Update on biomedical HIV prevention research: how does Nigeria need to prepare for trial results

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Outline

- Contraception: an interphase for SRH and HIV response
- HIV Pre-exposure prophylaxis – critical need for SRH response
- Other biomedical HIV prevention research and its importance for male and female SRH
- Conclusion

Contraception: an interphase for SRH and HIV response

What is hormonal contraception?

Hormones are substances in our body that regulate and affect many, many different processes: growth, fertility, hunger, emotions – and much more.

Hormonal contraceptives use synthetic forms of our bodies' hormones to prevent us from falling pregnant

There are many different kinds of synthetic hormones used in contraception these include: progestins, estrogins and others

The need for contraception

Women worldwide need family planning, and in Africa, the use of hormonal contraception, and especially Depo, provide women with a long-acting, reversible and safe option for birth control.

- More than 150 million women around the world use hormonal contraceptives

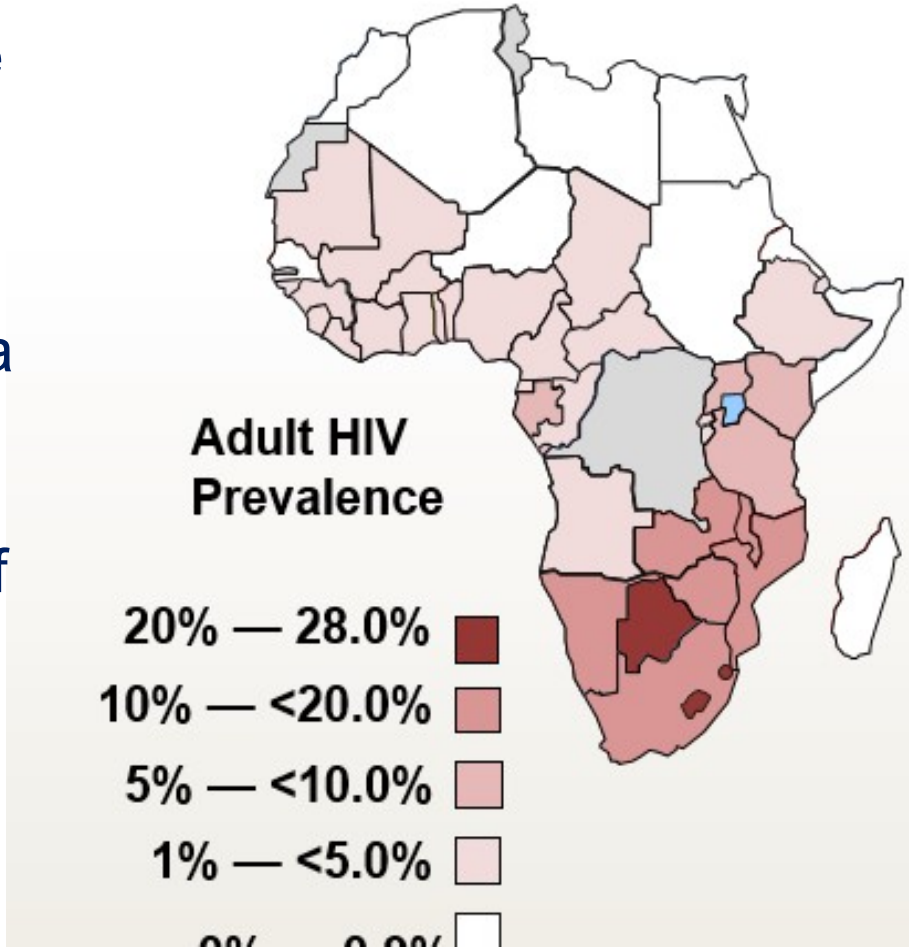
African women are at high risk of HIV.

