PROUD Participant Involvement meeting: Trial Design
Date: Tuesday 9th September 2014 18.00 – 20.00
Venue: MRC Clinical Trials Unit at UCL, Aviation House, 125 Kingsway, Holborn, WC2B 6NH
Contact person: Mitzy Gafos
Directions: Aviation House is situated on Kingsway, opposite Holborn Underground station (from Holborn station, cross Kingsway at the traffic lights so as Sainsbury's is in front of you, turn left at the lights so as Sainsbury's in on your right, pass Boots and the entrance to Aviation house is set back from the road on your right).

Discussion Points

**Note – at the month 12 visit, all participants are asked to complete a Study Acceptability Questionnaire (copy available at meeting). To date 152 participants have completed this questionnaire and we have used some of these responses to inform this discussion.*

Structure of the meeting (break into 3 groups of 5 people)

- Group 1 prioritise discussing questions 1 & 2 – then other questions of interest
- Group 2 prioritise discussing questions 3 – then other questions of interest
- Group 3 prioritise discussing questions 4, 5 & 6 – then other questions of interest
- Each group feedback on each question and facilitate discuss across the room

1) Study Update

From November 2012 (enrolment opened) to April 2014 (enrolment closed), 545 men joined the PROUD pilot study. We are currently negotiating funds to be able to offer all participants Truvada from the end of their follow up period (after 2 years in the study) until the very end of the study (when the last person completes the study in April 2016).
What are your thoughts on the following:

- If we are unsuccessful in getting this funding – access to Truvada will end once men finish their study follow up period.
- If we are successful in getting this funding, once men have completed their 2 years in the study we would hope to reduce study visits to every 6 months and collect only limited data on sexual behaviour and adherence at these visits.

2) Study Design

We are in the process of applying for funding to expand to a larger clinical trial which would require enrolling an additional 1200 men from mid-2015.
What are your thoughts on these ideas for the larger trial:

- Deferred group – is it still acceptability to randomise men to wait for 12 months to receive Truvada? When will it stop being acceptable: when we have proof of Truvada effectiveness in the UK? Only when it is licensed by the European Medicines Agency even if not yet available in the UK? Only when Truvada is available in the UK?
    - Note that in the month 12 acceptability questionnaire, 76% of men said that the chance of being in the deferred group might put 'other' men off joining the study.
    - Only 12/152 men reported the deferred design as being the thing they most disliked in the study.

- Third group – we could evaluate another drug in the same study so as men would be randomised to receive Truvada, a new PrEP drug, or be in the deferred group. After 12 months in the deferred group, men would then be randomised to receive Truvada or a new PrEP drug. What are your thoughts on this? What do you think about the criteria for the new PrEP drug i.e. expectations around effectiveness, safety/side effects, resistance, less frequent dosing, etc?

3) Data collection

Two important aims of the study are to a) measure changes in sexual risk behaviour over the course of the study (to understand if Truvada use increases risk behaviour) and b) measure adherence to Truvada. As such we ask men to report sexual behaviour and adherence on a number of questionnaires in the study (all questionnaires will be available at the meeting):

1. Baseline Sexual Behaviour Questionnaire (paper)
2. Daily diary (on-line)
3. Monthly Adherence and Sexual Behaviour Questionnaire (on-line or paper)
4. Annual Sexual Behaviour Questionnaire month 12 and 24 (on-line or paper)

On the Visit Questionnaire, clinicians also record if the participants has had 'any' condomless sex since the last visit, participant reported adherence, and pill counts.

