
Partners in Prevention

Lessons Learned

Importance of Network Culture & Feedback

Relevance for MTN

MTN Annual Regional Meeting,
Cape Town
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Clinical trials require....

- Important, clear & testable hypothesis
- Well-written protocol that is feasible to implement
- Focused & strong core team with clear roles & good communication
- Strong sites with motivated, dedicated study investigators where recruitment, retention, adherence & high quality data are everyone's priority (at CORE and sites)
- Realistic enrollment numbers with careful tracking
- Sufficient endpoint events

Principles & Objectives for Success of a Clinical Trial

- Team work & communication are essential
- A trial is only successful if there is strong commitment & leadership at all levels
- Competition is healthy
- Evaluation is necessary
 - ◆ Can only fix what you're aware of needing to be fixed
- Resources (ie budgets) should be linked to performance
 - ◆ We work better when we're incentivized

HPTN 039: HSV-2 suppressive therapy to prevent HIV Acquisition, N= 3272

HIV- HSV-2+
heterosexual women

Harare, Zimbabwe
Lusaka, Zambia
Johannesburg, SA

and

HIV- HSV-2+ MSM

Lima, Iquitos, Pucallpa: Peru
Seattle, San Francisco
New York

↓
Randomize

↙
Acyclovir 400 mg bid

↘
Placebo

1° endpoint: HIV infection
(estimated to be 3.5%/yr in placebo arm)

Lessons from HPTN 039 implementation

- Need to find ways to expedite protocol finalization, sponsor review & approval, SSP/SOP approval, IRB review & approval training, and study initiation
- Morale of protocol team and site staff is enhanced by seeing the trial get started
 - ◆ Requires efficiency & resourcefulness in problem-solving at multiple levels
- Need determined, effective, hands on investigators & protocol chairs and specialist

HSV-2 Suppression to Prevent HIV Transmission

3408 HIV- discordant couples with HIV+ partner also HSV 2-coinfected



Randomize HIV/HSV-2 + persons w/ CD4 \geq 250



Acyclovir 400 mg twice daily



Placebo twice daily



Follow couples for 1-2 years

1° endpoint: HIV infection in HIV-negative partner
(estimated 4% in placebo arm)

