World Health Organization

Preparing for PrEP implementation

Kevin R. O'Reilly

Prevention in the Health Sector, HIV/AIDS Department, WHO HQ

Outline

- **PrEP rationale**

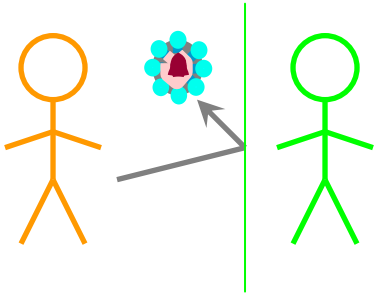
- Challenges ahead

World Health Organization

Why PrEP

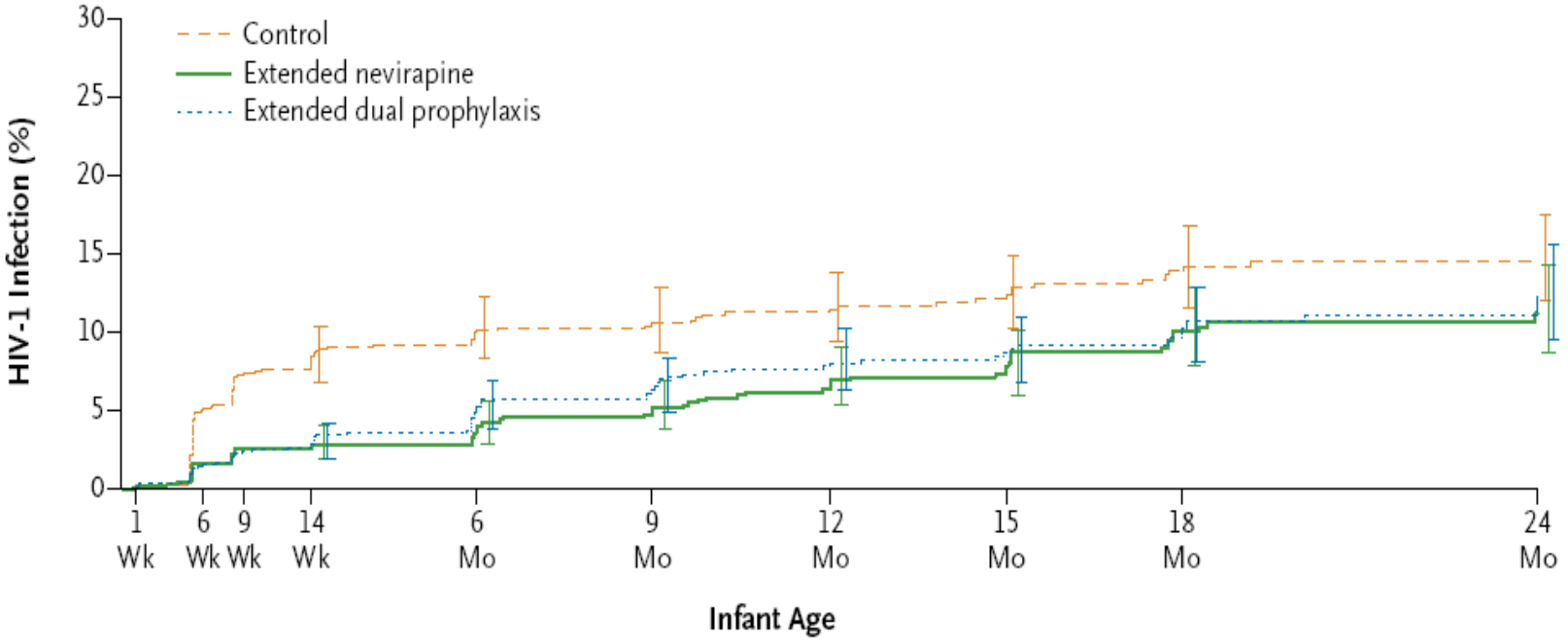
- In PrEP, an HIV uninfected individual takes antiretroviral medication(s) daily. By having these medications in the bloodstream, HIV may be unable to establish infection.

