ASPIRE

A Study to Prevent Infection with a Ring for Extended Use

Aspiring Toward Efficiency- Streamlining without Sacrifices

Patrick Ndase, MBChB, MPH
Katie Schwartz, MPH

MTN Regional Meeting 2012

MTN microbicide trials network

Efficiency Definition:

- Literary definition: *"skillfulness in avoiding wasted time and effort"*
- VOICE definition: *Was in terms of shortening participant visit length at research sites*
  - *Focus: 7 deadly wastes in improving clinic flow*
- ASPIRE: "*Efficiency is everything*"
  - *Per visit retention right from accrual stage, every effort to promote product adherence, safety & quality data*

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We MUST win on all “The Big Five”

Accrual

Adherence

Retention

Clinical and Laboratory Participant Safety

Data Quality and Timeliness

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Why efficiency is important

We're at crossroads for HIV prevention among women in developing countries

- Low level efficacy with TDF gel (39%)
- Oral PrEP didn't work in high risk women in VOICE (TDF) & FemPrEP
  - ? Biologic/Adherence challenges for VOICE
  - Adherence was low in FemPrEP
- The "Ring" is our best chance to prove efficacy if it indeed biologically works

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Adherence seems critical to ART based approaches to prevention

	Efficacy	Adherence*
Partners PrEP	75%	82%
iPrEx	44%	51%
Fem-PrEP	6%	26%

* Based on tenofovir levels in non-seroconverters

Baeten CROI 2012, Abstract 29
Donnell CROI 2012, Abstract 30
Grant NEJM 2010
Van Damme CROI 2012, LB32

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Potential ‘drivers’ of adherence

- Adherence may reflect risk perception & patterns of sexual behavior
  - *Baseline HIV risk assessment*
  - *Local HIV statistics matter (New HIV infections per day)*
    - *“Knowledge is Power”*
- Per visit retention rates (NOT overall retention) counts
  - *Missed visit = month of zero adherence*
- Good Participant Rapport is going to be “KEY”
  - *Staff must love what they do*
  - *Participants ought to feel a sense of belonging*

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What will it take to efficiently conduct ASPIRE?

- Community outreach must have its ***"ear to the ground"*** approach
- Participant discussions ought to change their perception of study participation to altruism
- Efficiencies in visit flow will be critical
- We have to "KNOW OUR PARTICIPANTS"
  - As messengers, we must be fully committed to the message
  - Examine if any inefficiencies will mar our ability to answer research question

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We're all part of the same team…

- No one knows how to do this perfectly
  - *We will need to keep an open mind….*
  - *Cross-site, cross-team sharing is important*
    - *Some of our ideas: job-specific list-servs, biweekly calls with FHI360, regular protocol team meetings that focus on site-led presentations*
  - *We need to constantly talk with each other…*

We shall need to keep an open mind…

- Every CRS is different
- There is “no once size fit all” message, but the guiding principles to efficiency improvements are the same:
  - Regular internal audits of your systems
  - Listen to your participants
  - Keep open to evaluating new ideas
  - Every step or process needs to add value

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General impressions from early assessments:

- Enthusiasm about running ASPIRE is high. KEEP IT UP!
- The outreach teams are making great effort to recruit women at highest risk of HIV acquisition
- Within research experienced communities like Durban, research naïve participants have been recruited to date
- Attention being paid to retention early on
- Data collection is streamlined and CRFs easy to use
- Sites have embraced a contraceptive method mix (Implants, IUCD's, Pills, Injectable all provided on site).

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Efficiencies Related to Accrual

- The right number, the right women
  - Modest site sample sizes = achievable number of recruitments
  - Critically evaluate each potential participant
    - Is she likely to return each month for a year+?
    - Is she motivated to use the study product? Why?
    - What is her risk level? Her risk perception?
    - Seeing this critical evaluation taking place at sites visited
  - Being selective at screening can save a lot of time and energy for the team down the road

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Efficiencies Related to Retention

- Focus here is both staff & participant retention
  - Good trained staff not easy to find (and training takes time)
  - Modest achievable sample sizes imply greater focus on quality enrollees *(risk perception & retention)*
  - Efficient clinic flow enhances overall retention (get in and get out)
    - Efficiency challenges when dealing with specific IRB requirements- more systems/procedures adds to length

