



Elizabeth Glaser
Pediatric AIDS
Foundation

*Until no
child has
AIDS.*

Use of PrEP in HIV-Negative Pregnant and Breastfeeding Women

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(and huge thanks to Lynne Mofenson)





Why Consider PrEP in Pregnant and Breastfeeding Women?

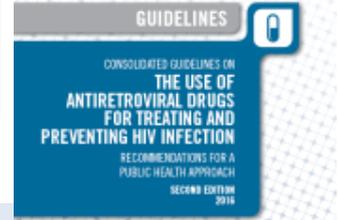
- *Increased HIV acquisition during pregnancy*
- *High HIV incidence during pregnancy in SSA*
 - *Increased MTCT with incident infection*



Recommendation

NEW

Oral PrEP containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches (*strong recommendation, high-quality evidence*).



Box 3. Defining “substantial risk”

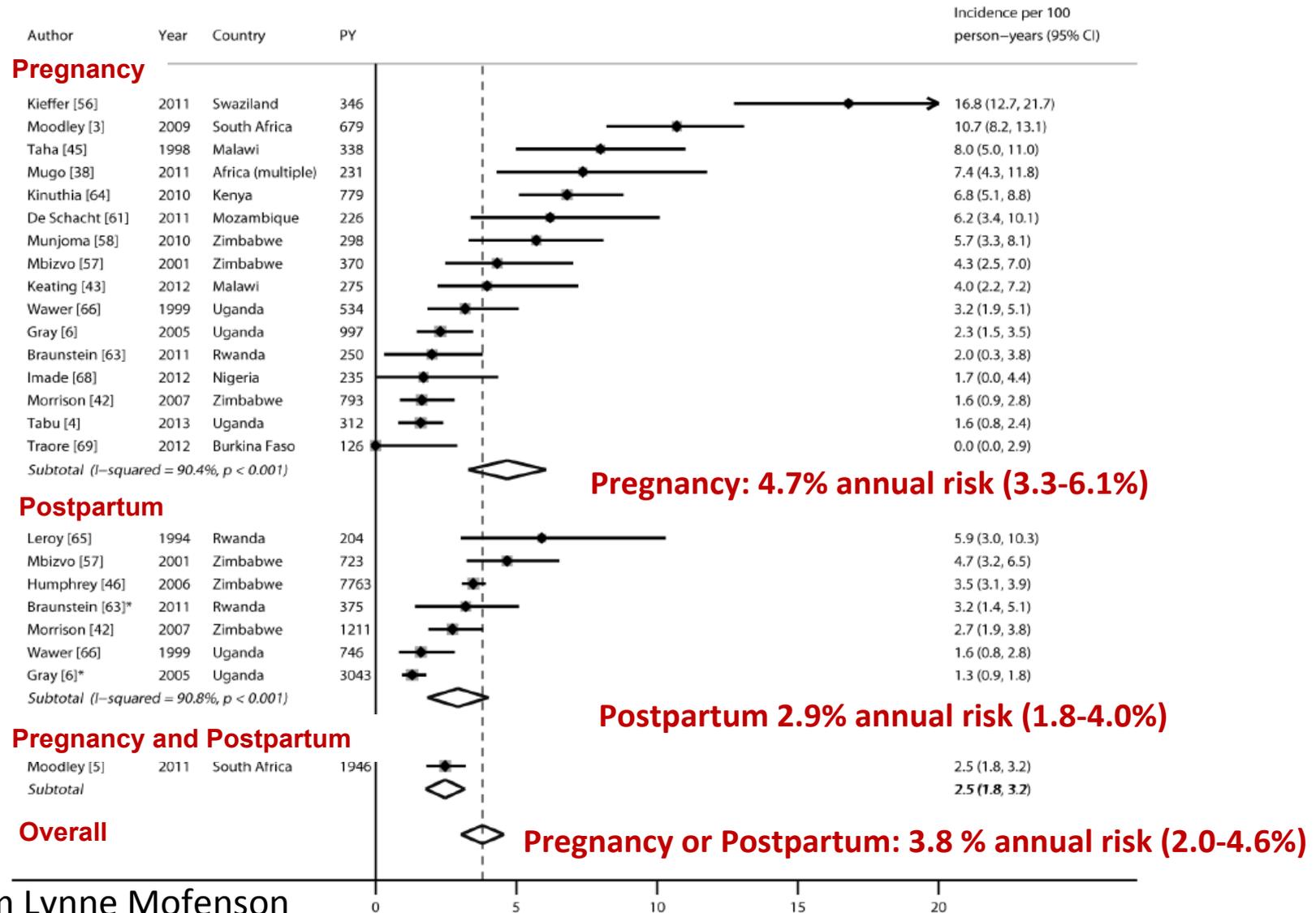
Substantial risk of HIV infection is provisionally defined as HIV incidence greater than 3 per 100 person–years in the absence of PrEP. HIV incidence greater than 3 per 100 person–years has been identified among some groups of men who have sex with men, transgender women in many settings and heterosexual men and women who have sexual partners with undiagnosed or untreated HIV infection. Individual risk varies within groups at substantial risk depending on individual behaviour and the characteristics of sexual partners. Most of the PrEP trials reviewed for this recommendation identified and recruited groups at substantial risk of acquiring HIV infection, as demonstrated by the HIV incidence rate among participants in control arms that ranged between 3 to 9 per 100 person-years in most studies. Indeed, the HIV incidence in control arms of PrEP trials was often higher than anticipated, suggesting that PrEP attracts people at particularly high risk (187). In locations where the overall incidence of HIV infection is low, there may be individuals at substantial risk who would be attracted to PrEP services.

HIV incidence greater than 2 per 100 person–years was considered sufficient to warrant offering oral PrEP in the recommendations issued by the International Antiviral Society – USA expert panel in 2014 (191). Thresholds for offering PrEP may vary depending on a variety of considerations, including available resources and the relative costs, feasibility and demand for PrEP and other opportunities.

High Rates of Incident HIV during Pregnancy/Breastfeeding

Drake AL et al. Drake A et al. PLoS Med 2014;11:e1001608

- Meta-analysis of data from 19 studies (all Africa)



Peripartum MTCT with Incident HIV Infection During Pregnancy

Range 10.7%-30.5%

| Author*/Year | Country | Year | Population/Method | N | % MTCT |
|----------------------------------|---------------|---------|---|--------|--------|
| Rollins N, 2007 (prior analysis) | South Africa | 2004-5 | 86% BF; surveillance (mat report prior neg) | 53/172 | 30.5% |
| Dinh T-H, 2015 | South Africa | 2011-12 | NS, national sample (mat report prior -/ record review) | 22/212 | 10.7% |
| Drake, 2014 | Meta-analysis | | | 30/194 | 17.8% |
| Tovo, 1991 | Italy | NS | FF, cohort (seroconvert) | 2/10 | 20.0% |
| Roongpisuthipong A, 2001 | Thailand | 1992-4 | FF, cohort (seroconvert) | 2/15 | 13.3% |
| Birkhead G, 2010 | NY | 2002-6 | FF, cohort (seroconvert) | 9/41 | 22.0% |
| Nesheim S, 2007-new | US | 1990-8 | FF, retesting in ANC | 1 / 4 | 25.0% |
| Singh, 2012-new | US | 2005-10 | FF, surveillance | 16/124 | 12.9% |

