

Dapivirine Vaginal Ring Pre-exposure Prophylaxis for HIV Prevention in South Africa

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Background

- A vaginal ring (VR) containing dapivirine (DPV) is under evaluation for pre-exposure prophylaxis (PrEP) for HIV prevention among women
- The potential impact and cost-effectiveness of DPV PrEP scale-up are unknown
- Cross-resistance is common between DPV and first-line antiretroviral therapy (ART) in resource-limited settings

Methods

Model overview

- We refined a deterministic mathematical model to simulate the HIV epidemic in KwaZulu-Natal, South Africa with the scale-up of DPV VR PrEP
 - The model population was stratified by gender, age, sexual behavior, HIV status and disease progression, male medical circumcision (MMC) status, ART or PrEP use, and drug sensitivity of HIV in blood and genital compartments
 - The model was calibrated to HIV prevalence and incidence data from KwaZulu-Natal using a Bayesian framework

Interventions

- Baseline:** ART + MMC scale-up
 - ART reaching 80% of HIV+ persons with CD4 \leq 500 cells/ μ L by 2020
 - MMC reaching 80% of men by 2017
- Unprioritized PrEP** (Baseline + 2.5%–15% overall PrEP coverage)
 - DPV VR PrEP scale-up reaching 5%–30% of women aged 15–54
- Age-prioritized PrEP** (Baseline + 2.5%–15% overall PrEP coverage)
 - DPV VR PrEP scale-up reaching 10%–70% women aged 15–24
 - DPV VR PrEP scale-up reaching 15%–85% of women aged 20–29
- Risk-prioritized PrEP** (Baseline + ~0.1% overall PrEP coverage)
 - DPV VR PrEP scale-up reaching 50%–90% of female sex workers (FSWs)

Cost-Effectiveness Analysis Characteristics

- Perspective:** modified societal
- Time horizon:** 2017–2027
- Outcome:** costs per infection prevented (IP)
- Discount rate:** 3% per year

Model Analyses

- Base case analyses:** interventions simulated using input point estimates (Table 1)
- Uncertainty analyses:** multivariate analyses of 10,000 simulations per intervention, using randomly-sampled inputs (Table 1)

Table 1. Key model inputs

Parameter	Base case	Range	Source
PrEP average adherence		40%–95%	
Low adherence scenario	50%		FACTS 001
High adherence scenario	95%		Montgomery et al. 2012 AIDS Behav
PrEP efficacy against wild-type HIV	90%	50%–99%	iPrEx, Partners PrEP, Nel et al. 2014 JACR
PrEP efficacy against PrEP-resistant HIV, relative to wild-type	100%	50%–100%	Penrose et al. 2015 CROI
Cross-resistance prevalence (% of ART-resistant HIV that is cross-resistant to PrEP)	80%	70%–100%	Penrose et al. 2015 CROI
Persistence time of DPV drug concentrations after ring removal	None	1–5 days	Nel et al. 2014 JACR
PrEP cost, per person-year	\$95	\$60–\$130	Stover et al. 2014 PLoS One
ART cost, per person-year	\$750	\$460–\$1040	Meyer-Rath et al. 2012 JAIDS
MMC cost, per surgery	\$110	\$70–\$150	Kripke et al. 2013