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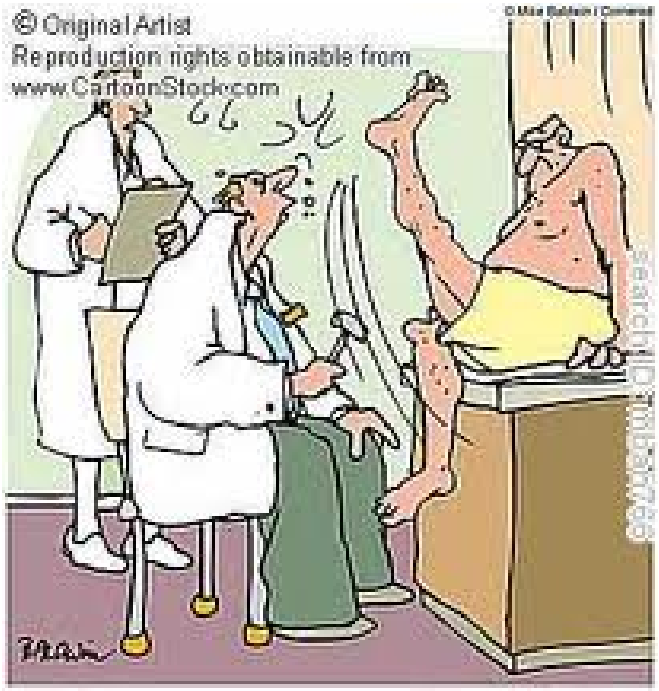
Efficiencies Related to Visit/Binder Flow

- Periodic visit and data flow assessments are necessary
- Sites already engaging in visit flow adjustments to lead to more efficient flows, reducing screening visits by hours
- Efficient visit flow procedures allows for time for effective QC during the visit
- Efficient movement of binders through QC1/QC2/DF ensures that timelines for faxing are met



"Reflexes seem normal. You kept him waiting over two hours."

Efficiencies Related to Adherence

- What it takes to get women to come, contribute to the study, and honestly report their experience
  - Critical for staff to promote comfort and openness in discussing ring experiences
  - ACE Approach- motivating and supporting the participant to develop strategies to improve adherence; allowing non-perfect adherence to be OK
  - High retention: *Missed visit = month of <u>zero</u> adherence*
    - The 'retention loop' as a key component to adherence counseling

Efficiencies Related to Data Quality

- Documentation systems:
  - Duplication → takes more time and more opportunity for discrepancies
    - Are there additional sources for this information? Can they be eliminated or reduced?
  - There must be value addition for every chart note
  - Using checklists and other source docs to document procedures done and less interactive processes (ID, co-enrollment verification, blood draws, test results, counseling procedures)

Chart-noting:

- Depending on the site, 1.5- 6 pages of chart notes for a screening visit. Keys to efficiency:
  - Focus on what needs to be documented in the chart notes per Source Doc SOP- otherwise it's duplicative
  - No need to rewrite what is in the site SOPs
  - Document interactions with the participant, not the procedures conducted
  - These are unique to the visit, not found elsewhere, help clue next staff member in to 'who' she is/what her experiences are
    - EXAMPLE: Post IC, nurses may address some residual questions about the ring or post BBA staff may address some of the worries she reported before randomizing

07SEP12	POST - TEST AND RISK REDUCTION
- 12:06	COUNSELLING DONE, PT'S READINESS
	FOR HIV TEST RESULT ASSESSED, SHE
	WAS READY THEREFORE HIV NEGATIVE
	RESULT DISCLOSED. PT WAS HAPPY
	TO RECEIVE SUCH RESULT. IMPORTANCE
	OF MAINTAINING HER STATUS
	DISCUSSED AND HOW SHE CAN
	ACHIEVE THAT EXPLAINED AND
	EMPHASISED. PARTNER TESTING AND
	COUNSELLING OFFERED. 20 STUDY
	MALE CONDOMS DISPENSED. ——

07SEP12	PPT IDENTITY CONFIRMED WITH SA
09:13	ID DOCUMENT. CO-ENROLLMENT
	DATABASE CHECKED PPT IS NOT CO-ENROLLED. PPT REGISTERED
	FOR SCREENING VISIT. AGE IS
	CONFIRMED PPT IS 33 YEARS
	OLD. PPT IS NOT ON MENSES.
07SEP12	SCREENING IC OBTAINED AND IC
10:00	COVERSHEET WAS COMPLETED AS
	PER STUDY SOP.

Things to Share…

- Peer Educator Model:
  - Former VOICE ppts aiding recruitment in some sites
    - Sites talking about utilizing this model for IUCD promotion as well
  - Waiting room support from participants who have had the ring inserted- ‘I can’t feel it!’
- Cross-pollination within CRS, CTU & across CTU’s
  - Interaction with ppt on ring use/experiences at various cadre ship levels of staffing
  - Between Clinicians/Nurses/Counselors/RA’s
  - Forum for exchange of successes & challenges

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We will now call upon…

Doerieyah Reynolds, Emavundleni CRS

- Share site experience around promoting efficiencies in the IC process
- How this system translates into greater participant ‘participation’ in the trial- comprehension, willingness/openness to use the produce, come to clinic etc

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National Institutes of Health

Statistical Center for HIV/AIDS Research & Prevention
SCHARP

fhi360

Malawi College of Medicine – JHU Research Project

WRHI

MRC SOUTH AFRICA

CIDRZ

UNC Project - Malawi

International Partnership for Microbicides

University of Zimbabwe, School of Medicine

Desmond Tutu HIV Foundation

CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA