# Turning off the tap: Prevention of infections in children, adolescents and adults

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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

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# 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

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# 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.

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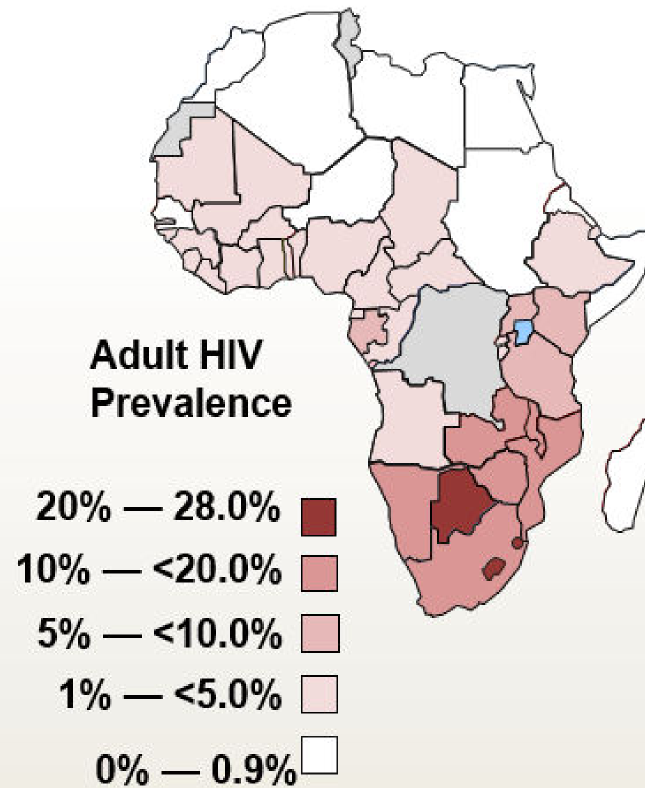
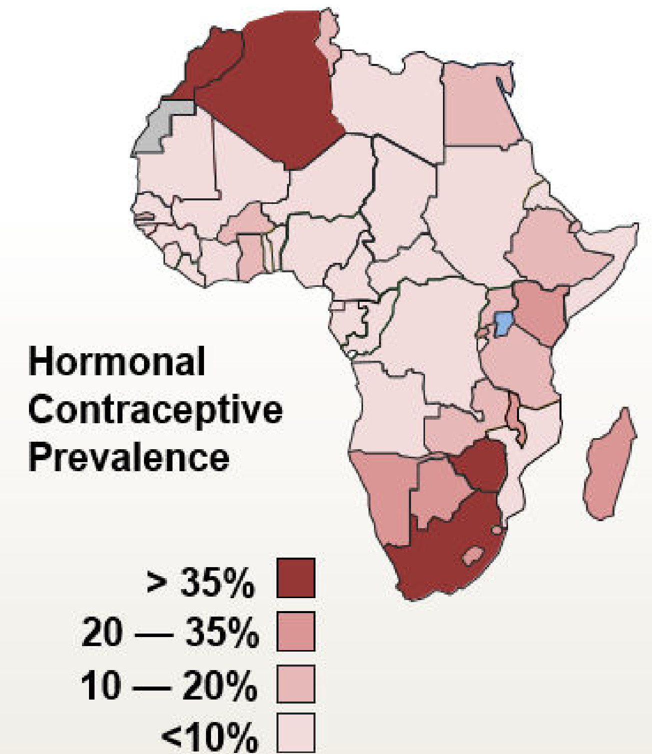
# African countries with HIV prevalence also have high rates of women using hormonal contraception

- 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.

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# 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.

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# 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

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# What is the ECHO Study?

The Evidence for Contraceptive options and HIV Outcomes is an open-label randomised clinical trial that will compare three highly effective, reversible methods of contraception to evaluate whether there is a link between use of any of these methods and increased risk of acquiring HIV infection.