Results

Base Case Analyses

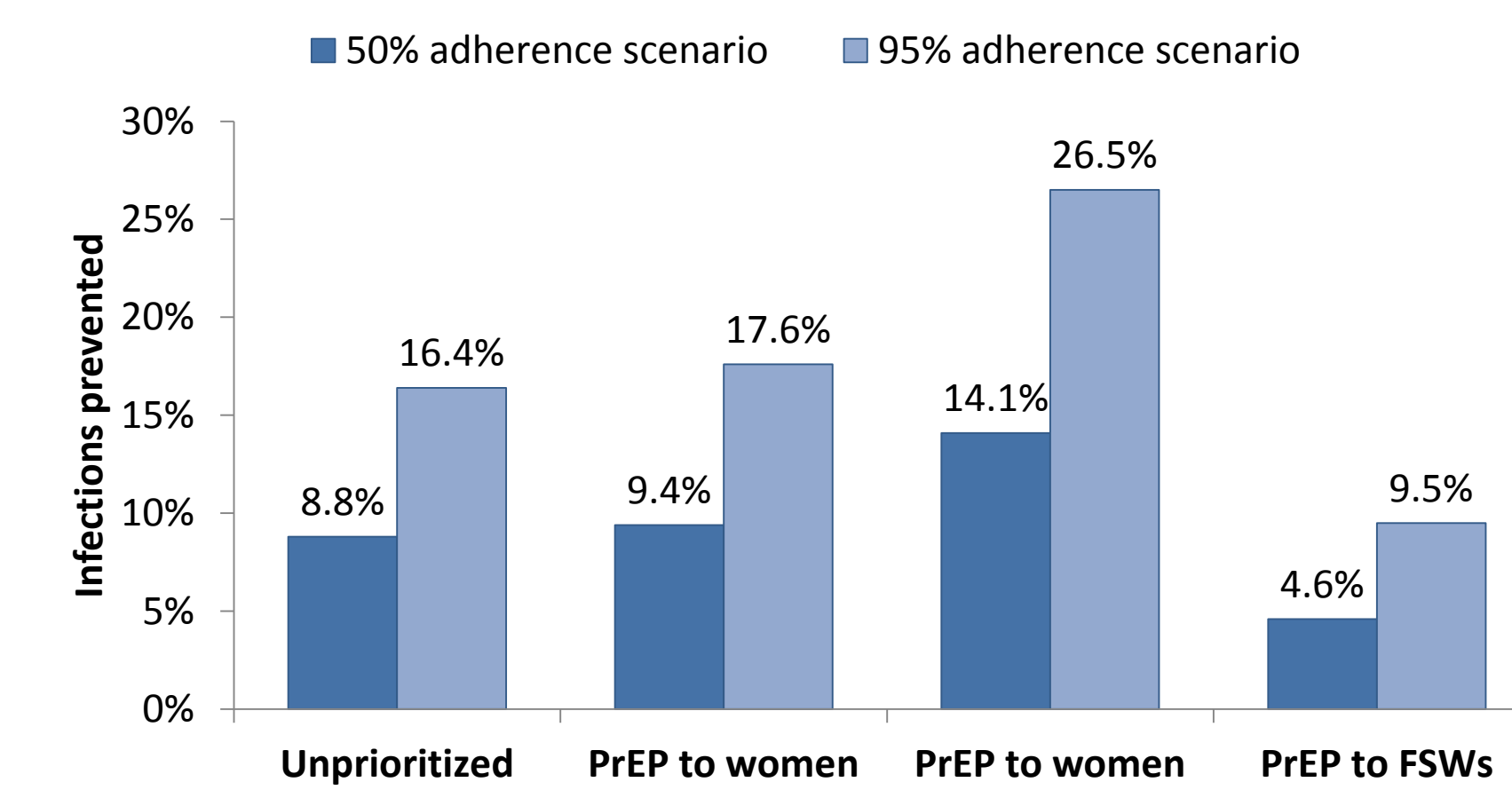


Figure 1. Cumulative (undiscounted) infections prevented by PrEP. Unprioritized and age-prioritized PrEP strategies covered 15% of uninfected adults aged 15–54

HIV Prevention

- 661,017 new infections occurred over ten years in the baseline scenario without PrEP
- 15% overall PrEP coverage prioritized to women aged 20–29 prevented the most infections (Figure 1)
- PrEP prioritized to 80% of female sex workers (FSWs) prevented the fewest infections, but required low (~0.1%) overall coverage
- PrEP prevented 86%–106% more infections at 95% vs. 50% average adherence

Healthcare Costs

- Without PrEP, cumulative discounted healthcare costs reached \$20,165.4 million over ten years
- At 15% overall coverage, unprioritized and age-prioritized PrEP strategies increased healthcare costs by \$316.8–\$420.8 million (Figure 2)
- Conversely, risk-prioritized PrEP reaching 80% of FSWs decreased costs by \$21.4 million (50% adherence) or \$45.3 million (95% adherence)

