NORTHWEST AIDS EDUCATION AND TRAINING CENTER

CROI 2015: HIV Prevention Updates

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NW AETC | echo

INFECTIOUS DISEASES

Doubts dispelled about HIV prevention

New studies show remarkable efficacy and versatility of drugs for uninfected

By **Jon Cohen**, *in Seattle, Washington*

…a bevy of new studies quelled most remaining doubts about the real-world effectiveness of what's known as pre-exposure prophylaxis (PrEP), showed practical ways to use it, and suggested that it could help change the trajectory of the epidemic.

Pragmatic Open-Label Randomised Trial of Pre-Exposure Prophylaxis: the PROUD study

MRC CTU at UCL
Sheena McCormack for co-authors

Sexual health service in England

- ~220 sexual health clinics, linked through professional guidelines
- Accessed by 110,000 HIV negative gay men per year
- Diagnoses made and services provided reported to Public Health England

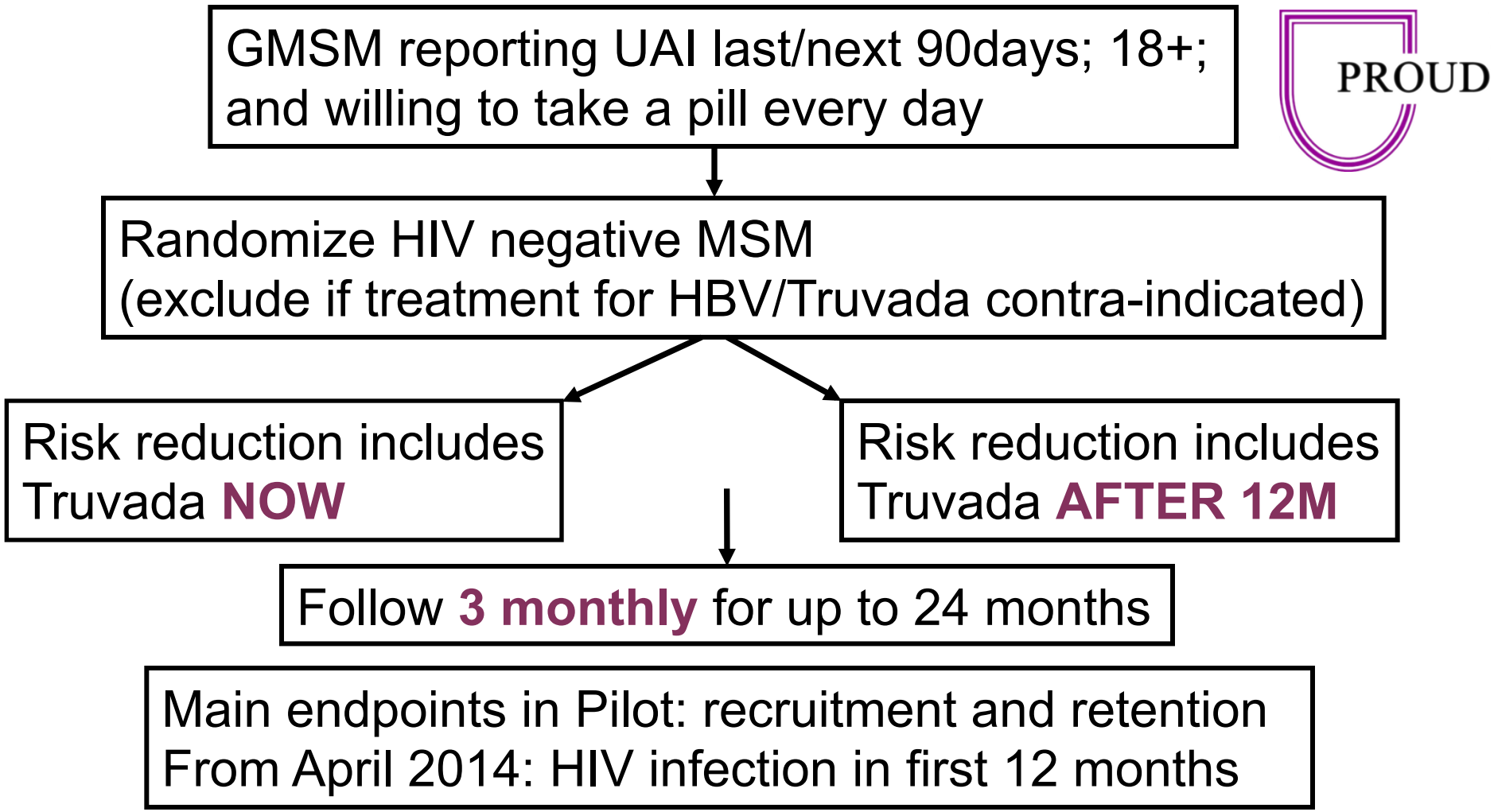
Rationale

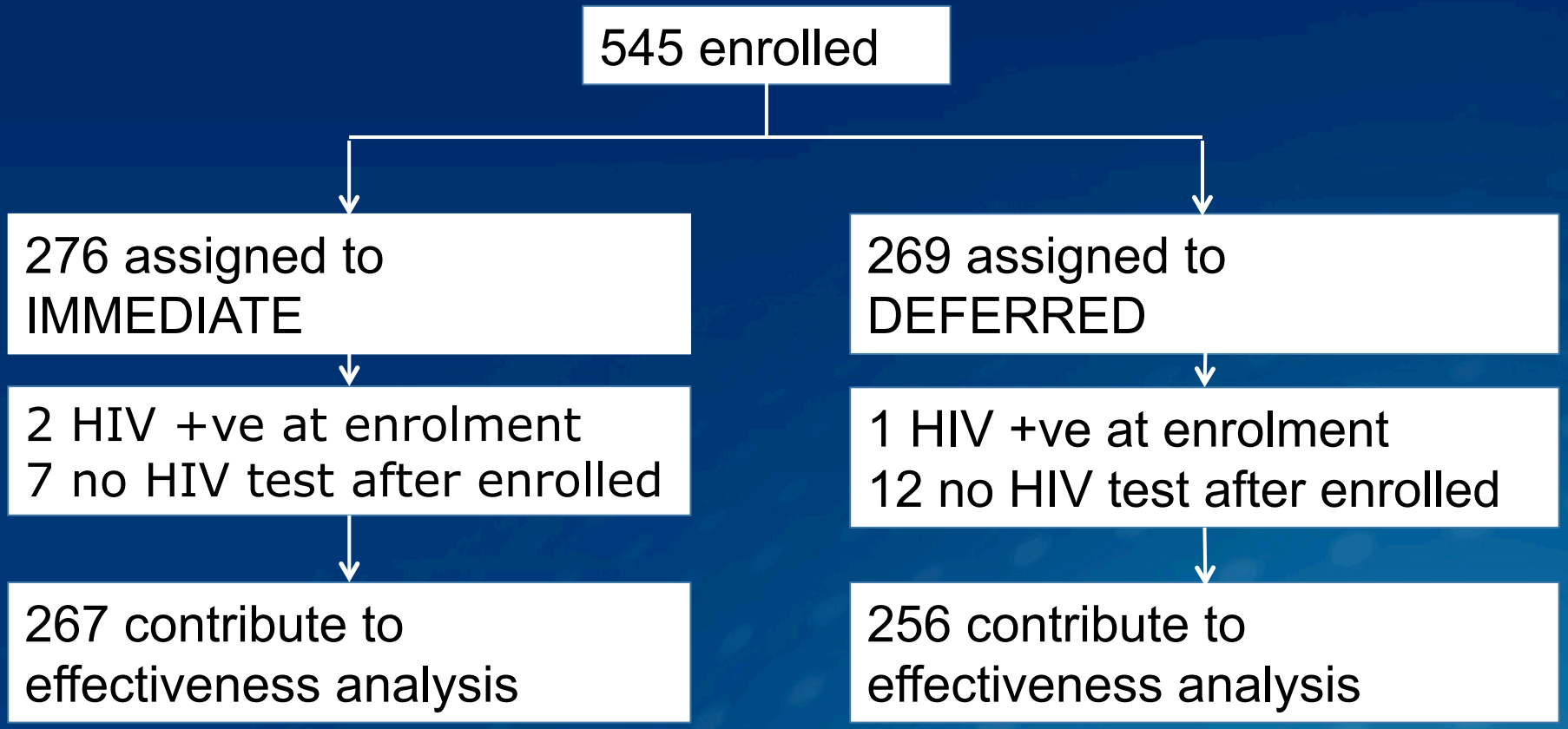
- To determine whether PrEP worked as well as iPrEx in this setting (44% reduction in HIV)

- Why might effectiveness be less in real world?
- Adherence less
  - trial schedules monthly
  - well resourced for adherence support

- Behaviour riskier
  - participants constantly reminded that they could be on placebo, and that effectiveness was unknown
  - well resourced for behaviour change interventions

PROUD Pilot


GMSM reporting UAI last/next 90days; 18+; and willing to take a pill every day
PROUD
Randomize HIV negative MSM (exclude if treatment for HBV/Truvada contra-indicated)
Risk reduction includes Truvada NOW
Risk reduction includes Truvada AFTER 12M
Follow 3 monthly for up to 24 months
Main endpoints in Pilot: recruitment and retention
From April 2014: HIV infection in first 12 months

