PROUD?

We are using two different approaches to answer the cost-effectiveness question. The first is a dynamic, individual based model of HIV transmission, progression and the effect of antiretroviral drugs. This will enable us to calculate the predicted long term (next 30 years) health outcome for gay men in the UK according to whether PrEP is introduced or not, as well as the costs over the same period. The health outcome will be measured in terms of quality adjusted life years (QALYs). We will consider the gain in QALYs from introduction of PrEP and relate this to the extra cost (if indeed the cost is higher with PrEP introduction).

The second approach is using a static decision analytical model to estimate the impact of year one of a PrEP Programme for 5,000 most-at-risk MSM, beginning in 2016, on their lifetime HIV incidence. It considers both the lifetime costs and QALYs averted as a result of the intervention.

The parameter values in both models are being synchronised, where possible.

NB: Interventions are generally considered cost effective in the UK if they result in a gain in QALYs at a cost of < £30,000 each.

27. How does the cost of PEP compare to the potential cost of PrEP?

In the cost effectiveness model, PHE estimate that 5% of at-risk MSM will use PEP in a given year. The cost of the drugs used for PEP (28 x Truvada and 56 x Raltegravir) is £772 per prescription, and the cost of providing PEP (the GUM tariff per PEP episode) is £225, resulting in a total cost of £997 per PEP episode.

The cost of Truvada used for PrEP is £360.92 a month (30 x Truvada) and based on the PROUD study protocol, the estimated cost of providing PrEP is £750 per year (although this may be an over-estimate and may differ in the clinical setting). Although PrEP provision would not require monthly visits, if we divided the annual costs of providing PrEP by 12 months (£62.50 per month), the resulting monthly cost of PrEP is £423.42.

28. When will Truvada come off patent?

Truvada will come off patent in the UK in 2018. Viread (TDF or tenofovir) will come off patent a little bit earlier in 2017.

29. Will PrEP be more cost effective when Truvada comes off patent?

The cost of Truvada is likely to reduce when it comes off patent. However, in the future, non-ART costs of HIV prevention and care will be proportionately greater than they are currently. As such, it is not straightforward to conclude that PrEP provision will be more cost-effective as drug costs reduce. Formal modelling analysis in the UK context is needed to confirm the impact of reduced drug costs on overall cost-effectiveness.

30. When will results from the cost effectiveness analysis be available?

PHE and UCL are presented results from the economic modelling to the March 2015 HIV CRG PrEP Policy Sub-Group (see policy section). The results were shared during the BASHH Spring conference (June 2015) and the groups are preparing manuscripts for publication.

See for example:

<http://www.bashh.org/documents/Events/Conf%202015/O1%20Valentina%20Cambiano.pdf>

POLICY

Key messages:

- PrEP offers a major new opportunity to curb newly acquired HIV infections in MSM in the UK, of which there were an estimated 2,800 in 2013.
- The PrEP policy sub-group of the HIV Clinical Reference Group is in the process of considering the evidence of effectiveness, cost-effectiveness and how PrEP might be commissioned in practice in England.
- BASHH and BHIVA updated their position statement after the release of the PROUD results and plan to issue guidelines regarding PrEP.

31. What are the next steps for NHS England in terms of making PrEP available?

NHS England recently announced that the review of all new clinical commissioning policy proposals for specialised services has been deferred to **June 2016**. This is the process which will decide whether HIV pre-exposure prophylaxis (PrEP) will be available on the NHS.

The HIV Clinical Reference Group (CRG) provide clinical advice to NHS England on the commissioning of HIV treatment and care. A subgroup of the HIV Clinical Reference Group has been working on a commissioning policy proposal for PrEP since September 2014. This has included a review of the clinical evidence, an impact assessment and stakeholder engagement. The group has broad representation from the community, PROUD study participants, academia, public health and NHS England and local authority commissioners. Before submission to NHS England for review in June 2016, the proposed policy will be released for public consultation. We

will post details about how you can get involved in the public consultation on our website as soon as they are available.

32. When will the PrEP Policy Sub-group recommendations be available?

The HIV Clinical Reference Group (CRG) will develop policy recommendations regarding the use of anti-retrovirals (ARVs) for PrEP based on the evidence review. These will then be considered through NHS England's process, which includes review by the Clinical Priorities Advisory Group (CPAG). Decisions about investment in new services will take place in June 2016 and if approved, PrEP could be available shortly thereafter.

33. If PrEP were to be commissioned who would be responsible?

NHS England are responsible for the commissioning of all anti-retrovirals (ARVs) for both treatment and prevention. Local Authorities are responsible for the commissioning of sexual health services (with 152 upper-tier authorities in England).

