AVAC

Global Advocacy for HIV Prevention

The State of PrEP Research and Preparedness

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Implications of new NPT research and development for people living with HIV
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Today's overview

- Reasonable to prepare for PrEP efficacy
- Ongoing PrEP research and timeline
- Remaining questions after trials
- PrEP challenges
- PrEP advantages
- What can advocates do to prepare for PrEP?

Comprehensive ARV Agenda

- Current uses of ARVs in HIV-positive and -negative people (treatment; vertical transmission; PEP)
- Strategies being researched (Oral pre-exposure prophylaxis (PrEP); ARV-based microbicides)
- Emerging uses of ARVs as prevention in HIV positive people (Tx as Px and earlier initiation of treatment; testing and immediate treatment)

What is PrEP

- **Pre-exposure prophylaxis (PrEP):** An experimental strategy using antiretrovirals to reduce the risk of HIV infection in HIV-negative people

(Can be local or systemic, various delivery systems—gels, rings, tablets, injection)

Reasonable to prepare for efficacy

- PrEP is biologically plausible
- There are concentrated levels of drugs in genital tract secretions
- ARVs work for *post*-exposure prophylaxis
- PrEP works in animal models
- PrEP proved safe in trial
- PrEP works for vertical transmission, malaria and AIDS OIs

Ongoing PrEP research

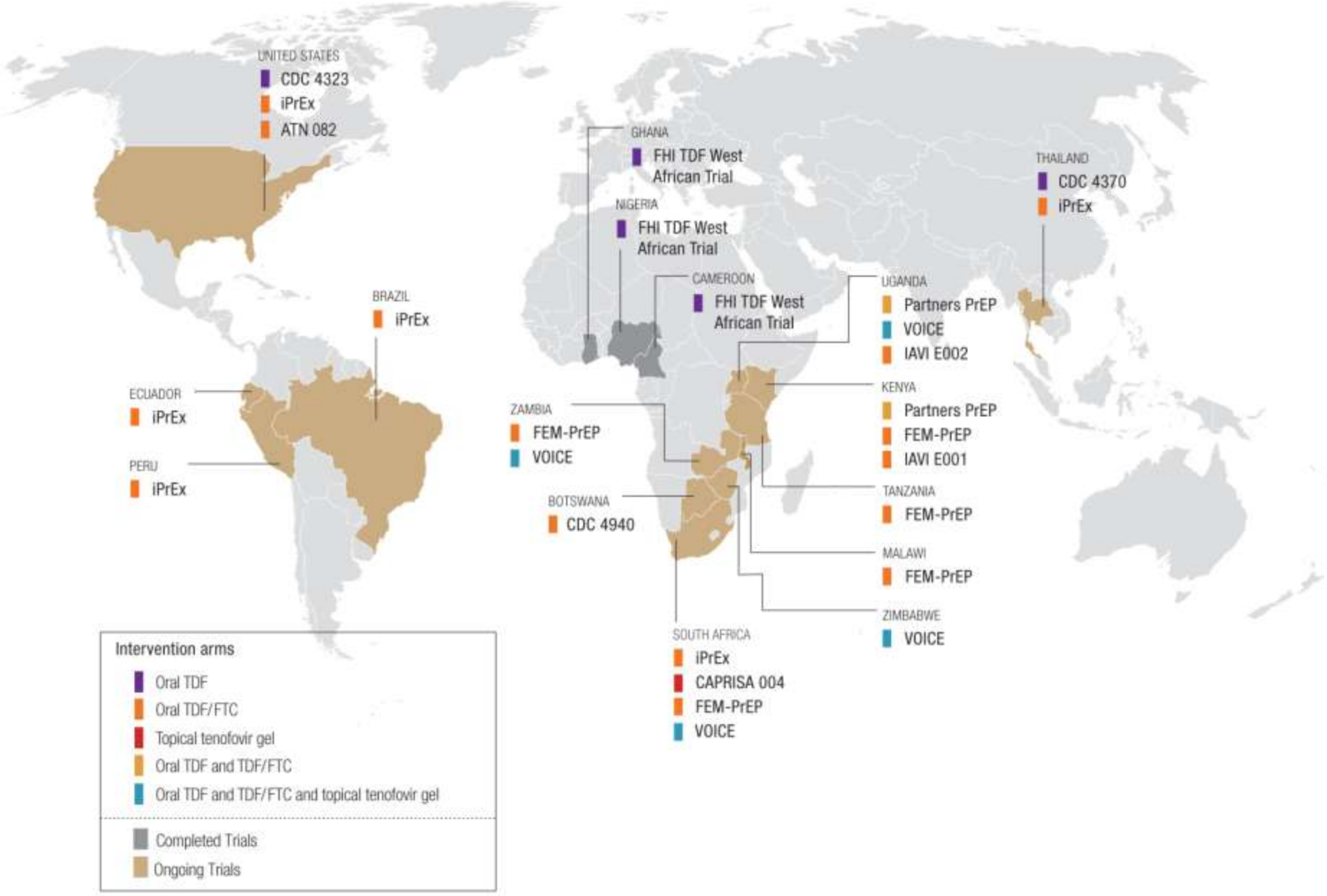
- Current oral PrEP effectiveness trials are testing:
  - *Tenofovir disoproxil fumarate* (TDF) *(Viread)*
  - A combination of TDF plus *emtricitabine (TDF/FTC) (Truvada)*
  - Once daily
- Trials also testing tenofovir (TFV) gel as a microbicide
- Nearly 20,000 people taking part in current PrEP trials