From the month 12 Acceptability Questionnaire (question 4), we received the following feedback (all responses in graph on last page):-

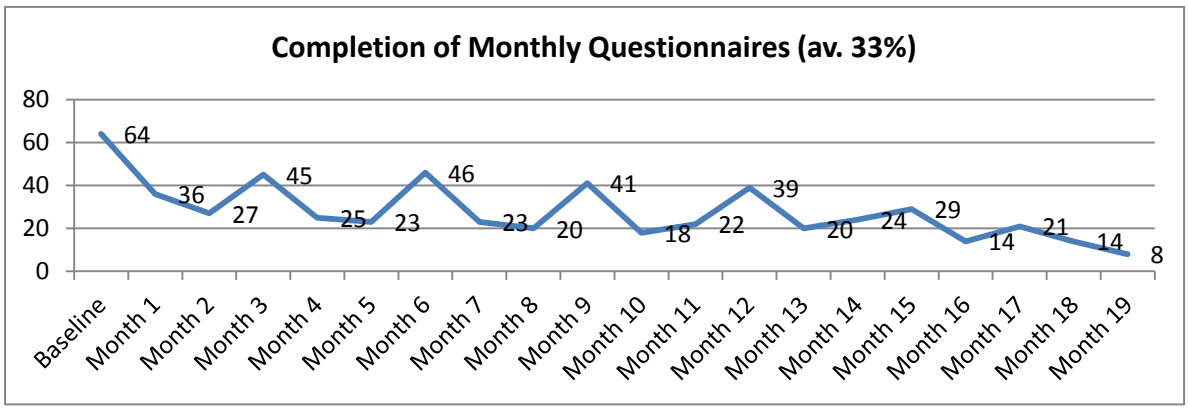
- 77% don't mind completing monthly questionnaires
- 59% like completing the questionnaires on line
- 59% don't dislike completing the diary
- 54% would prefer to complete questionnaires on a mobile app

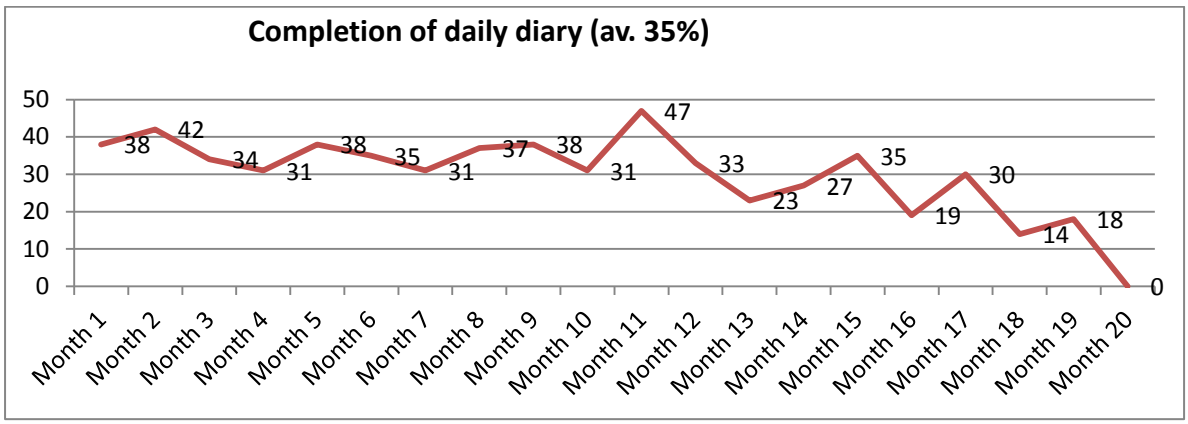
Men told us that the questionnaires and diaries were the study procedures they least liked! The main feedback related to:

- questions being confusing, difficult to answer accurately, frustrating, repetitive or too restrictive,
    - 36% of men said the questionnaires make it difficult to report sexual activity accurately,
- problems using the on-line system (not user friendly) and getting support to access it,
- too many questionnaires,
- difficult to remember to complete questionnaires (email reminder would be useful or mobile app),
- difficult to remember sexual activity over last 30 days or last 90 days,
    - 48% of men said it was difficult to remember sexual activity,
- diary cumbersome, fiddly and laborious to complete.