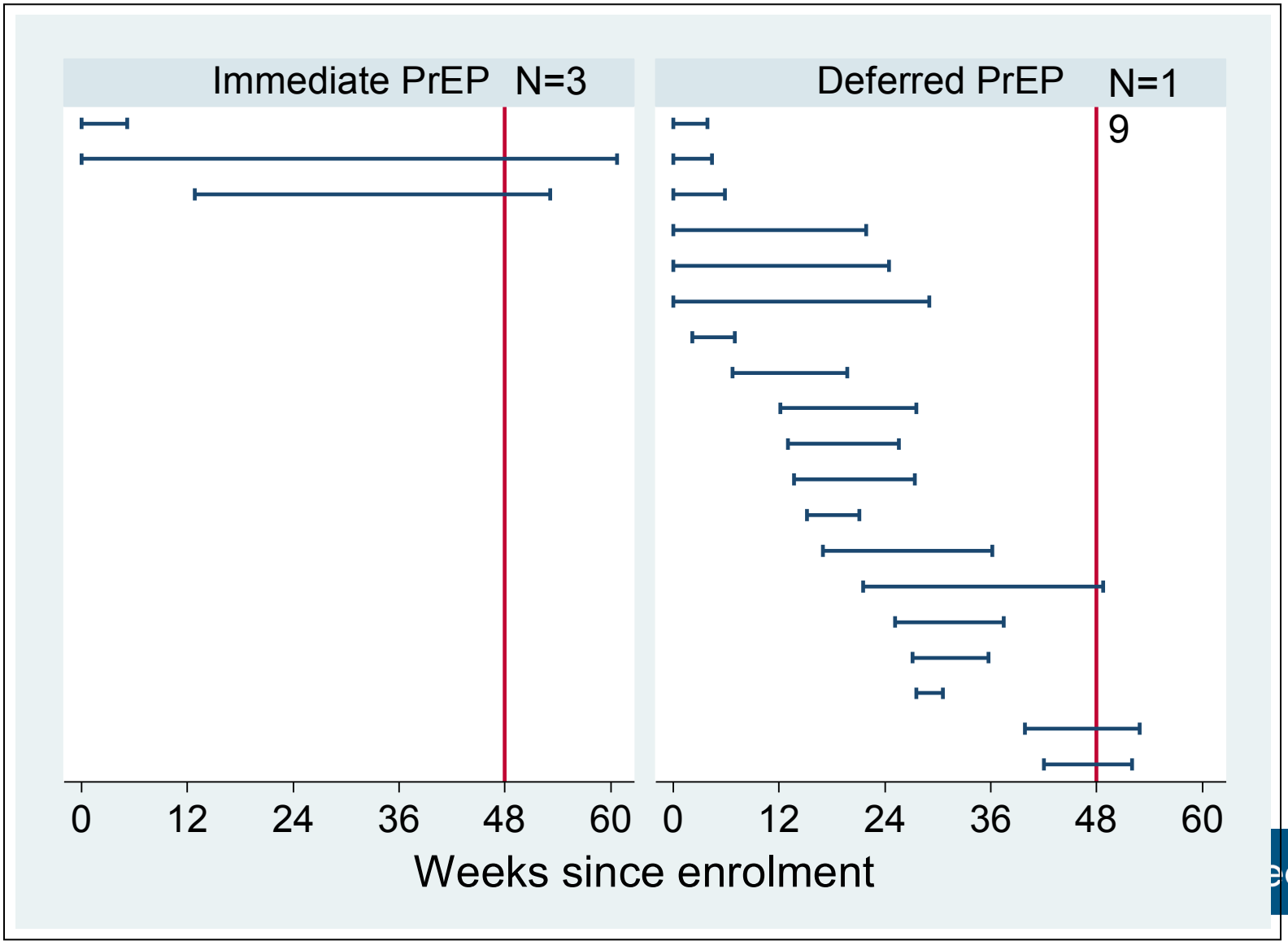


Calculation of person-years:

From enrolment to the first of the following

- HIV test at m12, or
- HIV test at the time of access to PrEP, or
- diagnosis of HIV infection

Individual incident HIV infections



HIV Incidence

Group	No. of infections	Follow-up (PY)	Incidence (per 100 PY)	90% CI
Overall	22	453	4.9	3.4–6.8
Immediate	3	239	1.3	0.4–3.0
Deferred	19	214	8.9	6.0–12.7

Efficacy =86% (90% CI: 58 – 96%)
P value =0.0002

Rate Difference =7.6 (90% CI: 4.1 – 11.2)
Number Needed to Treat =13 (90% CI: 9 – 25)

Reported sexual behaviour (preliminary)

Anal sex partners in last 90 days **BASELINE n=539**	**Immediate**Median (IQR)	**Deferred** Median (IQR)
Total number of partners	10.5 (5-20)	10 (4-20)
Condomless partners, participant receptive	3 (1-5)	2 (1-5)
Condomless partners, participant insertive	2.5 (1-6)	3 (1-7)

Anal sex partners in last 90 days **MONTH 12 n=349**	**Immediate**Median (IQR)	**Deferred** Median (IQR)
Total number of partners	10 (3-24)	8 (3-15)
Condomless partners, participant receptive	3 (1-8)	2 (1-5)
Condomless partners, participant insertive	3 (1-8)	3 (1-6)

