On Demand PrEP Dosing (2-1-1) for Women

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UNC Eshelman School of Pharmacy

HPTN Annual Meeting

Key Takeaways

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1. Women need On Demand PrEP options
2. PrEP pharmacology differs between vaginal vs rectal HIV transmission
3. Modeling and simulation can be used to optimize On Demand PrEP dosing for women

Fewer PrEP Options for Women

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PrEP for Rectal Transmission

- CAB 600mg IM q2 months
- FTC+TAF 200/25mg po daily
- FTC+TDF 200/300mg po
  - daily **OR**
  - #2 tablets 2-24h before sex, #1 24h after, #1 48h after **(2-1-1)**

PrEP for FGT Transmission

- CAB 600mg IM q2 months
- FTC+TDF 200/300mg po daily

FGT = female genital tract, CAB = cabotegravir, IM = intramuscular, FTC+TAF = emtricitabine + tenofovir alafenamide, FTC+TDF = emtricitabine + tenofovir disoproxil fumarate

PrEP Pharmacology is Multifactorial

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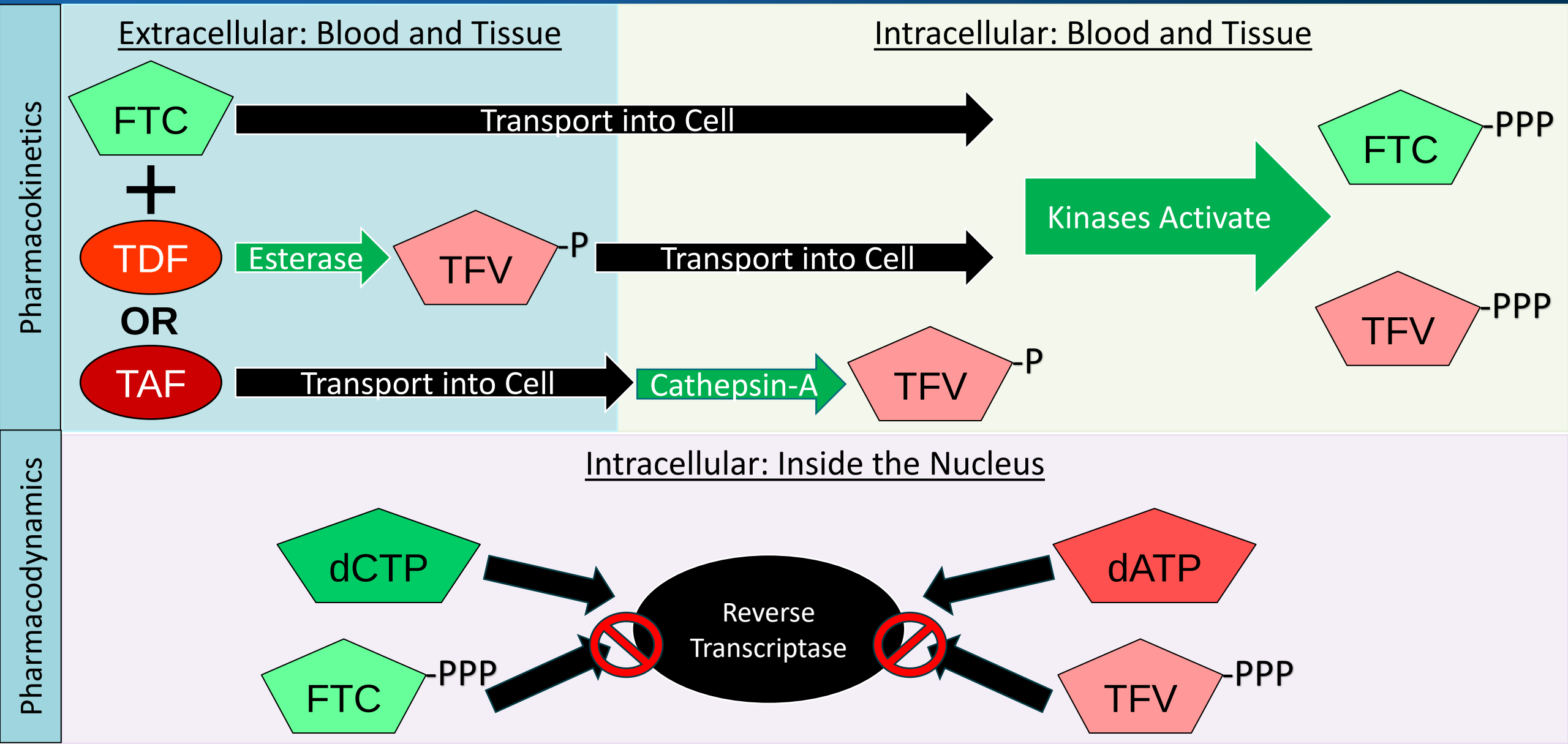