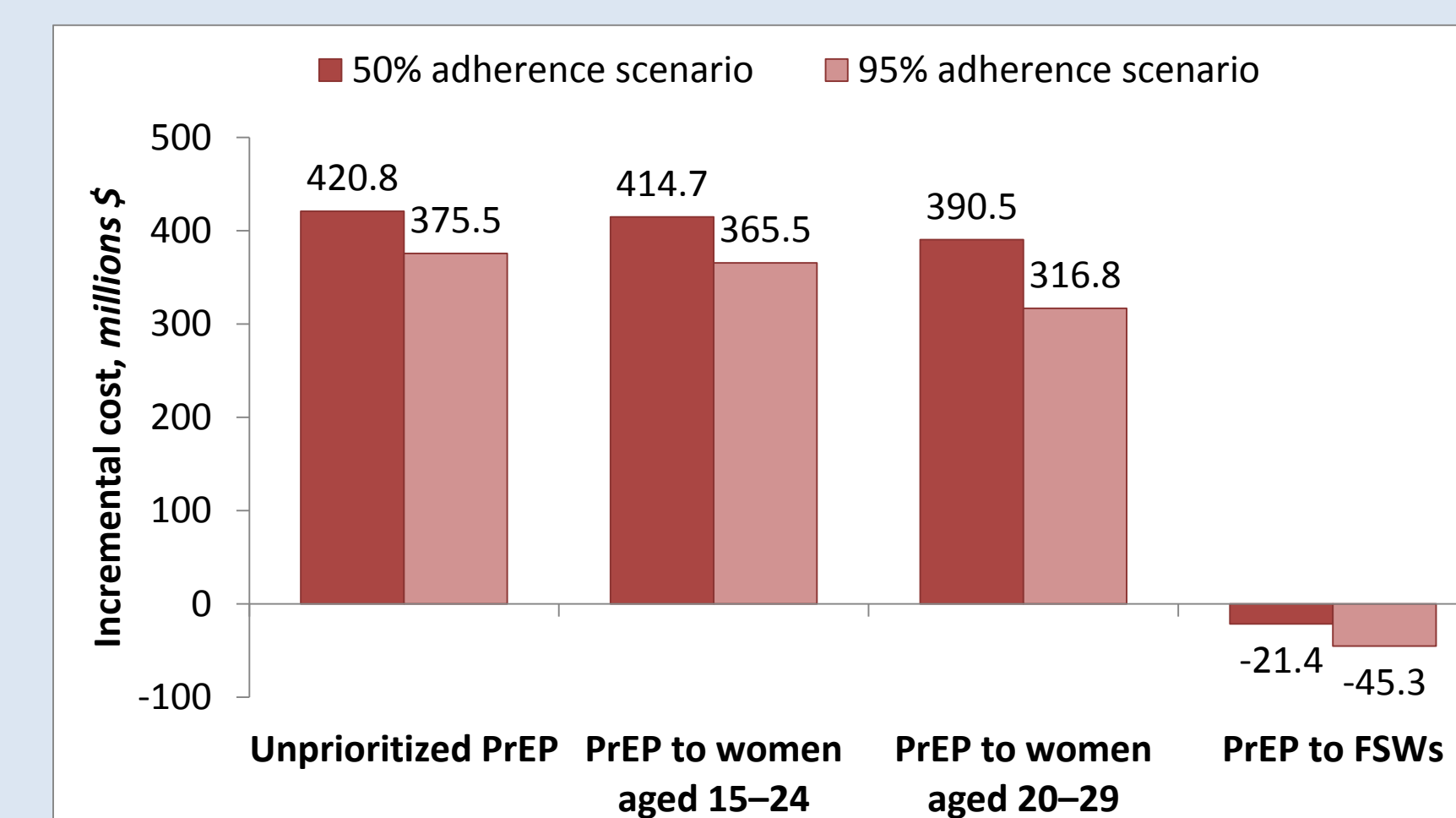


Figure 2. Incremental healthcare costs of PrEP strategies. Unprioritized and age-prioritized PrEP strategies covered 15% of uninfected adults aged 15–54

PrEP Cost-Effectiveness

- PrEP prioritized to 80% of female sex workers was cost-saving (Figure 3)
- PrEP use by women aged 20–29 dominated unprioritized PrEP and PrEP prioritized to women aged 15–24
- The cost and preventative impact of unprioritized and age-prioritized PrEP strategies increased proportionally to PrEP coverage levels
- Costs per infection prevented decreased by 52%–57% at 95% vs. 50% average adherence

