

Biomedical HIV Prevention Training Speakers Notes



Slide 1:

Welcome to this training developed by the Women's HIV Research Collaborative! [Introduce speakers.] This training is intended for anyone to be able to present. The slides come with speaker notes, so don't be surprised when you hear the speakers give supplemental information that does not appear on the slides. Anyone can download the slides and speaker notes from the HANC public website (www.hanc.info).



Slide 2:

The Women's HIV Research Collaborative, or WHRC, developed this training. Who is the WHRC? We are! As of September 2019, there are 23 WHRC members, most of whom are pictured here.

The WHRC is a group of women who are leaders in women's health and HIV from around the United States. With community and staff representatives from all five NIH-funded HIV/AIDS clinical trials networks, this group provides guidance and leadership in the HIV response focused on the research needs of cisgender and transgender women in the US.



Slide 3:

Here's where current WHRC members are located.

The WHRC focuses on advocating for HIV research with women living in the United States but operates with a comprehensive awareness of the potential for American women to benefit from HIV research that is being conducted internationally. To that end, WHRC's focus is domestic, but its interests are global.

Presentation Overview

- Women's Contributions to HIV Prevention Research
- The Urgency for HIV Prevention for Women
- HIV Prevention for Women: The Present
- HIV Prevention for Women: The Future
- How You Can Get Involved!

Slide 4:

[Read the information on the slide]

Women's Contributions to HIV Prevention Research

Slide 5:

Let's begin by acknowledging how women have helped to advance HIV prevention research.

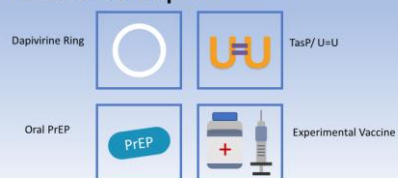
Women Play Vital Roles in Every Aspect of HIV Research

- All 5 NIH-funded research networks are led / co-led by women as Network Principal Investigators / Chairs
- Network Directors
- Laboratory Center Principal Investigators
- Statistical and Data Management Center Principal Investigators
- Women's Health Inter-Network Scientific Committee
- Advocates
- Front desk
- Managers
- Recruiters
- And many more

Slide 6:

[Read the slide info]

Women Advance HIV Prevention as Research Participants



Slide 7:

We'll be discussing all these prevention modalities in greater detail, but first we wanted to acknowledge the sheer contribution women have made to the field of HIV prevention as research participants. Thousands of women have participated in clinical studies of the HIV prevention approaches you see here [read the slide info]. We are grateful to all the cisgender and transgender women who have volunteered for these clinical trials, bringing us closer to an end to the HIV epidemic.

[Note to presenter: the information below is purely supplemental. If time is limited, skip it, highlight only a couple, or save it for Q&A.]

- Over 1,000 women participated in the studies leading to the U=U campaign (more on U=U coming...)

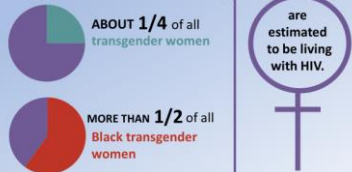
| | |
|--|---|
| | <ul style="list-style-type: none"> • Women and their infants in IMPAACT studies helped determine it was safe and effective to give infants a daily liquid ARV to prevent HIV acquisition • Cis and trans women's participation in Truvada as PrEP trials helped bring PrEP to licensure, and the same for transgender women's participation in getting Descovy licensed for PrEP. • The Dapivirine vaginal ring for HIV prevention is under regulatory review thanks to nearly 3,000 cisgender women who participated (and continue to enroll) in the MTN-led studies. Over 3,000 more cis women participated in non-MTN-led studies of this product. • Transgender women played a vital role in determining the safety and acceptability of a rectal microbicide gel, accounting for 18% of all participants in a pivotal Phase 2 MTN study. • 45% of all Phase 1 HVTN trial participants, 2002-2016, were women (over 1,500 cis and trans women) • 2% of all participants in the HVTN 505 study were transgender women • Ongoing: • Nearly 400 mother/infant pairs are enrolling in IMPAACT studies to test the safety of oral PrEP during and after pregnancy • Over 3,000 cis and trans women are enrolling in HPTN studies testing PrEP as a long-acting injection • Cisgender and transgender women around the world continue to join in the journey to find an HIV vaccine. Nearly 10,000 women have participated in studies by the HIV Vaccine Trials Network since they began testing HIV vaccine strategies! 7639 cisgender and transgender women are currently enrolled in HIV vaccine studies around the world. |
| | <p>Slide 8:</p> <p>The need for HIV prevention for women remains urgent. Let's take a look at some numbers in this next section of the training. Note that we have also included several quotes throughout the presentation from women who</p> |

"This is our struggle—we want to be free from HIV"

The Urgency for HIV Prevention for Women

have been involved with studies across the NIH-funded HIV/AIDS clinical trials prevention networks.

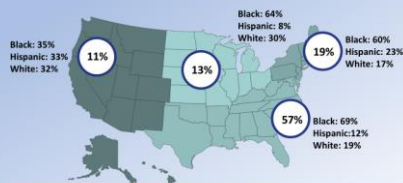
HIV Among Transgender Women in the US



Slide 9:

[Read the slide info.] Transgender women of color live at the intersections of racism, misogyny, and transgender-antagonism. These social and structural issues make transgender women more vulnerable to HIV; prevention is urgent.

