HIV Prevention Strategies
HIV Pre-exposure prophylaxis

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The findings and conclusions in this presentation are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention

HIV Prevention Research

- Behavioral Strategies
- Circumcision
- Antiretroviral therapy as prevention
- Vaccines
- Pre-exposure Prophylaxis (PrEP)
- Combination prevention strategies

Why Prevention Matters

- Safe and effective antiretroviral drugs (ARVs)
- Government, non-government, and philanthropic organizations making these drugs available
  - As of 2008, WHO estimates that 4 million on ARVs
- Still, 5.5 million remain untreated
- In 2007:
  - 1 million people were put on ARVs
  - 2.7 million more became infected
- Preventing new HIV infections key to controlling the HIV epidemic

This Presentation

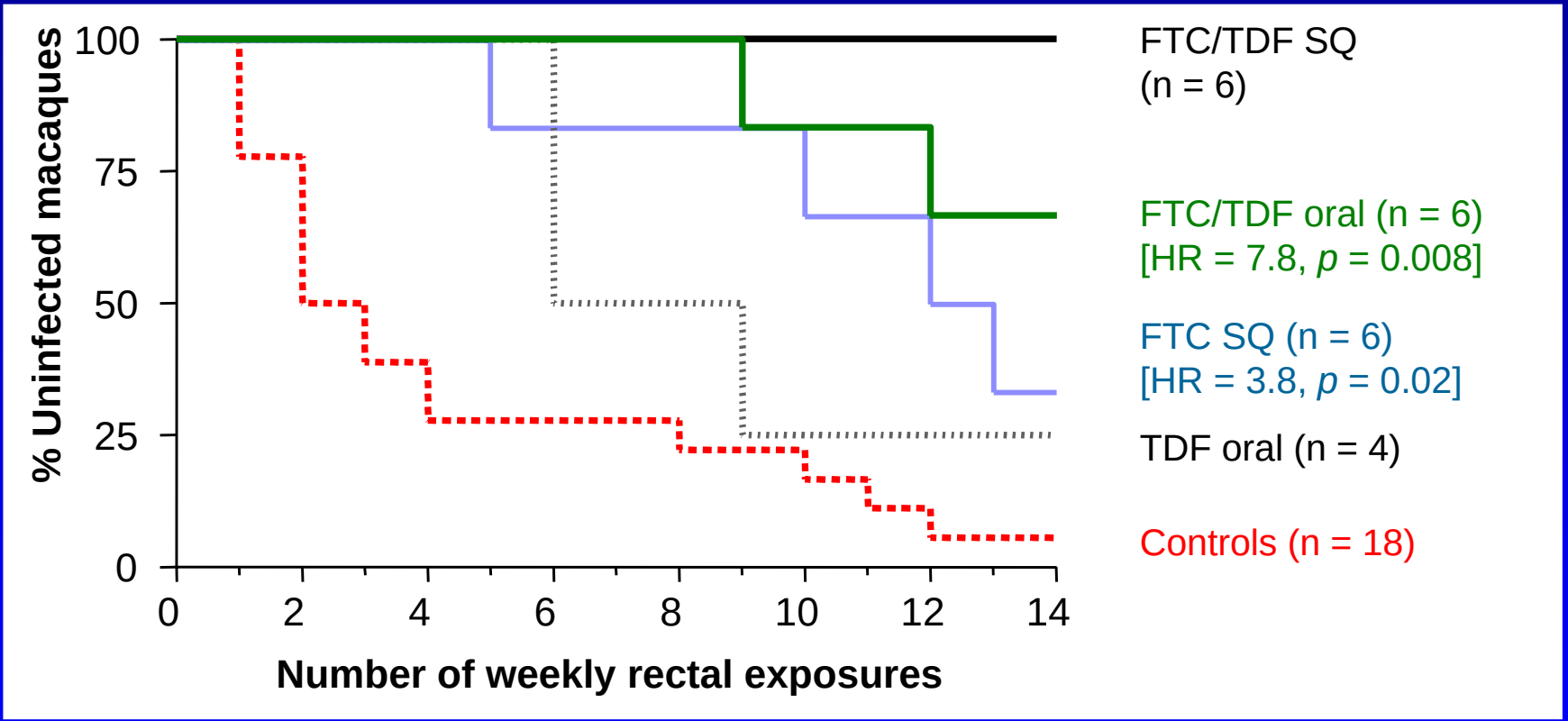
- Rationale for Pre-exposure Prophylaxis
- Describe completed and ongoing trials
- Summarize the populations and drugs
- Answers we should get from trials
- Next steps

