Why we need an MPT

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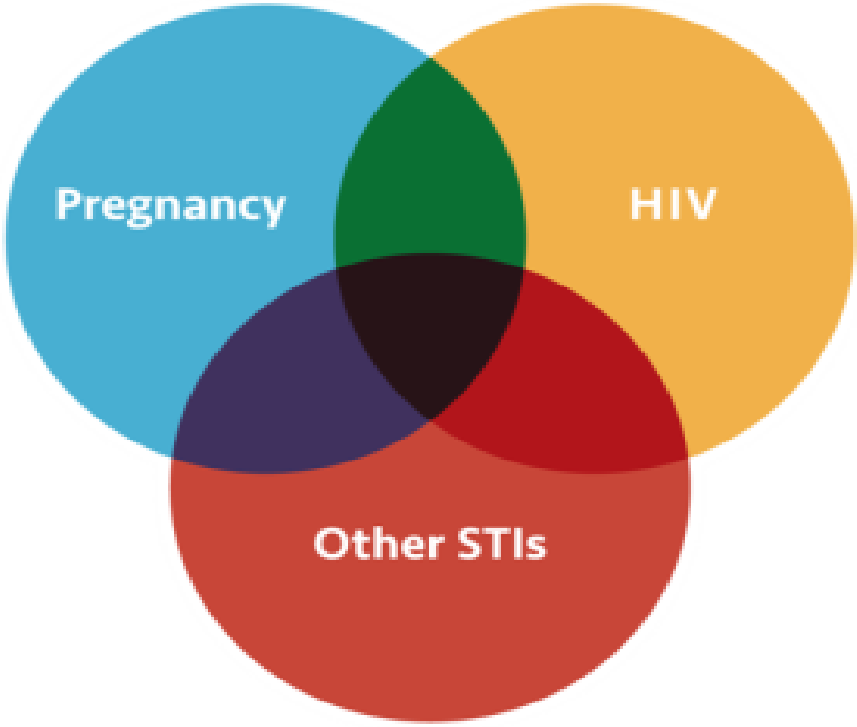
MTN Regional Meeting

Cape Town, Sept 20, 2017

Multipurpose Prevention Technologies

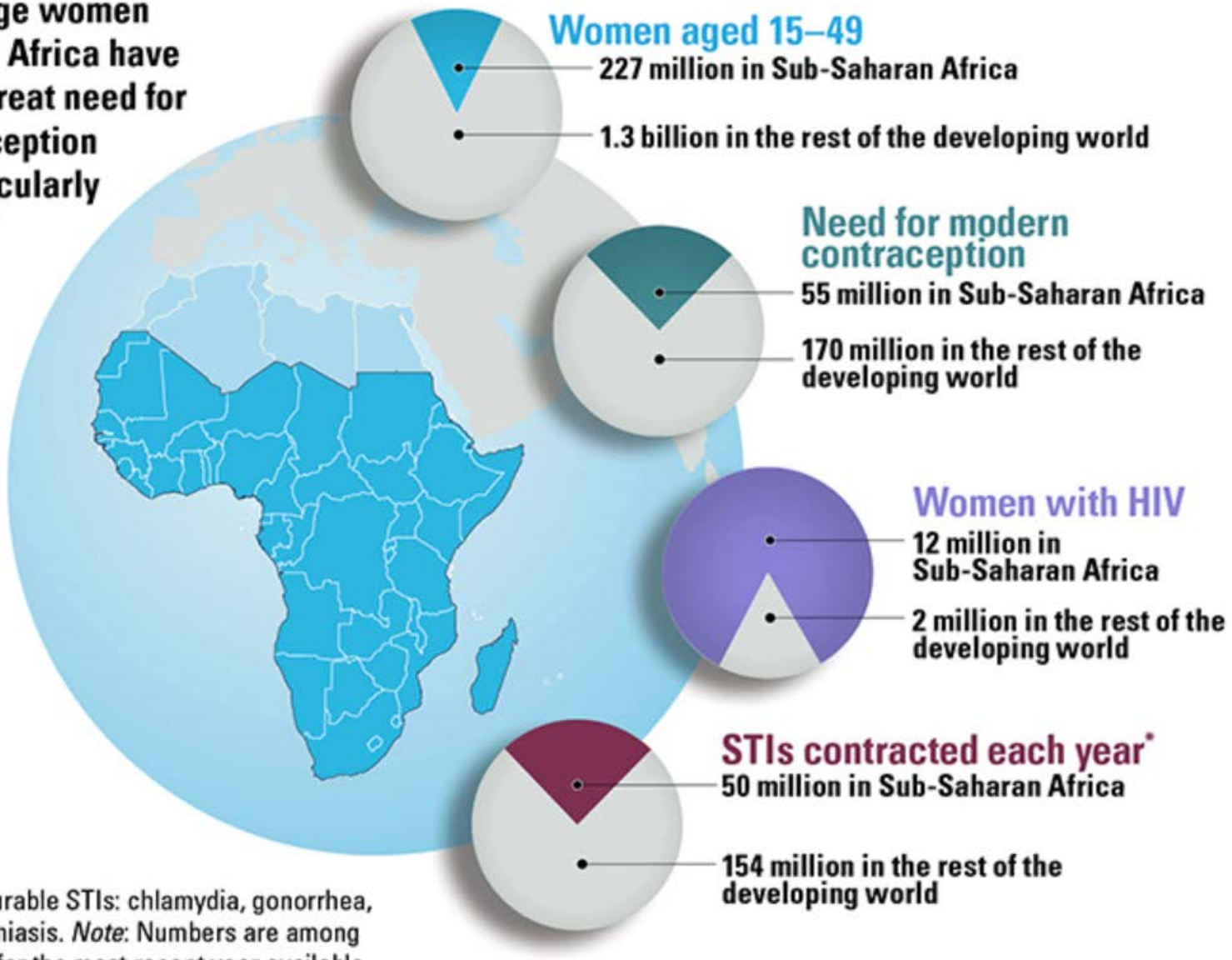
MPTs <u>combine protection</u> against:

- **Unintended pregnancy**
- **HIV**
- **Other STIs**



Greatest current focus is on Contraception + HIV prevention

Reproductive age women in Sub-Saharan Africa have a particularly great need for modern contraception and are at particularly high risk of HIV and other STIs.



* One of four major curable STIs: chlamydia, gonorrhea, syphilis or trichomoniasis. *Note*: Numbers are among women aged 15–49 for the most recent year available. *Source:* Guttmacher Institute.

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Why do we need an MPT?

- The end user wants an MPT
  - Women have told us they want a product that can do both

HOPE participant quotes

"I like the idea of having an MPT because it saves time, and hits two birds with one stone."

"The ring would be better if it was a two-in-one: protect from HIV and from pregnancy… to save women from using two different products."

"I prefer the ring and condom as the combination… the ring is inserted in you because partners sometimes lie and say they don't have condoms. My wish is for the ring to also prevent other things, like STI and pregnancies, because some women do not use contraceptives"

Why we need an MPT

- The end user wants an MPT
  - Women have told us they want a product that can do both
- Combined products have advantages
  - Reduces barriers to use
  - Reduces stigma
  - Increases potential user pool

Adherence is inversely proportional to barriers

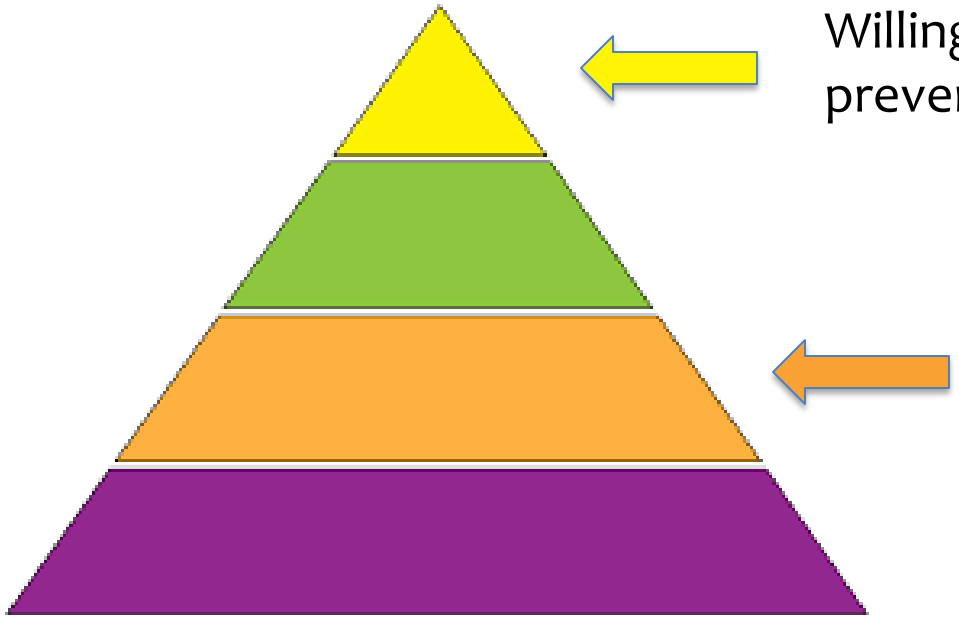
- Lessons learned from contraception: Decreasing (removing) barriers → increases use
  - Prescribe pills for 1 yr vs. 1 month at a time
  - Even better adherence with LARC methods (IUD/implant)
  - Contraceptive CHOICE project
    - Cost barriers
    - Education barriers
- Additional barrier associated with HIV prevention:

Potential user pool of reproductive age women

...most are at risk of pregnancy

.....many don't want to be pregnant

.....a few truly recognize/admit their risk of HIV



Willing to adhere to/pay for HIV prevention

Willing to adhere to/pay for contraception

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- Combined products have advantages
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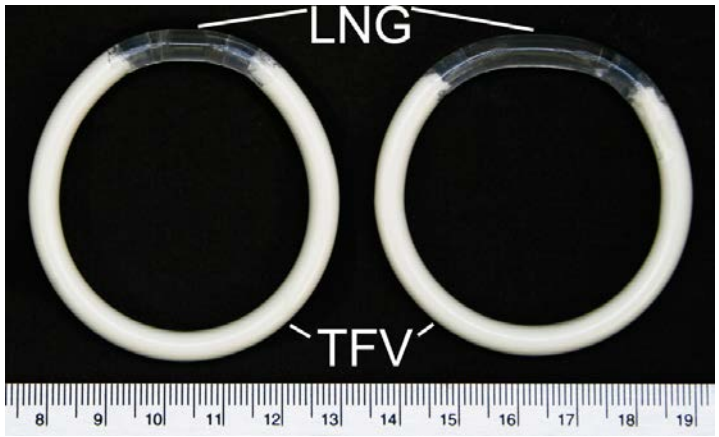
  - Increases potential user pool
- Increased synergy of family planning and HIV services
  - Better for programs and women

Bridging the silos between contraception & HIV prevention

MPT Products in Development: Tenofovir/ Levonorgestrol Ring (CONRAD)

- Prevention of HIV (HSV?) & pregnancy: 90 days
- Segmented polyurethane IVR produced via co-extrusion
- 90 day study in sheep
  - No adverse findings
  - Potentially effective levels of drug released over 90 days
- Phase 1 trial completed (1 month exposure)
  - No identified safety concerns
  - PK data to be published soon
- Phase 2 trial about to start (90-day)
  - Planned enrollment=60
  - 2 sites (EVMS & Domican Republic)

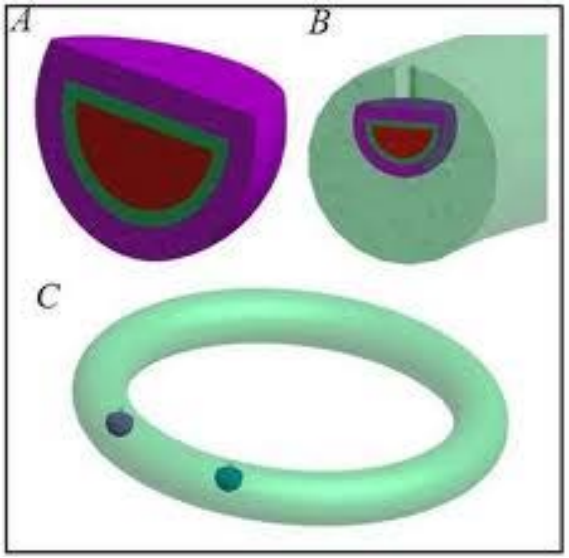


MPT Products in Development: Dapivirine/Levonorgestrel Ring (IPM/MTN)

- IVR with Dapivirine (NNRTI) + LNG
- Prevent HIV/pregnancy: 90 days
- Preclinical development of prototype is completed
- Phase 1 study: completed Aug 2017
  - Pharmacokinetic and safety study
    - 2 sites (Pitt and UAB)
    - 24 women randomized 1:1 (DPV vs DPV/LNG)
  - Data cleaning
  - Hopeful for submission of latebreaker abstract for CROI

