

Antiretroviral Prophylaxis:

**Point of convergence in the scientific agendas
for pre- and post-exposure prophylaxis,
microbicides & perinatal HIV prevention**

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Outline

- **Why the interest in PrEP...**
- **Why tenofovir?**
- **PrEP Trials**
 - **Active PrEP trials**
 - **Planned PrEP trials**
 - **Completed or halted PrEP trials**
- **Common challenges in antiretroviral prophylaxis**
- **Conclusion**

Introduction

- **Pre-exposure prophylaxis (PrEP) refers to an experimental HIV-prevention strategy that uses antiretrovirals (ARVs) to protect HIV-negative people from HIV infection**
- **PrEP for HIV prevention builds on the concept that medications can be used by healthy people to prevent certain infections, e.g. chloroquine by travelers to prevent malaria. INH prophylaxis to prevent TB**

Why the interest in PrEP....

- **Biological plausibility**
- **Numerous animal challenge since since 1995 show protection**
- **Success of post-exposure prophylaxis for needlestick exposure in observational data**
- **pMTCT: Proof of concept in humans**

Potential impact of PrEP

- **Mathematical modeling suggests substantial potential public health benefit of PrEP**
 - PrEP with 90% effectiveness and 75% coverage of the general population could lead to a 74% decline in cumulative HIV infections in 10 years.
 - Even with a 100% increase in at-risk behavior (disinhibition), there is still a beneficial effect (HIV reduced by 23%–63%)
 - 2.7 to 3.2 million new HIV infections could be averted in southern Africa in 10 years by targeting PrEP (if 90% effective) to those at highest behavioral risk

Source: Abbas UL, PLoS ONE 2(9): e875. doi:10.1371/journal.pone.0000875

Why Tenofovir for PrEP?

- **Effective therapeutic agent**
- **Very good safety profile**
- **Shows protection in over 20 macaque challenge studies**
- **Long half life**

Tenofovir as PrEP

- **Tenofovir (gel or oral) rapidly absorbed and detectable in genital tissues within 15 minutes after single dose**
- **Peak tissue concentrations reached by 2-4 hours, remain high well beyond 24 hours**
- **Plasma half-life is 17 hours**
- **Intracellular half-life is more than 170 hours**
- **Even a single pre-challenge dose of tenofovir, singly or in combination with FTC, is protective in monkeys**

Active trials: ARVs for prevention

- PrEP for IDU: CDC Thai – **tenofovir pill**
- PrEP for heterosexual transmission in women: CAPRISA 004 – **tenofovir gel**
- PrEP for heterosexual transmission in men & women: CDC Botswana – **truvada pill**
- PrEP for MSM: NIH-iPREX – Andean/US/SA – **truvada pill**

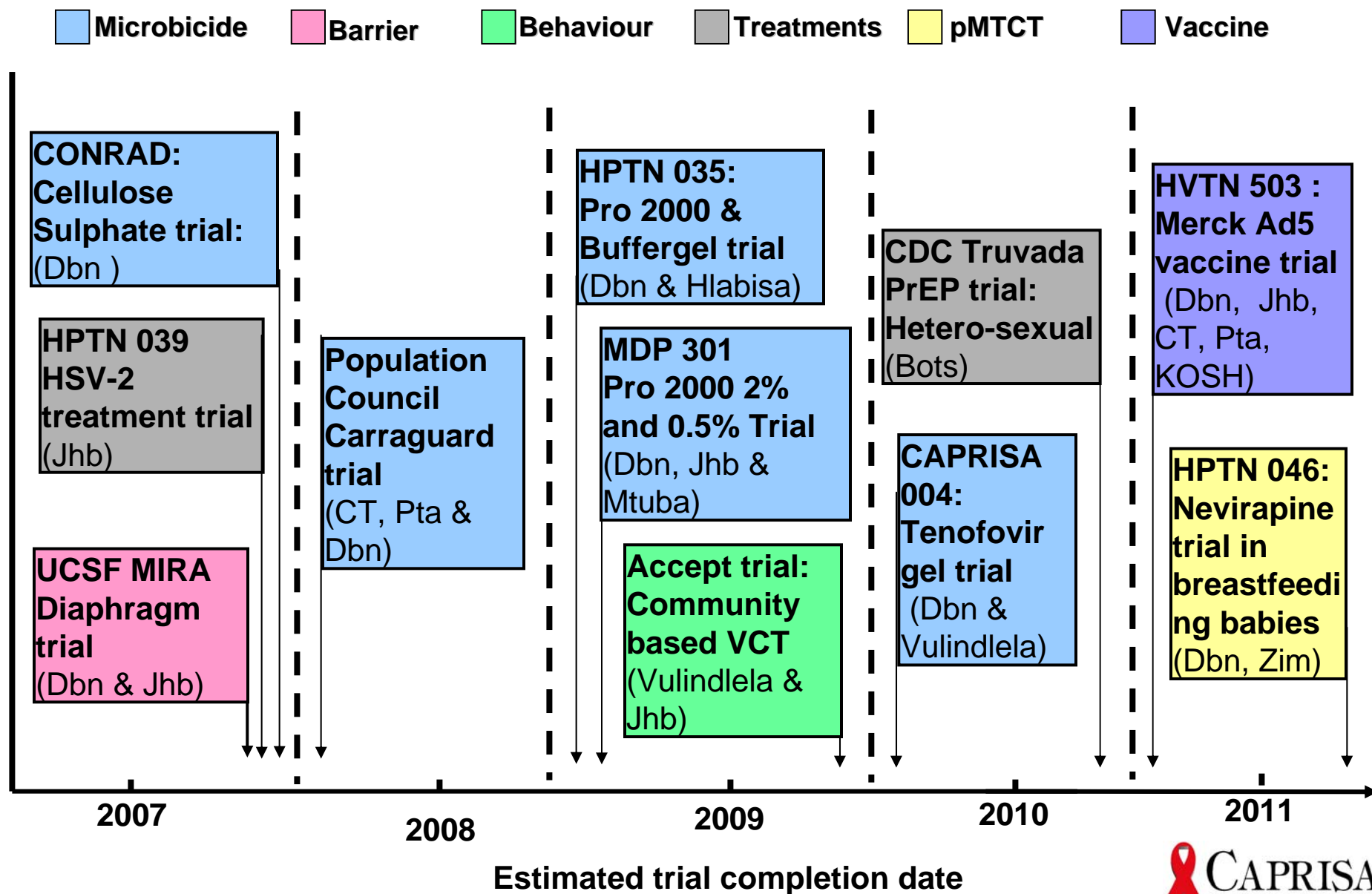
Planned trials: ARVs for prevention

- PrEP for heterosexual transmission in women: MTN 003 - VOICE – **tenofovir gel, truvada pill & tenofovir pill**
- PrEP for heterosexual transmission in women: IPM 009 – **dipavirine gel & ring**
- PrEP for heterosexual transmission in women: FHI FemPrep – **truvada pill**
- PrEP for discordant couples: Partners in prevention – **truvada pill**

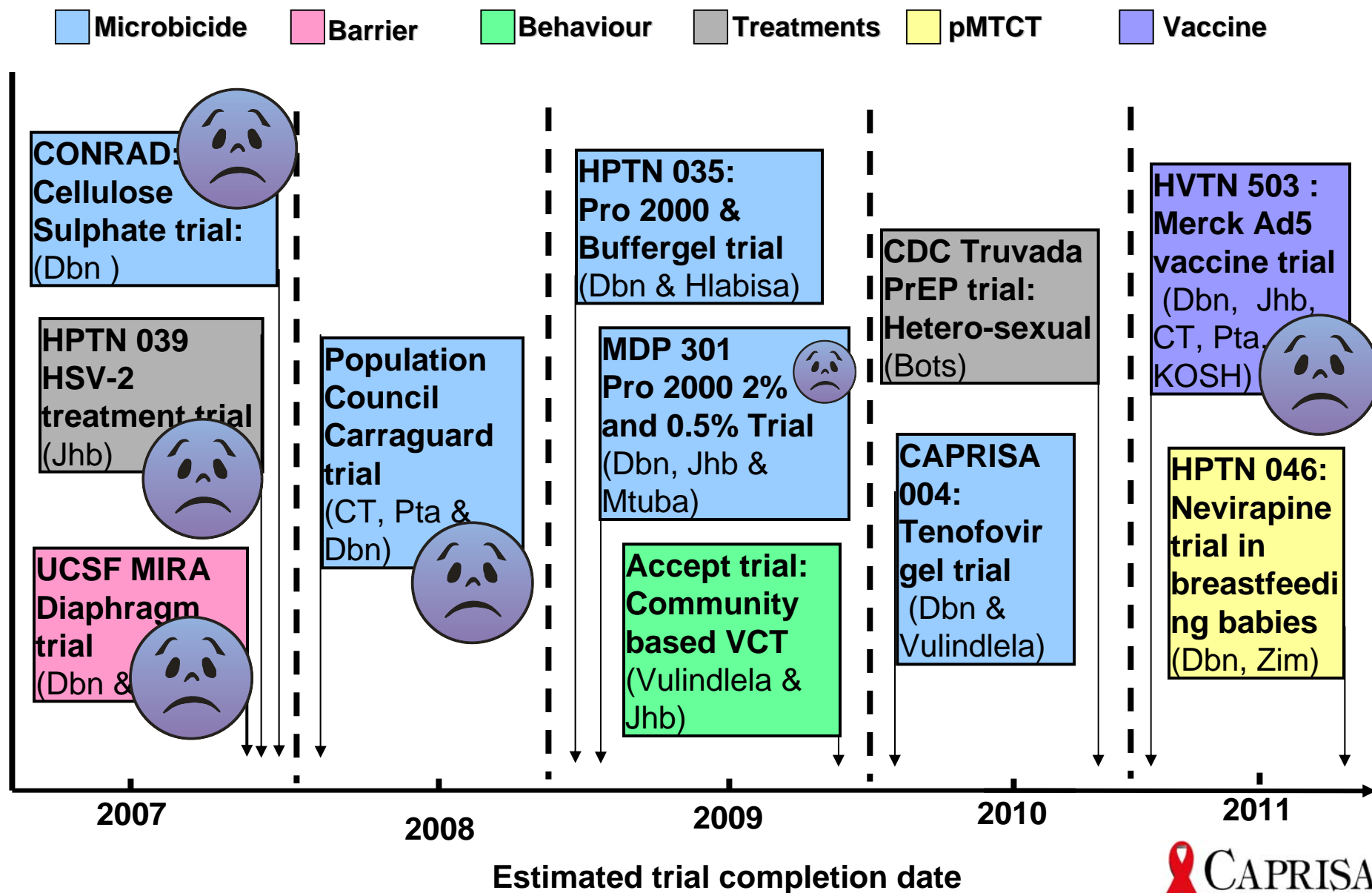
Completed, halted & cancelled oral tenofovir PrEP studies

Sponsor	Formulation / Design	Population	Sites
FHI	Completed	936 women	Ghana
NIH	Cancelled due to controversy stemming from activist groups ethical concerns	960 women	Cambodia
FHI	Halted following controversy of Cambodia trial	400 women	Cameroon
FHI	Halted before enrolment due to concerns by Malawi Ministry of Health	400 men	Malawi
FHI	Halted by trial sponsors due to concerns over site capacity	400 women	Nigeria

Anticipated South African prevention trial results



Anticipated South African prevention trial results



Antiretroviral tablets as oral PrEP



Tenofovir & Truvada pills being tested in multiple studies in the general population, drug users, gay men, discordant couples & high-risk women

New generation microbicides: Antiretroviral gels as topical PrEP

**CAPRISA 004: testing Tenofovir gel as PrEP for
male to female transmission of HIV**



ARVs as oral PrEP prevent HIV transmission from mother-to-child

Extending HIVNET 012 - single dose of nevirapine to mother and baby as PrEP prevents MTCT

HPTN 046: testing nevirapine syrup in babies during breastfeeding to prevent HIV transmission



Common challenges in PrEP

- **Is it safe to give ARV drugs to uninfected people?**
- **Will those who get infected have HIV that is resistant to the PrEP antiretrovirals? Will this affect their subsequent care and choice of ARV treatment?**
- **Will people adhere to tablets or gels for long periods?**
- **How often to do HIV testing on people on PrEP?**
- **Is there behavioural disinhibition / risk compensation?**
- **Is this an affordable and practical HIV prevention strategy for scale-up if it is efficacious?**

Conclusion

- **Several PrEP effectiveness trials underway**
- **Tenofovir & Truvada - safe in treatment; are they safe in healthy people over long periods**
- **PrEP Optimism - backdrop of disappointment**
- **PrEP is a promising new HIV prevention approach - we patiently await results of current human trials**
- **The diverse current trials are inter-dependent: DSMB decisions and results from any one of the trials will impact on all others**