

Designs under Discussion for “Unmet Prevention Need”

**Ideas emerging from Seattle Workshop
“HIV Prevention Efficacy Trial Designs of
the Future” Nov 5, 2018**

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Goal: Regulatory Approval of New Product

1. Safe

Sufficient total person years of experience
Safety established with 12+ months of use

2. Effective

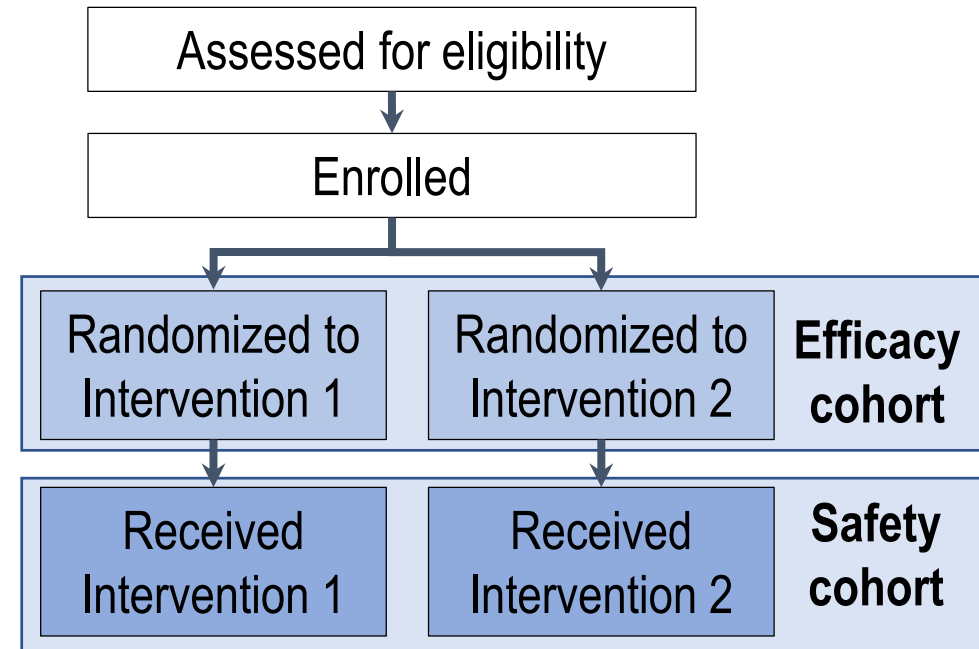
Unequivocal evidence of prevention of HIV infection

Standard for evidence

- Randomized Clinical Trial
- In populations at highest need

Current Era : FTC/TDF PrEP

- Current approved market leader is highly effective
- Dependent on daily adherence to pill taking



Data accumulating about PrEP non-persistence

- HPTN 067: < 2 pills/week (daily arm)
 - At 30 weeks
 - Young women in Capetown: 46%
 - MSM in Thailand: 4%
 - MSM in Harlem, US: 50%
- HPTN 073: < 4 days/week
 - Black MSM at 26 weeks : 36%
- HPTN 082: Undetectable DBS at 13 weeks
 - Young women in Africa: 16%
- US PrEP user pharmacy refills (Coy, 2019, JAIS)
 - At year 1 44%
 - At year 2 37%

With an effective product, three choices in future RCTs

1. Compare

Compare experimental product (EXP) to existing prevention (FTC/TDF)