PrEP Pharmacology Differs by Site of HIV Transmission Risk

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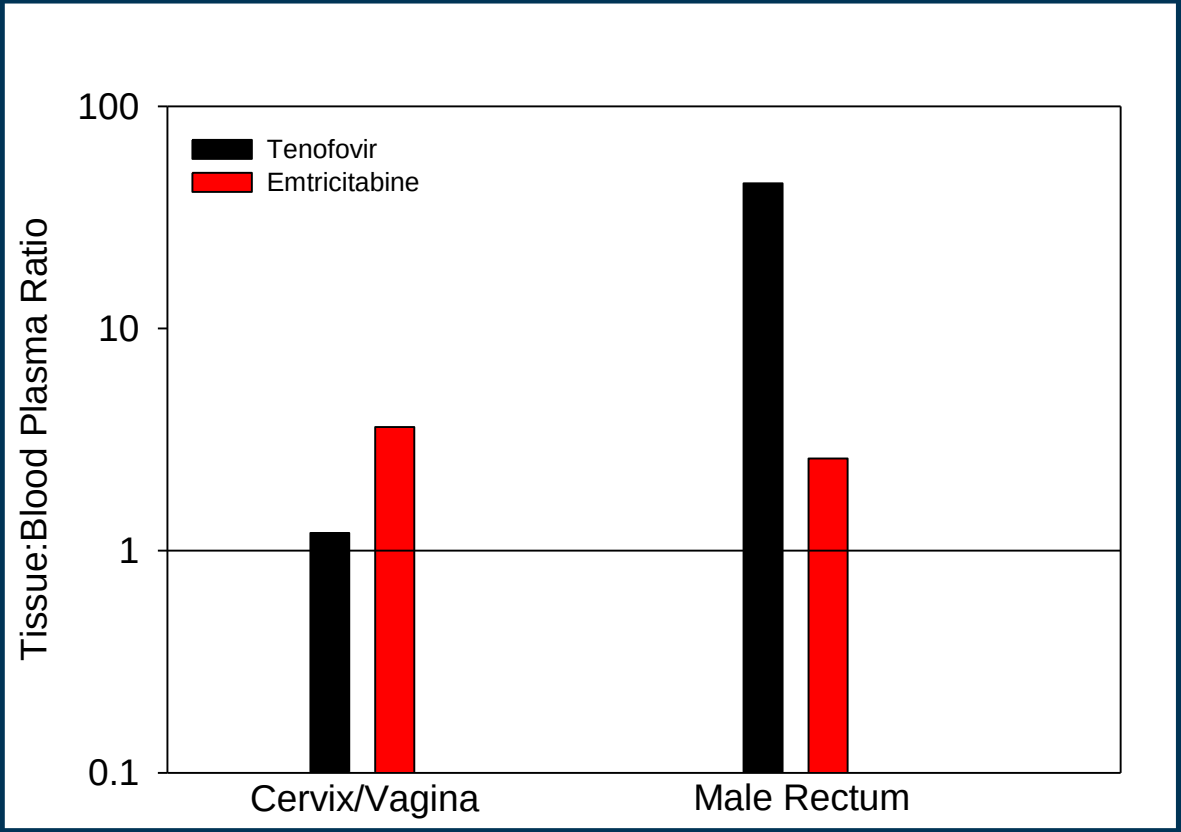
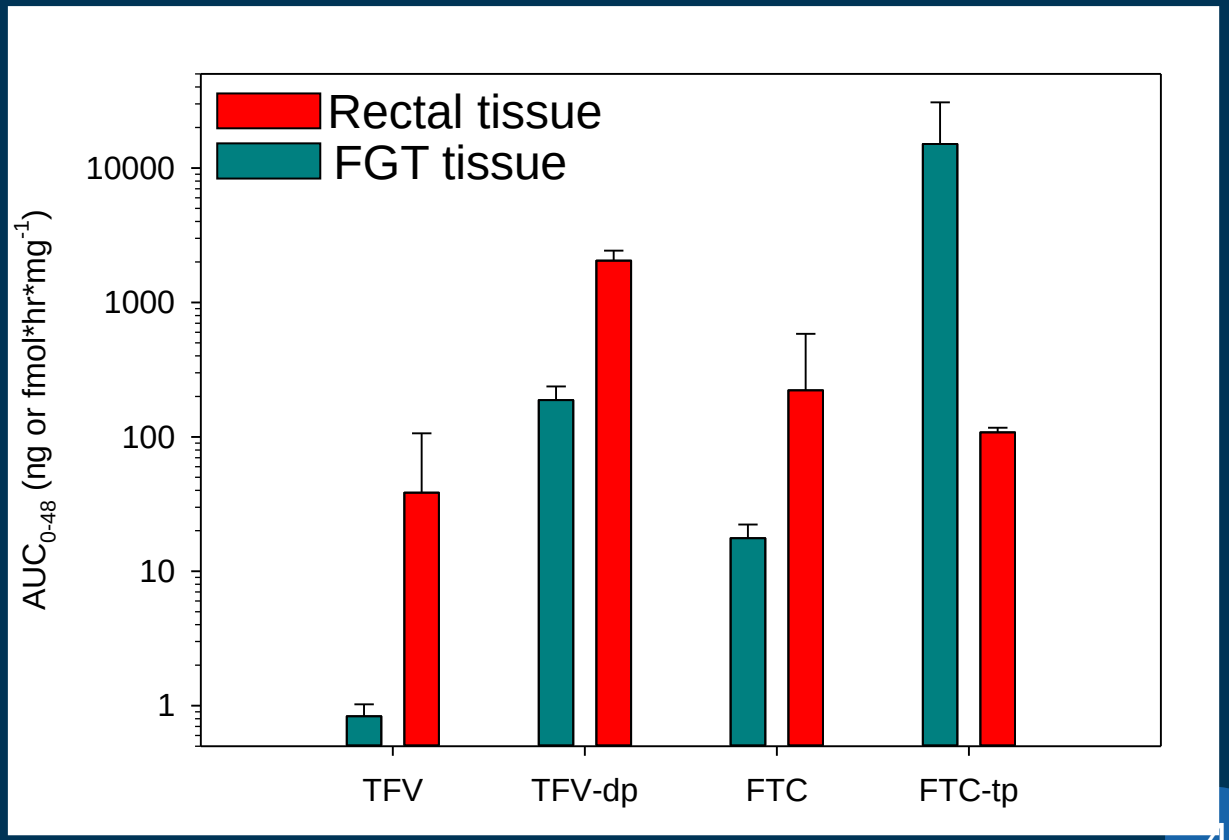
Lower TFV in FGT vs rectum



Patterson KB Sci Transl Med. 2011 Dec 7;3(112):112re4.

Lower TFVdp but higher FTCtp in FGT vs rectum



Adapted from Cottrell ML et al. *J Infect Dis*. 2016 Jul 1;214(1):55-64.

