CROI
18 February 2010

1st PARTNER Study Investigator meeting,
CROI 2010, Hotel Marriott Marquis, San Francisco

Agenda

- Welcome – history, organisation and immediate next steps
- Rationale and Design (Andrew)
- Community perspective (Simon)
- Implementation and requirements (Tina)
- Approach to recruitment (all)

History of the project

- Uncertainty exist to the extend that HIV pos persons on ART can transmit HIV
  - Idea to address this formed in Feb 2009
  - Preliminary site survey showed widespread interest
- Grant was submitted by April 2009
- NIHR grant awarded by end of 2009 (PI: Andrew Phillips)
- This project is one of several within the NIHR programme grant which aims to assess the prevention role of antiretroviral therapy in HIV transmission

Governance structure (1)

Executive Committee (EC)

- **Role: Oversee implementation of the study**
- **Convenes: bi-weekly**
- **Membership:**
  - **Andrew Phillips & Jens Lundgren (co-chairs), Alison Rodger, Tina Bruun, Simon Collins + 2-3 site representatives (tbd)**

Steering committee (SC)

- **Role: Assist the EC in its tasks; will be consulted on major study-specific decisions**
- **Convenes: quarterly (or more often if needed)**
- **Membership:**
  - **Members of the EC**
  - **Persons centrally involved in study (i.e. IT, statistics, virology, ethics and legal issues)**
  - **National representative (tbd; to be identified among site PI's in each country)**

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Governance structure (2)

Study Group

- Role: All inclusive group of investigators and other persons important for the success of the study
- Convenes: Investigator meetings (affiliated with conferences (in 2010: Vienna, Glasgow)). Communication via newsletters.
- Membership: All persons centrally involved in the study are automatically part of the PARTNER Study. Each site to identify 2 persons (+ one additional for every 30 partnership followed for 2 years)

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Organisation of the study

- Jointly lead by RFH and CHIP
- Sponsor: UCL
- Coordination: CHIP
  - All communication to and from site via CHIP
- Flow of study funds:
  - RFH foundation to CHIP
  - CHIP to sites
    - based on performance – see details later
    - based on contractual relation between CHIP and site

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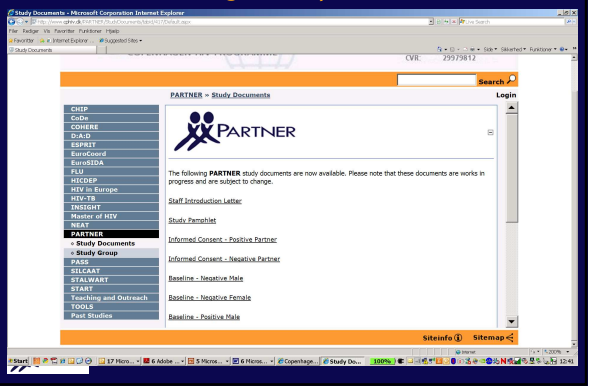
Study Group and authorship on publications

- Publications derived from the study will be authored by the "PARTNER study group".
- The top 20 recruiting sites will be guaranteed to have one person represented on the first major study publication. If the study results in more than one publication, rotation of membership of the writing committee will be made in a fair and geographically balanced way by members of the Study Group in conjunction with the Executive Committee.

Draft versions of all documents for commenting: hearing closes primo March



Next step

- Newsletter
- Hearing phase
  - Deadline for input to the protocol and study documents is 4th March 2010
- Investigator TC scheduled for Friday 5th March at 10.00 GMT (11.00 Central European Time)

Rationale and Design

Andrew Phillips

Background

- A proportion of people with diagnosed HIV report not always use a condom when having sex with partners of negative or unknown status.
- Appreciable evidence that virally suppressive ART reduces infectiousness of people with HIV through sex but precise estimates of risk are not Available, particularly for MSM
- Such estimates are needed both for counselling purpose, and for understanding the potential HIV prevention benefits of policy of expanding ART coverage to be offered to all people with diagnosed HIV.

Aims

To follow HIV serodifferent partnerships where the HIV+ partner is on ART and who report recently having had unprotected sexual intercourse to assess:

(I) the risk of HIV transmission in partnerships having unprotected sex and in which the HIV+ partner is on therapy with a viral load < 50 copies/mL

(II) why some partnerships do not use condoms, to describe the proportion who begin to adopt consistent condom use, and factors associated with this.

Design

- Observational study in which HIV serodifferent partnerships will be followed prospectively, with 4 monthly reporting of transmission risk behaviour and HIV testing for the HIV negative partner

Key Inclusion criteria

- HIV+ partner on ART (regardless of viral load)
- Partners have had unprotected penetrative anal or vaginal intercourse together in the past month
- Partners expect to have sex together again in the coming months

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Sample size

Aim to recruit and follow sufficient number of partnerships in order to collect a total of 3,333 persons-years of prospective follow-up. Initially, 1500 partnerships will be identified, with the intension to follow them for up to 2 years and 3 months. If for any reason a partnership chooses/is unable to contribute for the entire length of time, replacement will occur to achieve the overall target of 3,333 person-years. Follow-up for all partnerships will cease when this target has been meet.

Anonymization of data

Data on partnerships will be anonymized de-linked at intervals after the partnership is no longer under follow- up,including for partnerships where the HIV- person becomes infected.