PrEP Pipeline: Less frequently used classes and new drugs:(maraviroc, dapivirine, UC781 and TMC 278LA) might help minimize the risk of resistance or a “collision” of prevention and treatment options.)

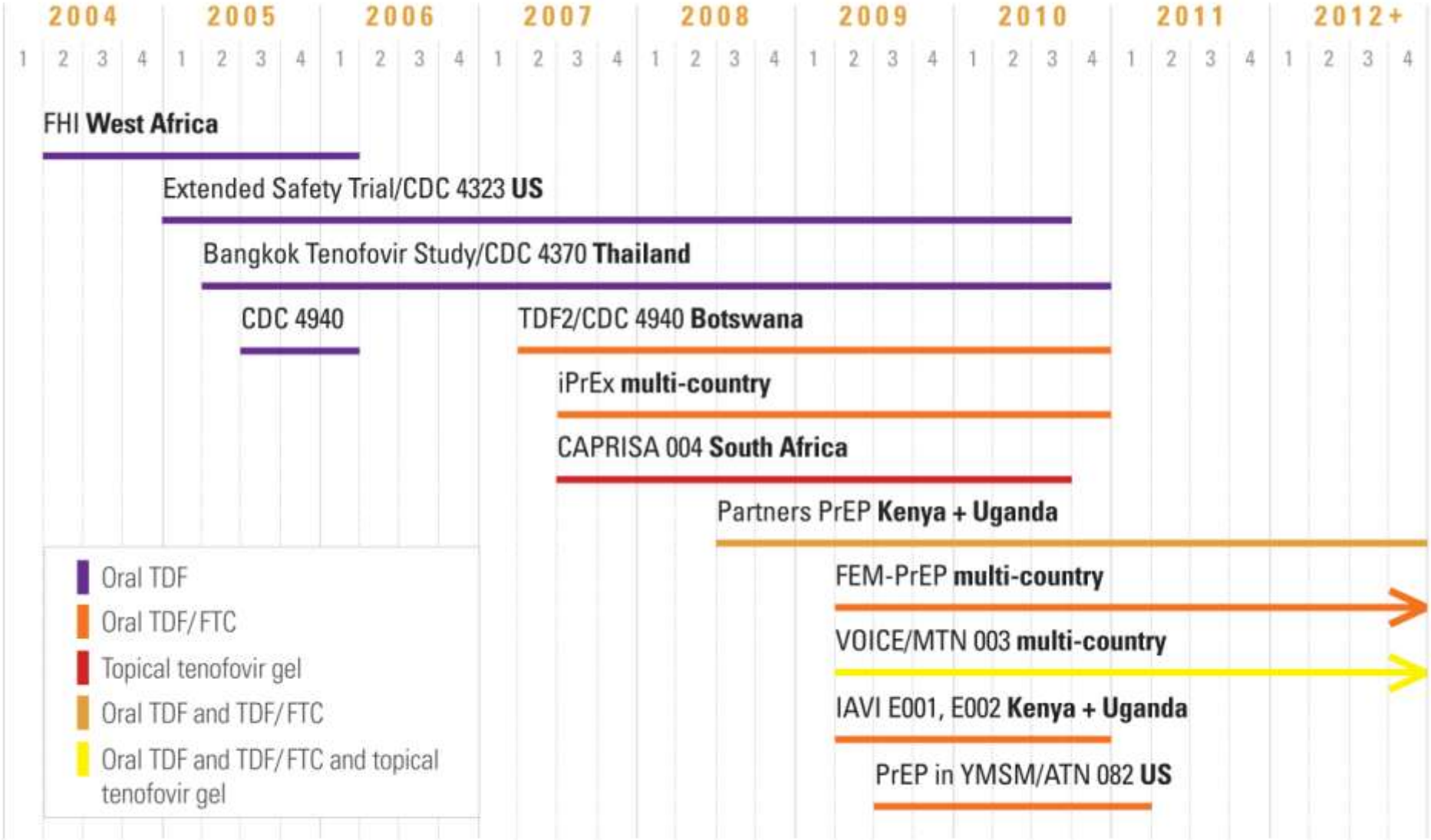
PrEP Timeline

- Look at *Px Wire*

Ongoing PrEP Trials (December 2009)



Timeline for Ongoing PrEP Trials (March 2010)



* The trial end-dates listed in this table are estimates. Due to the nature of clinical trials the actual dates may change. AVAC will continue to monitor trial progress and will update the timeline accordingly. To view or download an updated timeline visit *www.prepwatch.org*.

Ongoing and Planned ARV-based Prevention (Oral PrEP and Topical Microbicide) Trials (March 2010)

Study; Study phase	Location	Sponsor; Funder	Population (*mode of exposure*)	Intervention arm(s)	Status/ Results expected
US Extended Safety Trial (CDC 4323) Phase II, safety	United States	CDC	400 gay men and other men who have sex with men (*penile/rectal*)	Daily oral TDF	Completed / Q3 2010
Bangkok Tenofovir Study (CDC 4370) Phase II/III, safety and efficacy	Thailand	CDC	2,400 injecting drug users (*parenteral*)	Daily oral TDF	Enrolling / Q4 2010
CAPRISA 004 Phase II, safety and effectiveness	South Africa	CAPRISA, FHI, CONRAD, USAID, LIFElab	900 heterosexual women *(vaginal)*	Coitally dependent topical tenofovir gel	Completed / Q3 2010
iPrEx Phase III, safety and efficacy	Brazil, Ecuador, Peru, South Africa, Thailand, US	NIH, BMGF	2,499 gay men and other men who have sex with men *(penile/rectal)*	Daily oral TDF/FTC	Fully enrolled / Q4 2010