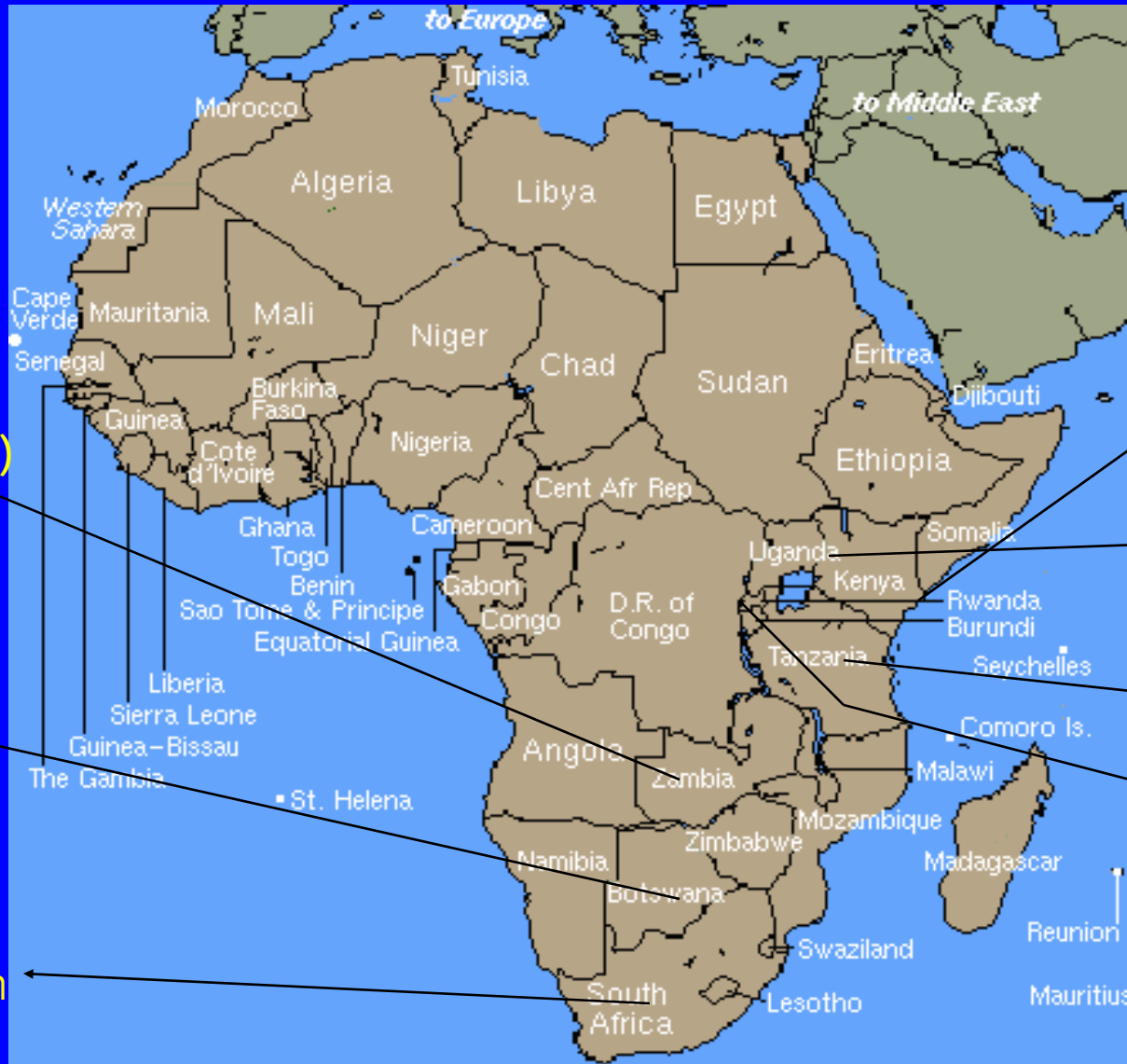


HIV discordant couples: Significance & additional challenges

- HIV transmission in Africa often occurs within HIV discordant couples in stable partnerships
- For each couple in which one partner is HIV-positive, ~50:50 chance their partner is HIV-discordant
- However, most couples are not aware of their HIV discordancy
 - ◆ HIV disclosure by HIV+ is low (~ 20%) due to stigma
 - ◆ Men are reluctant to be tested for HIV
 - ◆ Small proportion (~10%) test for HIV as couples
- Requires large community outreach & VCT collaborative effort



14 Sites for HSV-HIV Transmission Trial



Nairobi, Thika
Eldoret, Kisumu
Kenya (4)

Kampala, Uganda

Moshi, Tanzania

Kigali, Rwanda

Lusaka, Kitwe,
Ndola, Zambia (3)

Gaborone,
Botswana

Soweto, Orange
Farm, Cape Town
SA (3)



7 of 14 sites were new research sites



Kisumu, Kenya



Kampala, Uganda



Thika, Kenya

Multiple issues faced in Partners Trial

- **Recruitment**
 - √ 3400 enrolled (over 51000 couples of unk status tested, 6800 HIV DC screened)
- **Retention**
 - √ Goal: >90% at 12 months & 80% at 24 months
- **Adherence**
 - √ Goal: >90% of pills dispensed taken by pill count
- **Pregnancy**
 - √ 16% in index (~4% of study drug missed due to pregnancy)
- **Endpoints**
 - √ Need to track closely as may decline during follow-up
 - √ Follow-up of seroconverters & transmitting couples
- **Preparing for end of trial:**
 - ◆ Anticipating implementation challenges, assessing cost and other issues re. ACV
 - ◆ Preparing for media coverage