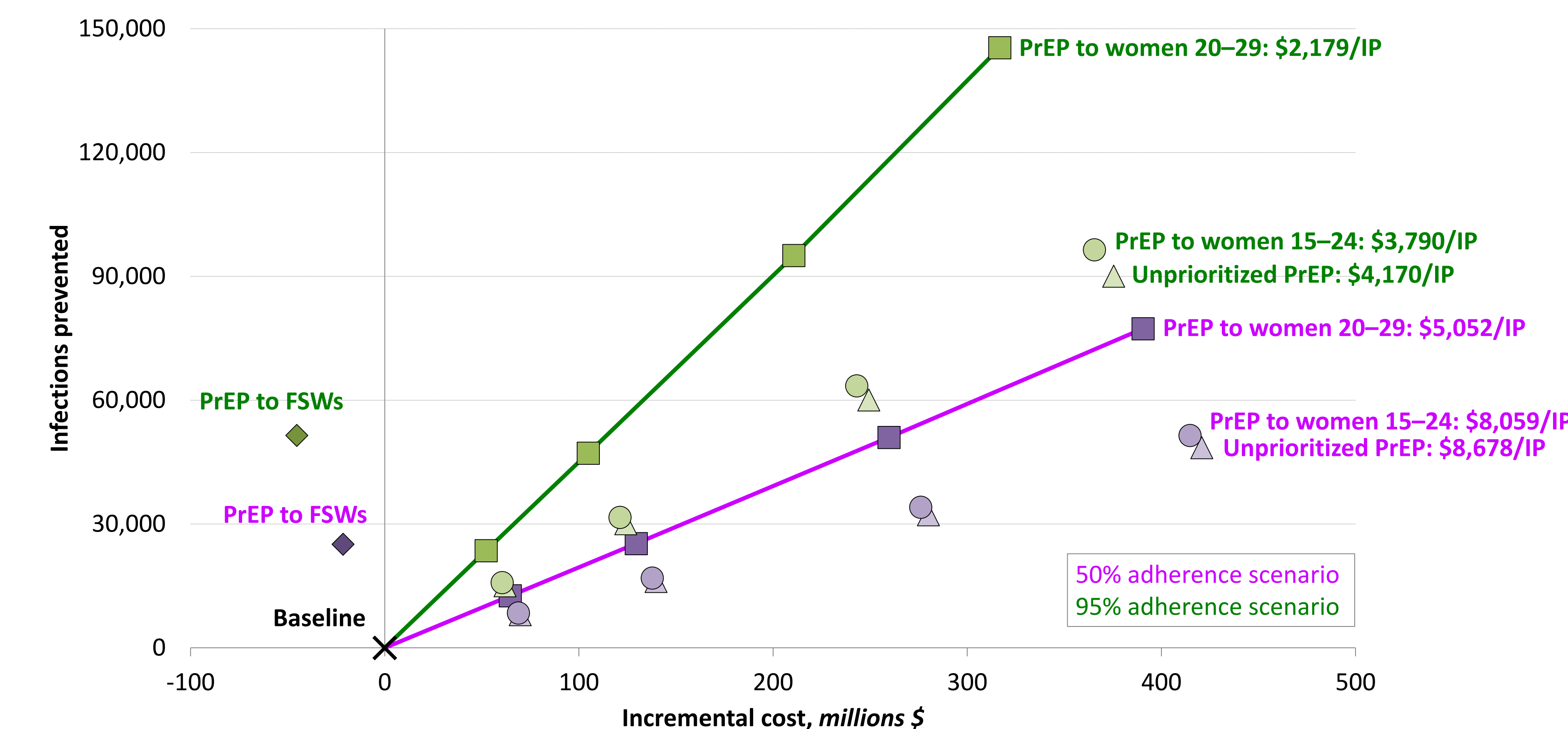


Figure 3. Cost-effectiveness frontiers for PrEP strategies. 2.5%, 5%, 10% and 15% overall coverage levels are shown for unprioritized and age-prioritized PrEP. Cost-effectiveness ratios (relative to baseline) are reported for 15% overall coverage. IP = infections prevented