Pre-exposure Prophylaxis (PrEP) Rationale

- Pre-exposure prophylaxis with ARVs might modify or prevent HIV infection
  - Malarial prophylaxis
  - ARVs used to prevent mother-to-child transmission
  - Post-exposure AZT 81% reduction in HIV infection
  - ARVs prevent/delay SHIV infection in macaques
- ARVs with long half-life allow once daily dosing
- Minimal drug-drug interactions
- Evidence from phase I/II/III trials: safe and effective for treatment of HIV

PrEP Macaque Studies

Macaques given weekly SHIV rectal challenges



García-Lerma et al. Prevention of Rectal SHIV Transmission in Macaques by Daily or Intermittent Prophylaxis with Emtricitabine and Tenofovir. *PLoS Med.* 2008 February; 5(2): e28.

Subbarao et al. Chemoprophylaxis with tenofovir disoproxil fumarate provided partial protection against infection with simian human immunodeficiency virus in macaques given multiple virus challenges. J Infect Dis. 2006 Oct 1;194(7):904-11.

Pre-exposure Prophylaxis Trials

Study	Site	Drug	Population
West Africa TDF Trial	Ghana, Cameroon, Nigeria	Tenofovir	936 women
US Extended Safety Trial	United States	Tenofovir	400 MSM
Bangkok Tenofovir Study	Thailand	Tenofovir	2400 injecting drug users
Botswana TDF2	Botswana	Truvada	1200 heterosexual men and women
Partners PrEP	Kenya, Uganda	Tenofovir, Truvada	3900 serodiscordant heterosexual couples
CAPRISA 004	South Africa	Topical tenofovir	1200 women
iPrEx	Brazil, Ecuador, Peru, South Africa, Thailand, US	Truvada	3000 MSM
Fem-PrEP	Kenya, Malawi, South Africa, Tanzania	Truvada	3900 women
VOICE (MTN 003)	South Africa, Uganda, Zambia, Zimbabwe	Tenofovir, Truvada, topical tenofovir	5000 women

Truvada = tenofovir-emtricitabine

West Africa TDF Trial

- Phase II randomized, double blind, placebo controlled trial of daily tenofovir
- Supported by Gates Foundation and FHI
- Women (n=936) in Ghana, Cameroon, Nigeria
- Conducted June 2004 - March 2006
- Study stopped prematurely in Cameroon and Nigeria

Peterson et al. Tenofovir Disoproxil Fumarate for Prevention of HIV infection in women. PLoS Clin Trials 2(5): e27.

West Africa TDF Trial Results

- No differences (placebo/tenofovir) in clinical or laboratory safety outcomes
- No evidence of risk compensation
- Inadequate power to assess efficacy
  - 8 HIV seroconversions: 2 Tenofovir, 6 placebo
  - Rate ratio = 0.35 (95% CI = 0.03-1.93)

Peterson et al. Tenofovir Disoproxil Fumarate for Prevention of HIV infection in women. PLoS Clin Trials 2(5): e27.