Lessons Learned from Partners in Prevention

- Site preparation took longer than expected
 - ◆ Cannot foresee all issues
 - ◆ Longer timelines than anticipated (IRB approvals, equipment importation, training 14 sites)
- Coordinating Center or Site delays = ↑ money
- Sites need experienced sr investigator & motivated junior investigator
 - ◆ Really invested in the trial
 - ◆ Sees professional opportunity if they make Partners work
- Some of our strongest sites were new sites
 - ◆ Focused on 1 study
 - ◆ Receptive to multiple strategies for recruitment of discordant couples

Site Challenges in Partners' Implementation -

- **Recruitment**

- ◆ Initial targets often unrealistic
- ◆ Need strong, multi-pronged recruitment strategies; need evaluation & revision
- ◆ Benefit of sharing strategies & lessons across sites

- **Retention & Study drug Adherence**

- ◆ Importance of systems & databases to track participants
- ◆ Assess participant concerns (eg., safety of study drug with alcohol)
- ◆ Provide tools (e.g. pill boxes)
- ◆ Retention & adherence are everyone's jobs

Evaluation

- is not a dirty word
- Evaluation is a necessary part of clinical trials to ensure best science & operations
 - ◆ For Core operations
 - ◆ For Site operations
 - ◆ For DAIDS
 - ◆ For participants
- We all benefit from feedback
- So how to do evaluation?
 - ◆ Examples from Partners in Prevention & IMPACT

Reports: Simple is beautiful



Enrollment Report as of 31 May 2007

SITE	Date of Enrollment Activation	Date of First Enrollment	# of Eligible Couples Enrolled during Month of:						Total Months of Enrollment	*# HIV Disc. Couples Screened	** Total Couples Enrolled	Average Monthly Enrollment
			Dec 06	Jan 07	Feb 07	Mar 07	Apr 07	May 07				
<i>Activation status: Activated</i>												
<i>PHRU</i>	17-Nov-04	25-Nov-04	5	9	9	4	5	2	29.9	433	240	8.0
<i>Nairobi</i>	23-Nov-04	01-Dec-04	12	18	21	23	15	2	30.2	771	416	13.8
<i>Gaborone</i>	02-Mar-05	08-Mar-05	13	7	11	13	2	4	26.4	553	325	12.3
<i>Kampala</i>	14-Mar-05	14-Mar-05	10	15	0	33	17	0	26.0	962	450	17.3
<i>Kisumu</i>	07-Apr-05	13-Apr-05	20	26	22	33	32	6	25.2	1227	532	21.1
<i>Eldoret</i>	16-May-05	31-May-05	18	11	20	13	18	5	24.0	485	268	11.2
<i>Kitwe</i>	27-Jun-05	28-Jun-05	0	0	0	0	0	0	10.1	192	91	9.0
<i>Moshi</i>	02-Jun-05	30-Jun-05	11	11	5	8	12	4	23.4	420	218	9.3
<i>Ndola</i>	27-Jun-05	13-Jul-05	0	0	0	0	0	0	10.1	241	161	15.9
<i>Cape Town</i>	10-Sep-05	05-Oct-05	10	10	8	15	9	4	20.1	383	196	9.8
<i>RHRU</i>	12-Aug-05	14-Sep-05	0	0	0	0	0	0	12.1	145	73	6.0
<i>Kigali</i>	27-Oct-05	31-Oct-05	0	0	0	0	0	0	6.1	219	153	25.1
<i>Lusaka</i>	30-Nov-05	15-Dec-05	0	0	0	0	0	0	5.0	104	72	14.4
<i>Thika</i>	28-Jun-06	30-Jun-06	14	35	24	23	22	4	10.5	474	213	20.3
Total All Sites			113	142	120	165	132	31		6609	3408	

Site Reports: Evaluation example from Partners in Prevention

- Developed site reports to focus on critical aspects of study implementation
 - ◆ Recruitment, retention, adherence to study drug, sample shipment, proficiency testing, responsiveness to issues, fiscal
- Provided data with comments & recommendations from Seattle Coordinating Center
- Sites appreciated reports but they were time-intensive to prepare for 14 sites

Example of site report from Partners in Prevention

Recruitment & Enrollment

Data Date: 25-Aug-06

Discordant But Not Enrolled Participants

Eligible but Not Enrolled	5 (4%)
Main reasons for Ineligibility:	
Not HSV-2 positive	41 (35%)
Low CD4 count	62 (52%)

Comments

Low CD4 count was a significant factor in determining the eligibility of screened HIV-discordant couples.

