

On the Horizon for Health Department Consideration: Biomedical Advances for Prevention

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BRIDGING SCIENCE, POLICY AND PUBLIC HEALTH

Prior to exposure

- Education & Behavior change
- Male circumcision
- **Preventive Vaccines**
- **Pre-exposure prophylaxis (PrEP)**
- **HSV2 suppression or vaccine**

Point of transmission

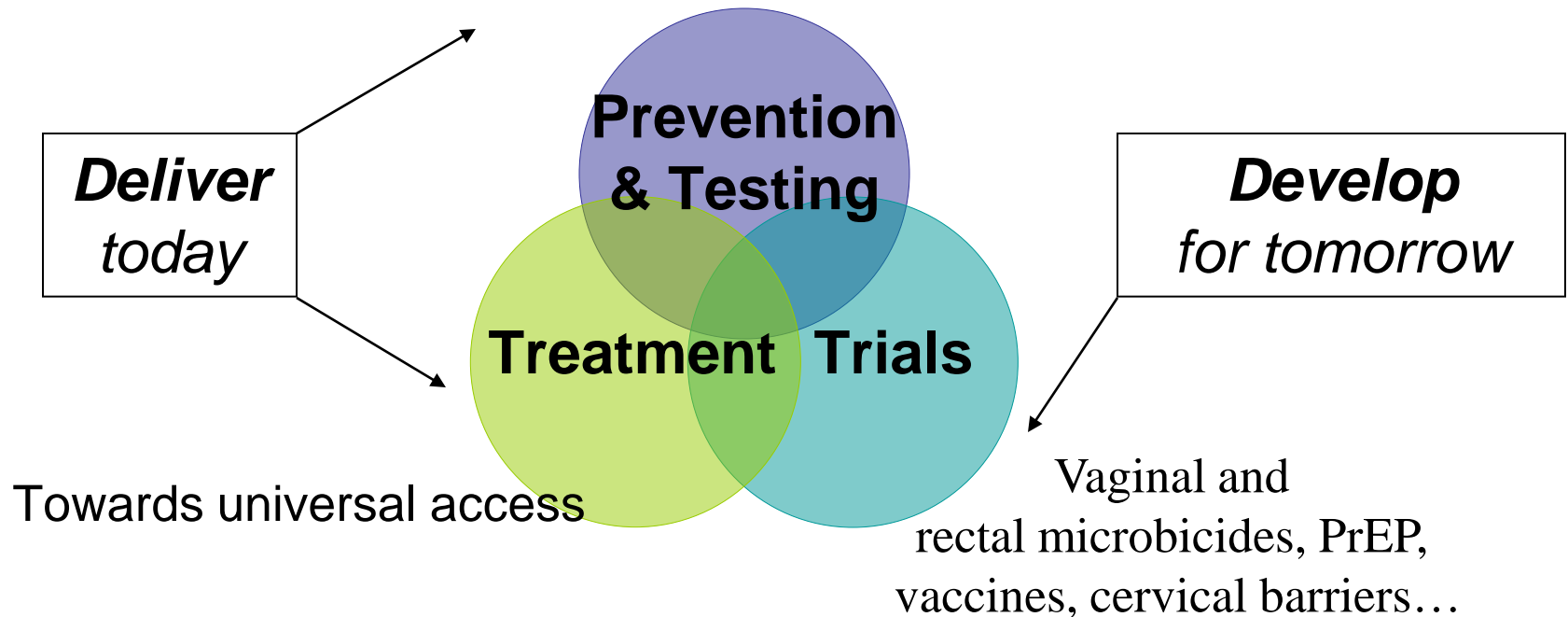
- Male and female condoms
- Antiretroviral therapy (mother-to-child)
- Post exposure prophylaxis (PEP)
- **Microbicides**
- **Diaphragm, cervical barriers & new FCs**

