



## **PROUD Study Key Messages, Q&A and further HIV PrEP trial information**

**For details of the study results see the PROUD Results Key Messages and  
Q&A  
(v2.0, 10<sup>th</sup> December 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 Truvada PrEP, the PROUD  
pilot and the PROUD trial.**

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## **PROUD Key Messages**

- HIV remains a major public health concern. An estimated 100,000 people are now living with HIV in the UK, with over 6,000 new diagnoses and around 700 HIV-related deaths annually. Over half of new HIV diagnoses each year are in gay men/ men who have sex with men (MSM). Additional approaches are needed, particularly for populations at higher risk of HIV, to tackle the HIV epidemic.
- HIV Pre-Exposure Prophylaxis (PrEP) is a new way to reduce the risk of getting HIV. HIV negative individuals receive a comprehensive risk reduction package (including behavioural support, regular HIV tests and free condoms) in combination with daily antiretroviral (ARV) drug treatment (to prevent the virus becoming an established infection if they are exposed to HIV).
- Large randomised controlled trials have shown the ARV PrEP treatment is biologically effective at substantially reducing HIV infection risk and is also well tolerated by HIV negative individuals.
- The degree of risk reduction delivered by HIV PrEP directly corresponds to treatment adherence. The iPrEx trial showed daily Truvada (tenofovir-emtricitabine) PrEP reduced the risk of HIV by an average of 44% vs. placebo. The quarter of participants who took Truvada every day reduced their HIV infection risk by 92% vs. placebo (although this could be an overestimate, as people who took their drug many also have had less risk).
- HIV treatment and care costs £800 million each year in England and an estimated £280,000-360,000 in undiscounted lifetime costs could be saved per HIV case prevented. Modelling studies using strict criteria show PrEP is cost effective in populations at higher risk of HIV infection.
- In 2012 in the UK, the British Association for Sexual Health and HIV (BASHH) and the British HIV Association (BHIVA) recommended that HIV PrEP is only used in clinical research projects to gather data on clinical- and cost-effectiveness, and acceptability to gay men/MSM. As of February 2015, BASHH and BHIVA are updating their position statement and guidelines regarding PrEP.
- Led by the Medical Research Council Clinical Trials Unit and Public Health England, the PROUD pilot intended to offer Truvada-PrEP (Truvada plus a comprehensive risk reduction package) to 500 HIV negative gay men, MSM and transgender women attending GUM clinics.
- The PROUD pilot aimed to inform whether a full scale HIV PrEP trial was feasible in the UK. The pilot aimed to look at the impact of the comprehensive risk reduction package, both with and without daily Truvada PrEP, on reducing the risk of HIV.
- Truvada PrEP is not a replacement for condoms, as condoms are the most effective way to prevent HIV and other sexually transmitted infections when used correctly and consistently. However, Truvada PrEP may be a useful additional risk reduction option in the UK in the future.

## **HIV PrEP PREVENTION STRATEGY**

### **Key messages:**

- HIV PrEP is a new risk reduction strategy, which involves HIV negative individuals receiving a comprehensive risk reduction package combined with daily ARV drug treatment.
- In clinical trials, both tenofovir and Truvada (tenofovir-emtricitabine) PrEP have been shown to reduce the risk of HIV infection.
- Currently, no ARV treatments are licensed for HIV PrEP in the UK.

### **1. What is HIV PrEP?**

HIV Pre-Exposure Prophylaxis (PrEP) is a new risk reduction strategy. HIV negative individuals receive a comprehensive risk reduction package (including behavioural support, regular HIV tests and free condoms) combined with daily antiretroviral (ARV) drug treatment, to prevent the virus becoming an established infection if they are exposed to HIV.

### **2. In which countries is HIV PrEP approved?**

Daily Truvada (tenofovir-emtricitabine) was approved for HIV PrEP use in the USA in 2012, to be offered as part of comprehensive risk reduction package. As of February 2015, no other countries have approved HIV PrEP.

### **3. Which ARV drugs can be used for PrEP?**

So far, the daily use of tenofovir and Truvada (tenofovir-emtricitabine) have both been shown to reduce the risk of infection, although only Truvada has been evaluated among gay and other men who have sex with men. Other ARVs are being evaluated for use as HIV PrEP.