Summary

105/578 18.2%

Postnatal MTCT with Incident HIV Infection During Breastfeeding

Range 16.0% - 53.3%

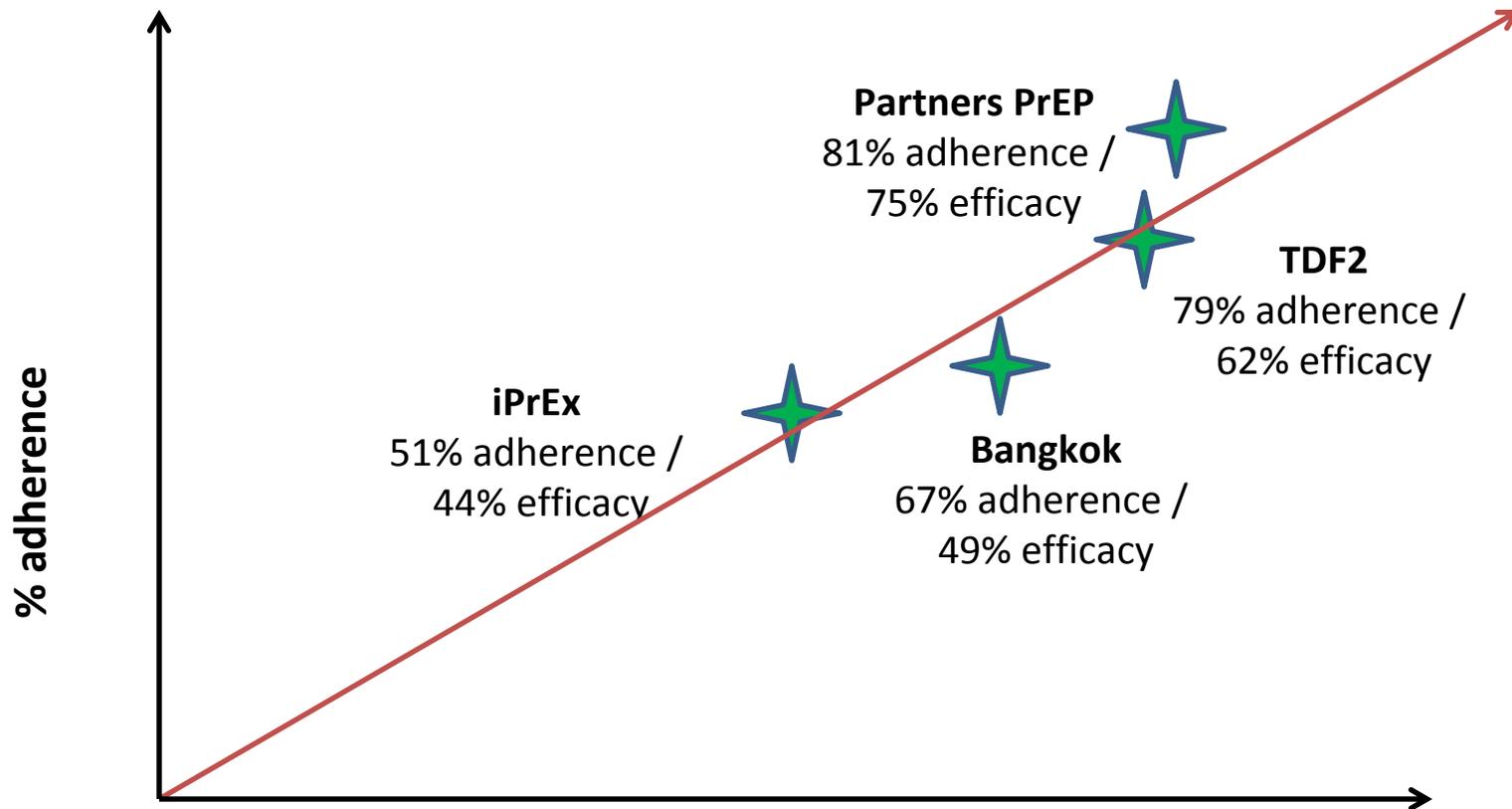
| Author/Year | Country | Year | Population/Method | N | % MTCT |
|--|----------------------|---------------|-------------------------|---------|--------|
| Van de Perre, 1991 (prior analysis) | Rwanda | 1988 | Prospect cohort | 8/15 | 53.3% |
| Dunn DT, 1992 (prior analysis) | Africa, Australia | 1980-90s | Meta-analysis | 12/42 | 28.6% |
| Ekpini, 1997 (prior analysis) | Cote d'Ivoire | 1990-4 | Prospect cohort | 2/12 | 16.7% |
| Embree, 2000 | Kenya | 1987-97 | Prospective cohort | 5/12 | 42% |
| De Schact, 2014 | Mozambique | 2008-11 | Prospect cohort | 6/29 | 21% |
| Drake, 2014 | Meta- analysis | | | 124/473 | 26.2% |
| Hira, 1990-new | Zambia | 1980s | Cohort | 3/19 | 16.0% |
| Humphrey | Zimbabwe | 1997- 2001 | Prospect Cohort | 79/334 | 23.6% |
| Palasanthiran, 1993 | Australia | 1980s | Retro Cohort (blood tx) | 3/11 | 27.0% |
| Colebunders, 1988-new | Zaire | 1980s | Cohort | 1/3 | 33.0% |
| Liang, 2009 | China | 2007 | Cohort (blood tx) | 38/106 | 36.0% |