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# Trends 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 |

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# 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 contraceptive method currently used, according to several surveys

| Method | 2003 KDHS | 2008-09 KDHS | 2014 KDHS |
|---|---|---|---|
| **Any method** | **39.3** | **45.5** | **58.0** |
| **Any modern method** | **31.5** | **39.4** | **53.2** |
| Female sterilisation | 4.3 | 4.8 | 3.2 |
| Male sterilisation | | 0.0 | 0.0 |
| Pill | 7.5 | 7.2 | 8.0 |
| IUD | 2.4 | 1.6 | 3.4 |
| Injectables | 14.3 | 21.6 | 26.4 |
| Implants | 1.7 | 1.9 | 9.9 |
| Male condom | 1.2[a] | 1.8[a] | 2.2 |
| Other modern method | 1.5 | 0.5 | 0.1 |
| **Any traditional method** | **7.0** | **5.3** | **4.8** |
| Rhythm | 6.3 | 4.7 | 3.8 |
| Withdrawal | 0.6 | 0.7 | 0.7 |
| Other | 1.9 | 0.7 | 0.3 |
| Not currently using | 60.7 | 54.5 | 42.0 |
| Total | 100.0 | 100.0 | 100.0 |
| Number of women | 4,919 | 4,928 | 18,549 |

[a] The question did not specify male condom.

***Kenya Demographic Health Survey, 2014***

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# 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

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# 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.

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# Purpose of the ECHO Study

**When comparing women's use of the contraceptives— Depo, Jadelle and IUD:**

•Is there an increased risk of acquiring HIV when they use one method over the others?

•Are there more or less side effects of each method?

•Are the pregnancy rates the same?

•How well do women stay on each of the three contraceptive methods?

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# ECHO Study Schema

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

# ECHO Sites

The study will take place at 12 sites across Eastern and Southern Africa, including sites in:

- Kenya - Kisumu
- South Africa
- Swaziland
- Zambia

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# 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.

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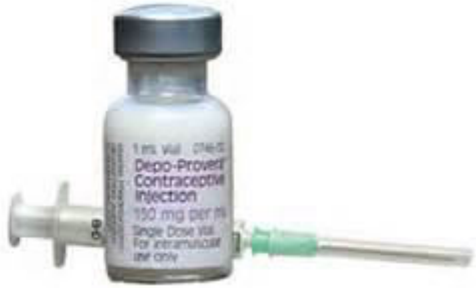
# Study products

### DMPA or Depo Provera



- Most widely used progestin-only injectable
- Given every 3 months as injection in arm
- Return of fertility is often delayed, by a minimum of four 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 intrauterine device (Cu-IUD) is a small, flexible plastic frame with copper sleeves or wire around it that is inserted in the uterus (womb)
- Once inserted, lasts up to 10 years, although one can have it removed at any time
- Return to fertility is immediate

# How the study works

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# Recruitment and Enrolling in the Study

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

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

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

# Study groups

- When a woman enrols in ECHO, she will be randomly placed in 1 of 3 groups:

**(DMPA) Depo Provera**

**OR**

**Jadelle Implant**

**OR**

**Copper IUD (Cu-IUD)**

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

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# 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.

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# Participant study visits schedule

Screening visit

Enrolment visit

One -month follow-up visit

Quarterly follow-up visits
(at Month 3, 6, 9, 12, and 15 months)

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# What happens during study visits?

**Appointment Reminder**

For: ______________________________________

With:______________________________________

On: Mon. Tues. Wed. Thurs. Fri. Sat.

________________________at_____________AM/PM

*This time is reserved for you. If you are unable to keep your appointment, please let us know at least 24 hours in advance so that we may schedule a new time for you. Thank you for your consideration.*

- 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

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# What 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

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# What happens to women during the study who:

**Become pregnant**

- 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

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# What happens to women during the study who:

Want 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

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# Participants 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.

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# What If No Trial

- The observational evidence base is unlikely to improve
- Without a trial, messaging will continue to be challenging for providers, policymakers, 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***

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# 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

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# What is NHVMAS Stance

- If DMPA or any other method increases women's risk of acquiring HIV – this 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 of the results of the trials
- Look out for the results of the study and push for policies to support the outcomes of the study results.

# HIV Pre-exposure prophylaxis – critical need for SRH response

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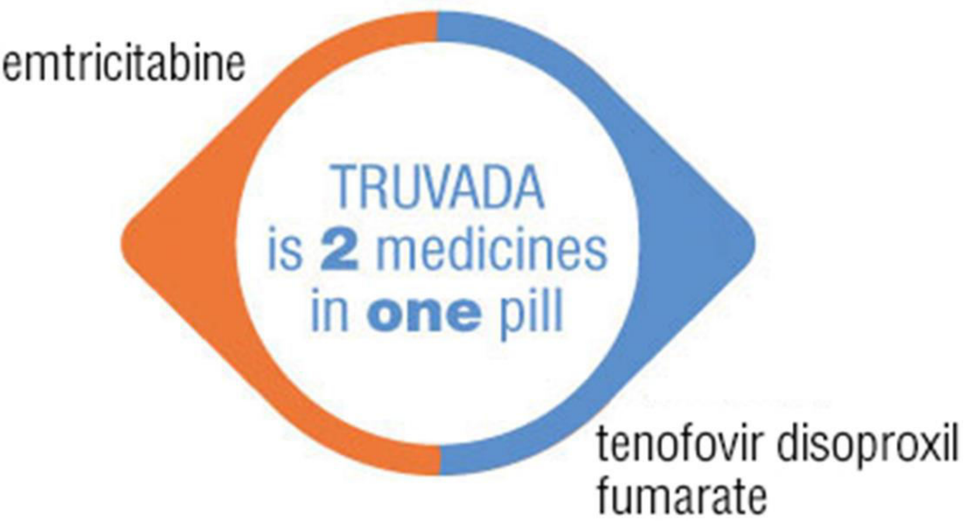
# PrEP

Pre-exposure Prophylaxis

Provides a way for people who do not have HIV, a way to *prevent* HIV infection by taking medication.



# 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

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# 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.

