MTN
microbicide trials network

HOPE
HIV Open-label Prevention Extension
Out of ASPIRE, there is HOPE

Top 10 Lessons Learnt from MTN-025/HOPE

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For and on Behalf of the HOPE Team

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MD, USA

UZCHS-CTRC
University of Zimbabwe College of Health Sciences - Clinical Trials Research Centre
Saving Lives Through Innovative Research Strategies

University of Zimbabwe,
College of Health Sciences

Outline

1. Stakeholder Engagement
2. Direct Data Entry
3. Retention
4. Choice and Adherence
5. Participant Engagement Activities
6. Options Counselling
7. Contraception
8. Visit Efficiency
9. Taking care of the carer
10. The secret to success

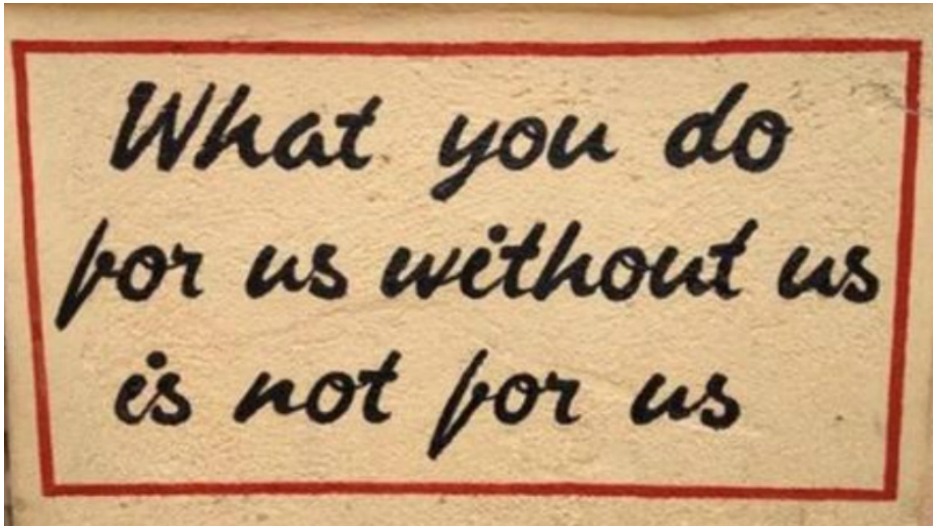
Beyond Phase III:
Seeking Civil Society perspectives into next steps with the dapivirine ring for HIV prevention in women

14 July 2014, Harare

Engagement needs to start early

- Civil society consultation took place even before ASPIRE was over to:
  - Discuss next steps should the ring be found safe and effective
  - Build understanding of what an OLE is and is not
  - Get feedback on MTN-025 design and implementation strategies
  - Provide foundation for continued engagement leading up to and during ASPIRE closure, results dissemination – and potential OLE
- Must be an on-going process
- What might have happened without early engagement?

Engagement needs to start early



❷ Direct electronic data capture

- Implementing any new IT system can be daunting and goes beyond the technology change
- As of Feb 2017, all sites were operating in full EDC
- Used direct data entry as much as possible
  - Reduced DUPLICATION
  - Minimized DISCREPANCIES

- Learning curve - efficiencies improved with experience
- *"Ah, sister this is better than all the paper you would complete whilst we waited in ASPIRE! We are spending less time at the clinic."*

Based on Maria Durkin, Improving Site Efficiency and Productivity, Applied Clinical Trials - Jul 01, 2009

Retention

Study Month	Retention
Month 1	98%
Month 2	98%
Month 3	99%
Month 6	98%
Month 9	96%
Month 12	99%
TOTAL	**99%**

- Of 9,296 expected follow-up visits across all sites to date, only 87 have been missed!

Retention

Staffing

Adequate staffing levels

Continuous refresher training

Task-shifting

Retain staff

Conducive Environment

Edutainment

Refreshments

Childcare

Visit Flow

Flexible working hours

Balance different types of visits/protocols

Reimbursement and appreciation tokens

Locator updates

4 Ring choice and adherence

- Does choice actually improve adherence?
  - At a site/study level, yes, it does
- There are still participants who accept without intention to use (social desirability)
  - *Trial experienced cohorts are conditioned in some way to act according to the parent protocol requirements… shifting ingrained thinking takes time* - Thes, Co-chair
  - *The one thing that I learnt is that it takes time for the women to understand change, CHOICE. They think they have to give a good report on ring use even when drug feedback results show otherwise.* Caroline, Counsellor, Spilhaus