After infection

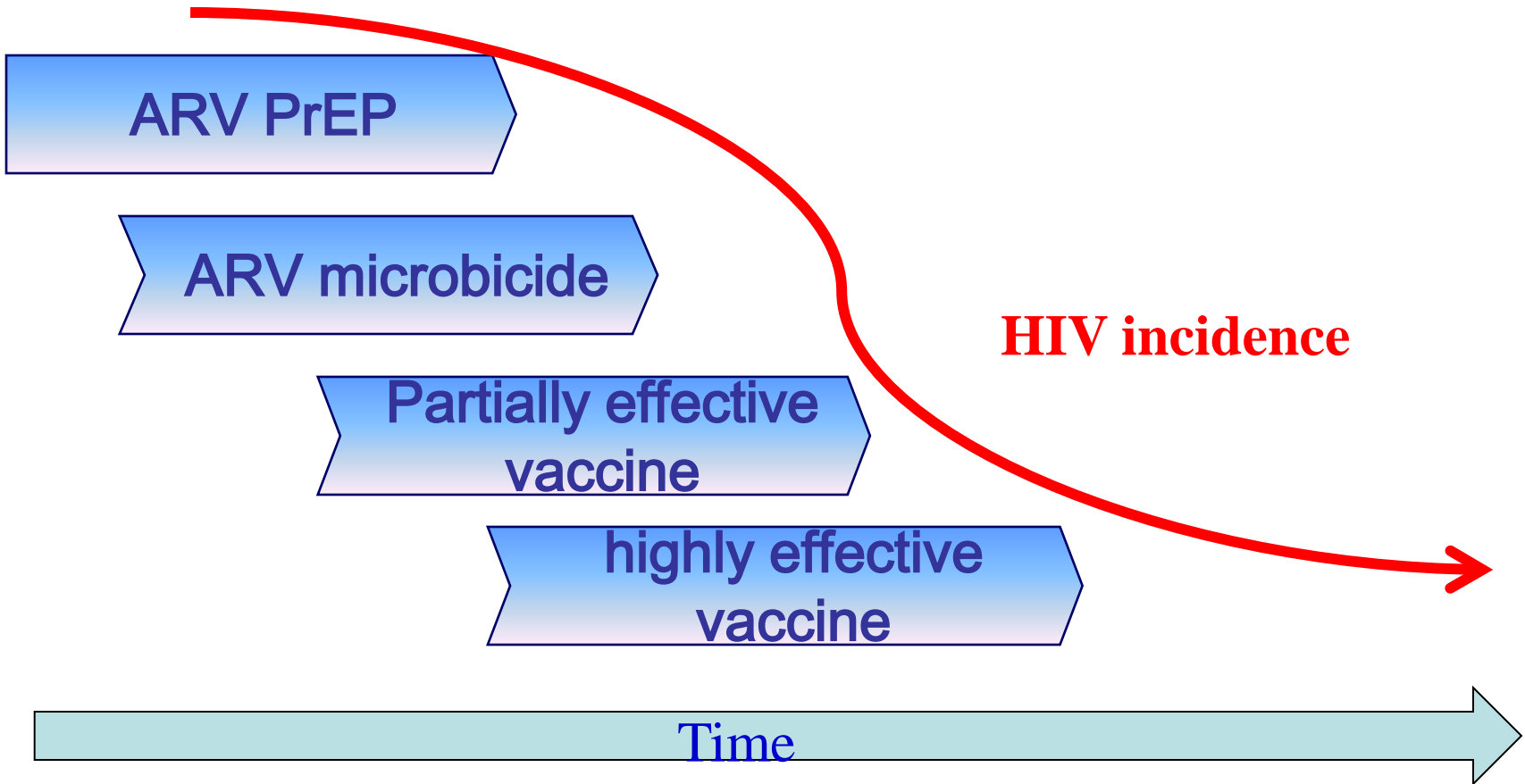
- Antiretroviral therapy
- Care
- Education & Behavioral change
- **Therapeutic Vaccines**

Comprehensive, integrated, sustained response

An expanded alphabet soup of prevention:
ABC (M&F), clean needles, male circumcision, VCT