34. Is NICE approval of PrEP required?

Currently NICE do not assess ARVs. NHS England does not require PrEP to have NICE approval before making a decision about whether to reimburse use of ARVs for PrEP.

35. If approved, when will PrEP be available on the NHS?

The HIV CRG PrEP policy sub-group intend to include PROUD results in their evidence review and policy recommendations. These findings will help develop proposals for the service delivery model for PrEP. Use of ARVs for PrEP has been identified by NHS England as a work area for 2016/7 for consideration for late 2016 implementation.

36. What is the role of the professional associations in making recommendations for PrEP?

BASSH and BHIVA have updated their position statement after the release of the PROUD results and plan to issue guidelines regarding PrEP later this year.

37. Who will be eligible for PrEP?

If PrEP is made available on the NHS, both the HIV CRG PrEP policy sub-group and BASSH/BHIVA guidelines are likely to recommend who should be eligible for PrEP. The HIV CRG PrEP policy sub-group are looking at evidence for all populations, not restricted to MSM.

38. Is European Medicines Agency (EMA) approval of PrEP required?

NHS England does not require PrEP to have EMA approval before making a decision about whether to reimburse use of ARVs for PrEP. This is likely to be the case in Wales and Northern Ireland although it appears Scotland would require EMA approval to use a drug licensed for treatment in an alternative designation for prevention.

39. Will Gilead submit an application to the European Medicines Agency (EMA) to license Truvada as PrEP?

Gilead have committed to submitting an application to the European Medicines Agency to license Truvada as PrEP. In December 2015, France became the first country in Europe to offer PrEP to at risk populations.

40. What about implementation in Wales, Northern Ireland and Scotland?

The process for review in the devolved authorities is not yet clear although it does appear that Scotland would require EMA approval of Truvada as PrEP in order to consider commissioning it for prevention.

PROUD PILOT STUDY

Key messages:

- The PROUD pilot study was able to provide evidence on the effectiveness of PrEP as HIV incidence in the deferred group was higher than anticipated and the effectiveness of Truvada was higher than expected.
- The PROUD pilot study will continue until its scheduled end in April 2016 and will continue to collect data on how participants incorporate PrEP into their other HIV prevention strategies.
- We have extended PrEP access to all PROUD study participants up to the end of the study in April 2016.

41. How come the pilot study provided evidence on effectiveness?

When planning the PROUD CLINICAL TRIAL, we anticipated observing a HIV incidence of 2.5 per 100 person-years in the deferred group (based on GUM data), an effectiveness of 50% (based on the iPrEX data and taking account of less than perfect adherence) and a loss to follow-up of about 15% of person-years. On this basis we calculated we would need to enrol up to 5,000 gay and other MSM to a large-scale clinical trial in order to evaluate the effectiveness of PrEP.

The PROUD PILOT study was undertaken to assess the feasibility of conducting a large-scale clinical trial like this.

Unexpectedly, the HIV incidence in the PROUD pilot more than 3 times higher in the deferred group than we anticipated and PrEP was highly effective which is related to high levels of adherence. It is because of these two factors, high HIV incidence and high effectiveness, that PROUD was able to provide evidence of effectiveness in such a small pilot study.

42. Have all participants randomised to the deferred group been offered PrEP?

Everyone who was still in the deferred period was invited to attend the clinic and offered PrEP.

43. How long will participants continue to get PrEP in the PROUD study?

We are continuing with the PROUD pilot study and now offering all participants PrEP. We have agreed funding to be able to continue to provide PrEP to all PROUD study participants up to April 2016. We are currently exploring opportunities to extend PrEP access for PROUD participants until NHS England announce the outcome of the policy review. The PROUD Trial Steering

Committee are scheduled to meet in January 2016 and will make a recommendation about how best to sustain PrEP access for PROUD study participants. We are committed to trying to sustain PrEP access for PROUD participants and will provide study participants with an update as soon as possible.

44. Why is the pilot study being continued?

By continuing to follow-up participants in the pilot study, we aim to sustain access to PrEP until it is hopefully available on the NHS. We will also learn more about when and how participants use PrEP and how they incorporate PrEP into their other HIV prevention strategies. We will also continue to monitor safety and drug resistance. Through more qualitative work, including one-to-one with participants, we will also learn more about participant's longer term experiences with PrEP.

45. What will happen if participants reach the end of the study and cannot access PrEP on the NHS?

Participants are highlighting this as a concern. We hope that by the time the PROUD pilot study ends, PrEP is available on the NHS and if that is the case, we will endeavour to arrange for a seamless transition into NHS provision for study participants. We will continue to monitor the situation carefully and discuss progress with participants. If, towards the end of the study it looks unlikely that PrEP will be available on the NHS, clinics will discuss other HIV risk reduction options with participants on an individual basis.