US Tenofovir Extended Safety Trial

- Collaboration of CDC, San Francisco Department of Public Health, AIDS Research Consortium of Atlanta, and Fenway Health in Boston
- Population: 400 MSM
- Objectives:
  - Evaluate safety and tolerability of daily tenofovir
  - Evaluate risk behaviors

US Extended Tenofovir Safety Trial

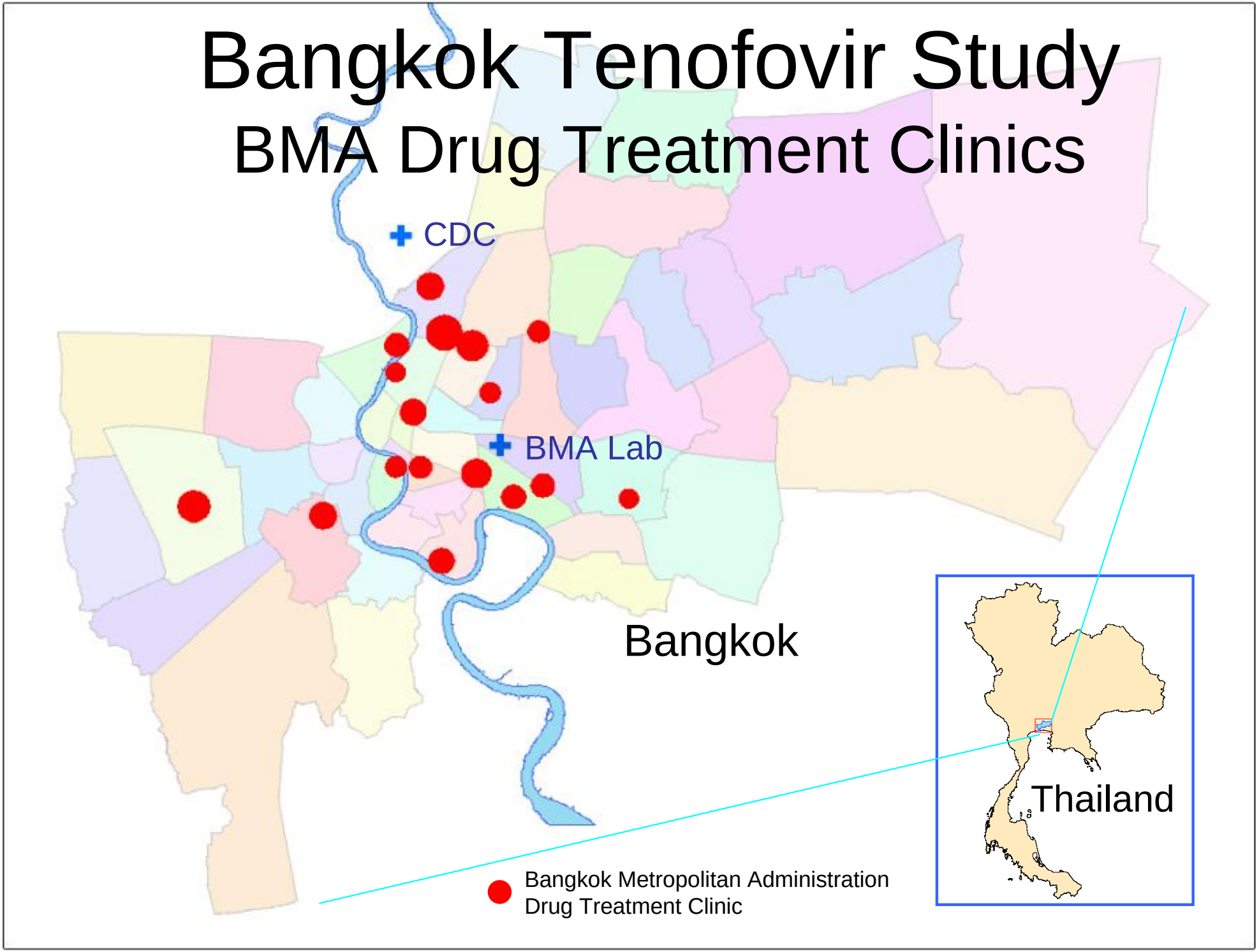
- Design:
  - Randomized, double-blind, placebo-controlled
  - Daily oral tenofovir vs. placebo
  - To compare risk behaviors of those taking a daily pill to those not taking pills, randomized to 4 arms
    - 2 arms receive either tenofovir or placebo immediately
    - 2 arms receive either tenofovir or placebo after nine months
- Status: Enrollment and follow-up complete, cleaning data, results expected early 2010

