Report on Second Participant Involvement Meeting

Date: 19th March 2014; 18.00 – 20.30
Location: Terrence Higgins Trust (THT)
Presenter: Mitzy Gafos (Sheena McCormack available for questions)
Facilitator: Justin Harbottle
Topic: Future HIV prevention research priorities: a discussion about research priorities in the event that PROUD demonstrates benefits of PrEP in the UK
Attendees: 17 study participants with representation from Dean St (8), John Hunter (3), Barts (2), St Thomas's (2), MMC (1), Homerton (1),

Format of Meeting

Presentation

- Entitled 'Background of PrEP Research' – summarises information on the pre-circulated hand-out

Aims of meeting

- Pilot study aims to assess the feasibility of conducting a larger clinical trial of PrEP using the deferred randomisation design in the UK.
- Pilot started Nov 2012 – we are close to full enrolment – so anticipate pilot ending by April 2016 at the latest.
- We have applied for funding to expand the pilot into a full-scale clinical trial by enrolling an additional 1800 men – if we get funding for this the trial could start in the first half of 2015 and continue until the end of 2018.
- The main questions we want to be able to answer in the trial are:
    - Effectiveness
    - Safety
    - Resistance
    - Adherence
    - Impact on sexual behaviour – risk mitigation/compensation
- It is possible that we could answer these questions sooner than we expect – certainly before 2018. Research planning and funding processes can take a very long time, and therefore we are starting to think now about the next research priorities for HIV prevention research in this country – and would welcome your input.
- The main question today is if the PROUD study demonstrates that Truvada reduces the risk of HIV infection among gay men in the UK – what are the next research priorities?

Breakout sessions (4 tables – 4 or 5 people per table)

In break out groups, the following three questions were discussed – although questions 1 and 3 merged into a single discussion:

1) **What are the next priorities for clinical trials in the UK?**
   Should we be testing different ways of using Truvada or new HIV prevention drugs? For example should we test Truvada with alternative dosing, Truvada with new ways to support adherence, different PrEP pills, monthly injectable PrEP, comparing pre to post exposure options, rectal microbicide gels, etc.

2) **How acceptable would various clinical trial designs be to test the priority clinical trial questions?**

All clinical trial designs require a control group in order to compare the test product. Based on the clinical trial priorities discussed in the last question, would it be acceptable for the next clinical trial to have the following as control groups:

- Placebo
- Deferred start (as in PROUD)
- Daily Truvada

3) What are the next priorities for clinical research around Truvada in the UK?

If PROUD shows Truvada to be effective in the UK, what are the other clinical research questions that we need to prioritise? For example evaluating the ways that Truvada is prescribed, evaluating ways to support adherence such as peer support, understanding more about how sero-discordant couples use PrEP and treatment as prevention, etc.

Summary of Feedback

1. **<u>Next clinical trial priorities</u>**

a. Truvada

- The majority of the group find daily pill easy to take and convenient to fit into the daily routine – as such few people saw a particular need for alternative dosing options. However, there was some recognition that while this may be true for men who chose to join PROUD, there may be other groups who may find daily pill taking a challenge.
- Intermittent PrEP such as 3 or 4 times weekly - majority of group preferred the daily model for themselves and also felt that the daily pill was simpler for people with more chaotic lifestyles. The majority also felt that the daily offers some forgiveness for people who may forget to take pills occasionally.
- Half dose Truvada – in response to comments with intermittent dosing each individual would use less drugs, so more people could have access to drugs, the group accepted that access was an important issue but still felt they would prefer a half dose of Truvada (if shown sufficient for effect) every day than reducing from daily pills. However some people questioned if it was worth taking the risk of halving a dose that there is a lot of confidence in.
- Before and After dosing – the general feeling was taking a pill before sex required a level of forward planning that was unrealistic for many men. For some people, the real benefit of PrEP was perceived as being a back up in the cases of unexpected sex, or unplanned condomless sex (such as after drug taking). It was also noted that this would be of least interest to very sexually active men. Also a question of if before and after dosing of PrEP would replace PEP.

b. Alternative ARVs as PrEP

- The majority find Truvada easy with no objections to the side effects (although some people experienced them initially) – as such, few people saw the need for alternative PrEP models for themselves.
- Any alternative would have to be expected to be at least as effective as Truvada
- The need for PrEP drugs that were not key to treatment regimens in other parts of the world was raised – and acknowledged as justification for new drugs. However, there was no real priority in this group, and the show of hands (where 9 people said they would participate in a trial of an alternative drug) showed a level of interest that did not come through strongly in the discussion.

c. Injectables (monthly)

- There were concerns raised about side effects – some people experienced initial side effects with Truvada and were concerned that being given a dose of drug to cover them for a month could dramatically increase the experience of side effects – and also remove the possibility to just stop taking the drugs if the side effects persisted
- Concern that anxiety levels may increase towards the end of the month, with concern about whether there was still sufficient drug on board to offer protection – this related to having a lack of control over the level of drug taking
- Most people would want the injectable to be at least as good as the daily pills
- Concern that there would be less leeway for late clinic appointments – being late for the injection could result in waning drug levels, whereas people can be given additional supplies of pills in case they are late for a clinic visit. Also comments that not all clinics offer appointments that suit peoples life/work schedule so this could be particularly difficult in those circumstances
- One benefit of a monthly injectable was that it would necessity a structure of monthly clinical contact which many people found favourable.
- There was a question of whether the injectables could be self-administered at home – but there were mixed views on the benefit of this.