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

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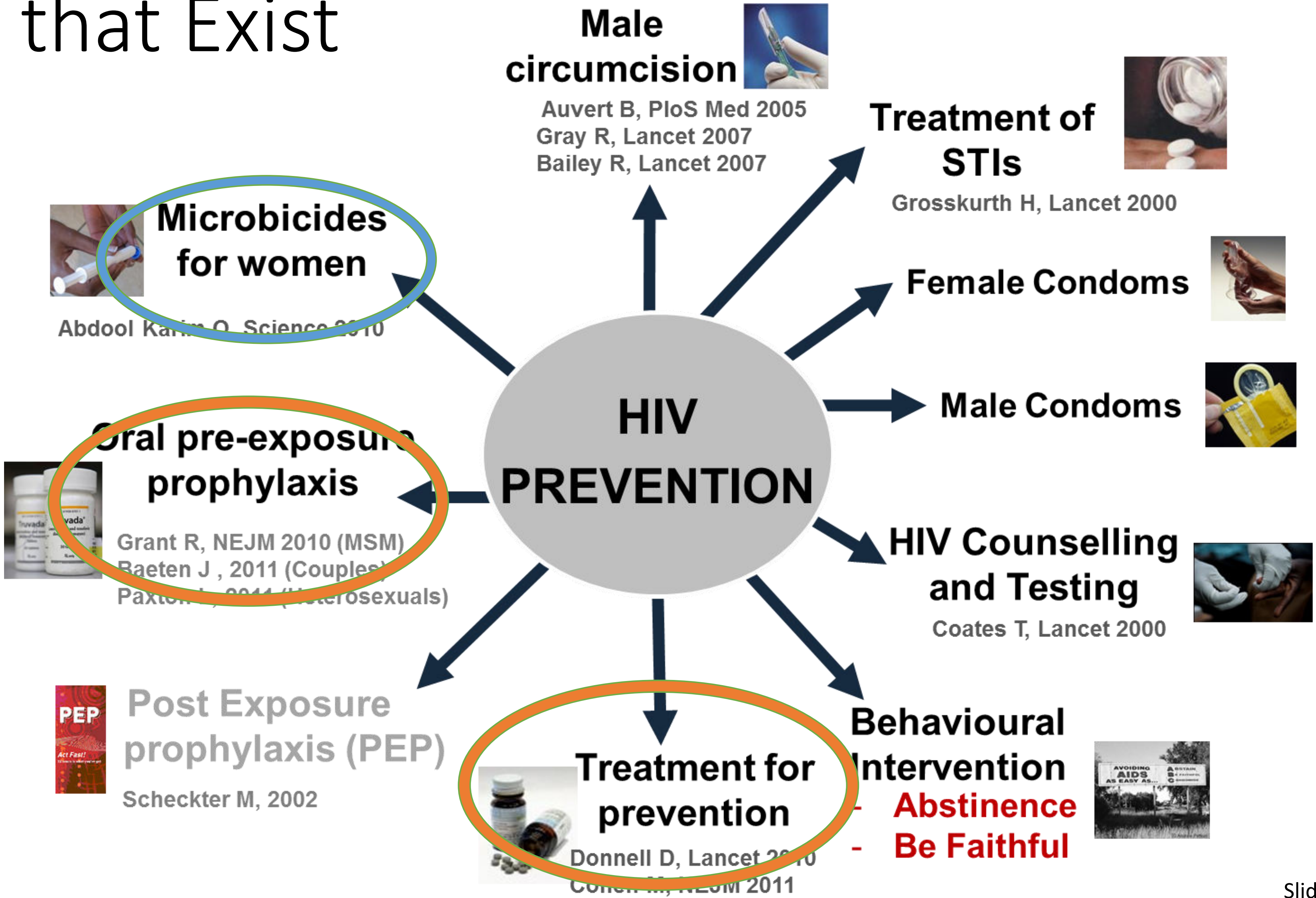
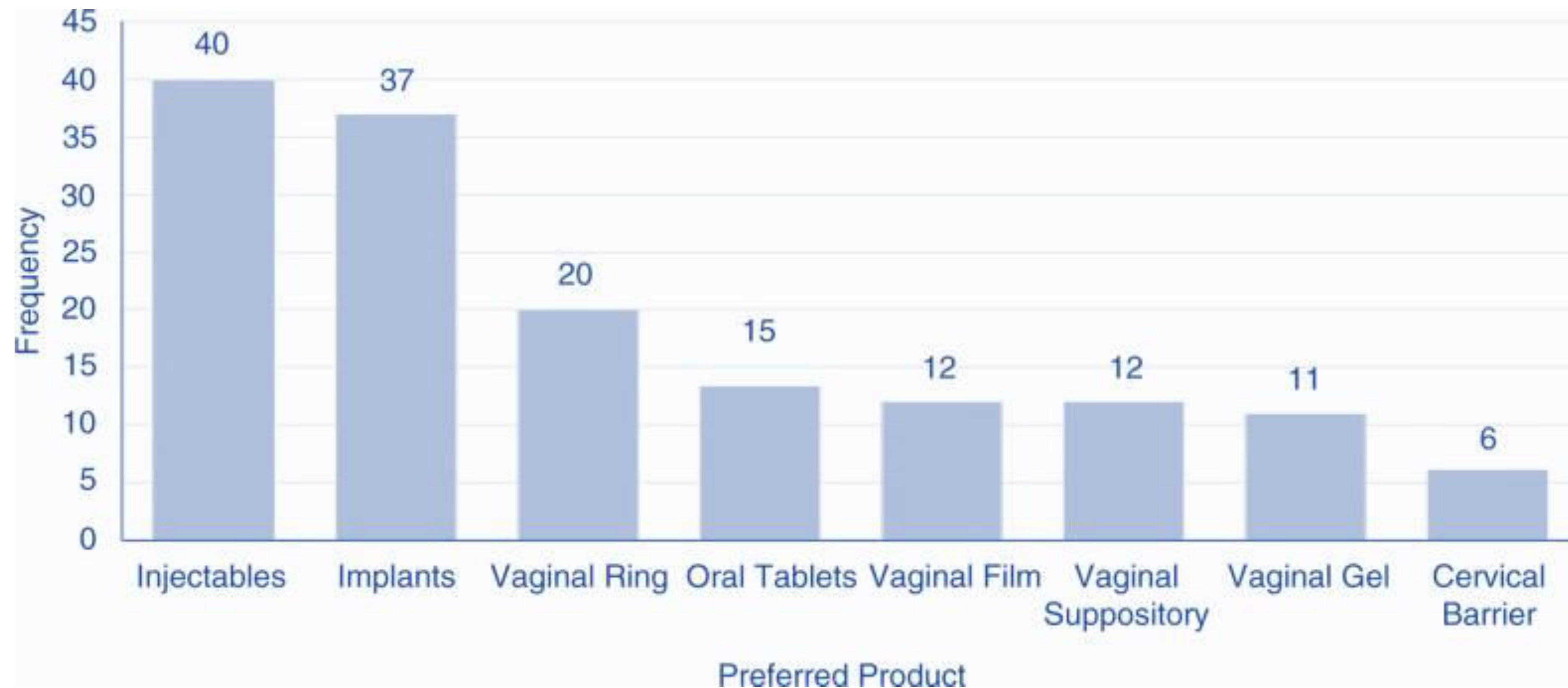
# Tools that Exist