Bangkok Tenofovir Study

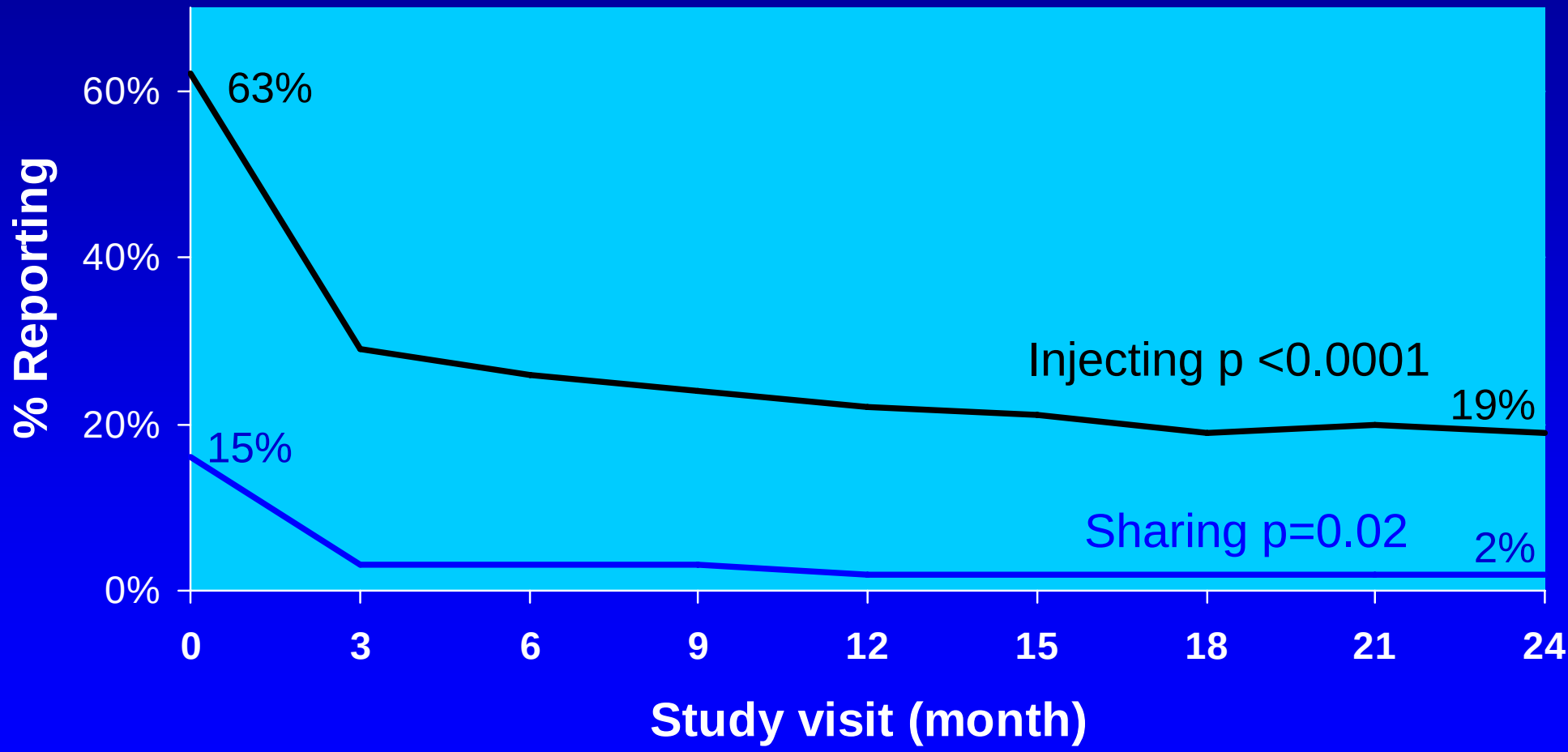
- Sponsor: CDC in collaboration with Bangkok Metropolitan Administration, Thailand MOPH
- Population: 2400 injecting drug users
- Objectives
  - Determine if tenofovir prevents HIV infection
  - Determine if tenofovir is safe
- Design
  - Randomized, double-blind, placebo-controlled study
  - Daily oral tenofovir vs. placebo