Conclusions

- HIV incidence in the population who came forward to access PrEP was much higher than predicted based on all MSM attending sexual health clinics
- Despite extensive use of PEP in the deferred period
- Our concerns about PrEP being less effective in the real world were unfounded

- MSM incorporated PrEP into existing risk reduction strategies which continued to include condom use
- There was no difference in STIs, which were common in both groups

- Clinics were able to adapt routine practice to incorporate PrEP

On Demand PrEP with Oral TDF/FTC in MSM Results of the ANRS Ipergay Trial

Molina JM, Capitant C, Spire B, Pialoux G, Chidiac C, Charreau I, Tremblay C, Meyer L, Delfraissy JF, and the ANRS Ipergay Study Group

Hospital Saint-Louis and University of Paris 7, Inserm SC10-US019 Villejuif, Hospital Tenon, Paris, Hospital Croix-Rousse, Lyon, UMR912 SEAS Marseille, France, CHUM, Montreal, Canada and ANRS, Paris, France

Study Design

Double-Blinded Randomized Placebo-Controlled Trial

- HIV negative high risk MSM
- Condomless anal sex with ≥ 2 partners within 6 m
- eGFR > 60 mL/mn

→ **Full prevention services* TDF/FTC before and after sex**

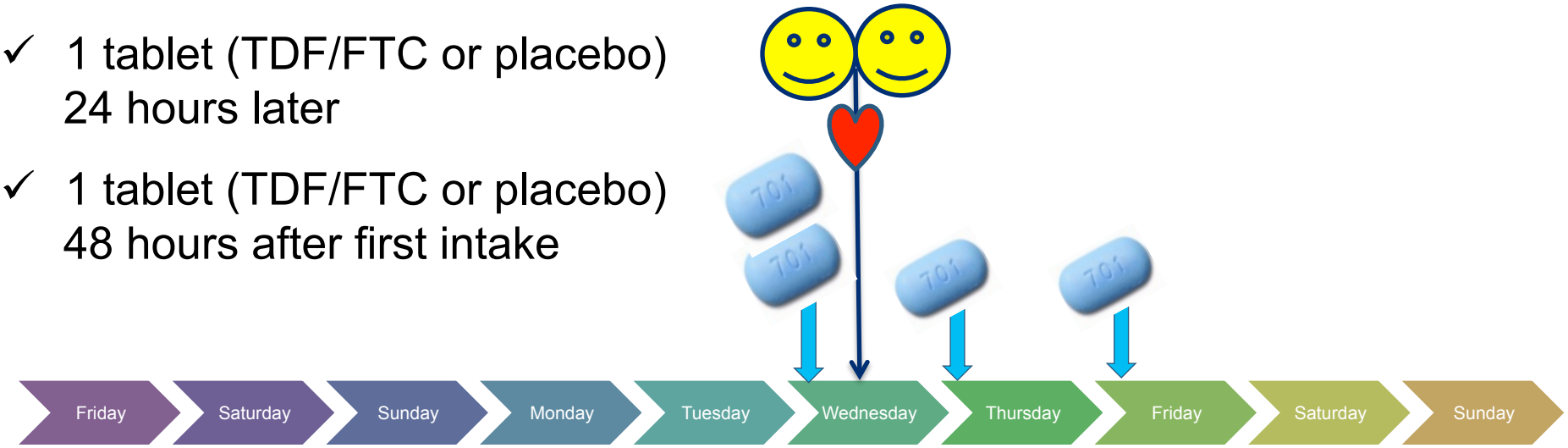
→ **Full prevention services* Placebo before and after sex**

* Counseling, condoms and gels, setting and treatment for STIs, vaccination for HBV and HAV, PEP