4 Ring choice and adherence

- There are still participants who accept the ring
  - but may face challenges to use or
  - their circumstances change, or
  - they just want the OPTION of the ring, but do not intend to use it all the time
- Participants want objective measures of adherence
  - but they want them *sooner,* and
  - they want them to be right
  - Measures can have a negative impact if perceived as inaccurate
  - Some participants are really not okay with the frequency/amounts of hair collected in HOPE

4 Ring choice and adherence

- The ring is not for everyone, and not for everyone all the time
- At Enrollment, 92% of women choose the ring as part of their prevention package
- Overall top reasons for decline are:
  - Prefers alternate HIV prevention method
  - Undecided /not ready
  - Participant not interested
  - Partner concerns/wants to inform partner before initiating use

Study Month	Ring Acceptors
Enrollment	92%
Month 1	90%
Month 2	88%
Month 3	87%
Month 6	84%
Month 9	80%

5 Participant & partner engagement

- Important to hold regular participant and partner engagement events to:
  - Make sure participant understand **choice, adherence,** and **accurate reporting**
  - Address adherence challenges
  - Keep participants motivated to complete the study and to recognize their contributions
  - To engage men in support of their partners and the study
  - Share important study updates
  - Resources and HIV prevention options post-HOPE

Study-Related Discussions

- Adherence, Choice, Open Reporting
- HOPE/ASPIRE differences
- What HOPE contributes
- Counseling, Residual Drug, Audio Recording
- Wait Time, Clinic Experience
- New Procedures
- PrEP
- LARC
- Study Exit/PUEV

Non-Study related engagement

- Meet the Staff
- Education about other ongoing research
- Communication Tips
- World AIDS Day
- Human Rights Day
- TB Awareness
- Local HIV Statistics
- Personal Hygiene
- Respect
- Life Skills/Healthy Living
- IPV Resources

Activities and Fun Events:

- Holiday Celebrations
- Motivational Talks
- How to write a CV
- Music, Dancing, Singing
- Model Walk off
- Games, Quizzes, Puzzles
- Reading
- Poetry
- Manicures, Hair Styling

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Options counselling

- Not easy to learn a new counselling intervention or to internalize a deep respect for a participant's choices
  - desire to help often leads one to try and persuade participants to take certain actions.
- Continuous support of counsellors builds client-centered counselling skills.
- Audio-recording the counselling sessions was sometimes challenging for participants and counsellors
- Facilitated individualized feedback for study counsellors
- Improvement in counselling skills and monitoring
- Options counselling was delivered with fidelity across study sites.

Contraception

"A particularly vexing problem relates to high pregnancy rates among participants. Women who become pregnant are routinely required to discontinue use of study products…."

Challenges to HIV Prevention — Seeking Effective Measures in the Absence of a Vaccine Stephen W. Lagakos, et al, *NEJM* 2008

7 Contraception in Sub Sahara Africa

- Women in SSA continue to have relatively high fertility rates
  - average 4.94 births per woman
  - range from 3.22 in Zimbabwe, through 4.68 in Kenya, and 6.05 in Uganda to 6.28 in Zambia
- Unmet need for contraception also high
  - 14% in Zimbabwe, >20% in other countries
  - South Africa - rates of unintended pregnancy demonstrate high levels of unmet need, especially among young black women.

Contraception in HOPE

- Enrol women already on contraception
- Probe on desire to conceive – various tools
- Provide contraception on site
- Assist participants access contraception in public health facilities
- Contraceptive counselling is an on-going process
- Establish Contraceptive Action Teams (CAT)
  - Capacity building, contraceptive mix and use of long acting reversible contraceptives
  - Minimize provider bias - *"The nurse told me that if I did not want the pill, then she would not recommend anything."* L. Ashford 2002
- ASPIRE: pre-CAT, IUCD uptake 2%, post – approx. 23%
- Beware of current lactation!
  - Most policies in the region set optimal infant feeding duration at extended lactation periods of 12 to 24 months N Mgodi *et al* 2015

8

8 Visit efficiency

- Lengthy visits are consistently cited as a top reason for participant dissatisfaction in previous studies and can lead to:
  - Disengagement
  - Poor adherence/retention
  - Increased risk of social harms
  - Staff fatigue

- Visit flow assessments started in February 2017 and repeated at key points throughout the study (e.g. at end of accrual, start of PUEV visits, etc.)
- Visit efficiencies working group was established and met regularly via teleconference to discuss strategies
- HOPE lessons learned and best practices are being put to use in new studies