- Question if an implant type devise could be considered – similar to contraceptives – but similar concerns with this as with injectable

d. Rectal microbicides

- No-one in the room had heard of microbicides. There was very little interest in it – partly due to the coitally dependent nature of it and difficulty of predicting sex. Some people saw a potential if it was used as a lubricant – and potentially available in sauna's etc.

In a show of hands – we assessed peoples interests in different clinical trial options

Drug regime	**Interest**
Half dose daily Truvada	9
Additional PrEP i.e. Maraviroc	9
Monthly pill	9
Monthly injectable	9
Rectal microbicides	4
Pills on alternate days	1
Pills 3 or 4 times per week	0
Pills before and after sex	0

2. <u>How acceptable would various clinical trial designs be to test the priority clinical trial questions?</u>

- Placebo control was not considered acceptable given the evidence around Truvada – the use of a placebo was viewed as putting the needs of science above the needs of patients. Also it was acknowledged that the use of a placebo would not pick up changes in behaviour as people would minimise risk in case on placebo. Alternative concern about people who would have a false sense of security in the study and put themselves at risk while on placebo.
- Deferred model was viewed as acceptable although could be a disincentive for some people to join or remain in the study. However, it was viewed as essential to collect evidence on changing behaviour and the related impact on STIs.
- Truvada (open label) as a control was generally considered acceptable – although there was an emphasis that this should be in the context where the next drug is expected to be at least as good as Truvada.
- Truvada (blinded) as a control was also generally acceptable – although from the views expressed maybe less so than open label given the strength of evidence for Truvada.

3. What are the next priorities for clinical research around Truvada in the UK?

- This question was merged into question 1 and as such was slightly less structured that the other questions
- The key question that emerged related to supporting adherence – and in the show of hands, 12 men said they would take part in this research. One suggestion was about text message type reminders – although many people in the group described the mechanisms they have developed for themselves and it could be interesting to collate these (i.e. phone aps with pill reminders etc).
- The possibility of home testing – for HIV and STIs – was also raised in relation to PrEP provision – with medications delivered at home as they are for treatment by some clinics.
- Discussed the option of comparing PEP (i.e. prepared packs for time of risk) to PrEP. The advantage of PrEP was viewed as the ease of the daily pill without need to 'worry' about sudden exposure – although the benefit of using alternative drugs (with less side effects) for a shorter

duration as PEP was acknowledged. The concern about the worried well was raised whereby people may overuse PEP if it is available at home.

- There was a lot of discussion about the stigma related to being on PrEP – although it was not clearly discussed as a research priority, there was a sense of a need to support people on PrEP to articulate their use of PrEP in a positive way – as an empowered statement of taking control of ones health such as stopping smoking.
- There were also a number of examples of poor clinical practice in terms of experiences at particular clinics and with some health care professionals - such as framing Truvada as poison. Again this was not articulated as a research priority but was noted as a potential barrier in the future.
- There were a lot questions about access to Truvada after the study – it was explained that PROUD are in the processes of negotiating access to drug so as at the end of follow-up each individual can keep accessing it until the last person exits the pilot study, or the clinical trial if additional funding is secured to expand the study. The hope is that the evidence from the study would support provision via the NHS. However, a few people felt that we should be prepared to assess the impact of loosing access to Truvada just in case access is limited for any reason.

4. How would you like social media to support participation?

- We asked an additional question right at the end of the meeting about participants interest in social media forms.
- There were benefits seen in having a space to share experiences of side effects, adherence etc.
- There were concerns that this would be perceived as a hook up site – for example as a Daily Mail headline
- Benefits of having a private forum with an anonymous handle opposed to using facebook real name accounts
- One question about whether anonymity was just between participants or also to the PROUD team – comment that PROUD team could potentially monitor registration without needing to know identity when in forum.
- Benefit of both private (participant forum) and public awareness raising forum to promote PrEP and challenge stigma.

In a show of hands – we assessed peoples interests in different social media models

Media	**Interested**
Something	12
Facebook – public	1
Facebook – anonymous	2
PROUD site forum	12

Notes

- Cost of Truvada was discussed (£418 per month) but also noted that it comes off patent in 2018 and can be made available in Africa for £150 per year
- A number of people draw on parallels with contraceptives in terms of thinking about pills v injections

Report prepared by Mitzy Gafos
Circulated 21st March 2014