PrEP Effectiveness May Differ by Site of HIV Transmission Risk

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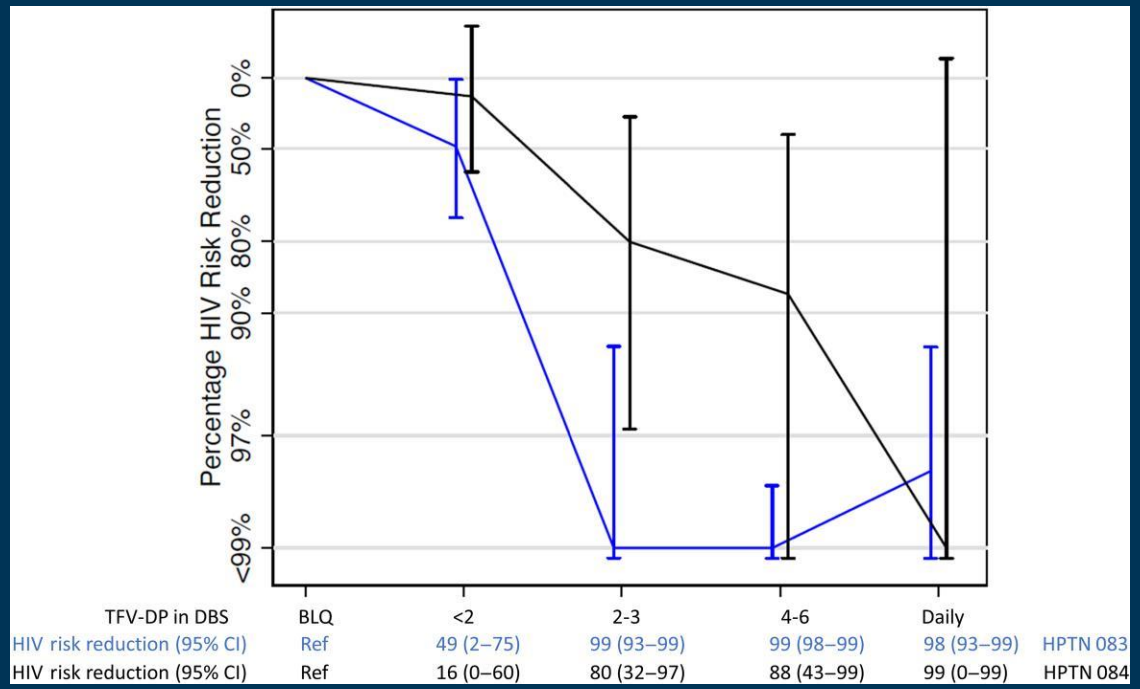
Lower risk reduction for women vs men with less than daily dosing



Anderson PL et al. *CID*. 2023 76(10):1850-3.

Low incidence among women reporting 4-6 doses/week

Doses Per Week	HIV incidence rate per 100 person-years (95% CI)
7	0 [Reference]
4-6	0.13 (0.02-0.92)
4-6 ↓ to 2-3	0.49 (0.22-1.08)
<2	1.27 (0.53-3.04)