Bangkok Tenofovir Study

BMA Drug Treatment Clinics



Injecting and Needle Sharing by BTS Participants Completing 24 Months (n=1227)



Bangkok Tenofovir Study

- Bangkok Tenofovir Study launched in June 2005
- Trial 97% enrolled
- DSMB safety reviews in 2006, 2007, 2008, and 2009 recommended continuation
- Expect to complete follow-up 2010

Botswana TDF2 Truvada Trial

- Sponsor: CDC and Government of Botswana
- Population: 1,200 HIV-negative heterosexual men and women, ages 18 to 39, Gaborone and Francistown
- Objectives
  - Determine if truvada prevents HIV infection
  - Determine if truvada is safe
- Design
  - Randomized, double-blind, placebo-controlled trial
  - Daily oral truvada vs. placebo

Botswana TDF2 Truvada Trial

- Trial launched using Tenofovir 2005
- Enrollment stopped March 2006 (N=71)
- Re-launched 2007 with Truvada
- Status: 98% enrolled; expected completion late 2010

Partners PrEP Study

- Management and funding:
  - U of Washington and collaborators at 9 sites: Kenya and Uganda
  - CDC and TASO, a Ugandan NGO, co-manage 2 sites
  - Funded by the Gates Foundation
- Objective
  - Determine safety and efficacy of once-daily tenofovir and truvada
- Population: 3,900 heterosexual sero-discordant couples in Kenya and Uganda
- Design
  - Randomized, double-blind, placebo-controlled study
  - HIV-uninfected partners are assigned to one of three groups: Tenofovir, Truvada, or Placebo