Slide Credit (HPTN, Karim & Cohen)

# What are the alternatives to Oral PrEP and TasP?

What women want in a Prevention Product

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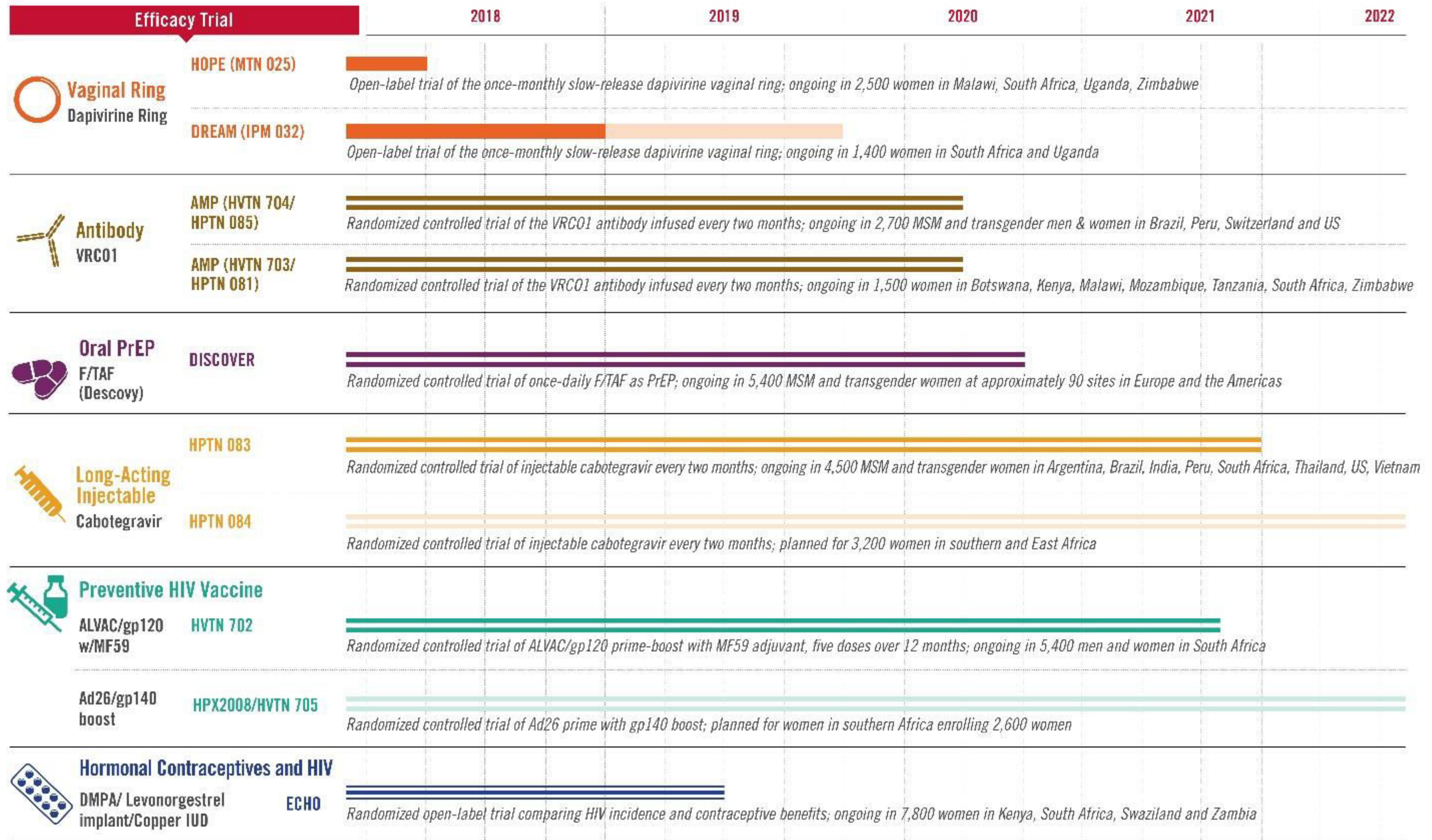