Other MPT Rings Containing Tenofovir

- Tenofovir silicone "POD" IVR (+Acyclovir, + HC)
  - Moss et al 2012
  - In vitro evaluation, and macaque safety and compartment delivery
  - Possible to add in drugs for desired range of activity
  - Problem: scale up could be difficult



Oakcrest-Auritec POD IVR (preclinical)

CONRAD/IPM IVR Status and General Issues

- Both targeting 90 days
- Both completed phase 1; CONRAD going into 2nd trial
- Justification for progestin only? LNG?
- Justification for LNG doses? Contraceptive efficacy?
- Clinical/regulatory strategy?

Slide courtesy of J. Romano

MPTs in the Pipeline

- Longer acting vaginal rings
- Films and tablets that could provide protection for a week after a single dose
- Injectables that combine contraception and infection prevention
- Nanofiber delivery systems
- IUDs and Implants

Sound familiar??

www.theimpt.org/documents/MPT-Pipeline-Table.pdf

Applying Contraceptive Modalities to HIV Prevention and Treatment

Method	Pros	Cons
Short-acting (Pills/Patch/Ring)		
Injectable (DMPA/Net-En)		
LARC (IUDs/Implants)	baseline (low dose)	

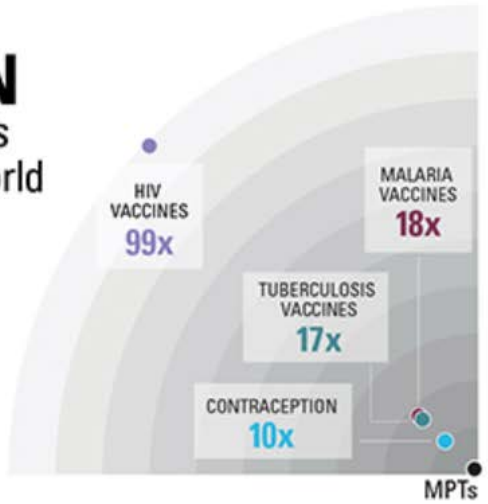
Major considerations for LARC MPTs

- Maximum insertion-removal interval?
  - Q6 months? Q12 months?
  - Longer is better
- Patient tolerance for removal/reinsertion
  - No other clear benefits when patient does not perceive continuing HIV risk
- End game
  - Importance of minimizing ARV 'tail'
  - Major issue when removal is most complex procedure and lack of trained clinicians

Challenges to MPT Development

COST

$6.5 MILLION
was invested in MPTs for the developing world in 2013. Investment was much higher for other prevention technologies.



TIME

On average, for any new drug

12 YEARS
IN DEVELOPMENT

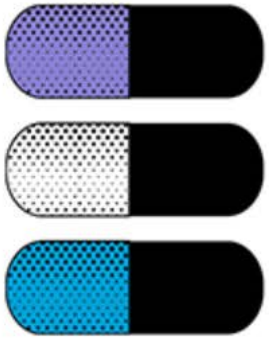
COMPLEXITY

MPT development relies on the simultaneous delivery of

2 or more active ingredients

directed at

2 or more indications



USE

Key to developing new MPTs is understanding

Interest

Motivation

Ability to use

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Can We Get to a Viable MPT for Women?

- Drug and Technology options are limited
  - Cannot match current contraceptive products
- Development will require broad expertise and careful strategic planning
- Timelines will likely be long
- Development costs will likely be high
- Risks will be significant

Slide courtesy of J. Romano

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Summary

- The idea of multipurpose protection for women is decades old
- 1st generation products will be vaginal rings containing antiretrovirals plus LNG and these are now in clinical trials
- Choice of options will be key for success

"We don't accept what we have now as the end of the story—this is the beginning of the story. Need longer-acting ring, need MPT ring, need other ARVs (more potent) and potential creation of LARC MPTs to optimize efficacy."

--Sharon Hillier 19 Sept 2017

Thank you!

MTN
microbicide trials network

National Institute of Allergy and Infectious Diseases

IMPT
for Reproductive Health

AVAC
Global Advocacy for HIV Prevention

fhi360
THE SCIENCE OF IMPROVING LIVES

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

CAMI Health