HPTN 083/084



FTC/TDF



EXP

2. Layer

Compare EXP to placebo (PBO) on top of use of existing prevention

AMP



Placebo

EXP

3. Combine

Compare existing prevention combined with EXP product



FTC/TDF+
Placebo



FTC/TDF +
EXP



The Prevention Mosaic



ORAL PREP

RING

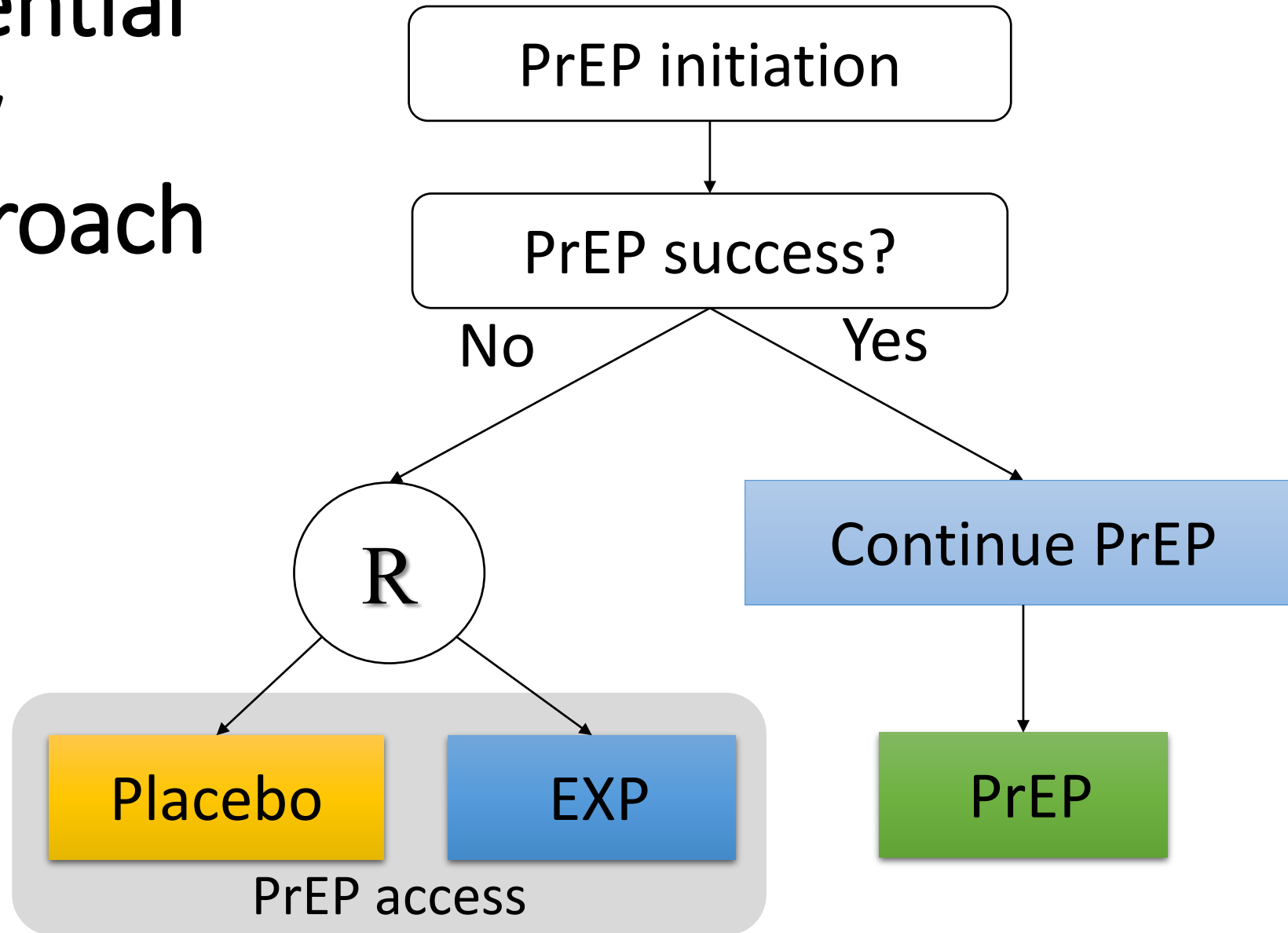
ABSTINENCE

The Prevention Mosaic

STILL UNPROTECTED

CONDOMS

Potential new approach

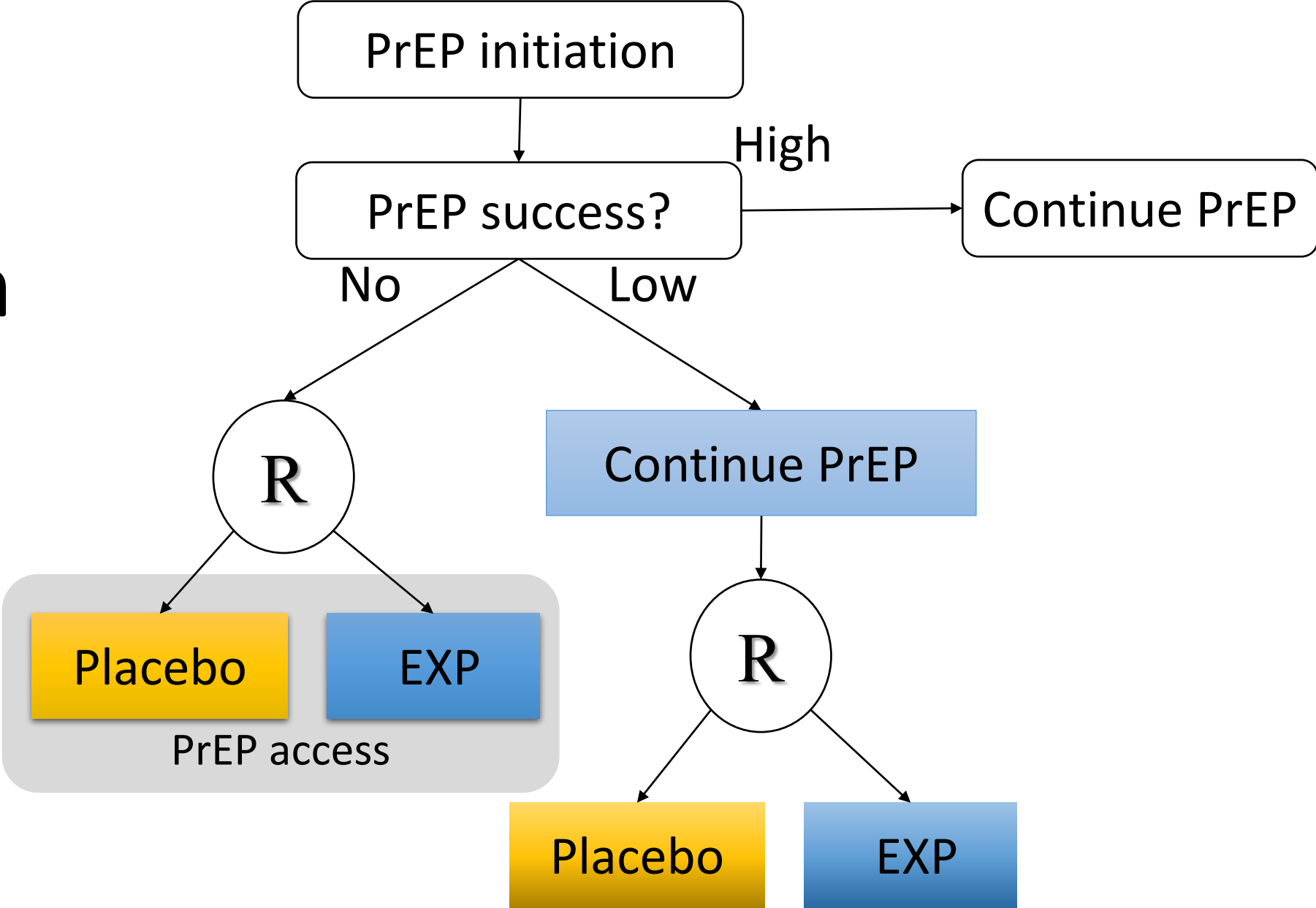


Sample size implications

- Incidence in those with unmet need is probably higher
- Difference between incidence placebo and active is projected to be bigger

Percentage on PrEP	Type: Powered for 60% efficacy of EXP	Total number of infections	Number of participants (Assuming 4% incidence)
100%	Non-inferiority	980	17,754
75%	Non-inferiority	192	3,033
50%	Superiority	196	2,745
25%	Superiority	104	1,308
0%	Superiority	70	799

Potential new approach



Explore innovative design ideas

- Challenge of advancing new products for prevention when existing products are very successful
- Need community, stakeholder and scientists engaged in robust discussion of prevention need, to discern a path forward together