HIV Diagnoses Among Cisgender Female Adults & Adolescents in 2017



Slide 10:

The percentages in the circles show regional differences in HIV diagnoses among cisgender women. As you can see, more than half (57%) of all diagnoses among cis women in the US occurred in the South. The additional percentages show racial and ethnic disparities within each region.

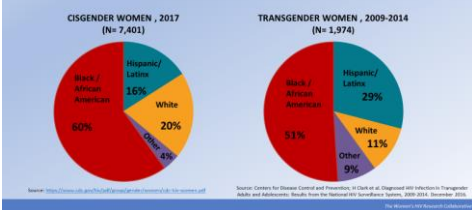
While HIV incidence among cis women has been steadily declining for the past decade or so, there are still over 7,000 cis women diagnosed with HIV in the US annually. That's about 20% of the new HIV diagnoses in the US. At the end of 2016, an estimated 258,000 cis women in the US had HIV. 1 in 9 cis women has HIV but doesn't know it. Prevention is urgent, and HIV prevention approaches *must* include women of color and women living in the US South.

[Information below is supplemental only. Skip if time is limited.]

Women who are receptive partners during vaginal and anal sex are more vulnerable to acquiring HIV than their insertive partners.

Women who experience violence / abuse are more vulnerable to acquiring HIV.

Diagnoses by Race: Women in the US



Slide 11:

- Women of color, particularly Black women, are especially vulnerable to HIV due to interlocking social and structural oppressions. As you can see, nearly 60% of the cisgender women diagnosed with HIV in 2018 were Black.
- You can also see that transgender women of color have the highest incidence among trans women. Over half of trans women diagnosed in 2009-2014 were Black, and almost a third were Latina.
- In 2013, the percentage of transgender people (the majority of whom were transgender women) who received an HIV diagnosis was 3 times the national average

[Supplemental info if time allows]:







A CDC study of HIV incidence among cisgender women from 2010-2016 found that 93% of the new HIV cases among cis Black women would not have occurred if the incidence rate for cis Black women were as low as the rate for cis white women. Meaning almost all of the new HIV cases among cis Black women can be attributed to racial disparities.

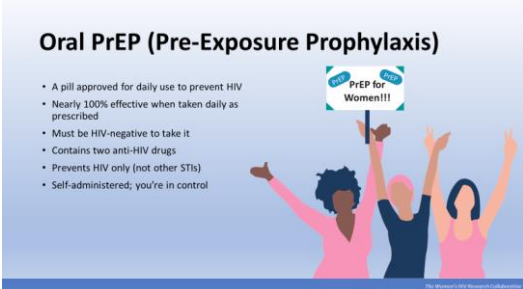
"It's time we placed our own health above our partner's desires."

HIV Prevention for Women: The Present

Slide 12:

Let's take a look at what's currently available for cis and trans women in terms of biomedical HIV prevention.

| | |
|--|---|
| <div data-bbox="175 233 703 527"> <h3>Available Now</h3> <div>  <p>Post Exposure Prophylaxis (PEP)</p> </div> <div>  <p>Treatment as Prevention (TasP)</p> </div> <div>  <p>Pre-Exposure Prophylaxis (PrEP)</p> </div> <p><small>The Woman's HIV Response Collaborative</small></p> </div> | <p>Slide 13:</p> <p>These are the biomedical options for HIV prevention available now. [Read the slide info]. In the following slides, we will look at each of these options in greater depth. Of course, there are other HIV prevention options available, but we will focus on the biomedical.</p> <p>Other available prevention options:</p> <ul style="list-style-type: none"> • Condoms and other barriers • Education and behavior modification • Treatment/ prevention of drug/alcohol abuse • Needle exchange • Interruption of vertical/perinatal transmission • Voluntary medical male circumcision • HIV and STI testing |
| <div data-bbox="175 814 703 1108"> <h3>Post-Exposure Prophylaxis (PEP)</h3> <div>  <p>The use of antiretroviral medicines after being potentially exposed to HIV to prevent the virus from taking hold in the body.</p> <ul style="list-style-type: none"> • Must be started within 72 hours after exposure in order to be effective • The sooner PEP is started, the better • Usually prescribed to be taken once or twice daily for about a month </div> <p>If someone thinks they may have been exposed to HIV, they should talk to their health care provider or an emergency room doctor about PEP right away.</p>  <p><small>The Woman's HIV Response Collaborative</small></p> </div> | <p>Slide 14:</p> <p>PEP stands for Post-Exposure Prophylaxis. This involves [read the slide info].</p> <p>[Supplemental info, only if asked about effectiveness]: There haven't been extensive randomized control trials to be able to give a percentage of effectiveness, but we know from implementation that PEP is effective if taken within 72 hours—just not 100% of course!</p> |
| <div data-bbox="175 1251 703 1545"> <h3>Treatment as Prevention (TasP)</h3> <ul style="list-style-type: none"> • The use of antiretroviral drug therapy (ART) by someone who has HIV • By taking ART as prescribed, people living with HIV can reduce the amount of virus in their bodies to "undetectable" levels • Under conditions of viral suppression, the chance of transmission to others through sex is ZERO • U=U  <p><small>The Woman's HIV Response Collaborative</small></p> </div> | <p>Slide 15:</p> <p>[Read the slide info, making the following commentary...]</p> <p>[After reading bullet 1]: The main purpose of people living with HIV taking HIV medicine is to stay healthy and prevent the progression of HIV. But there is also an added HIV prevention benefit! Treatment-as-prevention (TasP) refers to the use of ART by someone who has HIV to stay healthy and decrease the likelihood of HIV transmission to others through sex, needle sharing, or during pregnancy and birth.</p> <p>[After reading bullet 2]: TasP works by reducing the amount of HIV in the body of someone living with HIV to very low levels (called "undetectable"), thus making their blood, vaginal fluid, semen, and breastmilk less likely to pass HIV to others (though breastfeeding is not</p> |