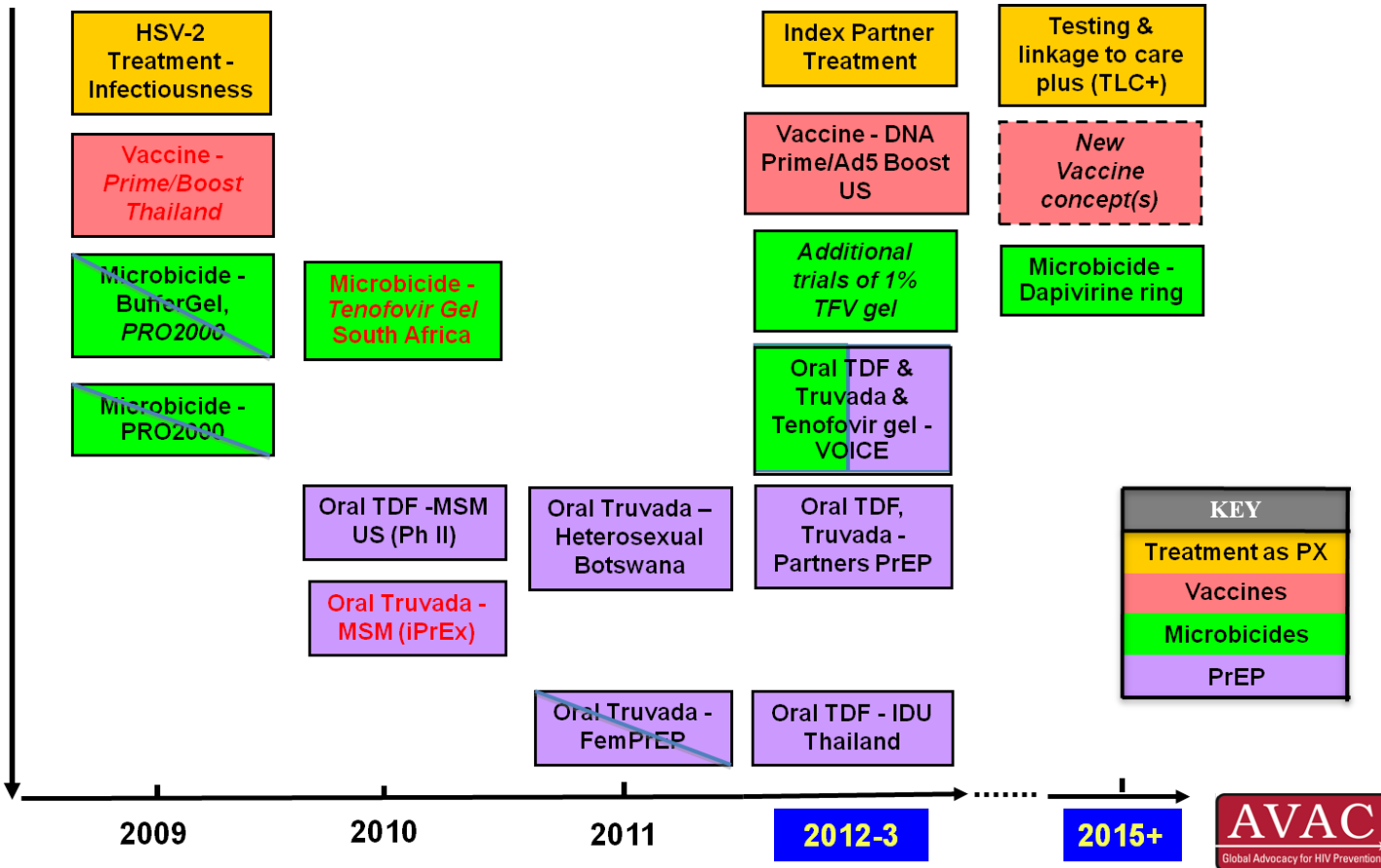


Pathway to reversing the epidemic



Robin Shattock, AIDS Vaccine 2010, Atlanta

HIV Prevention Research Landscape



Duration between discovery of microbiologic cause of selected infectious diseases and development of a vaccine

Virus or bacteria	Year cause discovered	Year vaccine licensed	Years elapsed
Typhoid	1884	1989	105
Haemophilus Influenzae	1889	1981	92
Malaria	1893	None	–
Pertussis	1906	1995	89
Polio	1908	1955	47
Measles	1953	1995	42
Hepatitis B	1965	1981	16
Rotavirus	1973	1998	25
HPV	1974	2007	33
HIV	1983	None	–

Trials Illustrate Key Concepts in HIV Vaccine Development

- We can learn important lessons from products that don't work or have modest efficacy.
- Science usually proceeds in small steps.
- Clinical trials are essential; humans clinical trials don't lie.
- Clinical, preclinical and basic research are all essential.
- Every study raises new questions.
- Humility.
- **An HIV vaccine is possible!**

**Join me in the effort
to stop HIV**

Are you a man between
18-45 years old and HIV
negative? Volunteer for
an HIV vaccine study and
turn hope into action.

HOPE TAKES ACTION

hopetakesaction.org

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- Studies in animals have reduced risk of infection if ARVs are administered before virus exposure.
- PMTCT: ARVs are given to HIV-positive mothers and their infants to help reduce the risk of HIV transmission to the infant.
- PEP: Post-exposure prophylaxis is an HIV risk-reduction method in which someone who thinks they may have been exposed to HIV takes a short-course ARV regimen to reduce the risk of HIV infection.
- Evidence that low viral load in an HIV-positive individual decreases transmission rate to HIV-negative partners.

Current uses of ARVs in HIV-positive and -negative people

- HIV treatment
- Prevention of vertical transmission
- Post-exposure prophylaxis (PEP)

Strategies being researched in HIV-negative people

- Oral pre-exposure prophylaxis (PrEP)
- ARV-based microbicides

Emerging uses of ARVs as prevention in HIV-positive people

- Treatment as prevention and earlier initiation of treatment
- Testing and immediate treatment

What happened in FEM-PrEP?