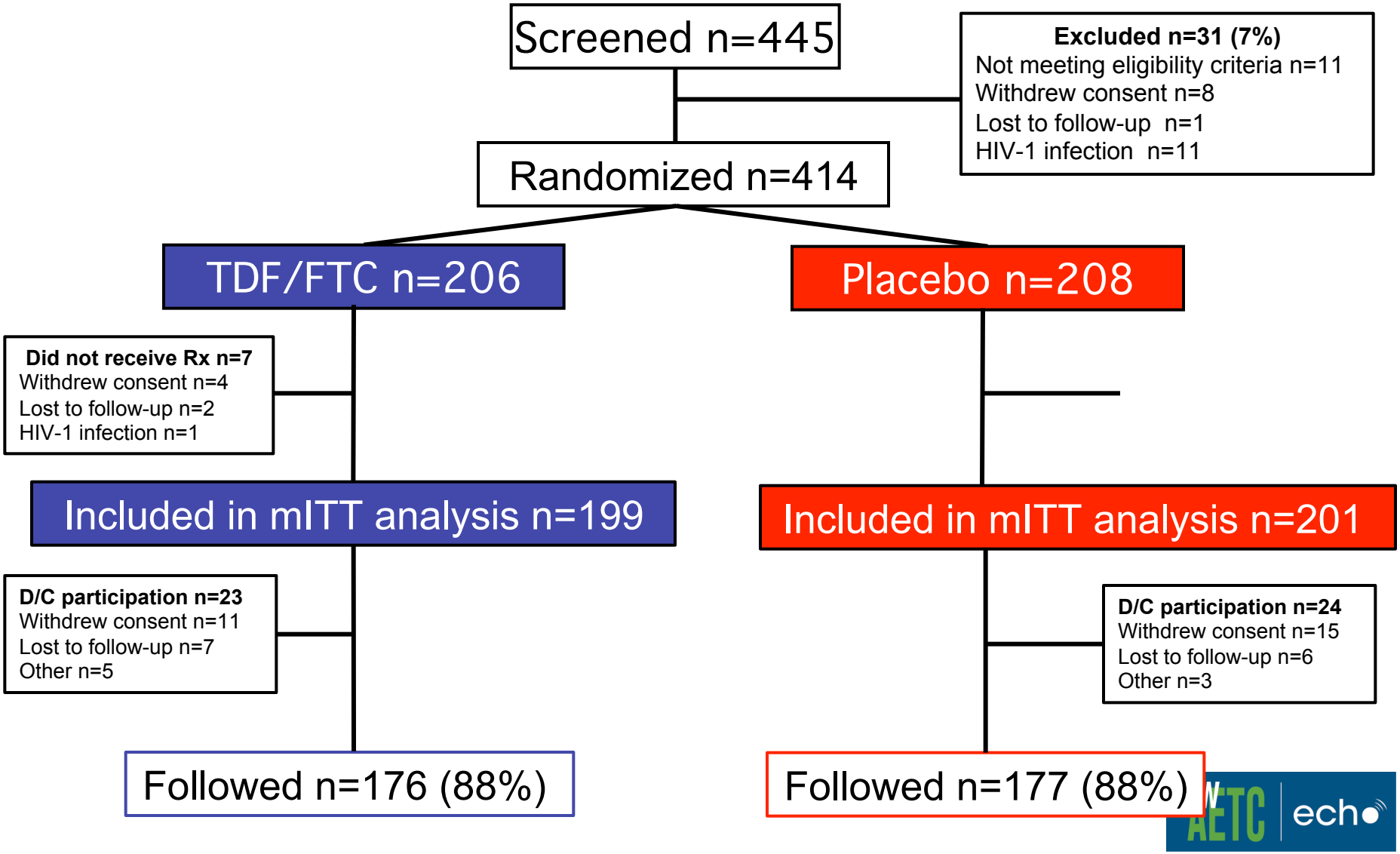
- End-point driven study : with 64 HIV-1 infections, 80% power to detect a 50% relative decrease in HIV-1 incidence with TDF/FTC (expected incidence: 3/100 PY with placebo)
- Follow-up visits: month 1, 2 and every two months thereafter