### **4. Which ARV drugs are approved for PrEP use in the UK?**

No drugs are currently approved for HIV PrEP use in the UK. As of February 2015, the British Association for Sexual Health and HIV (BASHH) and the British HIV Association (BHIVA) are updating their position statement and guidelines regarding PrEP.

### **5. For which populations is HIV PrEP an appropriate risk reduction strategy?**

HIV PrEP has been investigated in a range of clinical trials involving different populations: gay men, serodiscordant couples who were primarily heterosexual and young heterosexual adults. In the USA, daily Truvada is now licensed for use as HIV PrEP in 'otherwise healthy individuals who are at high risk of infection'.

### **6. How will HIV PrEP be used in the UK?**

The PROUD pilot study results will help inform if and how PrEP will be commissioned in practice – see RESULTS UPDATE – policy section

### **7. Would all gay men, men who have sex with men and transgender women be eligible for Truvada PrEP in the UK?**

In the PROUD pilot, we investigated Truvada PrEP use in gay men, men who have sex with men and transgender women who had condomless anal sex in the last three months and were likely to do this again in the subsequent three months. If Truvada PrEP is introduced in the future in

the UK, based on UK guidelines, clinicians will decide in consultation with an individual whether it is appropriate for them.

## **CURRENT EVIDENCE FOR HIV PrEP (based on evidence available as of October 2014)**

### **Key messages:**

- Trials undertaken in HIV negative populations have demonstrated that Truvada PrEP reduces the incidence of HIV infection, and is generally well tolerated.
- In trials to date, the degree of risk reduction delivered by HIV PrEP directly corresponds to the proportion of participants that had detectable drug level in their blood system – which is an indicator of how often people took the drug.

### **8. How effective is PrEP in reducing HIV infection rates?**

In the iPrEx trial, daily Truvada reduced the incidence of HIV infection by almost half (44%) in MSM. This result is supported by the TDF2 (enrolling heterosexual individuals) and Partners in PrEP trials (enrolling heterosexual couples) in Africa which found a 63% and 73% reduction. However, two trials (FemPrEP and VOICE) in heterosexual women did not demonstrate reduced HIV incidence with daily tenofovir or Truvada.

The degree of risk reduction delivered by HIV PrEP in the trials directly corresponds to the proportion of participants that had detectable drug level in their blood system – which is an indicator of how often they took the drug. In the iPrEx trial, the quarter of participants who took Truvada every day reduced their HIV infection risk by 92% vs. placebo (although this could be an overestimate, as people who took their drug may also have had less risk).

### **9. What is known about the safety of Truvada use as PrEP?**

The PrEP trials provide safety data in HIV negative populations and confirm that Truvada is generally well tolerated. To date the only safety concerns have been mild gastro-intestinal discomfort at an early stage of treatment, and mild creatinine elevations (which give an indication of how well the kidneys are working) that reversed when treatment stopped.

We know that stopping and starting ARV therapy whilst risk of HIV infection is ongoing should be avoided. This is because the risk of HIV resistance to one of the two drugs in Truvada developing is highest if Truvada is started just after an individual has become infected. We do not know about the long-term safety (10-20 years) of Truvada in HIV negative populations.

### **10. Why did you not start giving Truvada as PrEP in the UK without a pilot study, now that the USA has licensed it?**

The USA has private healthcare and there is therefore little burden placed on the national system by approving Truvada PrEP. However, in the UK it is vital that we understand the most suitable models of NHS provision and assess the cost-effectiveness based on level of interest and use. In 2012, BASHH and BHIVA recommended that, in the first instance, Truvada PrEP was only used in clinical research projects to gather the data required to inform its use in the UK.

## **HIV PREP - POTENTIAL CHALLENGES**

### **Key messages:**

- Trials conducted to date have found no evidence that Truvada PrEP (or placebo) leads to higher risk sexual behaviours.
- Development of ARV resistance was uncommon in the placebo-controlled trials, but most likely to occur in people who had become infected with HIV soon after they started taking Truvada.
- It is possible that someone who is on HIV PrEP may still become HIV positive. This is why it is vital regular HIV testing is included within PrEP risk reduction packages.
- Truvada PrEP is not a replacement for condoms, but may be a useful additional option for individuals at high risk of infection, and who do not or cannot always use condoms.

