Microbicide Trials:

Challenges and Opportunities

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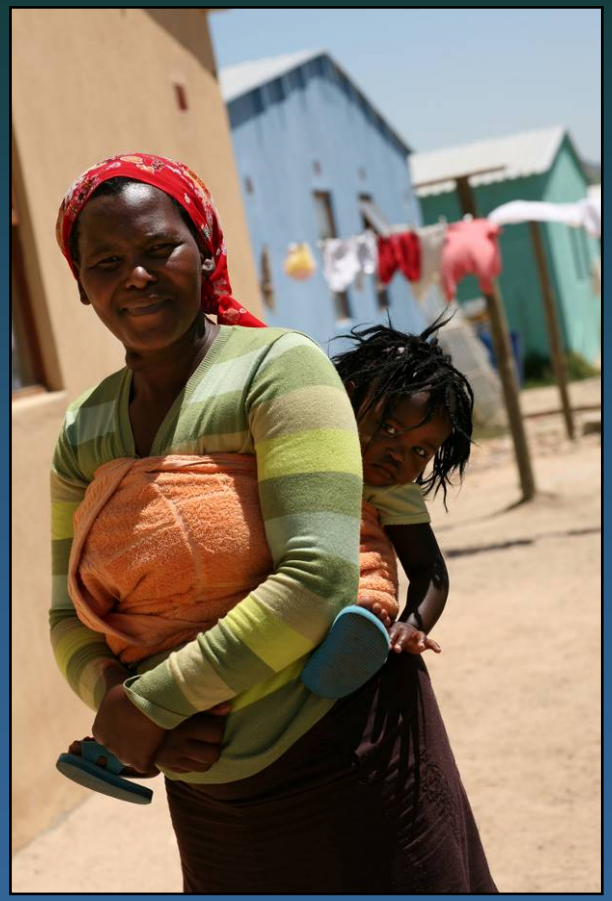
Women and HIV



- **New UNAIDS numbers**
  - Globally, 15.4 million women living with HIV, and the proportion of new HIV infections in women continues to rise
- **Face of HIV increasingly female, young**
  - In Sub-Saharan Africa, young women 15-24 up to 3 times more likely to acquire HIV than men
- **Married, monogamous women at high risk**
  - India: 22% of HIV cases in housewives with single partner
  - In Uganda 50% of new infections within marriage

Women's Vulnerability to HIV

- Biological, economic and socio-cultural factors:
  - Male-to-female transmission higher
  - Young women at even higher risk
  - Financial dependence on male partners
  - Inequality of women (exploitation and violence)
  - Cultural practices such as early marriages, intergenerational sex and marital infidelity
  - Paradoxically higher HIV rates seen in higher economic index women who live in urban areas

Why Test Microbicides in Developing Countries?

- Countries in greatest need of new HIV prevention options
  - Communities with high HIV incidence
  - Risk-benefit determination can only be obtained where the disease in question is endemic
- Test microbicides in contexts in which they will be used
  - Effectiveness, risk, and adverse events must be studied in relevant populations
  - Clinical and regulatory implications explored and prepared for
- Building understanding and support towards future access from a range of stakeholders

Clinical Research in Africa

Challenges	Opportunities
Microbicide trials • Unknown HIV incidence • True informed consent • Potential social harms • High pregnancy rates • Long-term ARV treatment	• Conduct epi studies • Ethics guidelines/ community engagement • Family planning/condoms • Referral networks/partnerships
Resource limitations • Clinical infrastructure • Ethics and regulatory	• Site development/staff training • Capacity building/development of clinical research guidelines
External environment • Politics, culture, media	• Relationship/trust building

Capacity Building at Research Centres

- Community engagement –establish CAB
- Referral networks for medical care/support
- Infrastructure and equipment
  - Build/purchase/lease and renovate space
  - Acquire medical and office equipment
- Staff development
  - Hire 15-20 per site with diverse expertise
  - Provide GCP, GCLP & study-specific training
- Communications, messaging and tools
- Financial management support

IPM Site Development to Date

- Strengthened or established capacity at 15 research centers (by end of 2008)

Country	Number of research centers	Established new
South Africa	9	6
Kenya	3	1
Rwanda	1	1
Tanzania	1	1
Malawi	1	1
TOTAL	15	10

KCMC, Moshi, Tanzania

New infrastructure and equipment

HIV incidence study completed
Clinical studies ongoing

Projet Ubuzima, Kigali, Rwanda

Completed IPM 003 dapivirine gel safety trial

HIV incidence studies ongoing
Clinical trials planned

Ladysmith, KwaZulu-Natal, South Africa

Site selection & renovation
Staff selection & training

HIV incidence study ongoing
Clinical trials planned

Ethical Guidelines for Clinical Trials

- Many studies taking place in developing countries

Key issues

- Community engagement
- Informed consent process
- Risk reduction counseling
- Family planning
- Management of pregnancy
- STI screening and treatment
- Testing positive at screening
- Participants who seroconvert
- Treatment for physical harms
- Services for study staff
- Post-trial access to products

Guidelines

- UNAIDS/WHO ethical guidelines in HIV prevention trials, 2007
- UNAIDS/AVAC good participatory practices, 2007
- South Africa GCP, 2006
- IPM ethical guidelines, 2006
- Nuffield Council on Bioethics, 2005
- GCM consensus points, 2005
- CIOMS biomedical guidelines, 2002
- WMA Declaration of Helsinki, 2000
- ICH GCP, 1996

Addressing Key Issues

- HIV transmission
  - Risk reduction counseling – at screening and during trial
    - Provision of male/female condoms
  - STI screening and treatment – also suggest to partners
- Pregnancy
  - Must be on stable form of contraception
    - Prior to study start and throughout study
    - Family planning counseling
  - If fall pregnant, continue with safety evaluation visits
    - Monitoring of pregnancy and baby up to one year
    - Referral to antenatal clinics
    - Pregnancy registry
    - If also seroconverted, referral for PMTCT
- Disease progression
  - Not specifically addressed in microbicide trials
    - May refer to acute infection protocols
    - Conduct follow up studies to assess resistance

Provisions for Participants Who Seroconvert During Trials

Microbicide field committed to providing appropriate HIV-related care and ARV therapy

- Implementing in multiple ways:
  - Guided referrals for HIV care, treatment, support
  - Pre-established partnerships with national/local institutions
  - Dedicated financing if national programs cannot sustain
  - Follow-up study protocols (for ARV microbicides)
  - Pursuing additional support from global donors
  - Advocacy for treatment scale up

Key Challenges

- Timeframe: participants may not need treatment until years after a trial
- Migration: how to ensure access for people who move out of the area or country
- Follow-up: how best to keep in touch with participants & inform them of choices
- Referral networks: how to ensure their strength over time
- Sustainability of appropriate long-term Rx