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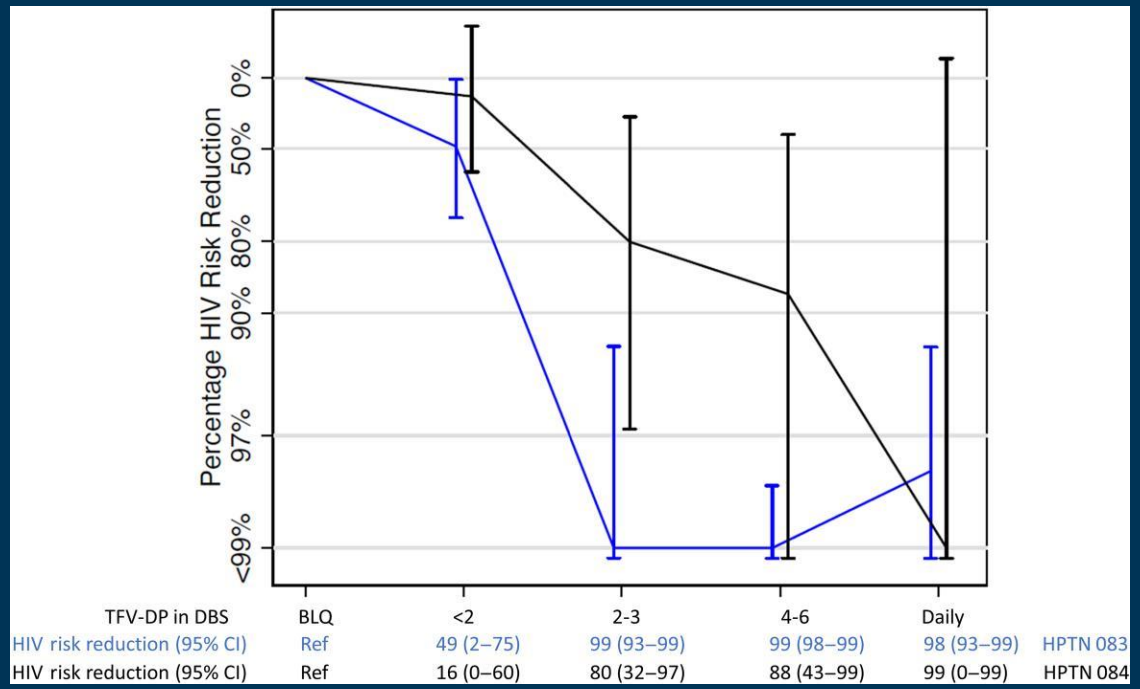

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Model Predicted PrEP Effectiveness Tracks with Clinical Estimates

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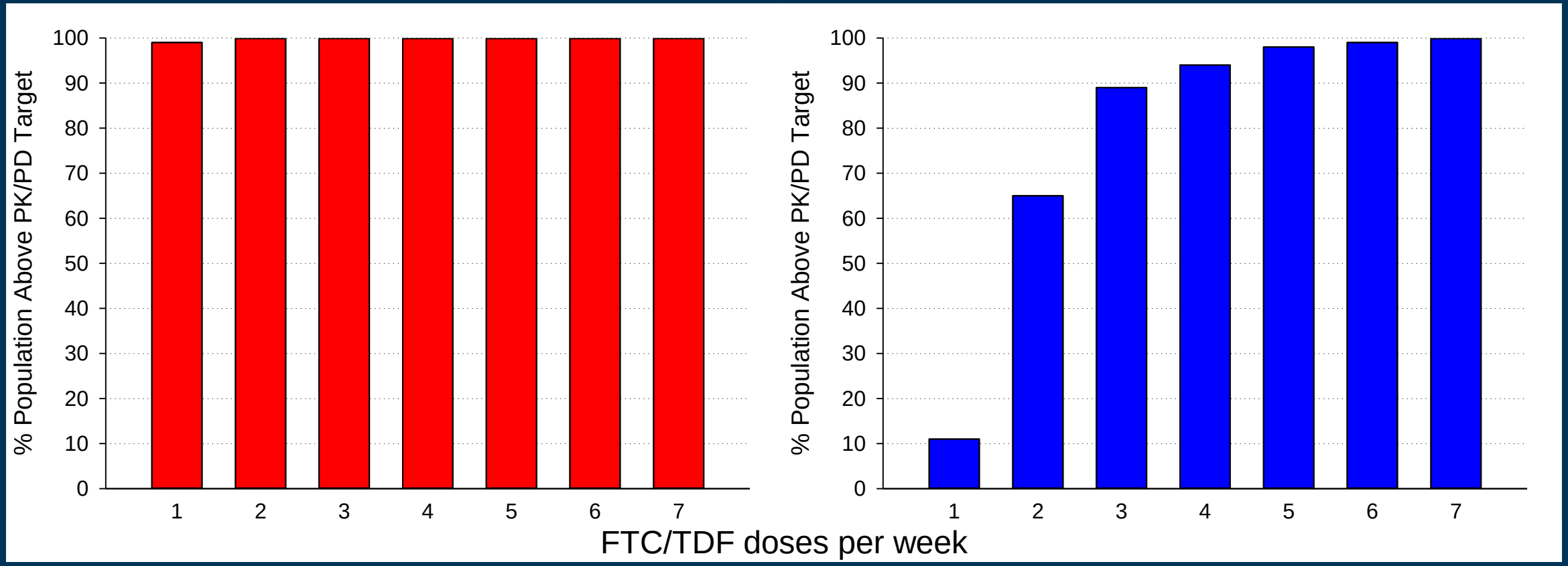
Rectal Tissue Simulations