### **11. Can someone still become infected when on HIV PrEP?**

Yes, it is possible that someone who is on HIV PrEP may become HIV positive. The evidence on Truvada PrEP collected in the Partners study suggests that HIV can be acquired even when drug levels suggest tenofovir (one of the two drugs in Truvada) was taken every day. That is why the PrEP comprehensive risk reduction package in PROUD includes regular HIV testing, to help ensure people remain aware of their HIV status.

### **12. Could HIV PrEP increase antiviral resistance if there is widespread non-adherence?**

There are concerns that Truvada PrEP could lead to the development of drug resistance, if people become infected while on PrEP or start on PrEP when already infected. Resistance was uncommon in the placebo-controlled trials, but most likely to occur in people who had caught HIV just before they started Truvada. Whether this will make a greater contribution than non-adherence to ARV treatment is not clear.

### **13. If someone thinks they are protected from HIV by taking Truvada, will they be more likely to engage in high risk sexual behaviours?**

Truvada placebo-controlled PrEP trials conducted so far have found no evidence that PrEP (or placebo) led to higher risk sexual behaviour. However, this is a question the PROUD pilot will be exploring – see RESULTS UPDATE – pilot study results section.

### **14. Is Truvada PrEP a replacement for condoms? Why prescribe an HIV medication when condoms are freely available and effective?**

When used correctly and consistently condoms are the most effective way to prevent HIV and other sexually transmitted infections. However, new HIV infections continue to rise each year in the UK. In 2013, 2800 MSM were newly infected with HIV in the UK. Condoms are not a sufficient option for all men and therefore new HIV risk reduction strategies are needed. Truvada PrEP may be a useful additional option for individuals at high risk of infection, and who do not or cannot always use condoms.

### **15. Why is PrEP needed when there are already HIV effective prevention methods available?**

We already have universal access to condoms, HIV testing, STI testing, HIV post-exposure prophylaxis and effective HIV treatments (that can reduce viral loads to undetectable levels and

therefore risk of onward transmission) but the number of new HIV infections continues to rise each year in the UK. In 2013, 2800 MSM were newly infected with HIV in the UK. Additional ways to tackle the HIV epidemic are needed. Offering Truvada PrEP will help clinics to engage with HIV negative populations, and the PROUD pilot was designed to help us better understand what is happening between negative and positive tests.

**16. Is there a chance that the perceived stigma around not using condoms may make some men reluctant to discuss/use PrEP?**

The SIGMA UK survey identified stigma relating to PrEP users being perceived as ‘irresponsible’ for not using condoms. Anecdotal feedback from PROUD recruitment centres has also identified some reluctance to report sex without a condom and concerns around stigma associated to non-condom use. An important part of ongoing HIV research will be exploring how to expand the dialogue around responsible sexual behaviour to reflect and encompass new HIV prevention strategies, e.g. TasP (Treatment as Prevention) and PrEP

**HIV PrEP COST EFFECTIVENESS**

**Key messages:**

- Data show Truvada PrEP is cost effective when targeted to populations at higher HIV risk.
- It is important to have reliable UK data on cost effectiveness. The PROUD study will investigate cost-effectiveness of Truvada PrEP in the UK.
- Introducing Truvada PrEP in the UK would not remove the need for ongoing investment in initiatives to improve HIV awareness, access to sexual health services, safer sexual behaviour and regular HIV testing. However, our efforts have not been sufficient to control the HIV epidemic to date and new strategies are needed.

**17. Is there evidence to show that Truvada PrEP is cost effective?**

A modelling study based on the iPrEx trial results found Truvada PrEP was highly cost effective if targeted at people at high risk of HIV, costing from US \$140 - \$1,400 per disability-adjusted life year with HIV averted, according to who was targeted and what their adherence rates were. Other modelling studies also found Truvada PrEP is cost effectiveness if given to people at high risk of infection.

**18. How can Truvada PrEP be funded when huge NHS cost savings need to be found?**

It is important to recognise we spend £800m every year in England on HIV care and treatment, and that an estimated £280,000 - £360,000 in undiscounted lifetime treatment costs could be saved for each case of HIV prevented. Data show Truvada PrEP is highly cost effective when targeted to populations at higher HIV risk. HIV PrEP may be a useful option to help reduce future HIV infections and, in the long-term, save the NHS money. It is important to have reliable UK data on cost effectiveness to assess this.