| | |
|--|---|
| | <p>recommended for PLHIV in the US whether on ART or not).</p> <p>[Read bullet 3, emphasizing that there is <i>zero</i> chance of HIV transmission through sex under conditions of viral suppression. TasP is not 100% effective at preventing HIV transmission for other modes of transmission like injection drug use and breastfeeding.]</p> <p>[Bullet 4]: U=U stands for Undetectable=Untransmittable. This phrase is now being used all over the world in different languages to emphasize that HIV cannot be passed on through sex when someone who has HIV is virally suppressed. [More references are available in the PPT notes for those who ask for resources]</p> |
|  | <p>Slide 16:</p> <p>[First read this info]: Pre-Exposure Prophylaxis (PrEP) is an HIV prevention approach for HIV-negative individuals to stay HIV-negative by taking anti-HIV drugs (antiretrovirals, or "ARVs"). By "oral PrEP," we mean [read slide info].</p> <p>Truvada was the first pill approved as HIV PrEP in 2012. In the US, it is recommended for all people vulnerable to acquiring HIV, including cis and trans women. It has also been approved as PrEP in many countries around the world. In 2019, the FDA approved another pill as HIV PrEP called Descovy, which contains slightly different drugs from Truvada. Unlike Truvada, Descovy is only approved to prevent sexual transmission of HIV, and it is not approved to prevent HIV transmission through receptive vaginal sex because this was not tested in the study leading to its approval. A trial is planned to test Descovy for HIV prevention through receptive vaginal sex with results by 2025. People interested in preventing sexual transmission of HIV through receptive vaginal sex should consider Truvada for PrEP.</p> <p>[Only if asked about side effects: The most common side effect is mild stomach upset. This can be reduced by taking it with food and/or taking it before bed.]</p> <p>[Only if asked about STIs: Note that it is recommended to use condoms with PrEP since PrEP protects only against HIV, not other STIs.]</p> |

[Resource available in PPT notes for those who ask for more info]

Who Should Take Truvada as PrEP?

- Anyone who is HIV-negative and vulnerable to acquiring HIV (Centers for Disease Control and Prevention or CDC), including (but not limited to):
 - Cis and trans women who do not use condoms during sex with partners of unknown HIV status
 - Cis and trans women in a sexual relationship(s) with a partner(s) who has HIV
 - People in sero-discrepant relationships – one partner has HIV, the other does not – including those who are considering getting pregnant or breastfeeding
 - Women who would feel more comfortable and confident using it

The CDC estimates that nearly 500,000 women in the US could benefit from taking PrEP. However, less than 1% of those 500,000 women are taking it!

Source: <https://www.cdc.gov/hiv/prep/>

Slide 17:

We will be focusing on Truvada instead of Descovy because Descovy isn't approved for use by all women, but Truvada is. Both work equally well to prevent HIV. Those interested in learning more about Descovy can discuss it with their doctors.

[Read the slide info]

[Only get into the following if asked:

It works for women!! Research has shown that adherence (taking the pill as prescribed) does not need to be as perfect for rectal exposure to HIV, but it does need to be near-perfect for it to work against vaginal exposure to HIV. Some research also suggests that it needs to be taken for a longer period of time before it becomes fully protective against vaginal exposure to HIV. CDC reports that it is fully effective against rectal exposure to HIV after 7 days of daily use, and fully effective against vaginal and injection drug exposure after about 20 days of daily use. Be sure to consult with your provider.]

Does Truvada as PrEP Work for Trans Women?

- The CDC recommends PrEP for all HIV-negative persons who are vulnerable to getting HIV, including transgender women.
- Research is ongoing with regard to interactions between hormone therapy and oral PrEP, but the CDC does not recognize any drug conflicts or interactions.
 - If you're worried that PrEP will affect your hormone therapy, ask your health care provider to check your hormone levels.
- Everyone taking PrEP should see their health care provider every 3 months for follow up, HIV tests, and prescription refills.
 - Combine PrEP visits with hormone therapy appointments.

Source: <https://www.cdc.gov/hiv/prep/>

Slide 18:

[Read the slide info.]

HIV Prevention for Women: The Future

Slide 19:

We have just reviewed what is currently available to women in terms of biomedical HIV prevention. All the HIV prevention approaches we have discussed so far are available for use right now! In this next section, we will be discussing biomedical HIV prevention approaches that are not yet available, but currently under research to see if they are safe and effective for people to use in the future.

Still Under Research

New PrEP & Integrated Strategies



New formulations and delivery methods to reduce the likelihood of transmission.

Microbicides



Products applied vaginally or rectally that may prevent HIV transmission.

Vaccines



Harnessing the immune system to help prevent a person from contracting HIV.

Slide 20:

We will focus on these three areas of ongoing biomedical HIV prevention research: New PrEP and Integrated Strategies, Microbicides, and Vaccines. Again, these approaches are not yet available for use because they are still being studied to make sure they're safe and effective.