8 Visit length improvements

	Average Visit Time in Hours					
	Total Visit Length		Procedure Time		Waiting Time	
	Feb 2017	Jan 2018	Feb 2017	Jan 2018	Feb 2017	Jan 2018
Follow-up Visits	5.0	**3.1**	2.4	**2.2**	2.4	**.9**

8 Recommendations

- As much as possible, streamline protocol requirements/visit procedures
  - In particular, consider ways to streamline and shorten ICFs.
  - Reduce number of required questionnaires, CRFs, samples, etc.
  - Consider carefully level of counseling that is needed.
- Consider staffing requirements carefully and have adequate staff on board from study initiation, especially when running multiple concurrent protocols
- Continued Challenge:
  - Managing participant load in the clinic
    - ingrained culture of not adhering to specific times when seeking medical care – can we ever hope to shift this?

8 Achieve balance

Do not compromise on quality!

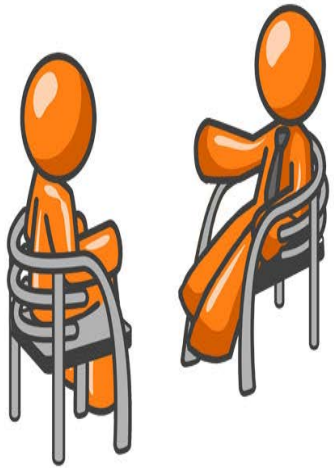
Maintain Quality

Maximise Efficiency

Quis enim carers curat?

9

Individual Counselling



9 Taking care of the carer

Compassion Fatigue • Burnout • Vicarious Trauma

- Regularly hearing and witnessing difficult stories can impact one's ability to feel empathy and provide supportive care
- Personal and professional demands without adequate rest can cause hard-to-relieve exhaustion
- Prolonged exhaustion can lead to psychological and physical impacts

9 Support on the HOPE teams

- Practicing open communication about mental health and wellbeing
- Taking breaks – during the day, the year, and away from the site as a team when possible
- Using "shared confidentiality" and laughter to debrief
- Seeking outside help and support
- Celebrating success individually and together!

9 Boosting staff morale

- Create a conducive working environment
- Team building activities
- Motivational incentives
- Appreciation of work done/ citations
- Does not need to be expensive!

10

The secret to success

Celebrating a product that works!

10 Celebrating a product that works

- It is exciting to work on something that has shown it works.
- Many years of Clinical Trials Unit funding, across multiple networks, and this is our first prevention product.
- People like you and me have worked hard for many years in order to contribute to a successful product that might one day get to African women.

10 Celebrating a product that works

- Amazingly the ring is poised on the edge of that place
- It is a prelude to other products (injectables, MPTs, implants, immune therapy) for the future
- Everything we are learning (at sites, core, lab, NIH) for regulatory readiness will apply to all of those potential future products.
- *There is no secret to success; it is the result of preparation, hard work and learning from failure* – Colin Powell
- Most of all, it results from the love of what one is doing

Thank you

MTN-025/HOPE Study Team

- **Leadership:** Jared Baeten (protocol chair), Thesla Palanee-Phillips (protocol co-chair), Nyaradzo Mgodi (protocol co-chair), Elizabeth Brown (protocol statistician), Katie Schwartz & Ashley Mayo (FHI 360), Lydia Soto-Torres (DAIDS medical officer)
- **Study sites:**
  - **Malawi: Blantyre site (Malawi College of Medicine-John Hopkins University Research Project):** Bonus Makanani, Taha Taha
  - **Malawi: Lilongwe site (University of North Carolina Project):** Francis Martinson, Lameck Chinula
  - **South Africa: Cape Town site (University of Cape Town):** Lulu Nair, Linda-Gail Bekker
  - **South Africa: Durban eThekwini site (Centre for AIDS Programme of Research in South Africa):** Leila Mansour
  - **South Africa: Durban – Botha's Hill, Chatsworth, Isipingo, Tongaat, Umkomaas, Verulam sites (South African Medical Research Council):** Anamika Premrajh, Arendevi Pather, Logashvari Naidoo, Nishanta Singh, Nitesha Jeenarain, Samantha Siva, Vaneshree Govender, Vimla Naicker, Zakir Gaffoor, Simone Hendricks, Shaamilah Suleman, Gita Ramjee
  - **South Africa: Johannesburg site (Wits Reproductive Health and HIV Institute):** Thesla Palanee-Phillips
  - **Uganda: Kampala site (Makerere University-Johns Hopkins University Research Collaboration):** Flavia Matovu Kiweewa, Brenda Gati, Clemensia Nakabiito
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