**19. Why doesn't the Government just run another national awareness campaign, rather than spending money giving drugs to healthy people?**

Introducing Truvada PrEP in the UK would not remove the need for ongoing investment in initiatives to improve HIV awareness, access to sexual health services, safer sexual behaviour and regular HIV testing. However, our efforts have not been sufficient to control the HIV epidemic to date. New HIV infections continue to rise in the UK, with gay men/men who have sex with men at highest risk - with 2800 new infections in the UK in 2013. Additional ways of tackling the HIV epidemic are needed in the UK, and Truvada PrEP may be a useful and cost-effective option.

## **PROUD PILOT & TRIAL**

### **Key messages:**

- The PROUD pilot was initially undertaken to measure the feasibility of conducting a large-scale HIV PrEP trial in the UK.
- It is a multi-centre, open-label RCT of immediate or deferred inclusion of Truvada, alongside a comprehensive risk reduction package. It aimed to enrol 500 gay men, MSM and transgender women to be followed-up for two years.
- The original plan was that if the PROUD pilot demonstrated feasibility, funding would be sought for a full scale trial to generate evidence on Truvada PrEP effectiveness and cost-effectiveness in the UK. The idea was that the open-label (no placebo) trial design would provide evidence on the level of protection provided by Truvada PrEP at the population level when used in a “real life” context.
- However, in October 2014, the PROUD pilot study answered the important question of how much protection daily Truvada can offer when provided in sexual health clinics in the UK so a full scale trial is no longer necessary.

### **20. Why was the PROUD trial planned?**

In 2012, BASHH and BHIVA recommended that clinical research be undertaken to gather the data required to inform Truvada PrEP use in the UK. Although studies in other countries have shown that Truvada used as PrEP can reduce the chance of becoming infected with HIV, people have different risk factors and behave differently with respect to pill taking in different parts of the world. How good PrEP is at reducing the risk of becoming infected with HIV for gay men in the UK is related to these differences. We needed to better understand these behaviours in the UK to avoid giving PrEP to people that don't need it, and to find out who wants to take it. As of February 2015, BASHH and BHIVA are updating their position statement and guidelines regarding PrEP.

### **21. Why was the PROUD pilot needed first?**

There are inherent risks and opportunity costs in carrying out an ambitious, large scale UK trial, which was estimated to require 5,000 participants. The main threats are the acceptability of randomisation and the willingness of otherwise healthy men to regularly attend clinic for follow-up visits. The pilot design aimed to assess the feasibility of conducting the main trial, as well as providing an opportunity to test the trial procedures are acceptable and sustainable in participating clinics, and to optimise data collection tools. As it turned out, a large scale trial was

unnecessary as the pilot study answered the important question of how much protection daily Truvada can offer when provided in sexual health clinics in the UK.

**22. What is the PROUD pilot design?**

The pilot is a UK multi-centre, open-label randomised control trial of immediate or deferred inclusion of Truvada, alongside a comprehensive risk reduction package. The pilot aimed to enrol gay men, men who have sex with men and transgender women attending GUM clinics. Recruited HIV negative volunteers were randomised into one of two groups; one group to use daily Truvada from the start of the pilot and the other after 12 months. Both groups were originally due to be followed-up for 2 years, but now all participants will be followed up (if they consent to the additional follow up period) until April 2016 regardless of when they joined the study (which could be anytime from November 2012 to April 2014).

All participants were offered a comprehensive risk reduction package including regular HIV testing, diagnosis and treatment of STIs, support to reduce high risk behaviour, free condoms, and other biomedical interventions such as post-exposure prophylaxis where relevant.

**23. In the pilot, why were half of participants randomised to a deferred start of Truvada after 12 months?**

The perception that PrEP protects against infection may lead to reduced use of condoms or riskier sexual practices (“risk compensation”). If this phenomenon exists, efficacy estimates from trials to date may exaggerate the actual protective effect of PrEP. The PROUD pilot study was designed to allow comparison of changes in behaviour between participants randomised to start Truvada immediately or after 12 months instead of using a placebo as the comparison group.

**24. What is the rationale for no placebo in PROUD?**

By removing the placebo arm, we are able to examine the level of protection provided by Truvada PrEP at the population level when participants are given a drug they know is effective at reducing the risk of HIV if they take it.

**25. Who is leading and funding the PROUD pilot?**

The PROUD pilot is being run and funded by the Medical Research Council Clinical Trials Unit at UCL and Public Health England, in partnership with 12 NHS trusts and members from community organisations. In addition, Gilead is donating Truvada.