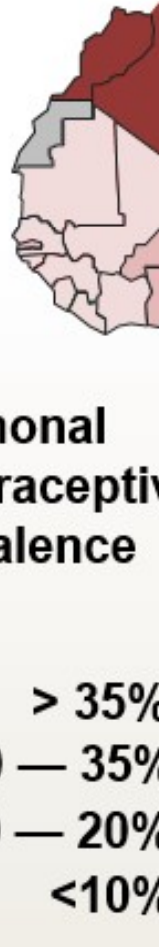
- 16 million women aged 15 years and older are living with HIV; 80% live in sub-Saharan Africa
- Young women 15–24 years old in sub-Saharan Africa are twice as likely as young men to be living with HIV.

ican countries with HIV prevalence also have high ra of women using hormonal contraception

The reasons for this are unclear.

There is confusing data about whether there is a link between using some contraceptives and an increased risk of contracting HIV.





What do we know about hormonal contraception and HIV risk

- For many years, there has been a question about whether some hormonal contraceptives affect women's risk of getting HIV
- The greatest concern has been about contraceptives that contain a specific progestin (a synthetic form of progesterone). This progestin is found in the injectable known as DMPA or "Depo".
- The evidence is mixed – some studies suggest that women who use DMPA are at higher risk of getting HIV than women who use other methods – but other studies do not.

Why is the evidence mixed? In part because of where it comes from

Observational Studies

An ***observational study*** takes place when researchers don't assign choices they simply observe them:

For instance, a study trying to find a connection between students who play an instrument and academic performance. Instead of assigning some students to learn an instrument the researchers simply *observed* student who did and did not play an instrument and recorded their grades.

- This is also an example of a ***retrospective study*** because researchers first identified subjects who studied music and then collected data on their past grades.

We can choose our beliefs, not our facts

- The World Health Organization has, since 2016, classified DMPA and another progestin-only contraceptive, NET-EN, as having a "theoretical or possible risk" of increasing women's risk of HIV
- There is no clear answer – right now, we do not know for sure.
- We may know soon, because of an ongoing trial called ECHO
- The goal of the rest of today is to talk about what we might do, depending on what ECHO shows

What is the ECHO Study?

e **E**vidence for **C**ontraceptive options and **H**IV **O**utcomes is an open-label ndomised clinical trial that will compare three highly effective, reversible method contraception to evaluate whether there is a link between use of any of these thods and increased risk of acquiring HIV infection.

nds in the Use of Contraception-Nigeria

Method	2003 NHDS	2008 NDHS	2013 NDHS
Any method	12.7	14.3	15.4
Any modern method	9.3	10.4	11.2
Female Sterilisation	0.2	0.3	0.3
Male Sterilisation	u	u	0.0
Pill	2.0	1.6	1.9
IUD	0.6	0.7	0.8
Injectables	1.6	2.0	2.5
Diaphragm	0.0	0.0	0.0
Male condom	3.4	4.7	4.6
Female condom	0.1	0.0	0.0
Implants / Norplant	0.0	0.0	0.3
Lactational Amenorrhea (LAM)	1.0	1.1	0.3
Foam/ jelly	0.0	0.0	0.0
Standard days method/beads	0.4	u	0.5
Any traditional method			
Rhythm or periodic abstinence	2.1	2.1	2.0
Withdrawal	1.3	1.8	2.2
Not currently using	87.3	85.7	84.6
Total	100.00	100.00	100.00
Number of women	7,620	33,385	38,948

Trends in the Use of Contraception-Kenya

Table 7.5 Trends in the current use of contraception

Percent distribution of currently married women age 15-49 by method currently used, according to several surveys

Method	2003 KDHS	2008-09 KDHS
Any method	**39.3**	**45.5**
Any modern method	**31.5**	**39.4**
Female sterilisation	4.3	4.8
Male sterilisation		0.0
Pill	7.5	7.2
IUD	2.4	1.6
Injectables	14.3	21.6
Implants	1.7	1.9
Male condom	1.2[a]	1.8[a]
Other modern method	1.5	0.5
Any traditional method	**7.0**	**5.3**
Rhythm	6.3	4.7
Withdrawal	0.6	0.7
Other	1.9	0.7
Not currently using	60.7	54.5

Kenya Demographic Health Survey, 2014

Objectives of the ECHO trials

Primary objective

To compare the risks of HIV acquisition between women randomised to DMPA, levonorgestrel (LNG) implants, and copper IUDs

Secondary and tertiary objectives

Pregnancy, safety, contraceptive continuation

Why do we need the ECHO Study?