HIV Drug Resistance

- ART scale-up in the baseline scenario without PrEP produced 476,019 prevalent drug-resistant infections at 2027
- PrEP scale-up decreased prevalent drug-resistant infections in base case simulations (Figure 4)
- Decreases in drug resistance diminished by 2%–12% when in addition to blood, resistance was also tracked in the genital compartment

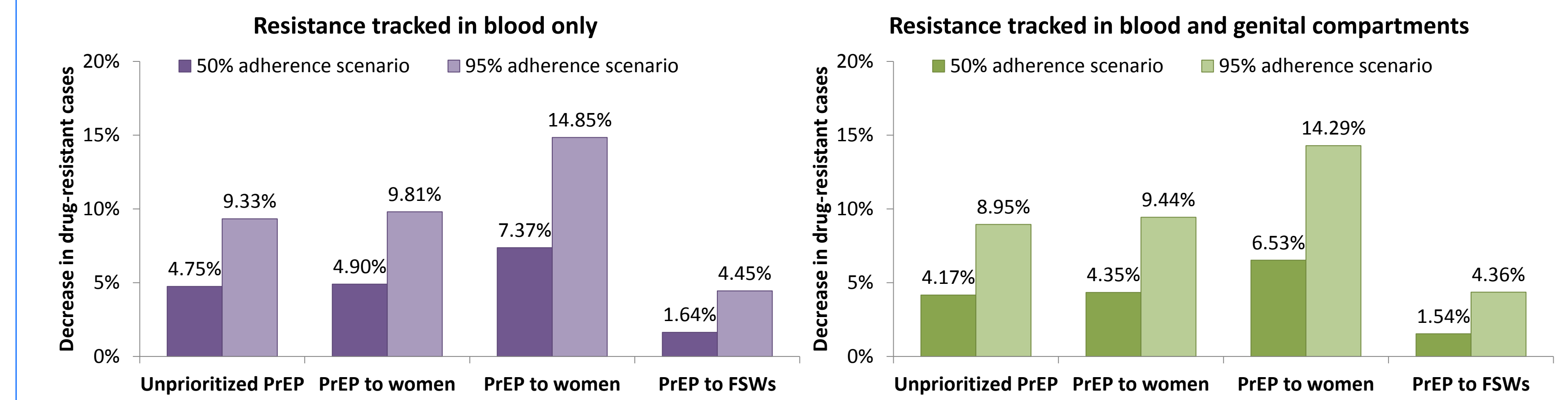


Figure 4. Decreases in (undiscounted) prevalent drug-resistant infections (relative to baseline) after ten years of PrEP scale-up. Unprioritized and age-prioritized PrEP strategies covered 15% of uninfected adults aged 15–54

Uncertainty Analyses

- Risk-prioritized PrEP was cost-saving in all simulations (Figure 5, Table 2)
- Age-prioritized PrEP was more likely to be cost-effective at ages 20–29 vs. 15–24
- Unprioritized PrEP was the least likely to be cost-effective
- At a willingness-to-pay threshold of \$7,500 (~ South Africa's GDP), PrEP's probability of cost-effectiveness was
 - 74% when unprioritized
 - 81% when prioritized to women 15–24
 - 98% when prioritized to women 20–29
 - 100% when prioritized to FSWs