**26. When did the PROUD pilot take place?**

The recruitment period commenced November 2012 and the study was fully enrolled with 544 volunteers in April 2014. The pilot study is funded until April 2016 offering PrEP to all participants.

**27. Where is the PROUD pilot running?**

The PROUD pilot involves 13 centres across the UK – London (8 sites), Brighton, Sheffield, York, Birmingham and Manchester.

**28. How many people did the PROUD pilot aim to recruit? Who was eligible to participate?**

The PROUD pilot aimed to recruit 500 volunteers, but finally enrolled 544 participants, who:

- were born male (gay men, men who have sex with men and transgender women)
- were HIV negative
- were 18 years or older
- had had anal sex with a man without a condom at least once in the last three months
- were likely to do this again in the next three months
- could visit one of the participating clinics for blood tests every three months.

**29. Will participants receive any financial reimbursement?**

Participants in the PROUD pilot will not receive any financial reimbursement.

**30. Why are black African and black Caribbean heterosexual populations not being included in PROUD?**

In the PROUD pilot, Truvada PrEP will be offered to gay men, men who have sex with men and transgender women accessing GUM clinics. In the UK, this is the only combined group in which HIV incidence is sufficiently high to enable the conduct of a large scale trial with clinical endpoints. Data are also available from two recent UK surveys confirming the likely acceptability of the intervention among gay men/men who have sex with men in the UK.

**31. What did you expect the PROUD pilot to show?**

We expected the pilot to show whether it would be feasible to conduct a large scale clinical trial of PrEP involving approximately 5000 gay men, men who have sex with men and transgender women in the UK. We aimed to find out if the randomisation process (immediate or deferred start of Truvada) would be acceptable. We hoped that the PROUD pilot would show if this population were interested in taking PrEP as part of a HIV risk reduction strategy, and if participants would be willing to visit the clinic every three months for two years. We also hoped that the PROUD pilot would provide some insight into sexual behaviour and adherence behaviour when on Truvada PrEP.

However, in October 2014, the PROUD Trial Steering Committee announced that participants in the deferred group, who had not yet started PrEP, should be offered PrEP ahead of schedule. This followed a recommendation from the Independent Data Monitoring Committee (IDMC), based on an interim analysis of the data that showed that PrEP was highly protective against acquiring HIV in this study population. In addition the rate of HIV infection was also much higher than expected compared to the general sexual health clinic attendees.

**32. What did you expect the PROUD trial to show?**

We expected to need a larger clinical trial in order to answer the important question of how much protection daily Truvada can offer when provided in sexual health clinics in the UK. However this question was answered in the pilot study so a full scale trial is no longer necessary.

**33. When will the results of the PROUD pilot be available?**

The PROUD pilot study released the HIV effectiveness results at the Conference on Retroviruses and Opportunistic Infections (CROI) on 24<sup>th</sup> February 2015. The results will be submitted to a leading scientific journal for peer review by April 2014. The pilot study is funded until April 2016, and we anticipate the release of subsequent results in mid-2016.

**34. When would results from a full PROUD trial be available?**

Given that the PROUD 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.

**35. Will PROUD participants continue on Truvada PrEP at the end of 24 months?**

Before enrolment, all participants were made aware that Truvada PrEP may not continue after the 24 month follow-up period in the pilot. However, in October 2014, the TSC recommended that follow-up, including the provision of PrEP, should be extended for all participants until the end of the study in April 2016.

**36. What are the potential risks and benefits of taking part in the pilot?**

Participants have access to genitourinary medicine experts, who routinely offer support packages designed to reduce higher risk sexual behaviour and maintain their overall health, plus they will receive Truvada PrEP. Participants were fully informed of any risks before they enrolled. This might include experiencing side effects associated with medication, although available data show Truvada is well tolerated.

**37. If PROUD pilot participants are non-adherent, will they be at risk of HIV infection?**

The evidence on Truvada PrEP suggests that drug adherence is crucial for preventing infection. In the iPrEx trial, in those whose drug levels showed they had been taking PrEP daily, the risk of HIV infection was reduced by at least 92% compared to a placebo. However, measured drug levels showed that 49% of trial participants had not been taking PrEP regularly.