For over 25 years, the world has lived with the uncertainty about whether or not use of hormonal contraceptives increases HIV risk.

ECHO aims to answer this critical public health question of the possible risks (HIV acquisition) and benefits (pregnancy prevention) of the three commonly-used, effective contraceptive methods among women who desire contraception

urpose of the ECHO Study

hen comparing women's use of the ntraceptives— Depo, Jadelle and IUD:

- there an increased risk of acquiring HIV when they e one method over the others?
- re there more or less side effects of each method?
- re the pregnancy rates the same?
- ow well do women stay on each of the three ntraceptive methods?

ECHO Study Schema

gn	Multi-center, open-label randomized clinical trial
y arms	Random allocation to one of three study arms: DMPA, levonorges (LNG) implant, copper IUD
ulation	Sexually active HIV-uninfected women, ages 16-35 years seeking highly effective contraception, willing to be randomized to any stu arm
ple size	7800 women (~2600 per study group), approximately 1000 wome were to be enrolled at Kisumu site
y Sites	12 sites in East and southern Africa
uitment ces	Family planning clinics, post-partum and post-abortion, clinics, Primary care clinics within Kisumu county and its environs
y Duration	Follow-up: 18 months per woman Total study duration of ~36 months

ECHO Sites

e study will take place at 12 sites
ross Eastern and Southern Africa,
luding sites in:

- Kenya - Kisumu
- South Africa
- Swaziland
- Zambia

Who can participate in the ECHO study

- Sexually active women 16-35 years old
- HIV negative and willing to be tested
- Seeking effective contraception
- Do not want to become pregnant for the duration of study participation
- Willing to be randomised to any of the three contraceptives being tested
- Willing to give consent to participate

Voluntary and confidential

All information shared with trial staff will kept confidential.

Women are asked to be honest at all times in their answers to staff.

Participation is voluntary and women may leave the study at any time they wish.

Study products

A or Depo Provera

st widely used
gestin-only injectable
en every 3 months
njection in arm
urn of fertility is often
ayed, by a minimum
our months

Jadelle Implant

- Consists of two thin, flexible rods filled with synthetic progestin that are inserted just under the skin of a woman's upper arm
- Once inserted, lasts up to 5 years, although one can have it removed at any time
- Rapid return to fertility once removed

Copper IUD (Cu-IUD)

- The copper-bearing intra
  device (Cu-IUD) is a sm
  flexible plastic frame wit
  copper sleeves or wire a
  it that is inserted in the u
  (womb)
- Once inserted, lasts up t
  years, although one can
  removed at any time
- Return to fertility is imme

How the study works

ecruitment and Enrolling in the Study

otential participants have beeen invited to the trial site to learn about the study.

uring initial visit, they learnt about the risks and benefits, and also about what cluded in the visits (known as informed consent).

omen learnt about the 3 contraceptives being tested and asked if they were lling to use any of the 3 products.

tudy groups

hen a woman enrols in ECHO, she will be randomly placed in 1 o
oups:

DMPA) Depo Provera

OR

Jadelle Implant

OR

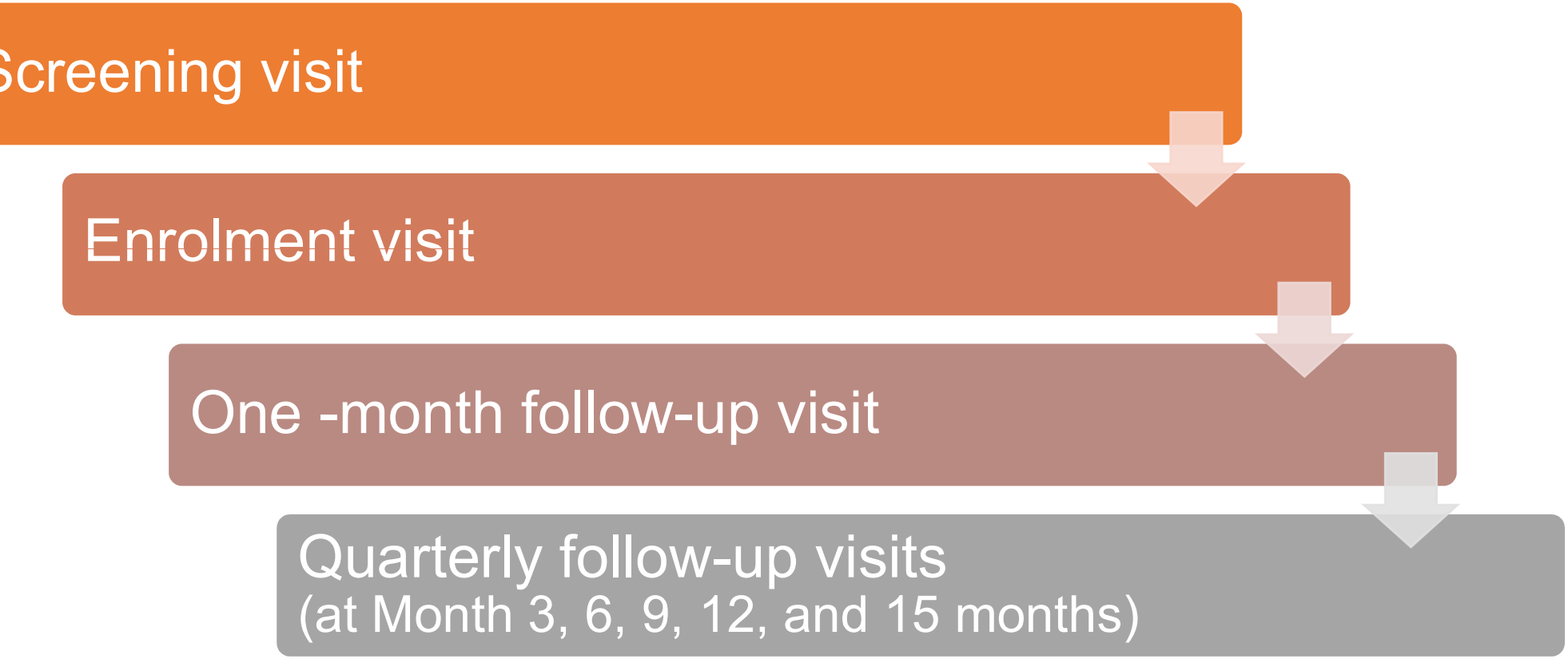
Copper IUD (Cu-IUD)

icipants in all groups will be given the same standard
ention package (condoms, HCT, STI treatment)

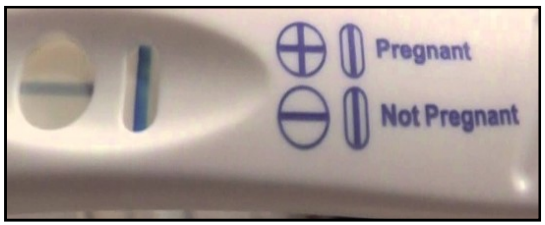
The study groups, continued

- All women have an equal chance of being placed into each group.
- Neither she nor the staff can choose which product each participant will receive.
- Selection into a group is random, like rolling a dice.
- Once a participant is in a group, she will be encouraged to remain on her assigned method for the duration of the study.

Participant study visits schedule



What happens during study visits?