No single HIV prevention approach will be acceptable to all people. The best option for one person may not be the best option for others. Research is critical to develop and test new prevention options that offer people more choices.

Note that there is ongoing research in HIV treatment as well, but we will be focusing on primary prevention.

[Only read if anyone asks about microbicides being a type of PrEP:

Rectal and vaginal microbicides are also forms of PrEP (products used for prevention before exposure to HIV), but they are different in that they are non-systemic research products (used only where they are needed) as opposed to oral, injectable, and implantable research products, which distribute the drug(s) systemically (throughout the whole body).]

Continuing Research: PrEP & Integrated Strategies

The HIV Prevention Trials Network (HPTN), funded by the National Institute of Allergy and Infectious Diseases, the National Institute of Mental Health, and the National Institute on Drug Abuse, is dedicated to discovering and developing new and innovative strategies to reduce the acquisition and transmission of HIV.



Slide 21:

[First read this info]: We've already discussed oral PrEP, a daily pill for HIV prevention. Oral PrEP is the only type of PrEP currently approved in the US, but scientists and community members are helping to find other forms of PrEP and integrated strategies, which we will discuss in this section.

[Then read slide info.]

Integrated Strategies

- No single HIV prevention intervention will work for all women.
- Effective HIV prevention programs require a combination of behavioral, biomedical and structural interventions.
- Evidence-based and cost-effective strategies to meet women's needs.



Slide 22:

Integrated Strategies or Combination Prevention is a framework used for HIV prevention. [Read slide info.]

Advancing HIV Prevention Research

- Oral PrEP is now a real option for HIV prevention. What's next?
- Improving PrEP and evaluating new PrEP agents and delivery methods
 - Developing and evaluating integrated combination prevention strategies
 - Optimizing application of new knowledge to women (and other key populations)



Slide 23:

[Read slide info]

PrEP 2.0

- **Injectable PrEP Studies**
 - HPTN 083
 - 43 sites in 7 countries (including US)
 - Minimum recruitment target of 10% transgender women (~450 transgender women)
 - HPTN 084
 - 3,200 cisgender women in 7 African countries



Slide 24:

These injectable PrEP studies are all based on studies of injectable ART for treatment of HIV. Those studies were successful, and injectable ART is now being considered as a potential option for people living with HIV. This is important because, remember, treatment is prevention!

The concept with injectable PrEP is that people would receive 6 injections per year (every 8 weeks). There would be an extra shot in the first year to ensure drug levels are high enough when starting injectable PrEP; the first two injections would be 4 weeks apart, and then all subsequent injections would be 8 weeks apart. The first injection would also be preceded by taking an oral pill form of the drug for a certain amount of time to make sure people don't have adverse reactions before

receiving the shot, which lasts for a long time and can't be removed.

In May 2020, the HPTN reported the very exciting news from HPTN 083 that this form of injectable PrEP was highly safe and efficacious among the cisgender men and transgender women who participated in the study. The study also exceeded the 10% TGW enrollment goal and actually enrolled 12% TGW.

A few months later, the HPTN reported news from HPTN 084: this form of injectable PrEP was highly safe and efficacious for the cisgender women in the study. Now that we know that this form of injectable PrEP is both safe and effective for HIV prevention, injectable PrEP could become approved and available for use with a prescription.

It is important to have a variety of options for PrEP...

Potential advantages

For those who don't like to or have trouble swallowing pills, an injection could be an alternative.

It would also be long-acting. Taking only 6 shots per year instead of 365 pills per year could help women who have trouble with adherence, pill fatigue, etc. We also know that oral PrEP must be strictly adhered to for it to protect against vaginal acquisition of HIV, so an injection 6 times a year would lend more flexibility.

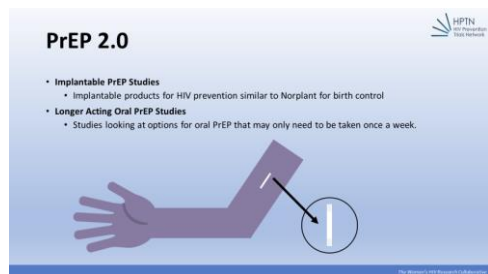
Injectable PrEP also has different side effects than oral PrEP (e.g. redness, pain, and/or swelling at the injection site). Both products were very safe and well-tolerated in clinical trials.

Potential disadvantages

The long-acting medicine is a potential advantage, but this may have potential disadvantages too. The medicine is injected into the buttock and cannot be removed once it's administered; studies have shown that it can last in the body for about a year. Some women may prefer shorter-acting options for HIV prevention. This may also mean that if a person stops taking the injections, they might have to take oral PrEP until the injectable drug has left their system so they are protected not only from

acquiring HIV but also from acquiring HIV that could form resistance to low levels of the injectable drug. Right now we don't have answers to these questions because injectable PrEP is not yet available outside clinical trials.

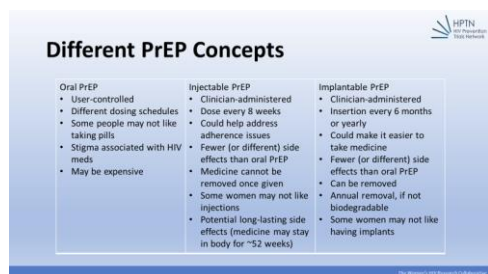
[Quickly read the slide info]



Slide 25:

Implants delivering HIV prevention medicine could be long-lasting from 2-3 months to a year, maybe longer. These are in the very early stages of development.