Ipergay : Event-Driven iPrEP

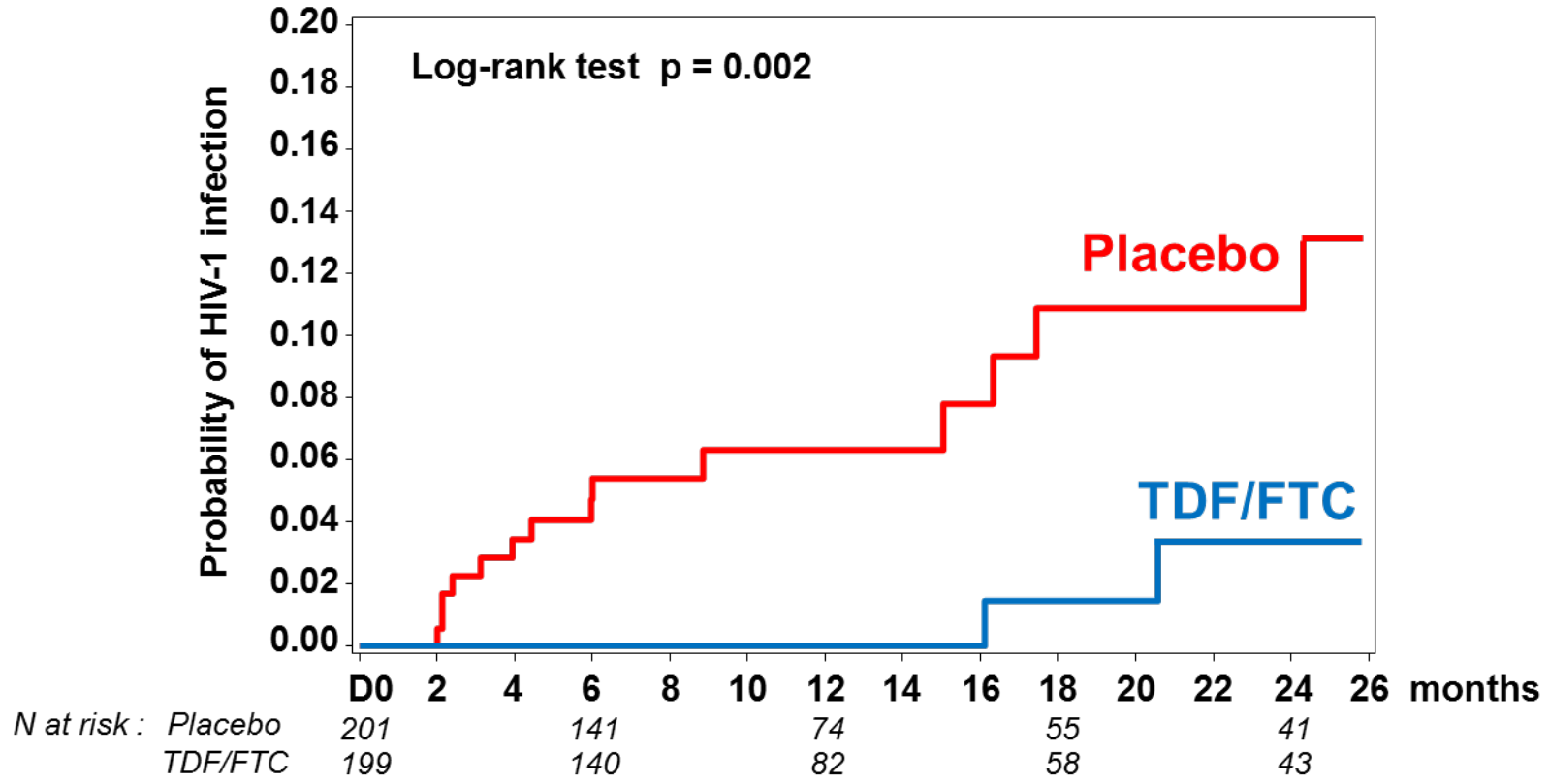
- ✓ 2 tablets (TDF/FTC or placebo)
  2-24 hours before sex
- ✓ 1 tablet (TDF/FTC or placebo)
  24 hours later
- ✓ 1 tablet (TDF/FTC or placebo)
  48 hours after first intake



Study Flow-Chart



KM Estimates of Time to HIV-1 Infection (mITT Population)



Mean follow-up of 13 months: 16 subjects infected

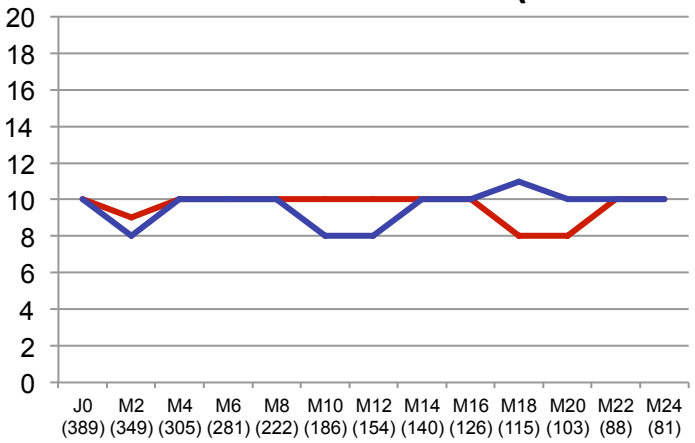
14 in placebo arm (incidence: 6.6 per 100 PY), **2 in TDF/FTC arm** (incidence: 0.94 per 100 PY)

86% relative reduction in the incidence of HIV-1 (95% CI: 40-99, p=0.002)

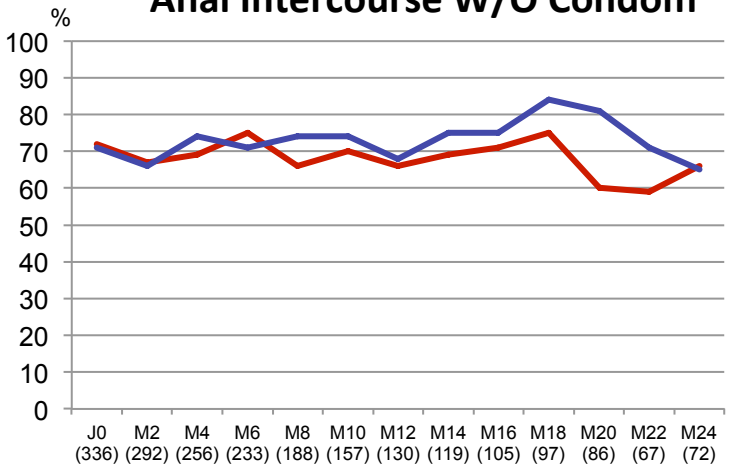
NNT for one year to prevent one infection : 18