Summary:

Slide from Lynne Mofenson

157/583 26.9%

When PrEP is Taken, It Works



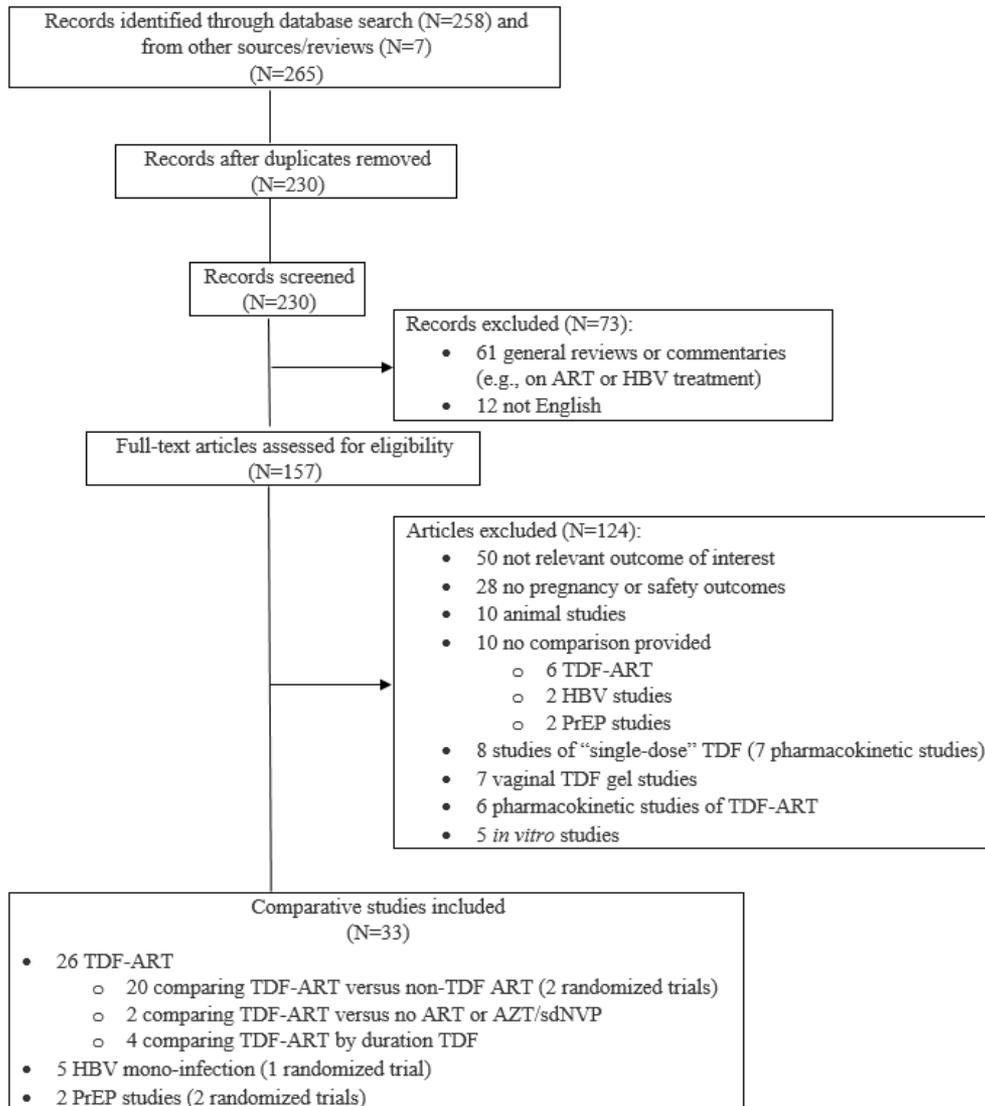
HIV protection effectiveness

PrEP trials where the majority of subjects were adherent demonstrated HIV protection, with higher protection estimates when more of the population was adherent.