[Read slide info]



Slide 26:

To summarize, this table is another way to visualize potential pros and cons as well as the many types of PrEP research that are being conducted to improve options for PrEP.

[Read slide info]



Slide 27:

If you'd like to learn more about PrEP and Integrated Strategies research conducted by the HPTN, check out these resources. Additional questions can be sent to the community program management team at 083CPM@HPTN.org. You can also learn more about the HPTN and its research agenda by visiting its website. Please also follow the HPTN on social media for study updates and events.



Slide 28:

Microbicides are products applied vaginally or rectally that may work to prevent HIV acquisition. We will look at some of the different formulations of microbicides.

What Are Microbicides?

- Microbicides are products applied inside the vagina or rectum to protect against HIV through sex.
- They deliver high levels of anti-HIV drugs to the site of potential HIV transmission, with very little drug absorbed into the body.
- Microbicides formulated as vaginal rings, films, gels, douches, fast-dissolving inserts, and suppositories are being developed and tested to provide additional options to prevent HIV acquisition during sex.
- These products could fulfill the need for a non-systemic and/or short-acting method for HIV prevention that can be used around the time of sex.



Slide 29:

[Read the slide info.] Although microbicides are not yet available for widespread use, researchers are making significant strides in the development and clinical evaluation of both vaginal and rectal microbicide products.

In January 2021, the World Health Organization recommended the dapivirine vaginal ring as an option for HIV prevention for cisgender women.

Why Microbicides?

- Truvada as PrEP is a safe and very effective method to prevent HIV, but taking pills daily may not be possible or desirable by everyone.
- To make a global impact on the HIV epidemic among cisgender and transgender women who may have vaginal and/or anal sex, we need new and creative ways to prevent HIV that recognize diverse preferences and choices.
- Products that could be used around the time of sex or that conform to already practiced sexual behaviors might be desirable to some women, giving them more control over their own health and sex lives.

Slide 30:

[Read the slide info.] Just as there are multiple choices in contraception to prevent unintended pregnancy, a microbicide could give people an additional option for HIV prevention.

Dapivirine Vaginal Ring

- Flexible silicone monthly ring that slowly releases Dapivirine inside the vagina, with low systemic absorption.
- Regulatory approval being sought based on multiple studies with more than 6,600 cisgender women, finding:
 - strong safety profile; reduces HIV transmission; more effective when used consistently – not used consistently by younger women & girls
- Ongoing study with cisgender girls and young women in Africa will provide more information on ring use in this population, as well as daily PrEP, and assess their preferences for the approaches.
- Other studies being planned will evaluate the safety of the ring in women who are pregnant and breastfeeding.



Slide 31:

[Read the slide info.] The dapivirine vaginal ring is the first biomedical HIV prevention option recommended by the WHO specifically for cisgender women.

To-date, the ring has only been tested among cisgender women, so it is not known whether it can be safely used in women with neovaginas.

Next Generation Rings

- Rings that can be used for up to 3 months
- Rings that can also prevent unintended pregnancy
- Rings that could protect against both HIV and other sexually transmitted infections, such as herpes



Slide 32:

[Note to presenter: read this information.]

While a ring used for a month at a time may appeal to some women, others may prefer a product they replace every three months, or a ring that provides contraception in addition to protecting against HIV. Others may want a ring that offers protection from other sexually transmitted infections, or STIs, in addition to HIV.

Toward this end, the MTN is evaluating next generation rings: a dual-purpose ring containing both a hormonal contraceptive and dapivirine and a three-month dapivirine ring. Other ring studies are combining anti-HIV drugs with products active against certain STIs, like herpes.

Rectal Microbicides

- Anal sex is a common sexual practice enjoyed by cisgender and transgender women around the world.
- Currently being developed and tested, rectal microbicides could...
 - Provide protection around the time of anal sex ("on-demand" products)
 - Conform to already practiced sexual behaviors such as rectal lubes and/or douches ("behaviorally congruent" products)
 - Encourage a feeling of safety & confidence by recognizing the importance of pleasure in the lives of cisgender and transgender women.
- Several early rectal microbicide studies have been completed to date that have enrolled more than 100 cisgender and transgender women.



Slide 33:

According to estimates, 10 percent of the world's population engages in anal sex. [Read the slide info.]

Rectal Microbicides & DESIRE

- DESIRE (Developing & Evaluating Short-acting Innovations for Rectal Use) launched in 2019 and is the first study to explore multiple placebo methods for delivering a rectal microbicide – a douche, suppository, and fast-dissolving rectal insert.
- DESIRE, whose results are expected in 2020, will:
 - Include 210 transgender men and women and cisgender men who have sex with men from Malawi, Peru, South Africa, Thailand, and the U.S. (Birmingham, Pittsburgh and San Francisco)
 - Aid in the design of HIV prevention products that fit into people's lives, rather than expecting their lives to fit into standard prevention methods
 - Directly impact the development of intervention strategies for future studies of rectal microbicides



Slide 34:

[Read the slide info.] DESIRE is an important step to developing a rectal microbicide that is not only acceptable, but *desirable* for people who are vulnerable to HIV from anal sex.

Additional Information

- www.mtnstophiv.org
- <https://www.facebook.com/microbicidetrialsnetwork/>
- www.bethegeneration.org
- www.nih.org

Slide 35:

Continuing Research: HIV Vaccines

A number of public and private organizations, in partnership and individually, are working together to find a vaccine that could end the HIV epidemic.