- Provide contraceptive counselling
- Provide HIV counselling and testing
- Ask questions about sexual behaviour
- Do a pregnancy test if needed
- Check health – for STIs and side effects to products
- Update contact information
- Schedule next appointment
- Give reimbursement for transport

at happens to women during the study who:

Become HIV-positive

- Receive counselling
- Referred to local HIV care providers for on-going care according to the National guidelines
- Remain in the study until completion and continue receiving services
- Collection of data relevant to the additional study questions

at happens to women during the study who:

ecome
egnant

- Receive care or referred for further care
- Discontinue her assigned method
- Remain in the study until completion
- Collection of data on HIV acquisition
- If pregnancy ends before completion of study, the woman will be encouraged to resume her allocated method or offered a choice of any method available at the clinic

at happens to women during the study who:

ant to switch or stop contraception

- Advised to come to the clinic to discuss her concerns and experience with the method
- Some women may wish to switch to another method after receiving counselling and treatment for any side effects
- Participants may change methods at any time during the study
- Women who switch methods will remain in the study and will be seen accordingly

articipants safety and monitoring

An independent Data Safety Monitoring Board (DSMB), comprised of global experts in reproductive health and HIV will meet regularly (six monthly) to oversee the well being of participants.

DSMB will review the data regularly (six monthly) to ensure the safety of participants and to determine if the study should continue.

The study site investigators (PI) are responsible for continuous safety monitoring of all participants.

What If No Trial

he observational evidence base is unlikely to improve

Without a trial, messaging will continue to be challenging for providers, olicymakers, and patients. Essentially:

- If HIV risk exists *in truth*, unnecessary infections will continue to occur.
- If HIV risk does not exist *in truth*, policies and/or individual women's choices may alter, with potentially serious negative consequences for maternal morbidity/mortality

Women need accurate information to exercise informed contraceptive choices

What can we expect when the results are released

- Official statement from the trial team itself
- Statements from advocates, WHO, stakeholders, opinion leaders
- A rapid entry of data into the news cycle and onto social media
- Depending on results, WHO could convene a review group to examine data and evaluate results' implication for MEC (the classification system for hormonal contraceptives)
- Countries and funders may say they will wait for WHO decision – or may decide to take independent decisions

What is NHVMAS Stance

If DMPA or any other method increases women's risk of acquiring HIV – thi does not necessarily mean that that method should be removed immediately, or even ever.

- Unplanned pregnancy increases women's risk of death and poor health outcomes
- Pregnancy increases women's risk of acquiring HIV by up to fourfold

Women do not accept a tradeoff between HIV prevention and safe effective contraception; nor do we endorse a hasty, dangerous shift in method availability based on data.

If a method impacts HIV risk—funders, national governments and others must be able to offer, immediately, comprehensive HIV prevention to women who want to use that method, while next steps are mapped out.

What role can you play?

- Continue to learn and ask questions about the ECHO Study whenever needed.
- Start to discuss about decision making options with critical stakeholders ahead
  he results of the trials
- Look out for the results of the study and push for policies to support the outcom
  of the study results.

HIV Pre-exposure prophylaxis – critical need for SRH response

rEP

-exposure Prophylaxis

ides a way for people
do not have HIV, a way
event HIV infection by
g medication.

e

TRUVADA
is **2** medicines
in **one** pill

tenofovir disoproxil
fumarate

What is PrEP?

Oral pre-exposure prophylaxis (PrEP) – the use of the antiretroviral drugs tenofovir and emtricitabine (TDF) - dramatically reduces the risk of HIV infection for men and women who take it as directed.

It is apt for persons at substantial risk for HIV infection.

In Nigeria, couples in HIV serodiscordant relationships are being prioritized for access to PrEP. The results of a PrEP demonstration project in Nigeria will determine how to dispense PrEP for serodiscordant couples in the count

Who should use PrEP?

NHVMAS advocates that beyond couples in sero-discordant relationships, adolescents should be prioritized for access to PrEP.

Evidence suggests that the HIV prevalence among adolescents is increasing while that among adults is decreasing in Nigeria.

The anatomy of a female adolescent increases her risk for HIV infection - a risk significantly higher than that of a female adult.

Teenage pregnancy is high. The risk of HIV infection increases 2-3 times during pregnancy and about 4 times 6 months postpartum.

What does this mean for SRH-HIV response?

These figures highlight the need to counsel female adolescents with high HIV risk behaviour – early sexual debut, multiple sex partners, transactional sex, having sex partners who are 10 years or more older than her – on the need for dual protection.