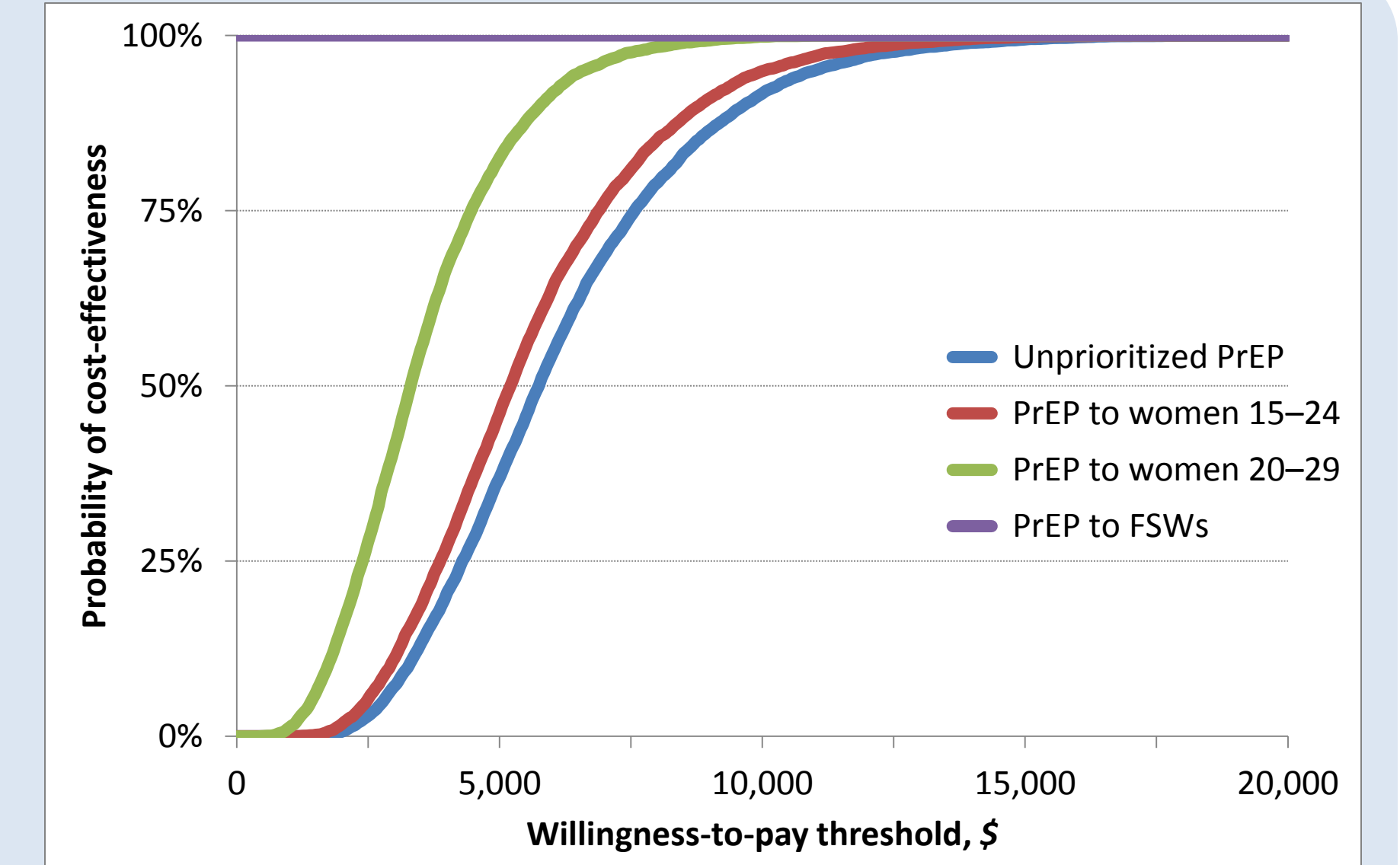


Figure 5. Cost-effectiveness acceptability curves of PrEP strategies (relative to baseline). The probability that PrEP is cost-effective at some willingness-to-pay threshold is the proportion of simulations with cost per infection prevented below that threshold

Table 2. Median (interquartile range) outcomes of PrEP scale-up

Outcome	Unprioritized PrEP	PrEP to women 15–24	PrEP to women 20–29	PrEP to FSWs
Infections prevented	5.1% (3.2%–7.2%)	5.5% (3.5%–7.9%)	8.0% (5.1%–11.5%)	3.4% (2.6%–4.5%)
Incremental cost, millions	\$213 (\$137–\$310)	\$209 (\$134–\$305)	\$192 (\$122–\$284)	–18 (–26 to –13)
Cost per infection prevented	\$5,747 (\$4,291–\$7,573)	\$5,209 (\$3,870–\$6,888)	\$3,309 (\$2,390–\$4,462)	cost-saving

Conclusions

- DPV VR PrEP could have considerable impact on HIV prevention at compelling economic value when prioritized to women by age
- DPV VR PrEP could decrease drug resistance, even if adherence is modest

Acknowledgements

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