TDF2 (CDC 4940) *Phase II, safety and adherence*	Botswana	CDC	1,200 heterosexual men and women *(penile and vaginal)*	Daily oral TDF/FTC; *switched from TDF Q1 2007*	Fully enrolled / Q4 2010
Partners PrEP Phase III, safety and efficacy	Kenya, Uganda	BMGF	4,700 serodiscordant heterosexual couples (*penile and vaginal*)	Daily oral TDF; daily oral TDF/FTC	Enrolling / 2012
FEM-PrEP Phase III, safety and effectiveness	Kenya, Malawi, South Africa, Tanzania, Zambia	FHI, USAID, BMGF	3,900 heterosexual women *(vaginal)*	Daily oral TDF/FTC	Enrolling / 2013
VOICE (MTN 003) Phase IIb, safety and effectiveness	South Africa, Uganda, Zambia, Zimbabwe	MTN, NIH	4,200 heterosexual women (*vaginal)*	Daily oral TDF; daily oral TDF/FTC; daily topical tenofovir gel	Enrolling / 2013
IAVI E001 & E002 Phase I/II, safety, acceptability, adherence	Kenya, Uganda	IAVI	150 serodiscordant couples and men and women *(vaginal and penile/rectal)*	Daily oral TDF/FTC; intermittent oral TDF/FTC (twice weekly + coital dosing)	Fully enrolled / Q4 2010
PrEP in YMSM (ATN 082) Phase II, safety, acceptability, feasibility	United States	ATN, NICHD	99 young men who have sex with men (YMSM) *(penile/rectal)*	Daily oral TDF/FTC	Enrolling / 2011
PrEP Using TMC278LA Phase I/II, safety and pharmacokinetics	United Kingdom	St. Stephens AIDS Trust	100 men and women (*vaginal and penile/rectal*)	TMC278LA injected intramuscularly	Enrolling / 2011