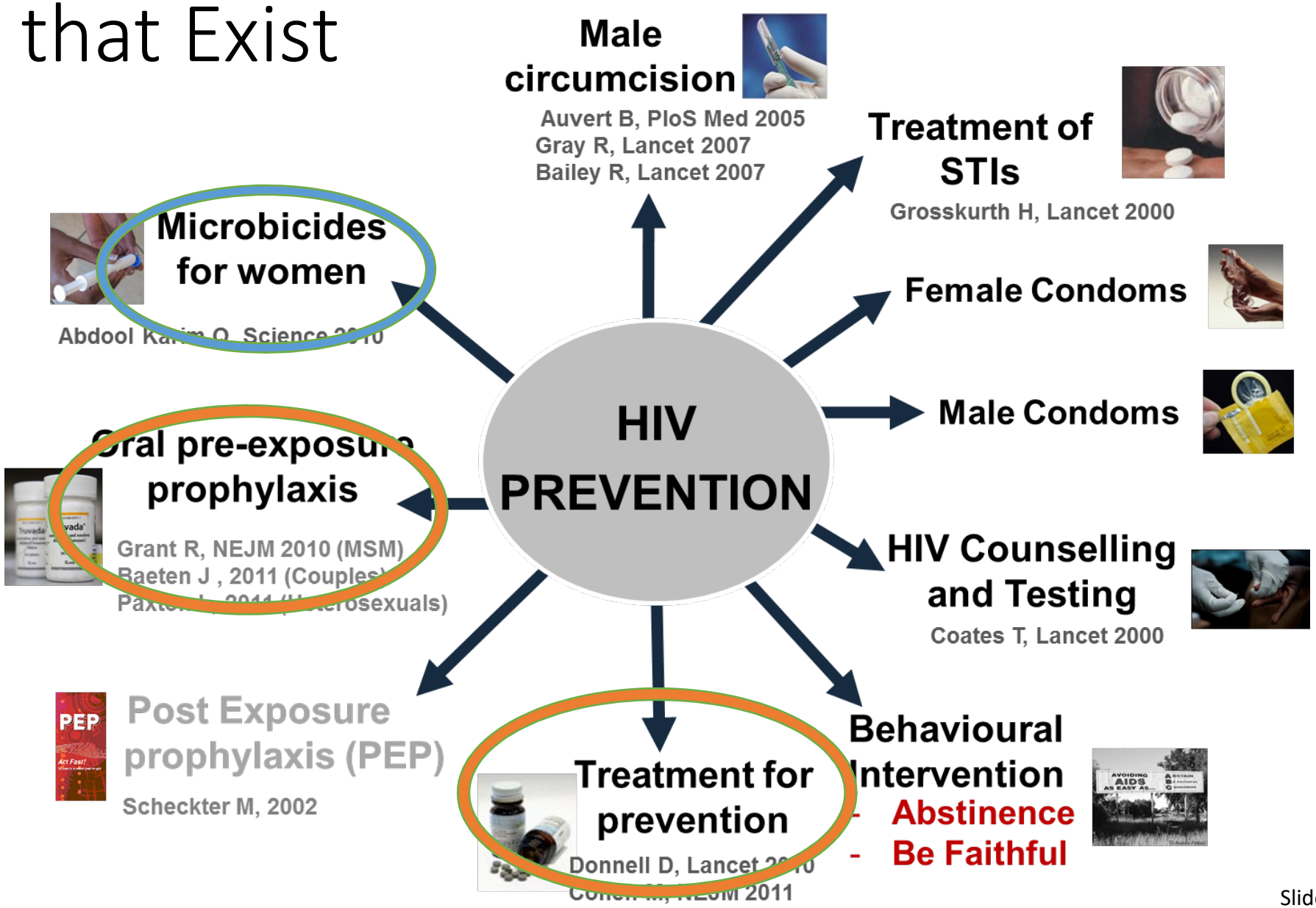
For individuals who do not use condoms, PrEP is **the** alternative.

Service providers need to watch out for the results of the ECHO trial to learn how to counsel appropriately on DMPA.