- **The primary objective of FEM-PrEP was to assess the safety and effectiveness of once-daily Truvada to prevent HIV acquisition, among HIV-negative women, between the ages of 18 and 35, at risk of HIV through sexual intercourse.**
- **FEM-PrEP was an “event-driven” trial (scheduled to run until a pre-determined number of HIV infections had taken place – not until a specific date.**
- **FHI announced on April 18, 2011 that the trial was closing as it couldn’t demonstrate efficacy even if it continued.**

What is the bottom line message from the FEM-PrEP trial?

- **FEM-PrEP did not close because of any safety issues in the trial. If there had been, other trials using the same product might have also been halted or paused.**
- **It is inconclusive about why the trial did not show effectiveness. It is not clear whether this result is due to low adherence to the study product by women, whether TDF/FTC just does not prevent HIV in the trial populations where it was conducted, or whether TDF/FTC given in this regimen simply does not prevent HIV in women.**
- **Detailed analyses are needed to understand why this outcome was obtained.**

What is the bottom line message from the FEM-PrEP trial?

- **While the outcome of the trial – zero effectiveness – is clear, the reason for this outcome is unclear.**
- **There was no effectiveness after 56 infections had occurred. This represented 77 percent of the anticipated HIV infections. Continuing the trial to 72 endpoints in an attempt to demonstrate the effectiveness of TDF/FTC in preventing HIV was futile in these circumstances.**
- **In terms of clinical trials, futility means that a trial will not be able to answer the question or questions it set out to explore.**

- **The study, known as HPTN 052, was designed to evaluate whether immediate versus delayed use of ART by HIV-infected individuals would reduce transmission of HIV to their HIV-uninfected partners and potentially benefit the HIV-infected individual as well.**
- **The Data Safety Monitoring Board has concluded that initiation of ART by HIV-infected individuals substantially protected their HIV-uninfected sexual partners from acquiring HIV infection, with a 96 percent reduction in risk of HIV transmission.**

- **HPTN 052 is the first randomized clinical trial to show that treating an HIV-infected individual with ART can reduce the risk of sexual transmission of HIV to an uninfected partner.**
- **This rigorously conducted clinical trial demonstrates that ART dramatically reduces HIV transmission from an infected partner to an uninfected spouse or partner**
- **Strategies for scaling up knowledge of HIV status and increasing treatment coverage are critical next steps to realizing the public health benefits of this finding.**

- In iPrEx, daily TDF/FTC helped prevent HIV among HIV-negative gay and bisexual men when used PrEP with condoms and other HIV prevention methods.
- iPrEx evaluated one particular HIV drug as PrEP (TDF/FTC – *Truvada*). Other HIV drugs are being considered for oral PrEP, but there are no data on other oral agents.
- PrEP is not yet recommended for use. iPrEx showed that PrEP using TDF/FTC is safe and effective in gay men who were instructed to take the drug daily, received monthly HIV testing and ongoing monitoring for side effects and who received comprehensive HIV prevention services. There are risks including possible HIV drug resistance and side effects that can only be minimized through ongoing monitoring and testing.

- You can still get HIV when taking PrEP. iPrEx found that PrEP using TDF/FTC is only partially effective. If approved for use as an HIV prevention strategy, it should be used with – not instead of – condoms, safer sex practices and other HIV prevention methods.
- PrEP is not a “vaccine” or a “morning-after” pill. The strategy as studied involves ongoing pill-taking. In the trial, participants who reported taking the TDF/FTC pill consistently had the highest levels of protection.
- PrEP is not for everyone at risk of HIV. The iPrEx trial showed that the TDF/FTC pill was partially effective for some gay and bisexual men at high risk of HIV, who took the pill regularly, were counseled to reduce HIV risk behavior and were closely monitored.

- **CDC Interim Guidance (Released January 2011)**
- **Technical Assistance**
- **Monitoring and Evaluation**
- **Implementation Research**
- **Policy**
- **Communication**
- **Stakeholder Engagement**
- **Public Health Guidelines (Expected end of 2011)**

*CDC Does not plan to fund PrEP medications or clinical care

NASTAD continues to monitor the PrEP landscape ...

National PrEP working group, PrEP Fact Sheet, Issues for Consideration, and NASTAD bi-monthly update memo.

CDC Consultation(s)

Benefit Managers and Insurers

Moving forward with PrEP implementation for MSM in the US

Public Health Guidelines

Gilead Community Meetings

Community Education Needs

Fair Pricing Coalition

Pricing of Truvada for PrEP

- Do we have the capacity for PrEP implementation?
- Is PrEP even feasible?
- Will people take a pill consistently?
- What about drug resistance and HIV testing?
- What are the long-term safety issues?
- What about other populations?
- How much will it cost and who pays?
- What about PrEP in other prevention trials?
- Where do vaccines trials fit in this conversation?

Can we deliver on the promise?