46. Will the PROUD clinical trial still go ahead?

Given that the pilot study has answered the important question of how much protection daily Truvada can offer when provided in sexual health clinics in the UK, there is no need for the planned larger clinical trial. As such, we have withdrawn our funding application to reopen the PROUD study for new recruitment.

47. What are the next PrEP research priorities?

We are in the process of talking to our partner organisations in order to identify which PrEP research questions we should address next in the UK. There are a range of other PrEP options in various stages of research that we could consider including alternative ARVs as PrEP, slow release long acting injectable PrEP, and the use of ARVs in rectal microbicides.

48. When will the PROUD results be published?

The PROUD study results were published in the Lancet and are supported by a policy briefing paper, both of which are available on the website

[http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(15\)00056-2/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(15)00056-2/fulltext);
<http://www.proud.mrc.ac.uk/pdf/PROUD%20results%20policy%20brief%20final.pdf>.

We are awaiting the publication of a paper describing the baseline study population in the Trials Journal. We are also in the process of preparing additional manuscripts and hope to submit a series of papers to scientific journals for peer review within the next six months.

OTHER AT RISK POPULATIONS

Key messages:

- The PROUD study results heighten the need for community based consultation with other populations at risk of HIV in the UK.
- Community consultations are needed to build a common understanding of what PrEP as a new HIV prevention tool could mean for specific population groups.
- Community consultations are also needed to map out the critical implementation questions that need to be addressed to support access, uptake, and use for specific population groups.

49. What do the PROUD study results mean for other populations at risk of HIV in the UK?

The PROUD study results heighten the need for community based consultation with other populations at risk of HIV in the UK, both to build a common understanding of what PrEP as a new HIV prevention tool could mean for specific population groups, and to map out the critical implementation questions that need to be addressed to support access, uptake, and use for specific population groups. It will be important to understand the needs of black-African women and men; trans-women, trans-men and non-binary populations; intravenous drug users; and gay, bi-sexual and MSM from black, Asian and minority ethnic (BAME) groups, and other populations at risk of HIV in the UK.

50. What evidence is there for the role PrEP can play for heterosexual women and men?

Evidence from the Partners PrEP and TDF2 studies in East and Southern Africa demonstrated that oral PrEP is highly effective against HIV for heterosexual women and men, either in sero-discordant relations (as in Partners PrEP) or not (as in TDF2). However, the FEM-PrEP and VOICE trials highlighted the challenges that women in Africa faced in adhering to a daily pill regime. It is important to remember that all of these studies were placebo controlled trials so women did not know if they were receiving the investigational drug or the placebo, or if the investigational drug would offer protection from HIV. These factors are bound to have diminished the perceived benefit of taking a pill every day. However through implementation research it will be important to consider the range of other socio-behavioural factors that are likely to influence PrEP uptake and use.

51. What evidence is there for the role PrEP can play for trans-women, trans-men and non-binary individuals?

Less than half a dozen trans-women joined the PROUD study although 339 trans-women joined the iPrEX study. An analysis among trans-women in iPrEX was recently published ([http://www.thelancet.com/pdfs/journals/lanhiv/PIIS2352-3018\(15\)00206-4.pdf](http://www.thelancet.com/pdfs/journals/lanhiv/PIIS2352-3018(15)00206-4.pdf)). To date, randomised controlled trials have not recruited trans-men or non-binary individuals.

52. What evidence is there for the role PrEP can play intravenous drug users?

The Bangkok Tenofovir study demonstrated a 49% reduction in HIV among intravenous drug users randomised to daily tenofovir (one of the two drugs in Truvada) verses placebo. The

number of infections acquired through injecting drug use remains low in the UK with an estimated 130 new HIV diagnoses in 2013.

53. Were gay, bi-sexual and MSM from BAME groups included in PROUD?

The PROUD study attracted a largely white, highly educated, employed, group of men mainly in their mid-30's who self-identified as gay and accessed sexual health clinics frequently. The varied needs of other gay, bi-sexual and MSM, especially from Black, Asian and Minority Ethnic groups, need to be considered in the planning of future PrEP implementation.

IPERGAY STUDY RESULTS

54. What are the implications of the IPERGAY study results?

IPERGAY evaluated “on demand” or “event-driven” PrEP in a double blind, placebo controlled randomised trial in France and Canada. They enrolled just over 400 gay men and other MSM who were instructed to take two Truvada pills between 2 to 24 hours before sex, a third 24 hours after the first dose, and a fourth 48 hours after the first dose. It is very exciting that PrEP ‘on demand’ was shown to be highly effective in the IPERGAY study. The HIV CRG PrEP Policy Group, as well as BASHH and BHIVA, will consider the IPERGAY results as part of their review of PrEP policy for the UK.