- Evidence that PrEP may work to prevent HIV
  - PMTCT
  - Animal studies
  - PEP
  - iPrex



World Health Organization

Pre- and post-exposure ART prevents vertical HIV transmission



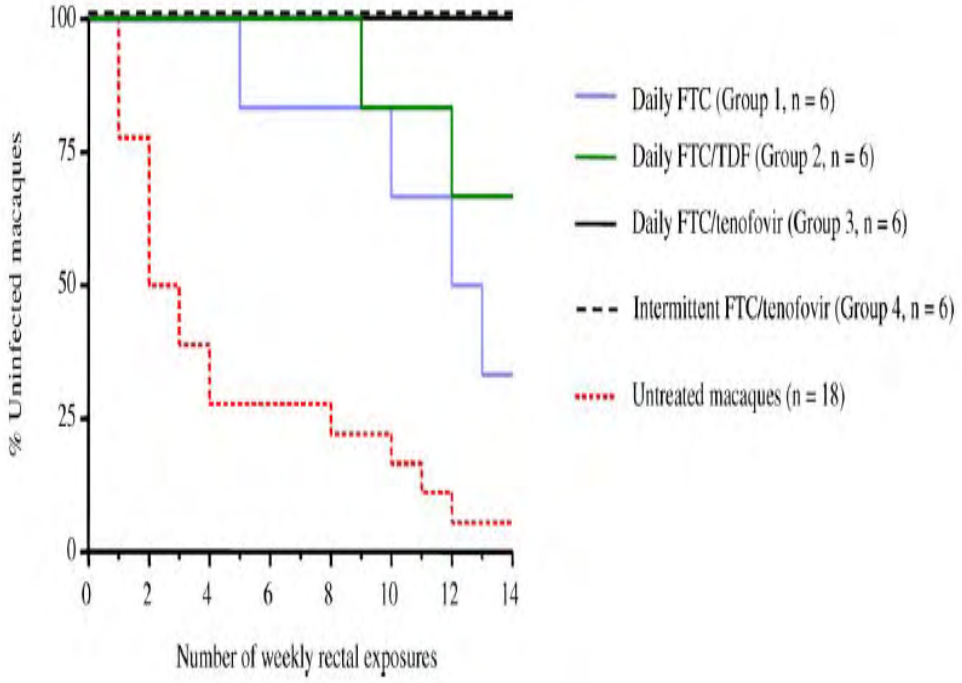
Prolonged nevirapine or nevirapine/zidovudine prophylaxis to breastfeeding infants from Malawi decreased postnatal HIV transmission by half

Kumwenda et al. NEJM 2008

World Health Organization

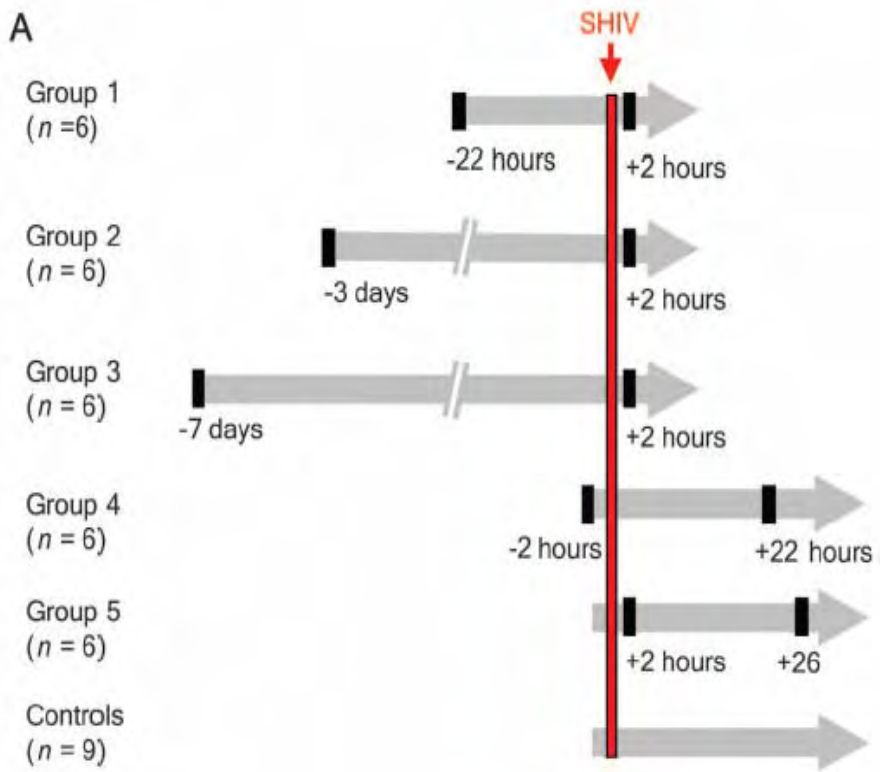
Preclinical Evaluation of Tenofovir (TDF) and TDF-Emtricitabine (FTC) (N=40)