Current & Projected Enrollment

Site Activation for Enrollment	[REDACTED]
HIV-Discordant Couples Screened	[REDACTED]
Site Enrollment Yearly Enrollment Targets	[REDACTED]
Percentage of Target Enrollment Achieved	85%
Average Enrollment Since Activation	[REDACTED]
Average Enrollment in Last 3 Full Months	15
Current Enrollment	[REDACTED]
Projected Enrollment by April 30, 2007	[REDACTED]

Comments

The [REDACTED] site has demonstrated exceptional performance in recruitment and retention of study participants since enrollment activation. The site pioneered recruitment strategies, messages and methods that have subsequently been adopted by other study sites. However, data supplied in the screening template is not reflective of the site's efforts. The site will work to provide more information on the screening template as of October 1, 2006.

Characteristics of Enrolled Participants

Female Enrolled Index Participants	[REDACTED]
Male Enrolled Index Participants	[REDACTED]
Female Enrolled Partner Participants	[REDACTED]
Male Enrolled Partner Participants	[REDACTED]
Median Index CD4/CD8 Count	410 (CD4) 938 (CD8)
Median months known HIV-positive	8.0
Partners HSV-2 Index \geq 3.5	84 (48%)

Comments

The data characteristics for [REDACTED] are generally consistent with the study's overall average. A lower percentage of [REDACTED] participants report being married to their study partner (38%) than the study's overall average (74%). Participants also have known their HIV serostatus longer (8 months) than study participants in general (4 months).

Plans for Partners PrEP Evaluation

- Reports:

- Simple, easy to interpret reports with 1 pg summaries each about site-specific recruitment, retention, study drug adherence
- Sites, CC staff, and protocol chairs can readily see progress & issues

PARTNERS PrEP
Enrollment Report -- report run September 8, 2008
Reflects data received by September 8, 2008

Site	Date of first enrollment	Number of couples* enrolled during month of:						Total couples enrolled*	Average monthly** enrollment over the past 3 months	Number of HIV-discordant couples screened***	Screen/enroll ratio
		07-2008	08-2008	09-2008	10-2008	11-2008	12-2008				
Kabwohe	20AUG2008		10	5				15	8.6	23	1.5
Kampala	03JUL2008	9	5					14	4.8	14	1.0
Total		9	15	5				29		37	1.3

- Frequent communication:

- Weekly to biweekly calls between site coordinators and sites
- Weekly priority emails from site coordinators to sites
- Discuss specific issues about PrEP trial (recruitment, adherence, lab, AE management etc)

IMPAACT Clinical Research Site Evaluation

Accrual	Data Mgt	Regulatory	Monitoring	CAB	Comments	Evaluation Score
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Accrual is rated as the average # subjects on intervention study for 12 month period

Outstanding: more than an average of 20 subjects on study

Adequate: 19 – 15 subjects of study on average

Requires attention: 14 – 10 subjects on study on average

Requires immediate attention: less than 10 subjects on study on average

Data management

Excellent = score is greater than 0.