The HIV Vaccine Trials Network (HVTN), funded by the National Institute of Allergy and Infectious Diseases (NIAID), is an international collaboration that conducts all phases of clinical trials to test HIV vaccines.

The HVTN's mission is to fully characterize the safety, immunogenicity, and efficacy of HIV vaccine candidates with the possible goal of developing a safe, effective vaccine as rapidly as possible for prevention of HIV globally.



Slide 36:

The HVTN's mission is to develop a safe and effective vaccine.

Suggested Activity: So to warm us up we are going to do an activity...

- 1) Please raise your hand if you have had a vaccination in the past year? (please keep your hand up)
- 2) Please raise your hand if you got a flu shot last year? (please keep your hand up)
- 3) Please raise your hand if you travelled internationally and had to get a yellow fever shot, or typhoid? (please keep your hand up)
- 4) Please raise your hand if you have been bitten by a dog and gotten a rabies shot? (please keep your hand up)

Thanks, you can put your hands down.

What this demonstrates is so important because many of us think of vaccinations as something babies or young

children get, and we forget that there are many vaccinations given to adults all the time. There are even vaccines specifically recommended for older adults, such as pneumonia and shingles. The term “vaccine” is not common in our vocabulary, and it’s important to remember that the shots people get ARE vaccines.

Preventive Vaccines Historically Have Ended Epidemics

Used for decades around the world, most commonly in children

Very safe when manufactured and used properly

Very cost-effective compared to treatment

Eliminated smallpox worldwide, soon polio

2006: 1st vaccine for girls and young women against a cancer-causing virus, human papilloma virus (HPV), and 2009-10 approval for boys and young men.

Slide 37:

With the activity we have just done in mind, [Read slide info]

Note to presenter: HPV is a sexually transmitted infection.

Vaccine Research in Perspective

| VACCINE | DISCOVERY OF VIRUS | VACCINE DEVELOPED FOR HUMAN USE | YEARS TO VACCINE |
|-----------------|--------------------|---------------------------------|------------------|
| H. Influenzae-B | 1892 | 1985 | 93 |
| Herpes (HSV-1) | 1919 | Not available | >90 |
| Pertussis | 1906 | 1926 | 20 |
| Polio | 1909 | 1954 | 47 |
| Yellow Fever | 1900 | 1935 | 35 |
| Influenza | 1933 | 1945 | 12 |
| Measles | 1911 | 1957 | 46 |
| Hepatitis A | 1973 | 1995 | 22 |
| Hepatitis B | 1967 | 1984 | 17 |
| HPV | 1974 | 2007 | 33 |
| HIV | 1983 | Not available | >30 |

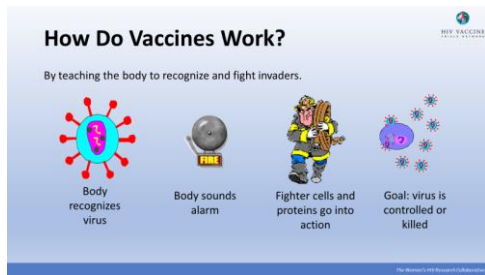
Slide 38:

Take a look at this slide. Notice that it has taken decades to develop vaccines for some of these diseases, sometimes more than 90 years! And yet, once developed, these vaccines have become a regular part of public health initiatives to prevent and control epidemics. This shows that it can take a long time to develop a vaccine, even after we know the cause of a disease. While the time is especially frustrating with HIV, because so many lives are being lost, we are actually on par with the timelines seen for other diseases. Also, there are no vaccines for any other retroviruses. And while it may take time, once we have them, vaccines have significantly reduced or eliminated a number of deadly infectious diseases. We hope one day to be able to add an HIV vaccine to this list.

[Background knowledge for presenter only]:

Haemophilus Influenzae Type B, or HiB, is one of the causes of meningitis.

A retrovirus is any [virus](#) which copies itself as part of the cell's [DNA](#) by [reverse transcribing](#) its [RNA](#). Since the cell cannot reread the step-in which RNA is converted back to DNA. this makes the retrovirus's RNA change often. This makes it harder for retroviruses to be attacked by drugs. [HIV](#) is a retrovirus, which makes it very difficult to overcome using drugs.



Slide 39:

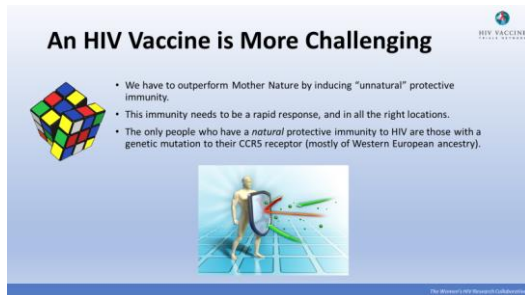
So how do vaccines work? Vaccines teach your body to recognize the virus, sound the alarm to activate your immune system, and instruct your fighter cells and proteins to go to work. The goal is that the virus will be killed or controlled.



Slide 40:

[Read slide info]

The myth that a vaccine already exists but is being withheld is a fairly widespread myth. It is commonly encountered among groups that have a history of being mistreated in past research. When speaking about this, it is sometimes effective to point out that the scientist who develops a vaccine is likely to become a “science superhero,” win the Nobel prize, etc. – not many people would be willing to keep this discovery a secret!



Slide 41:

So why is an HIV vaccine so challenging to develop?