Sexual Behavior

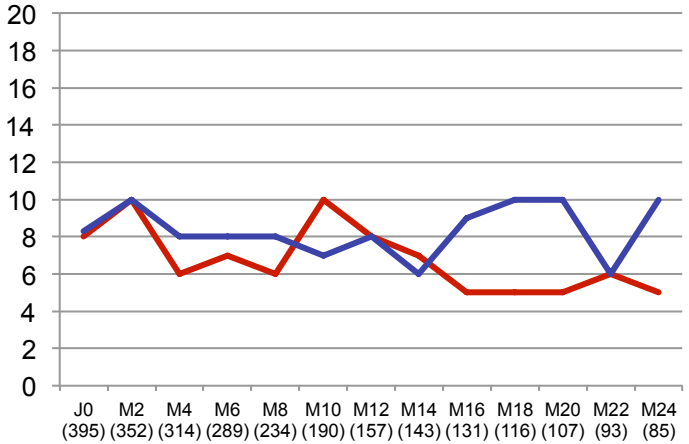
Median Nb of Sexual Acts (last 4 weeks)



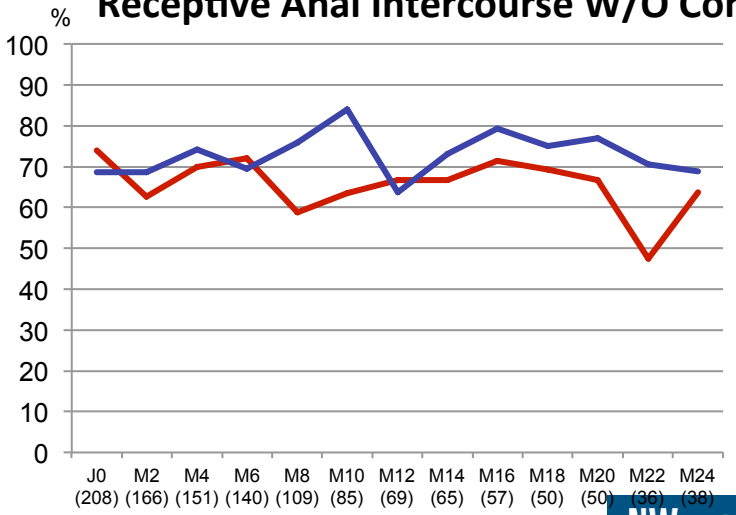
Anal Intercourse W/O Condom



Median Nb of Sexual Partners (2 months)



Receptive Anal Intercourse W/O Condom



Conclusions

- In this population of high risk MSM, incidence of HIV-1 infection in the placebo arm was higher than expected
- “On Demand” oral PrEP with TDF/FTC was very effective with a 86% (95% CI: 40-99) reduction in HIV-incidence
- Adherence to PrEP was good supporting the acceptability of “on demand” PrEP
- Safety of “on demand” TDF/FTC was overall similar to placebo except for gastrointestinal AEs
- No evidence of risk compensation
- On demand PrEP: attractive alternative to daily PrEP in high risk MSM who do not use condoms consistently

Near elimination of HIV transmission in a demonstration project of PrEP and ART

Jared M. Baeten, Renee Heffron, Lara Kidoguchi, Nelly Mugo, Elly Katabira, Elizabeth Bukusi, Stephen Asiimwe, Jessica E. Haberer, Deborah Donnell, Connie Celum, for the Partners Demonstration Project Team