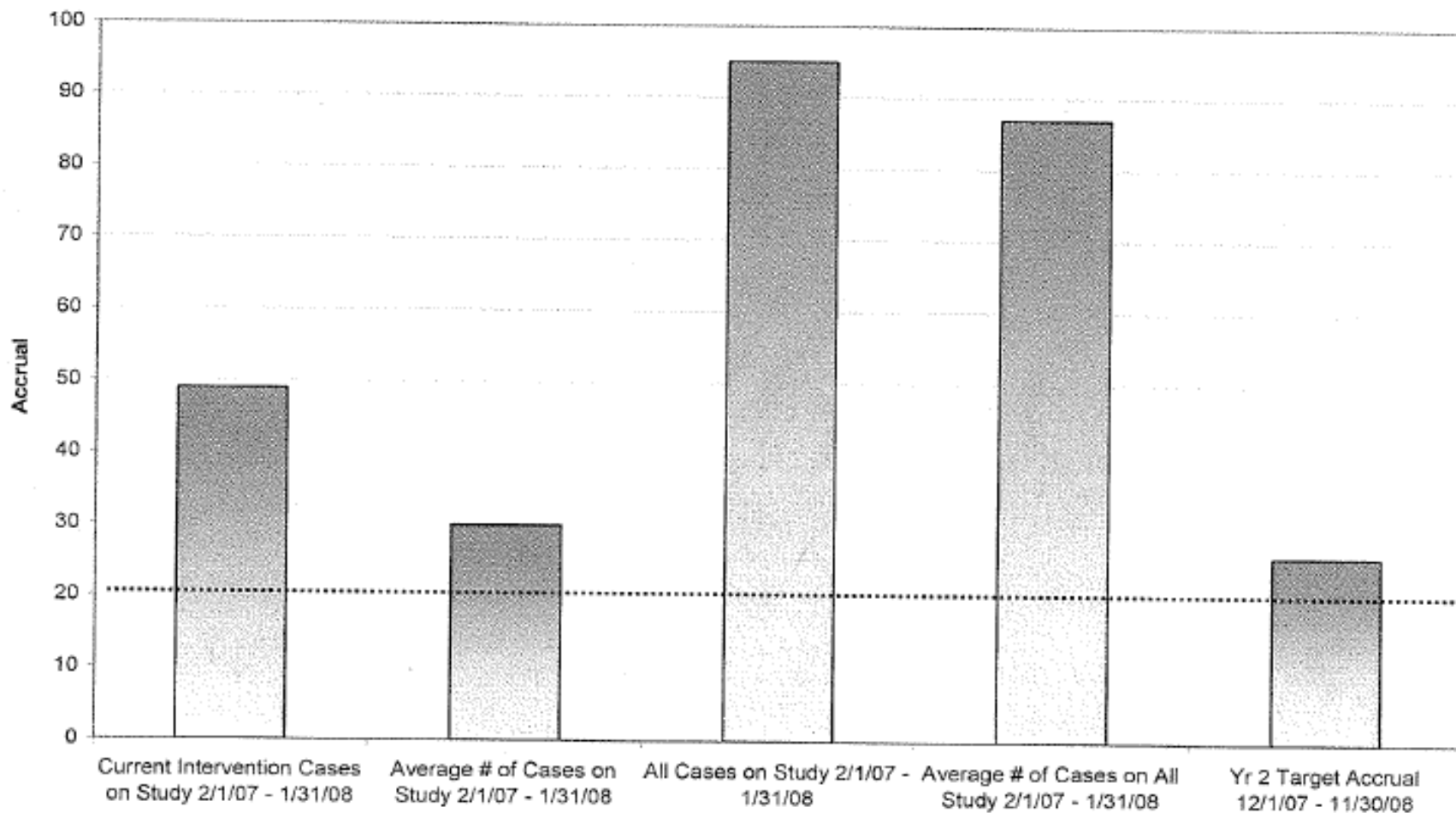
Satisfactory = score is between -10 and 0

Problematic = score is between -20 and -10

Unsatisfactory = score is less than -20

Example of IMPAACT report on Site Protocol Accrual

Accrual for a 12-month period from 2/1/2007 - 1/31/2008



MTN Evaluation Process Status

- Sites and CORE will be evaluated
- Specific evaluation reports are under development
- MTN Evaluation Specialist has been hired: Kym Smith

My Hope for MTN

- To cultivate a culture of strong teamwork & healthy competition
- Recognition that sites have invaluable expertise to share with each other re recruitment, retention, adherence, implementation
- Appreciation that evaluation is necessary & useful
- CORE and sites to simultaneously feel pride and be motivated to improve
- For MTN to do important trials as efficiently as possible with highest quality data



*If you want to go fast, go alone.
If you want to go far, go together.*
– African proverb