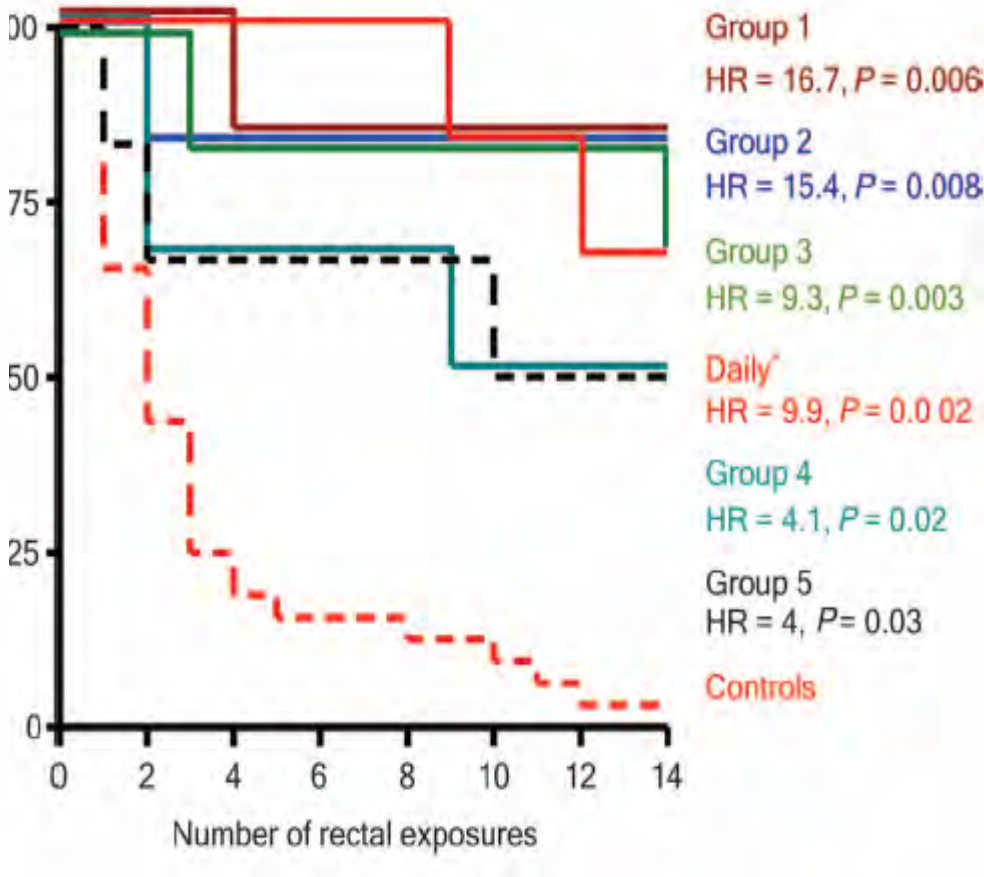
- Either FTC or TDF were protective
  - 70% to 100% Effective/expos
- Emtricitabine + Tenofovir
  - The combination was 100% effective
  - Even after repeated rectal exposures (14)
- The prophylactic activity probably reflects
  - Long intracellular half life
  - Activity in macrophages
  - High concentration in genital tissues



World Health Organization

Macaque data indicating Intermittent PrEP may be feasible





World Health Organization

Garcia-Lerma, Sci Trans Med 2010

Considerations re TDF & FTC/TDF for PrEP

POTENT:

- ✓ **Broad antiviral activity** (HIV-1 subtypes, HIV-1&-2)
- ✓ Active against virus types found both in early and late HIV infection (i.e., R5 & X4 viruses)
- ✓ Acts early in the life cycle of HIV (pre-integration) so it can **block initial infection**
- ✓ **Rapidly active** (suggesting even intermittent use might be possible)

SAFE:

- ✓ Favorable safety and tolerability
- ✓ High barrier to resistance, and limited cross-resistance

EASY:

- ✓ **Relative easy to use** (low pill burden, no food restrictions, no drug interactions with contraception/TB meds/antibiotics)

Evaluation of both TDF and FTC/TDF because of potential for different cost, resistance, and efficacy