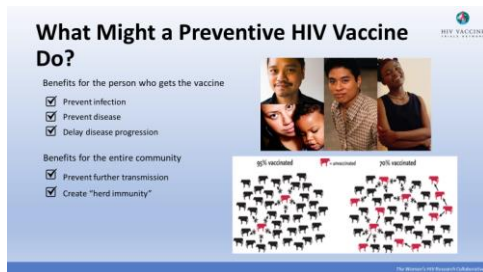
- [Read first bullet]. Mother Nature didn’t give us the power to successfully fight back against HIV, so the challenge we face is that we have to come up with an immune response that is better than what most people have naturally. The immune response we need must work for all the different modes of HIV transmission too.
- [Read second bullet]
- [Read third bullet]. CCR5 is one of the receptors found on the surface of our T-cells that HIV can bind onto. For those who have the genetic mutation, their CCR5 has changed such that HIV is not able to attach to it. It is like trying to put a key into the wrong lock; HIV is unable to fit, and there it cannot get into the cell. The mutation can be found in approximately 10% of Europeans, but it is rare in people of African and Asian descent.

[Background knowledge for presenter only]:

- There are very few human examples of someone clearing HIV from their body naturally (http://www.aidsmap.com/page/3511496/?utm_source=NAM-Email-

Promotion&utm_medium=hiv-update&utm_campaign=hiv-update and <https://leapsmag.com/exclusive-the-worlds-first-known-person-who-conquered-hiv-without-medical-intervention-goes-public/>). The next best example we have is the group of people known as “long term non- progressors,” also known as “elite controllers,” who still have HIV in their bodies, but their immune systems are able to control HIV and maintain a low viral load, often without a need for anti-retroviral treatment.

- (see a nice summary on Wikipedia for more information: <http://en.wikipedia.org/wiki/CCR5>)



Slide 42:

So when we find it, just what might a preventive HIV vaccine do? There are several possible ways that scientists believe a preventive vaccine could work.

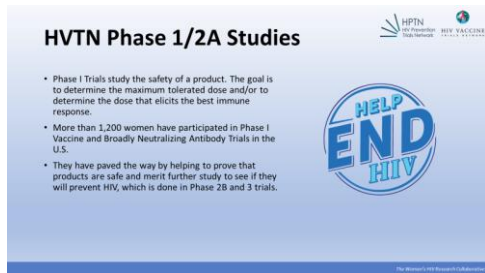
- The first way a vaccine might work is by triggering a strong antibody response. That would be the “gold medal” standard [refer to first check on the slide], to completely prevent infection.
- The second way [refer to second check on slide] would be a vaccine that could trigger a really strong T-cell response which might be able to combat an infection and clear it from the body to prevent disease, just like we are able to fight back against a cold or the flu. This would be the “silver medal” approach.
- The third idea [refer to third check on slide] is also related to T-cells. Perhaps we couldn’t completely fight off the infection, but only partially control it. This could result in slowing down HIV by helping to control viral load. This would be the “bronze medal,” and that could still be very important because we know that people with an undetectable viral load are healthier and cannot transmit HIV to others through sex, which is known as U=U or Undetectable equals Untransmittable.

[Refer to bottom half of slide] There would also be benefits for the wider public in addition to the vaccinated individual. For example,

- U=U
- Herd immunity, as seen here on the slide, or the idea that even if only some people get vaccinated, then the wider community will be afforded some protection as a result of fewer new cases of HIV overall. It may not be necessary to vaccinate everyone, but with fewer overall HIV transmissions, the larger public could still benefit.

We are seeing an example of this in the US today, where we are losing our herd immunity to measles and pertussis (whooping cough). Since these diseases have not been a problem for many years, parents may think it is not important to vaccinate their children or themselves. In recent years, there have been huge increases in the numbers of measles and pertussis infections in adults and children, so now there are big efforts underway to encourage people to vaccinate their kids, and for adults to get a booster injection.

[Background for Presenter only]: T-cells are like soldiers who seek and destroy invaders and support other **immune** cells for a combined **response** to invading viruses, like HIV.



Slide 43:

The HVTN is conducting innovative trials to help better understand how to tackle the complexity of HIV.

[Read bullets 1 and 2]

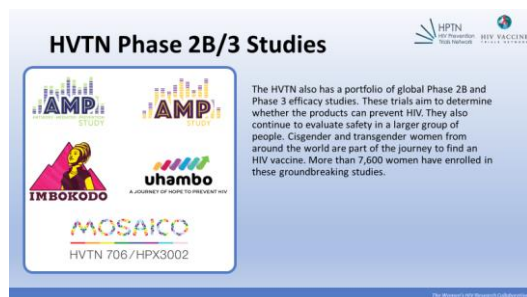
A vaccine study tests the safety of the vaccine and whether the immune system responds to the study vaccines. It takes many of these studies to produce a safe, effective vaccine. The vaccines being tested are not made from live HIV, killed HIV, or human cells containing HIV. They cannot cause HIV or AIDS.

Who has heard of broadly neutralizing antibodies, or “bnAbs”? Antibodies are one of the natural ways that our bodies fight infections. Some of the antibodies that are used for preventing infections are made in laboratories. Manufactured antibodies have been used successfully to prevent other diseases, and lab tests show that bnAbs can protect cells from many different strains of HIV around the world. The bnAbs being tested

are also not made from live HIV, killed HIV, or human cells containing HIV. They cannot cause HIV or AIDS. They are made in a lab using the same kinds of processes used to make other medicines. Some of these studies are done in partnership between the HIV Vaccine Trials Network and the HIV Prevention Trials Network. These two networks have joined forces to combine strengths on many current and upcoming studies to see if bnAbs will work to prevent HIV. These studies are happening all around the world. [refer to bullet 3] The women in these studies have paved the way by...