ATN – Adolescent Trial Network; BMGF – Bill & Melinda Gates Foundation; CAPRISA – Centre for the AIDS Programme of Research in South Africa; CDC – US Centers for Disease Control and Prevention; FHI – Family Health International; FTC – emtricitabine; IAVI – International AIDS Vaccine Initiative; MTN – Microbicide Trials Network; NICHD – National Institute of Child Health and Human Development; NIH – US National Institutes of Health; Q1-4 – quarters 1-4; TDF – tenofovir disoproxil fumarate; USAID – United States Agency for International Development

Remaining Q's after current trials

- Are there dosing strategies other than ongoing, once-daily dosing that could be used with oral PrEP drugs to reduce risk?
- Can PrEP strategies be developed for adolescents and pregnant women—two groups not included in current effectiveness trials?
- Can other compounds be developed for potential PrEP drugs?
- What are the long-term safety consequences of PrEP use?
- What are the rates of drug resistance associated with individuals using PrEP who seroconvert?
- How does this impact future treatment options?

PrEP Challenges

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PrEP Challenges

- **Target population:** discordant couples, MSM, sex workers, etc.
- **HIV testing:** health system burden, human rights concerns
- **Adherence:** daily, iPrEP, pre- or post-coital, varies in trials
- **Drug resistance:** circulating resistance decreases PrEP, development of drug resistance, requires rigorous testing
- **Risk compensation:** depends on effectiveness, increased or decreased condom use, useful in couples trying to conceive, pleasure
- **Costs (effectiveness and who pays?):** Depends on effectiveness, target small but highly exposed, monitor adverse events and extent of risk compensation
- **Ethics:** Competing resources with treatment, overburdened health systems, toxicity and resistance, “saving” PrEP drugs for prevention only

PrEP advantages

- Gender neutral
- Covert use is feasible
- Coitally independent
- May work for more than one type of exposure (e.g., IDUs who also have sex)
- Already approved drugs
- Can stop during low risk periods
- Periodic risk-reduction counseling and HIV testing
- Opportunity to link to preventive care
- Increase health system capacity
- Pleasure

PrEP program assumptions (US)

CDC will issue recommendations based on trial results;

All PrEP programs will include:

- Screening: HIV negative with ongoing risk of acquisition
- No contraindication to meds (lab tests)
- Visits 3-6 months
  - HIV rapid test
  - Assess side effects and adherence
  - Risk reduction counseling
  - Med refill
  - Periodic assessment of ongoing risk and safety labs
- Consider public sector provision of PrEP
  - Un/underinsured
  - Health departments (STD, family planning, community health clinics)

What can advocates do

Advocate for:

- Studies on feasibility are needed now
- Address concerns around ethics of access and feasibility of rollout
- Address concerns around risk compensation
- Drug procurement and distribution strategies
- Address issues of and ongoing voluntary counseling and testing
- Clinical monitoring and adverse event follow-up
- Behavioral monitoring
- For seroconverters, viral resistance testing and access to second-line therapy, if needed
- Usage guidelines
- Communications strategies
- Ensure a robust pipeline of approved and experimental compounds

What is AVAC doing?

And need to do more of?

- Building PrEP literacy (challenges and advantages)
- Creating platforms for debates and discussion
- PrEP think tanks (intermittent PrEP; financing; European PrEP)
- Px ROAR (US)
- National Stakeholder Engagement (Kenya, South Africa, Uganda, US)
- WHiPT (Kenya, Uganda, South Africa, Namibia, Swaziland)
- Prevention Research Advocacy Fellows

Get involved in PrEP/AVAC

- *PrEP Primer* and www.prepwatch.com
- *Vienna Px Research Roadmap*
  - Satellite session on Sunday, 18 July, 15:45–17:45: mini room 6: *The Promise and Perils of ARV-based Prevention: Making it a reality on the ground*
- Advocacy Fellows – deadline 19 July
- *Px Wire*
- *AVAC Report 2010: Turning the Page*
- Advocates' Network
- *www.avac.org*