World Health Organization

Outline

- PrEP rationale

- **Challenges ahead**

World Health Organization

Reality check

- Experience of moving from trials to implementation
  - Real world effectiveness is usually less than trial efficacy
  - implementation usually more complicated than planned
  - pace of scale-up usually much longer than expected
- Thorny issues to be addressed include
  - cost of daily PrEP (possibly greater than treatment for national budgets?)
  - motivation for daily PrEP (why would uninfected take it?)
  - experience with other daily prevention like OCs
  - political challenge of advocating scarce resources for socially marginalized groups
    - sex workers, MSM, IDU
    - readily available drug

Reality check: Setting the tone

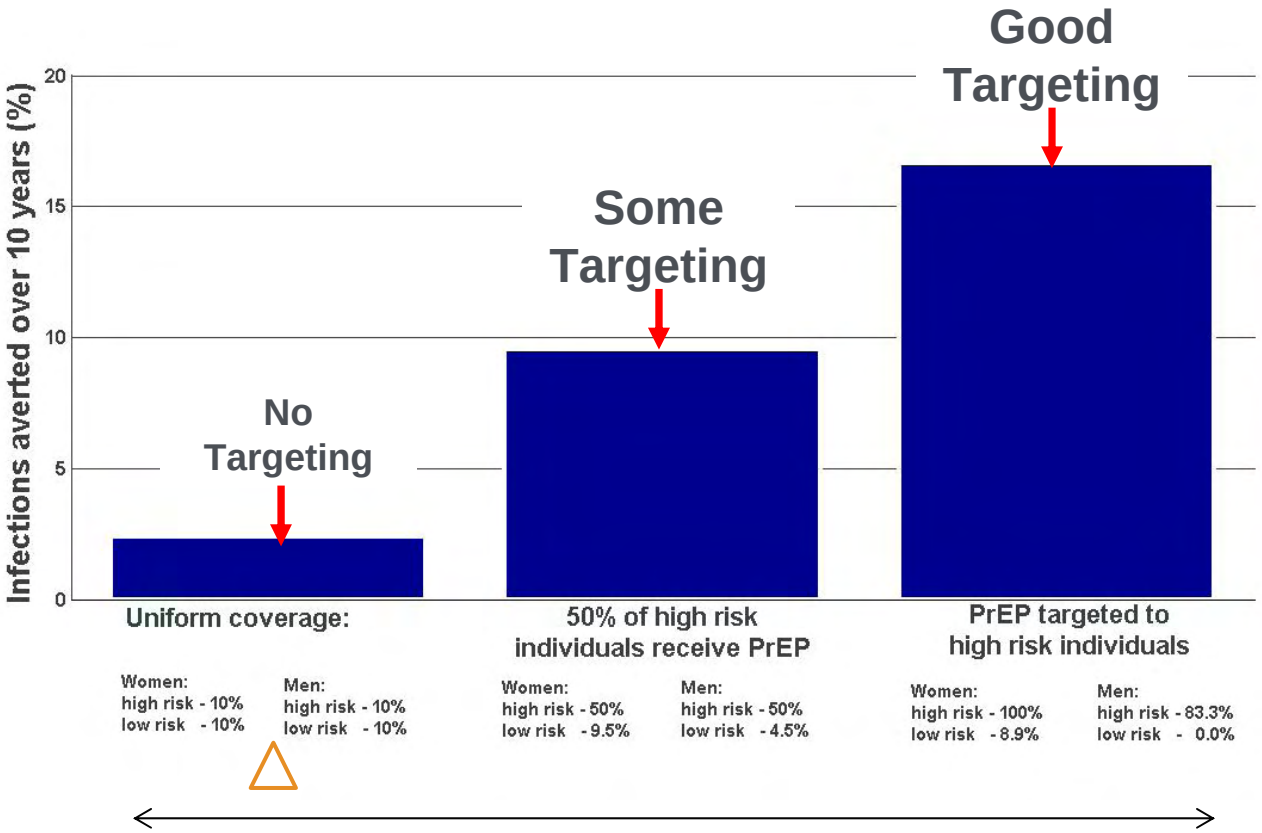
- PrEP will not be a ‘magic bullet’
  - PrEP integrated into current HIV prevention programs
- Regulatory approval and manufacturing capacity
- Potential for developing resistance
- Potential for adverse reactions
  - Renal dysfunction, hepatitis B flares
- Possibility of risk compensation or disinhibition
  - People on PrEP may have more sex, use condoms less

Challenges for PrEP implementation

- resistance, HIV testing & counselling, and re-testing
- resources constraints
- how best to provide PrEP, targeted or general distribution?

- Effective Targeting

For the same number of people staring PrEP, **effective targeting** to those at most risk can substantially amplify impact.



World Health Organization

Thank you !

World Health Organization