In such cases, virus from the HIV+ and (formerly) HIV- partner will be compared after anonymization.

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Primary outcome analysis

To estimate the rate of transmission of HIV per person year of unprotected sex in persons on ART with plasma viral load < 50 copies/mL.

Comparison of viruses

If the HIV- partner becomes infected this will be assumed to have been from the HIV+ partner unless there is evidence from viral nucleoside sequence comparison that viruses are different by more than a certain distance.

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Community perspective

Simon Collins

PARTNER: community perspective

i) Current lack of data on transmission

- Not to stop condom use, but to inform; especially after analysis of risk detailed in the Swiss statement
- Limited data for MSM - historically based on heterosexual monogamous couples
- Impact of risk for anal sex, at low viral loads
- Further data at <50, <5 and <1 c/mL
- Impact of different ARV combinations (TDF?)

PARTNER: community perspective

ii) Condom use and behaviour changes

- Additional results will inform on real world behaviour and risks
- Potential to reduce transmission risk for people in the study
- May support earlier studies showing that partners are *not* source partner
- *May* find that these currently perceived risk reductions have little significance when viral load is <50

PARTNER: community perspective

iii) Importance of PARTNER study

- To accurately define risk
- To inform both perceived and actual risk
- To impact on quality of life for both partners
- To inform and target more effective preventative and educational interventions
- Ideal study for wide community involvement

PARTNER: community perspective

iv) Community involvement

- Ideal trial for community involvement
- No safety issues, many potential safety advantages
- Address questions that patients want answered
- Ideal for community press, articles, leaflets etc
- Community awareness for HIV-negative partners (MSM press etc)

Implementation and requirements

Tina Bruun

Participating Centres

- Call for collaboration sent to 80 centres early January
- Responses received from 40 centres by 11 Feb
- Enormous interest and enthusiasm

Timeline 2010/11

February/March
- Final selection of centres
- Finalise protocol

Early Spring
- Ethical approvals initiated
- Contracts finalised

Late Spring—Summer
- Ethical approvals received
- Study initiation

Summer 2011
- All partnership are recruited

Site Requirements

Every site will need to follow 40 partnerships (on an average) for 27 months

Of note, it does not have to be the same 40 partnerships throughout the 27 months

Scenarios:

1. The same couple is followed for the entire 27 months period
2. The HIV positive partner get a new negative partner
3. The couple breaks up and a completely new serodifferent partnership replace them

We estimate that it will take approximately 1 year to recruit the partnerships and therefore we will by summer 2011 have all 1500 partnership recruited

Visitation schedule (1)

- Enrolment: baseline visit

  Can be done separately or with the two partners together - please ensure that both are fully informed about study and that participation from both is voluntary

  - HIV positive partner:
    - Complete CRF and sent to CHIP via FAX
    - Ask partner to complete questionnaire, place it in sealed envelope (to be send to CHIP in batches)
  - HIV negative partner:
    - Ask partner to complete questionnaire, place in sealed envelope (to be send to CHIP in batches)
    - Do a HIV test
    - Complete CRF and sent to CHIP via FAX

Visitation schedule (2)

- Follow up visits: Every 4 month (visit window: 3-5 months)
- For as long as the partnership want/can to continue or until the study has gathered sufficient follow-up
  - HIV positive partner:
    - Complete CRF and sent to CHIP via FAX
    - Ask partner to complete questionnaire, place it in sealed envelope (to be send to CHIP in batches)
  - HIV negative partner:
    - Ask partner to complete questionnaire, place in sealed envelope (to be send to CHIP in batches)
    - Do a HIV test
    - Complete CRF and sent to CHIP via FAX
- The maximum number of follow up visits per partnership will be 6
- The positive partners follow up visit can be conducted the same time as their regular clinic visit

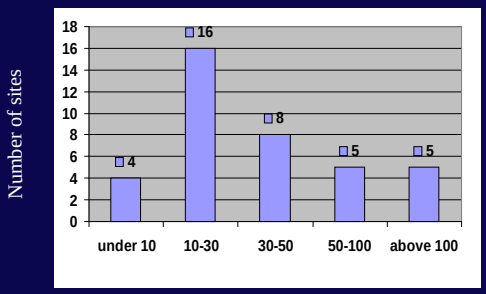
Visitation schedule (3)

- Procedures if HIV negative partner becomes HIV positive
  - Collect blood sample from both partners - ship to CHIP
    - Prior to sequencing, the pair of blood samples will be anonymized and unlinked
  - Request both partners fill out specific questionnaire

Approach to recruitment

All

Preliminary site estimation of recruitment



Numbers of partnerships

How to recruit partnership?

What causes the differences in the different site estimations?

- Number of patients in the clinic
- Recruitment strategies
  - It may be appropriate for the project nurse to screen patients so that the treating physician or contact-nurse only informs the patient about the study and refers them to the project nurse. This will enable people to keep their study participation separate from their routine care.
  - Publicity through leaflets and posters around the clinic will allow patients to self refer to the research nurse
- Other

Financial issues

Payment pr site pr. year

(estimation done with 38-40 partnership)

- Bonus for site establishment within timeframe: 750 £
- Reimbursement for submission fees: 666,50 £
- Site reimbursement per completed eligible partnership year: 180 £

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