**38. What is in place in the PROUD pilot to encourage and monitor adherence?**

Participants have access to genitourinary medicine experts, who routinely offer support packages designed to reduce higher risk sexual behaviour and maintain their overall health, plus they will receive Truvada PrEP. This includes education on the importance of treatment adherence and of regular HIV testing.

Participants were asked to report on their own adherence using monthly self-completed web-based questionnaires, daily diaries, and by regular pill counts. A subsample of approximately 50 participants was asked to provide additional blood samples for pharmacokinetic testing of drug levels. Another subsample of approximately 50 participants either has been or will be invited to participate in in-depth interviews to discuss adherence.

**39. Would PROUD be continued if European Medicines Agency licenses Truvada for PrEP?**

The PROUD trial steering committee (TSC) includes representatives from community groups as well as commissioners, policy makers, and researchers independent of the PROUD pilot. The TSC would advise the PROUD team on the most appropriate course of action if an application is submitted and approved by the European Medicines Agency for the use of Truvada as PrEP in Europe.

## **TREATMENT AS PREVENTION (TasP)**

### **40. What is 'Treatment as Prevention' (TasP)?**

Treatment as Prevention (TasP) is another important HIV prevention strategy. This involves prescribing ARV therapy to people as soon as they test positive for HIV instead of waiting for previously established clinical markers. With consistent adherence, ARV treatment suppresses their viral load and therefore significantly reduces infectivity. In the context of monogamous stable discordant couples this is a very promising strategy.

### **41. What clinical evidence is available for TasP?**

The HPTN052 study in stable discordant couples found that treating the HIV positive partner reduced the risk of the HIV negative partner becoming infected by 96%. It is worth noting that about a quarter of infections caught in HPTN052 came from other sexual partners (i.e. not the stable discordant partner). This highlights the ongoing need for additional HIV prevention options for negative women and men.

### **42. If viral load is reduced sufficiently in a large enough proportion of HIV positive people within a population, does this reduce overall infection rates?**

There is indirect evidence that if viral load is reduced sufficiently in a large enough proportion of HIV positive people within a population, this can reduce new HIV infections. However, this strategy is reliant on people knowing their HIV status, receiving treatment soon after infection, and strict adherence to their treatment regimen.

## **TRUVADA**

### **43. What is Truvada?**

Truvada is an antiretroviral drug licensed for the treatment of HIV in the UK, US and many other countries around the world. Truvada is a fixed dose combination of emtricitabine (200mg) and tenofovir disoproxil fumarate (300mg), and is manufactured by Gilead Sciences. As of 13<sup>th</sup> February 2015, Truvada costs £355.73 for a month's supply of daily tablets (BNF list price).

### **44. What are the known side effects with Truvada?**

Truvada is generally well tolerated. Side effects in the placebo-controlled PrEP studies were generally mild (e.g. mild nausea) and seen in the first few weeks. Mild gastro-intestinal discomfort at an early stage of treatment, and mild creatinine elevations that reversed when treatment stopped (which give an indication of how well the kidneys are working), have also been seen. Serious side effects such as changes in bone mineral density (how much calcium and other minerals are in your bone) are rare, especially in HIV negative people, and usually reversed when the drug was stopped.

We know that stopping and starting ARV therapy whilst risk of HIV infection is ongoing should be avoided. This is because the risk of HIV resistance to one of the two drugs in Truvada developing is highest if Truvada is started just after an individual has become infected. We do not know about the long-term safety (10-20 years) of Truvada in HIV negative populations.

## **HIV IN THE UK**

### **45. How many people currently have HIV in the UK?**

It is estimated that there were around 107,800 people living with HIV in the UK in 2013. An estimated 43,500 MSM were living with HIV in the UK in 2013, which is equivalent to 59 per 1000 MSM aged 15-59 years, or 1 in every 17. The Public Health England 2014 report on HIV in the United Kingdom is available at:

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/401662/2014\\_PHE\\_HIV\\_annual\\_report\\_draft\\_Final\\_07-01-2015.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/401662/2014_PHE_HIV_annual_report_draft_Final_07-01-2015.pdf)

### **46. How many new cases were diagnoses in 2013?**

There were 6,000 new HIV diagnoses in 2013 in the UK, with a total of 3,250 new diagnoses in MSM, of which 2,800 were infections acquired in the UK.

### **47. How much does this country currently spent on managing HIV patients?**

In England, over £800 million is spent each year on the care and treatment of HIV patients.

