HPTN 071: Population effects of antiretroviral therapy to reduce HIV transmission (PopART)

Overview and progress April 2014
Outline of presentation

• Trial design
• Timelines
• Progress 2013/14
• Major challenges
Trial Design

3 arm cluster-randomised trial with 21 communities (N ≈ 1.2million total population)

- **Arm A**: Full PopART intervention including immediate ART irrespective of CD4 count
- **Arm B**: PopART intervention except ART initiation according to current national guidelines*
- **Arm C**: Standard of care at current service provision levels including ART initiation according to current national guidelines*

*currently CD4-count <350 cells/mm³

- 21 communities in 3 arms
  - 12 communities in Zambia
  - 9 communities in South Africa

- Average of ~50,000 in each cluster (~ 50% adults)
- Incidence measured in *Population Cohort*: 2,500 adults in each cluster, followed up after 1, 2 and 3 years
PopART Intervention Package

Universal testing: annual door-to-door HBT

Service promotion and referral for:
- HIV care for HIV +ve including PMTCT
- VMMC
- TB
- STI

Support for:
- Retention in care
- Adherence to treatment

Universal treatment for HIV +ve irrespective of CD4 count

Facilitated by CHiPs

CHiPs: Community HIV-care Providers
PMTCT: Prevention of Mother to Child Transmission
VMMC: Voluntary Medical Male Circumcision
TB: Tuberculosis
STI: Sexually Transmitted Infections
Outcome data

**Population Cohort**
- HIV incidence
- HSV-2 incidence
- ART retention, adherence and viral suppression*
- Community viral load*
- ART drug resistance*
- Sexual risk behaviour
- HIV-related stigma

**CHiPs/Clinic**
- Uptake of intervention components
- Time between HIV diagnosis and initiation of care
- Retention in HIV care and ART adherence
- HIV disease progression and death
- ART Toxicity
- TB notification and mortality

* If funded
Why is a trial needed?

• Not known whether a UTT intervention can be delivered with high uptake and acceptability
• Many uncertainties in model parameters
• Population-level impact of (feasible) intervention package is not known
• Many potential adverse effects, such as toxicity, drug resistance, sexual risk disinhibition, HIV-related stigma, overload of health services
• A rigorously designed trial can measure the costs and benefits of this strategy and provide reliable evidence on cost-effectiveness for health policy makers
Additional studies

• Mathematical modelling
• Health economics
• Qualitative research
• Case-control studies of factors associated with uptake
• Ancillary studies
  – Phylogenetics
  – Stigma
  – ? Impact on TB prevalence
  – ? Impact on HIV-free infant survival
## Modified timeline

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### Household Mapping of communities

- **2012 Q3**: Initial visits to all households
- **2013 Q4**: Return visits to households
- **2014 Q1**: Return visits to households
- **2015 Q2**: Return visits to households

### CHiPs Intervention

- **2012 Q3**: Enrollment (PC0)
- **2013 Q4**: Return visits to households (PC12)
- **2014 Q1**: Return visits to households (PC24)
- **2015 Q2**: Return visits to households (PC36)

### Population Cohort

- **2012 Q3**: Enrollment (PC0)
- **2013 Q4**: Return visits to households (PC12)
- **2014 Q1**: Return visits to households (PC24)
- **2015 Q2**: Return visits to households (PC36)

### Interim Assessment

- **2013 Q4**

### Population Cross Sectional Survey

- **2014 Q1**: Case Control Study 1 and 2
- **2015 Q2**: Case Control Study 3

### Qualitative Studies

- **2014 Q3**: Rapid Community Assessment 2
- **2015 Q3**: Assessment of community response to intervention, ethnography, longitudinal study of testing behaviors

### Analysis and Reporting

- **2016 Q4**

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1. Requires additional Funding
2. To be described in and conducted according to an ancillary protocol
3. Full completion of the analysis is likely to extend beyond Q4 2017
Progress: 2013/14

- Protocol development/approvals
  - All approvals for main study received May 2013
  - Ancillary studies
- Public Randomisation - February 2013
- Research activities
  - Formative research completed
  - Census completed
  - Population cohort enrolment underway
- Intervention activities
  - Community
  - Clinic
- Meetings/governance
Research activities

• Formative research
  • Broad brush surveys completed in all 21 study communities
  • Background information on geographical, cultural, socio-economic, health-related characteristics
  • HIV landscape: Attitudes, perceptions, services
  • Key stakeholders
• 82 FGD in Zambia, 48 in SA = 130 total
• 65 KII in Zambia, 30 in SA = 95 total
• Observations in 13 different locations per community (day and night, transport, clinic, hair salons churches, bars etc)
CONCEPT MAPPING, COMMUNITY MAPPING AND CHARACTER CARD ACTIVITIES
Findings: Key barriers and catalysts to HPN 071 (PopART) trial implementation

**Catalysts**
- Availability of HIV service providers
- Community openness about HIV and HIV treatment
- Community exposure to non-clinic based HIV testing
- Community experience and acceptance of lay health workers
- Reported reduction in levels of stigma

**Barriers**
- Differential definitions of ‘community’
- Health system ART constraints
- Concerns: sustainability of treatment
- Low awareness of ART as prevention
- Resistance to MMC
- Fears of confidentiality (CHiPs)
- Stigma (disclosure of status ART clinic; contact with the CHiPs)
- Lack of shared understanding commitment amongst stakeholders
- Poverty, livelihood constraints, crime
- Mobility of people
- Alcohol and drug
- Illicit use of ARVs: increased availability ARV - black market
- Flooding during the rainy season
- Faith healing & traditional medicine

5. Catalysts and Barriers
Research activities

• Population cohort
  • Preparation of questionnaires and data collection tools
  • Development and testing of Electronic Data Capture systems
  • Acquisition and testing of robust tablet computers running Windows 8
  • Completion of household census in all 21 communities
    • Addition of neighbouring areas in 2 Arm C communities
    • Delineation of intervention and PC enrolment areas in large Lusaka communities
Community Overview - Zambia
Research activities

- Population cohort
  - Recruitment and training of PC research teams in both countries
- Start of enrolment
  - Zambia: November 2013
  - S Africa: January 2014
  - Pause in Zambia in December (IRB)
- To date 5,484 participants enrolled (target 52,500)
Intervention activities

- Design and development of Intervention Manual
- Working with implementation partners to prepare clinics and other services
- Recruitment and training of CHiPs
- Preparation and testing of CHiPs EDC including acquisition of equipment
- Clinic/CHiPs activities commenced
  - Zambia: Nov 2013, S Africa: Jan 2014
- Development/approval of Intervention Performance Communication Plan (monitoring against targets)
Meetings/governance

• PopART annual meeting in Africa
• International Advisory Group established: First meeting at HPTN Annual Meeting (May 2013), second meeting Cape Town (Feb 2014)
• DSMB meetings: April 2013, October 2013
• Trial Management Committee in-country meets quarterly
• ZIMT meets monthly
• DIMT and Community Advisory Boards meet monthly
Major challenges

• Delays
  • Development/testing of Population Cohort EDC
  • Problems with EDC equipment
  • Delays in IRB approvals/changes in Zambia
  • Delays in approval to start in S Africa due to ART funding arrangements

• Couple counselling Issues

• Intervention challenges
  • Men
  • Hard to reach populations
  • VMMC
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Dr. Sarah Fidler
Dr. Helen Ayles
Dr. Nulda Beyers

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