PrEP is Effective in Preventing HIV Infection Among African Young Women

- In meta analysis of 18 studies, adherence was a significant moderator of PrEP effectiveness (*Fonner AIDS 2016*)
 - Age & sex did not moderate effect of HIV PrEP on HIV acquisition
- Substantial number of young women were enrolled in PrEP studies that ascertained efficacy
 - In Partners PrEP: 33% women were age <30 yrs (*Baeten NEJM 2012*)
 - TDF was 77% & FDF/FTC 72% protective (*Murnane AIDS 2013*)
 - In TDF 2 Botswana study, 45.8% of cohort on PrEP were women (*Thigpen NEJM 2012*)
 - VOICE study sub analysis of women with detectable tenofovir in plasma demonstrated 53% protective effect (*Dai JID 2016*)

Systematic Review of TDF Safety in Pregnancy/BF



- Conducted systematic review of safety for WHO March 2016 meeting; recently updated through August 2016.
- Identified 33 comparative studies where TDF was compared to non-TDF regimen
 - 26 HIV+ women on ART
 - 7 HIV- women
 - 5 HBV mono-infection
 - 2 PrEP

Review Conclusions

- Safety data are reassuring.
- Most studies from HIV+ women on ART, presenting “worst case” scenario, as HIV+ women have ↑ adverse pregnancy outcomes than HIV-uninfected women.
 - TDF ART similar to other ART regimens in terms of maternal, pregnancy and infant growth outcomes; limited TDF exposure during breastfeeding.
- Fewer studies in HIV-uninfected women; adverse event rates much lower than HIV+ women, and no differences between TDF or TDF/FTC and control.
- PrEP benefits in women at high risk of HIV appear to outweigh any risks observed to date; as PrEP is implemented, will be important to continue surveillance of maternal, pregnancy and infant outcomes to confirm safety.

From Evidence to Implementation:
What do we need to ensure uptake,
access and adherence?

Raising Awareness and Demand

Balancing risk, access and potential stigma

- Risk will vary by geography & population
 - Pregnant in a hyper-endemic geographic location
 - All women or use criteria to select those at high risk?
 - Concentrated epidemics
 - FSW, members of special populations
 - HIV sero-discordant couples across geography
- Education of health care workers, women and CHWs
- Ensuring PrEP is delivered without stigma
- Provision across a number of health entry points
 - STI clinics, family planning – may target populations with noted risk factors
 - Provision in primary health centers will increase access and normalize PrEP

Innovations in PrEP Delivery

What innovations may facilitate adherence in this population? What models or delivery methods are best fit to sub-populations?

- On-demand/seasonal vs daily PrEP
- Adherence and psychosocial support: PrEP supporters, peer normalization, SMS reminders
- Dapivirine ring
- Long-acting injectables (e.g. during breastfeeding?)

Ensuring Access to PrEP

How can we ensure access to PrEP for all who need it?

- Design country guidance considering risk-benefit of particular population of pregnant women and current evidence on safety and effectiveness of PrEP
- Overcome regulatory barriers
 - Package inserts vary greatly by country on use in pregnancy and/or breastfeeding
 - May lead to confusion or hesitance to use PrEP in pregnant women at high-risk for HIV acquisition
- Delivery models for implementation: private sector, integration into family planning
- Addressing patent barriers to ensure access to affordable generics in middle-income countries

Leveraging PrEP to reach 90-90-90

Beyond helping pregnant and breastfeeding women and their infants stay HIV negative...

- May help facilitate regular testing
- Leading to early diagnosis
- Population is linked to services and for those who become infected, may facilitate early initiation of ART
- Normalize the concept of ART across populations

Thanks For Your Attention!

Acknowledgements:

Lynne Mofenson

Yannis Mameletzis

COUNTDOWN TO ZERO



GLOBAL PLAN TO
AMONG CHILDREN
2011-2015