All females who want to access contraception needs to test for HIV.

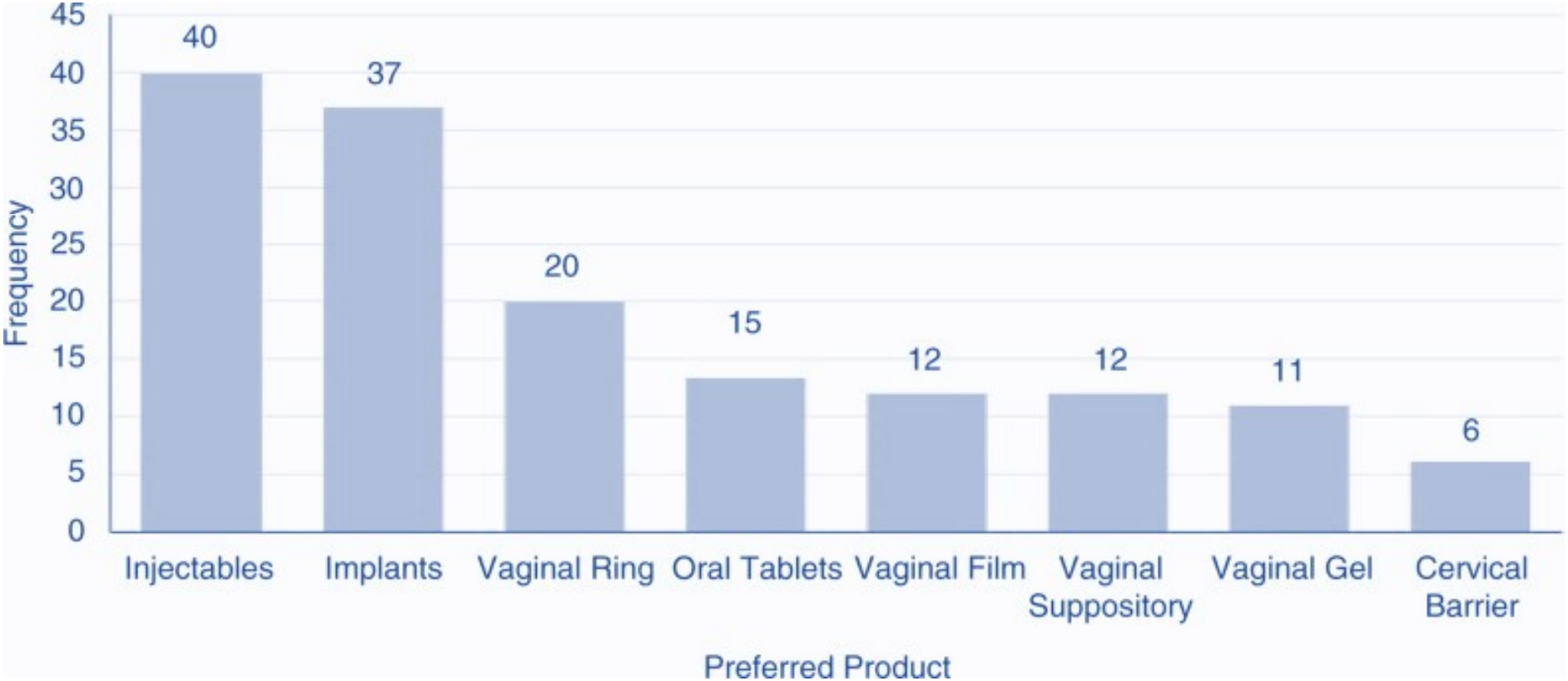
Other biomedical HIV prevention research and its importance for male and female SRH

ols that Exist



Slide Credit (HPTN, K

What are the alternatives to Oral PrEP and TasP?
What women want in a Prevention Product



Luecke et al

AVAC
Global Advocacy for HIV Prevention

The Years Ahead in Biomedical HIV Prevention Research

Status of select biomedical HIV prevention clinical trials

AVAC www.avac.org October 2017

is all about Choice!

ven the most effective product cannot protect against HIV f it is not used

product that best suits one's lifestyle and needs is more likely to be used

Vomen's preferences are not all the same - just as women have choices in ontraception, they should have choices for HIV prevention, too

Figure 1. MTN-003D stage 2 HIV prevention potential product formulation discussion card.