FGT Tissue Simulations



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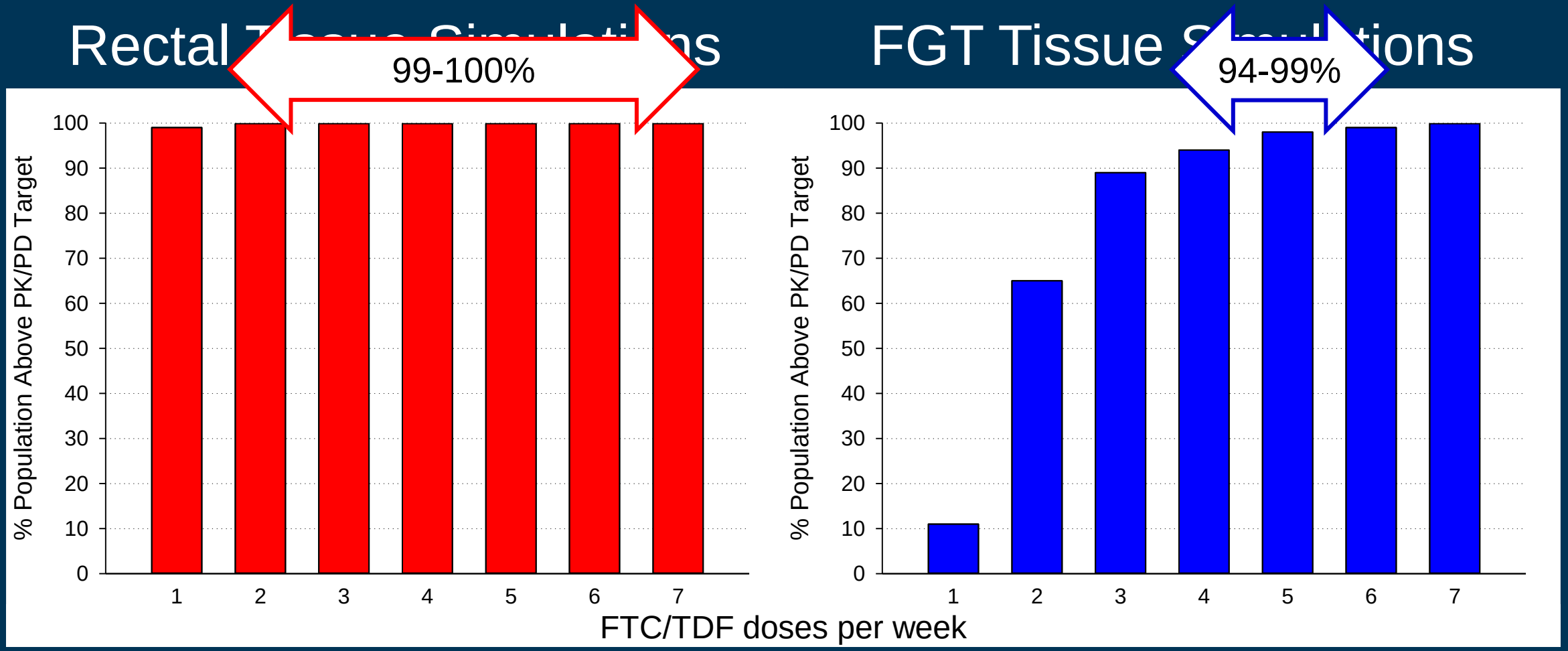