CROI 2015, Seattle

Design

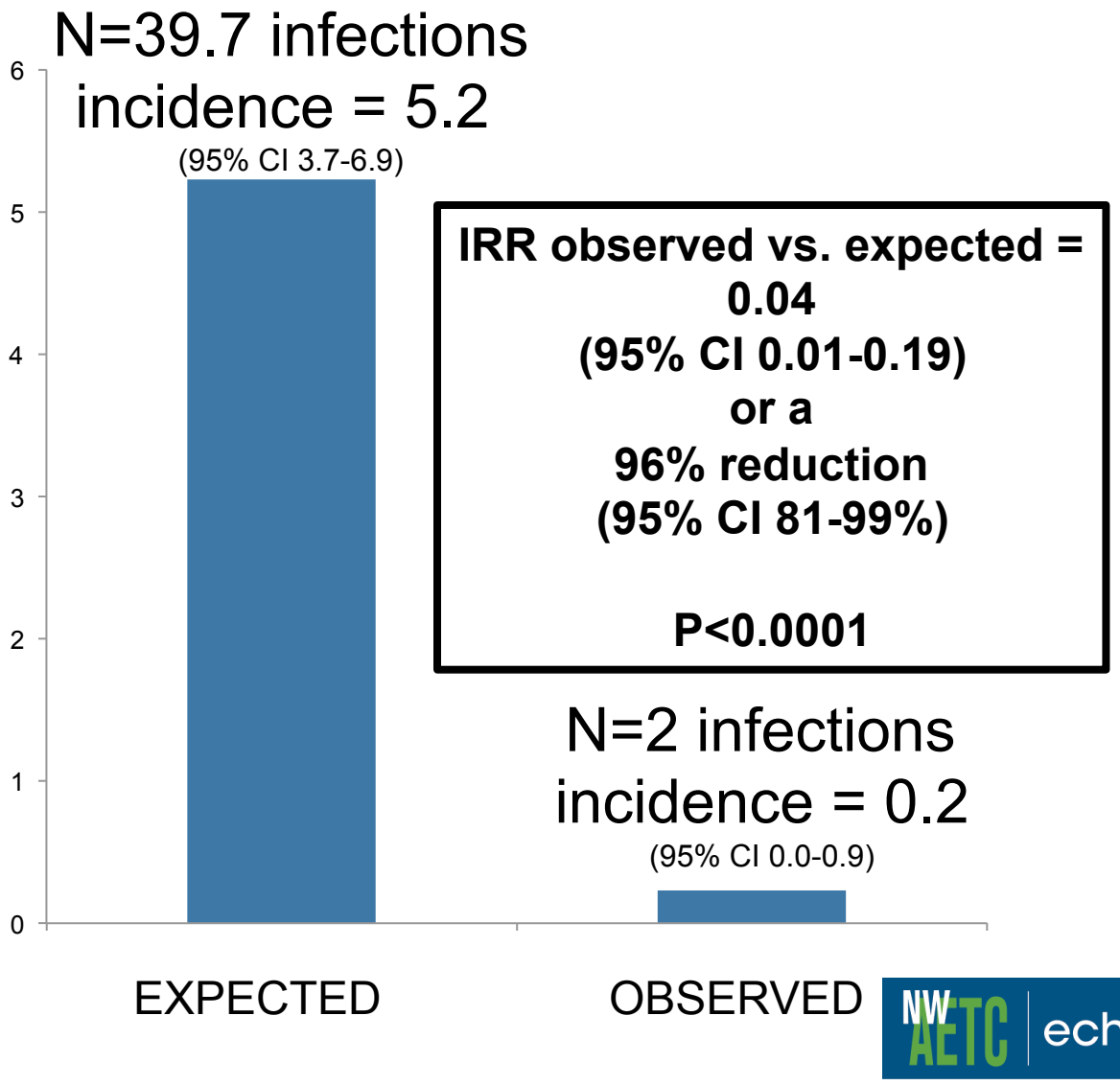
- Population:
  - Heterosexual HIV serodiscordant couples, not using ART or PrEP and ***with characteristics defining higher risk for HIV transmission***
  - *None participated in the Partners PrEP Study trial of PrEP*
- Intervention:
  - ART offered per Kenya/Uganda guidelines, which recommend ART for all infected partners in serodiscordant couples, regardless of CD4 count
  - PrEP (daily oral FTC/TDF, Truvada®) offered to the uninfected partner until the infected partner has been on ART for 6 months, permitting time to achieve viral suppression ***(=PrEP as a bridge to ART)***
- Follow-up:
  - Month 1 and then quarterly thereafter, for up to 24 months, including HIV testing, risk reduction, brief adherence support, and primary HIV care

Results: Follow-up

- To date, a total of 858 person-years have been accrued
  - The study is ongoing, with ~42% of planned person-time accrued so far
  - Retention is currently >85% at each quarterly visit
  - Pregnancy incidence is ~20%/year
- Uptake of PrEP and ART are high:
  - *PrEP:* >95% have initiated. Adherence is high (Heffron et al., CROI 2015, abstract #969)
  - *ART:* ~80% have initiated, >90% are achieving viral suppression
- For 48% of follow-up accrued to date, couples used PrEP alone (prior to initiating ART), 27% is PrEP & ART overlapping, and 16% is ART alone.
  - ART increases & PrEP decreases over longer follow-up, reflecting the use of PrEP as a bridge to ART in the partnership.
  - 9% of follow-up time has neither ART nor PrEP in use in the partnership.

HIV incidence

- The observed incidence is a **96% reduction** compared to expected, a result that was highly statistically significant



Summary

- In this open-label demonstration project of integrated delivery of ART and PrEP for prevention in HIV serodiscordant couples, we have observed a 96% reduction to date in incident HIV, compared to expected rates.
- Our study differs substantially from randomized trials of PrEP and ART in its open-label, implementation science approach and its focused recruitment of higher-risk couples.
- Our results demonstrate that PrEP as a bridge to ART is not only feasible but highly effective in preventing HIV transmission in this population.
  - Notably, the majority of person-time accrued to date is PrEP-exposed, emphasizing an important PrEP effect for our results.

Summary

- In real world settings daily PrEP works to avert HIV infections
- Intermittent PrEP has the potential to substantially decrease HIV incidence
- PrEP as a bridge to ART for high-risk serodiscordant couples works in low resource settings
- Implementation science studies will examine durability, barriers and facilitators, and peri-conception use of PrEP
- Ultimate goal is to inform public policy