Partners PrEP Study

3900 HIV-discordant couples

Randomized HIV- Partner

Tenofovir

Truvada

Placebo

Follow couples for 36 months

CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

CAPRISA IS A UNAIDS COLLABORATING CENTRE FOR HIV PREVENTION RESEARCH

CAPRISA 004 Tenofovir Gel Trial

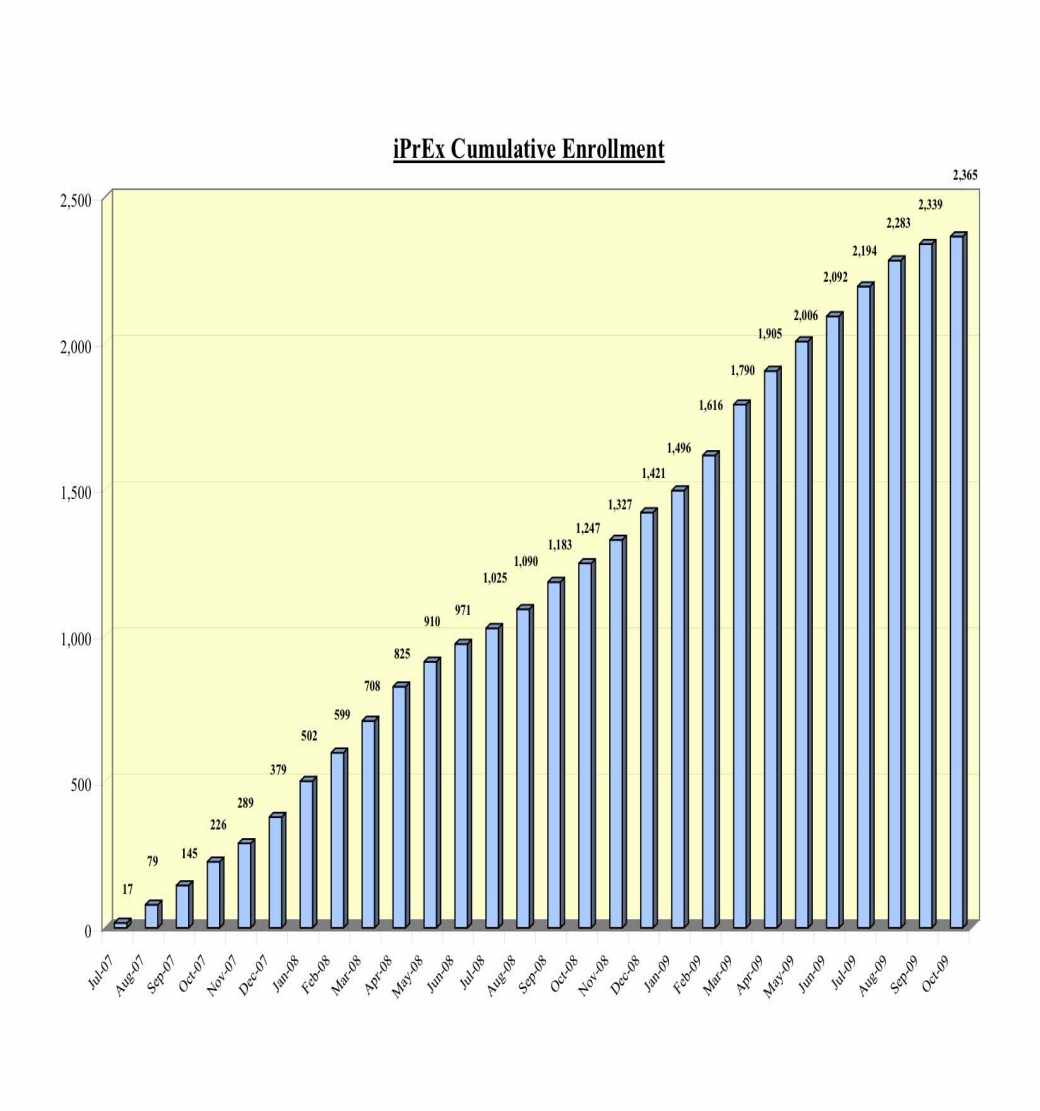
- Sponsor: CAPRISA, Conrad, FHI, LIFElab, USAID
- Population: 980 women in South Africa
- Objective: assess safety and effectiveness of 1% Tenofovir microbicide gel
- Design
  - Phase IIb, randomized, double-blind, placebo-controlled trial
  - 1% tenofovir gel vs placebo used 12 hours before and as soon as possible after intercourse
- Status: Began May 2007, enrollment complete, results expected 2010

iPrEx Truvada Trial

- Sponsor: US NIH, BMGF
- Population: 3000 MSM in Peru, Ecuador, US, South Africa, Brazil, Thailand
- Objective: Determine safety and efficacy of once-daily Truvada
- Design
  - Randomized, double-blind, placebo-controlled study
  - Daily Truvada vs Placebo