[Additional Resources for presenter only]:

- Phase 1 studies website: <https://helpendhiv.org/>



Slide 44:

[Read slide info]

1. The AMP studies are being conducted by two groups, the HIV Vaccine Trials Network and the HIV Prevention Trials Network. “AMP” stands for “Antibody-Mediated Prevention,” where study participants are receiving IV infusions of bnAbs to see if the bnAbs will protect them from acquiring HIV. The AMP Studies involve 2 trials, 2 cohorts, one design.

HVTN 704/HPTN 085

MSM+TG men + TG women

Brazil, Peru, Switzerland, US

HVTN 703/HPTN 081

Cisgender women

Sub-Saharan Africa: Botswana, Kenya, Malawi, Mozambique, South Africa, Tanzania, Zimbabwe

2. Uhambo (HVTN 702) – This was a clinical trial based on the Thai Trial, RV144, which was the first HIV vaccine efficacy trial to show partial effectiveness, reducing new cases of HIV by about 32%. Uhambo is a Zulu word meaning “journey,” and the journey of this particular experimental vaccine began in cisgender men and women in Thailand. Researchers adapted this experimental vaccine to the HIV subtype that predominates in southern Africa, where it was tested in South African cisgender women. The research team had hoped for better results, but unfortunately, it was announced in January 2020 that the experimental vaccine being studied in HVTN 702 did not work to prevent HIV. While these results are disappointing, we can still learn from them. We now know that this particular vaccine design did not work in this particular context. Other HIV vaccine trials remain ongoing.

3. Due to the HIV-1 diversity worldwide, scientists thought to create a vaccine candidate known as a mosaic that could work against all of the strains of HIV found around the world. Imbokodo (HVTN 705/HPX2008) is the most recent of the series of studies of this mosaic concept. The word Imbokodo comes from a Zulu expression that became well known during apartheid: *Wathinta abafazi, wathinta imbokodo!* which means, “You strike a woman, you strike a rock! This saying conveys the strength of women and their central role in African communal life. The trial is ongoing in cisgender women in Sub-Saharan Africa: Malawi, Mozambique, South Africa, Zambia, Zimbabwe.

4. The Mosaico study (HVTN 706/HPX3002) is testing the same mosaic vaccine concept in...

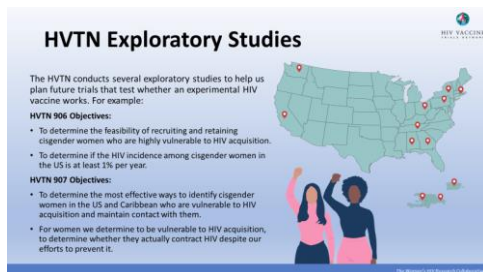
MSM +TG Men + TG Women

USA (24 sites)

Latin America: Argentina (4 Sites), Brazil (9 Sites), Mexico (3 Sites), and Peru (5 Sites)

Europe: Italy (3 Sites), Spain (6 Sites) and Poland (3 Sites)

Background information for presenter: The two AMP studies and HVTN 705 were fully enrolled in Fall 2019. Mosaico opened for enrollment in Fall 2019.



HVTN Exploratory Studies

The HVTN conducts several exploratory studies to help us plan future trials that test whether an experimental HIV vaccine works. For example:

HVTN 906 Objectives:

- To determine the feasibility of recruiting and retaining cisgender women who are highly vulnerable to HIV acquisition.
- To determine if the HIV incidence among cisgender women in the US is at least 1% per year.

HVTN 907 Objectives:

- To determine the most effective ways to identify cisgender women in the US and Caribbean who are vulnerable to HIV acquisition and maintain contact with them.
- For women we determine to be vulnerable to HIV acquisition, to determine whether they actually contract HIV despite our efforts to prevent it.

Slide 45:

[Read slide info]

HVTN 906 & 907 were conducted in the continental US as well as Haiti, Puerto Rico and the Dominican Republic.



Women Around the Globe

Women around the globe continue to contribute to helping us find new ways to prevent HIV.

Slide 46:

[Read slide info]

These are the MTN, HPTN, and HVTN sites across the world. Their work wouldn't be possible without the cisgender and transgender women contributing as research staff and participants around the world.



Slide 47:

So how can you get involved with this work?

Optional: read quote from the poem on the slide.

Note: Renowned poet Mary Bowman died on May 16, 2019.



Slide 48:

If you want to get involved, please consider joining us!

Membership on the WHRC involves participating on bi-monthly conference calls and/or working on the topic/area of your interest with other members (e.g. planning a webinar, authoring an abstract, collaborating as a community partner, assisting with developing the annual work plan). You decide your level of involvement!

For more information, contact Brian Minalga:

bminalga@fredhutch.org



Slide 49:

Here are some resources to get informed. Knowledge is power!



Here are some other ways to get involved [review slide info]

For CAB and trial participation info, visit the Network websites and/or clinicaltrials.gov.

Slide 51:

Acknowledgements

The Women's HIV Research Collaborative is grateful to the Division of AIDS at the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, for making this research possible by funding the vital work of the biomedical HIV prevention networks.

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Coordination

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Coordination

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