### **48. Who is most at risk of HIV infection?**

We know that the UK HIV burden is not shared equally, by population or by region. Gay men (or men who have sex with men) and people from Black African communities are two populations at most risk.

### **49. How much money could be saved per prevented case of HIV?**

It is estimated that £280,000 - £360,000 in undiscounted lifetime treatment costs could be saved for each case of HIV prevented. If the 2,800 new HIV infections acquired by gay men/men who have sex with men in the UK 2013 had been prevented, between £0.8 - £1.0 billion lifetime treatment and clinical care costs would have been saved.

## **NEW INFORMATION RELEASED OCTOBER 2014**

### **50. Why was the PROUD pilot study design changed in October 2014?**

The independent data monitoring committee (IDMC) compare the rates of HIV infection between the two randomisation groups (immediate and deferred arms). In their review on 6<sup>th</sup> October 2014 they observed that PrEP is highly protective against HIV infection in the study population. On the 9<sup>th</sup> October, the Trial Steering Committee (TSC) accepted the IDMCs recommendation that the deferred arm should no longer continue and participants in the deferred period should be offered PrEP.

### **51. How quickly were the protocol changes implemented?**

In October 2014, we revised the study protocol to discontinue the deferred arm and submitted the protocol to the Medicines and Healthcare products Regulatory Agency (MHRA) and Research Ethics Committee (REC) for review. Once approvals from these two authorities were in place we applied for approval from the NHS Trusts involved in the study. The whole process took

approximately three to four weeks. The new protocol was implemented across the 13 PROUD study clinics in October and November 2014.

**52. What were the implications for participants still in the deferred period?**

We informed all participants about the new information and asked them to contact their study clinic. As recommended by the TSC, we aimed to offer all participants still in their deferred period an appointment by the end of November 2014. As of 9<sup>th</sup> October 2014, there were 133 HIV-negative participants still in the deferred period, of which so far 108 have accepted the offer of PrEP, 10 have declined the offer (mainly because they no longer felt at risk), and 15 have not yet returned to the clinic.

**53. What were the implications for participants already on PrEP?**

We informed all participants about the new information. As recommended by the TSC, we aimed to see all participants by the end of 2014 for HIV and STI screening. This was important to allow us to determine the definitive effectiveness of PrEP in the study.

**54. What were the implications for participants who had stopped attending the study clinics?**

We made a special effort to contact all participants who did not attend their last clinic visit in order to update them on the new information and offer them PrEP. As of 20<sup>th</sup> February 2015, only 15 participants who were still in the deferred period as of the October protocol change, have not returned to the clinic.

**55. What happened if participants didn't want to start or continue to use PrEP?**

Participants do not have to start PrEP if they do not want to and there is no obligation to continue to take it. Participants can discuss their specific circumstances and HIV risk factors with the clinic teams in order to decide if they want to incorporate PrEP in their risk reduction package now or in the future. As of 20<sup>th</sup> February 2015, 10 participants who were still in the deferred period as of the October protocol change, declined the offer of PrEP, mainly because they no longer felt at risk of HIV.

**56. How long will the study continue now that you know Truvada PrEP is highly effective?**

We will continue the study schedule for all participants until April 2016. We will ask everyone to continue to have three monthly checks of HIV and STIs as well as periodic hepatitis C screening and kidney function tests. Although we know that Truvada is highly effective, we want to continue the study in order to collect more robust data on PrEP adherence and the impact of PrEP on sexual behaviour and the rate of STIs.

**57. How effective was Truvada in the PROUD study?**

We released these results on the 24<sup>th</sup> February 2015 – see the RESULTS update.

**58. How come the pilot study has 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,

MSM and transgender women 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 was 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.

**59. What will happen when participants reach the end of their two-year follow up period?**

Participants were originally due to be followed-up for 2 years, but now all participants will be followed up until April 2016 regardless of when they joined the study (which could be anytime from November 2012 to April 2014). For more details on PrEP access at the end of the study—see RESULTS UPDATE – PROUD pilot study section.

**FURTHER INFORMATION**

- PROUD study: <http://www.proud.mrc.ac.uk/default.aspx>
- Ongoing PrEP trials and demonstration studies: <http://www.avac.org/trial-summary-table/prep>
- Medical Research Council clinical trials unit: <http://www.ctu.mrc.ac.uk/>
- Public Health England: <https://www.gov.uk/government/organisations/public-health-england>