We also know:

- On average only 33% of participant's complete the questionnaire each month – highest at the clinic visits but still always lower than 50% after enrolment.
- On average only 35% of participant's complete the dairy – this is less influenced by clinic visit but still always lower than 50%





What are your thoughts on the following:

- Continue or drop the diary?
- Continue or drop the monthly questionnaires?
- Continue or drop all on-line data completion? We could just ask participants to complete paper questionnaires at the study visits.
- Which questions should we use to most accurately collect data on adherence?
- Which questions should we use to most accurately collect data on sexual behaviour?

4) Study visits

To reduce study costs for the clinical trial, we thought about reducing the study visits to every 6 months. However, in previous participant meetings men have told us they like the quarterly visits and find them useful in managing their risk. In the month 12 acceptability questionnaires, 91% of men said is was not a problem to visit the clinic every 3 months, 93% liked having regular HIV tests, and 89% liked having regular STI tests. In addition, approximately a quarter of men reported regular check ups as the thing they 'most liked' about the study.

- What are your thoughts about having clinic visits every 6 instead of 3 months?

PROUD

5) Patient and Public Involvement (PPI)

UK research funding bodies, such as the National Institute for Health Research (NIHR), recommend the involvement of patients and the public in the design and conduct of research studies. We also involve participants – like yourselves. To date participants and representatives of community organisations have volunteered their time for free. The NIHR guidelines suggest we pay participants for their time.

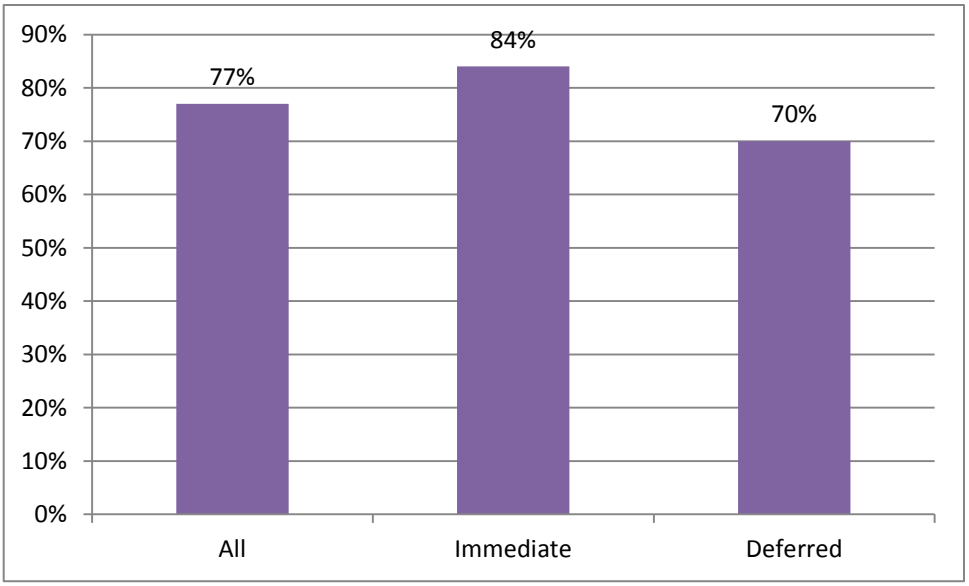
- What do you think would be a fair payment for your future attendance at a meeting such as this?

6) Reimbursing participants for visits during the period of deferment

In order to answer the key study questions, we need complete data which means we need at least 85% of men returning regularly for clinic visits. At the moment about 77% return and this is mainly due to lower return among men in the deferred group (70% in deferred compared to 84% in immediate).

- One suggestion has been to pay men in the deferred group to attend their month 3, 6, and 9 visits (i.e. when they are not receiving Truvada). What do you think about this idea, any alternative ideas, and if we did pay, how much should it be?

Visit attendance by study group



Month 12 Acceptability Questionnaire Data – question number 4 – only completed by 152 men to date as many men not yet reached their month 12 visit