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# It is all about Choice!

- Even the most effective product cannot protect against HIV  f it is not used
- A product that best suits one's lifestyle and needs is more likely to be used
- Women's preferences are not all the same - just as women have choices in contraception, they should have choices for HIV prevention, too

Vaginal Gel

Oral Tablets

Injectables

Vaginal Film

Vaginal Ring

Barrier Methods

Vaginal Suppository/Tablets

Implants

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

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# 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



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# What are Vaccines?

Vaccines teach your body to recognize and fight invaders.

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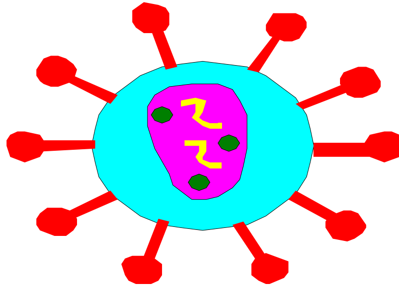
# How Does a Vaccine Work?

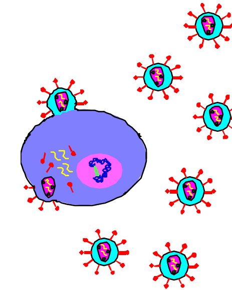
By teaching the body to recognize and fight invaders.



Body Recognizes HIV Virus

Body – Sounds Alarm

Fighter Cells Go Into Action



GOAL - HIV is controlled or killed

# Current vaccine studies for HIV Prevention

**HVTN 705**

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

**HVTN 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

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# 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)

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# 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?

AMP STUDY

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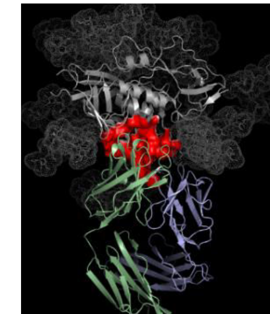
# Summary 1

- 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

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# Thank you!

Salamat!

Tatenda!

Grazie!

Siyabonga!

Zikomo!

Dankie!

Ngiyabonga!

спасибо

謝謝

Obrigado!

Twatotela!

Gracias!

Merci!

Webale!

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