iPrEx Truvada Trial

- Launched June 2007
- 78% enrolled
- Results 2010



Fem-PrEP

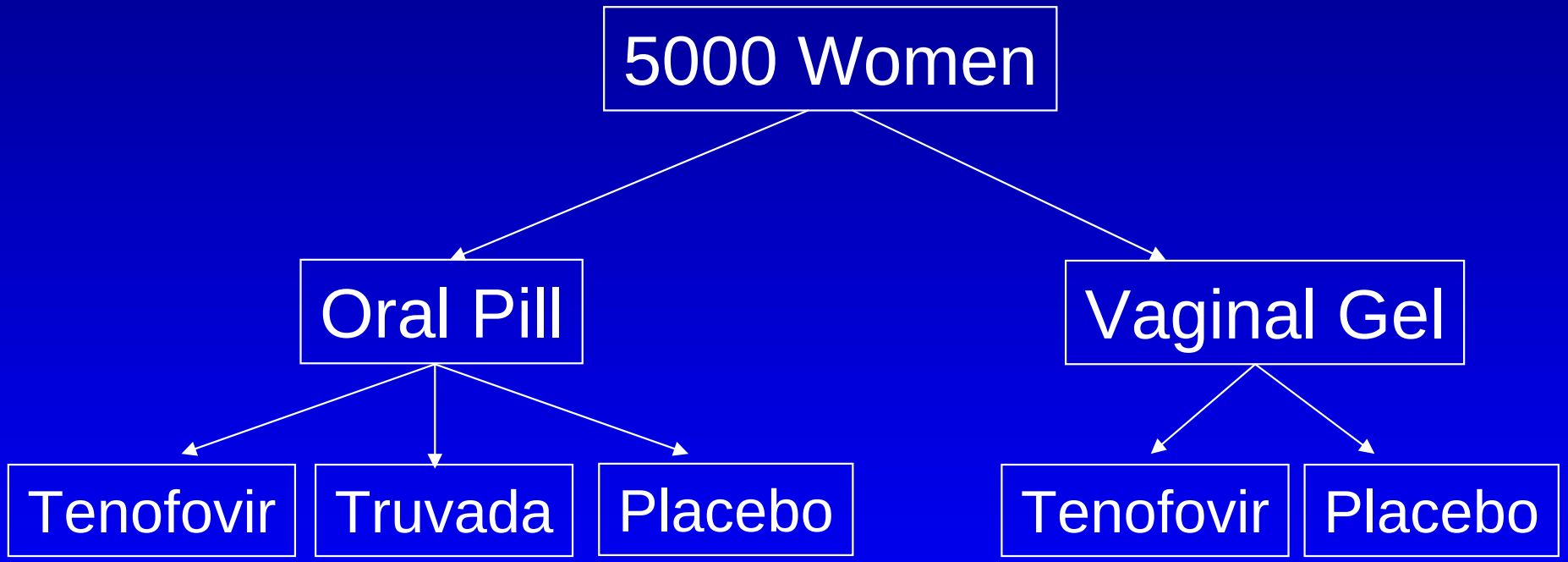
- Sponsor: FHI, USAID, BMGF
- Objective
  - Determine safety and efficacy of once-daily truvada
- Population: 3,900 HIV-negative women (ages 18 to 35 years) in Kenya, Malawi, South Africa, Tanzania
- Design
  - Randomized, double-blind, placebo-controlled study
  - Daily Truvada vs Placebo
- Status: Enrolling May 2009, expected to complete 2012

VOICE (MTN 003)

- Sponsor: Conducted by Microbicide Trials Network with funding from NIH
- Population: 5000 women in Uganda, South Africa, Zambia, Zimbabwe, (Malawi)
- Objective: Determine safety and efficacy of once-daily oral Tenofovir, oral Truvada, and Topical Tenofovir
- Design
  - Randomized, double-blind, placebo-controlled study
  - Daily oral Tenofovir vs oral Truvada vs Placebo
  - Once daily topical 1% Tenofovir gel vs Placebo
- Status: began Sept 2009, enrolling, expect to complete 2013

VOICE
VAGINAL + ORAL INTERVENTIONS TO CONTROL THE EPIDEMIC

VOICE (MTN 003)



VOICE
VAGINAL + ORAL INTERVENTIONS
TO CONTROL THE EPIDEMIC

Summary of PrEP Efficacy Trials

Risk group	Participants	Drugs tested
IDUs	2400	Tenofovir
Heterosexual men and women	3150	Tenofovir, Truvada
Women	9880	Tenofovir gel, Truvada, Tenofovir
MSM	3000	Truvada

Possible Outcomes of PrEP Trials

- The unexpected
- High efficacy in all populations
- Low efficacy in all populations
- Mixed results with safety issues

Additional Research Needed

- If daily PrEP works, what about intermittant PrEP? Exposure driven?
- More effective ARVs and combinations
- Other ARV formulations: patches, injectables

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