Vaccines Explained

A vaccine can be **preventive**, **therapeutic**, or both

Preventive HIV vaccines for HIV-negative populations are being developed to control the spread of HIV and are not a cure for AIDS

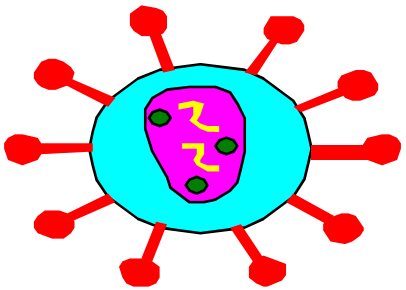
Researchers are also evaluating **therapeutic** vaccines to treat people who are already HIV+ or living with AIDS

What are Vaccines?

Vaccines teach your body to recognize and fight invaders.

How Does a Vaccine Work?

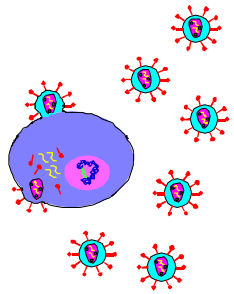
By teaching the body to recognize and fight invaders.



Body Recognizes HIV Virus

Body – Sounds Alarm

Fighter Cells Go Into Action



GOAL - HIV is controlled or killed

Current vaccine studies for HIV Prevention

VTN 705

Randomized controlled trial of Ad26 prime and MVA boost; planned for men and women in the Americas and Southern and East Africa

VTN 702

Randomized controlled trial of ALVAC/gp120 prime-boost with MF59 adjuvant, five doses over 12 months; ongoing in 5,400 men and women in South Africa

AMP = Antibody Mediated Prevention

Can a passively infused monoclonal antibody prevent HIV-1 infection in high risk adults?

Two harmonized protocols:

The AMP Studies:

HVTN 704/HPTN 085

(2700 MSM and TG in the Americas, Europe)

HVTN 703/HPTN 081

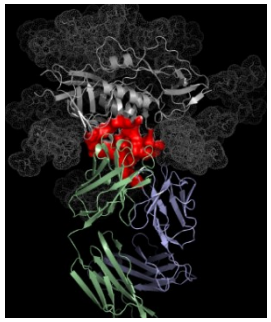
(1500 Women in sub-Saharan Africa)

The AMP Study - SSA

- This is the first trial to assess if intravenous VRC01 can be used to prevent HIV infection (similar to how antibodies prevent other diseases).
- 20 sites - 7countries in SSA
- Main study questions:
  - Is the VRC01 antibody safe to give to people?
  - Are people able to "tolerate" the antibody without becoming too uncomfortable?
  - Does the antibody lower people's chances of getting infected with HIV?
  - If the antibody does lower people's chances of getting infected with HIV, how much of it is needed to provide protection from HIV?

Summary 1

- Reasonable likelihood that we will conquer
- It will take our combined effort to curb the epidemic…
  - Through an bNAbs
  - Or through an HIV vaccine
  - Or through an intra-vaginal ring
  - Or through oral PrEP
  - Or through a long acting injectable agent
  - Or a combination of all or some of these.



"The secret is to gang up on the problem (HIV), rather than compete against each other" - *adapted,* Thomas Stallkamp

Summary 2

- HIV is about sexual and reproductive health
- Humans are not disease silos
- Winning health care challenges will require managing diseases process as an integrated process – run clinics that makes it possible for individuals to access serves through a one-stop-shop phenomenon as much as possible
- To start that process especially for women, we need to make effort to integrate SRH-HIV services

Thank you!

Salamat!

Tatenda!

Grazie!

Siyabonga!

Zikomo!

Dankie!

Ngiyabonga!

асибо

謝謝

Obrigado!

Twatotela!

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