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Modeling & Simulation Can be Used to Optimize On Demand PrEP for Women

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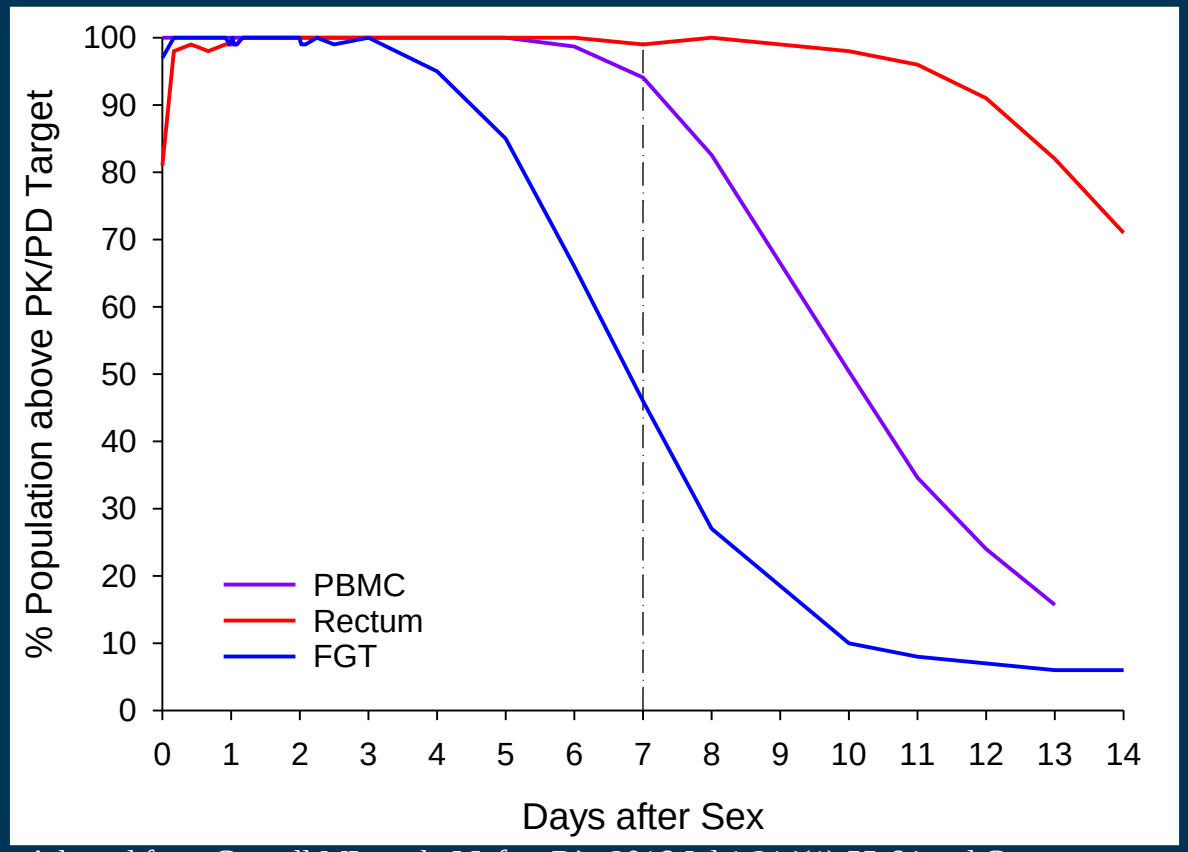
Lowest 2-1-1 efficacy predicted in FGT vs blood and rectum



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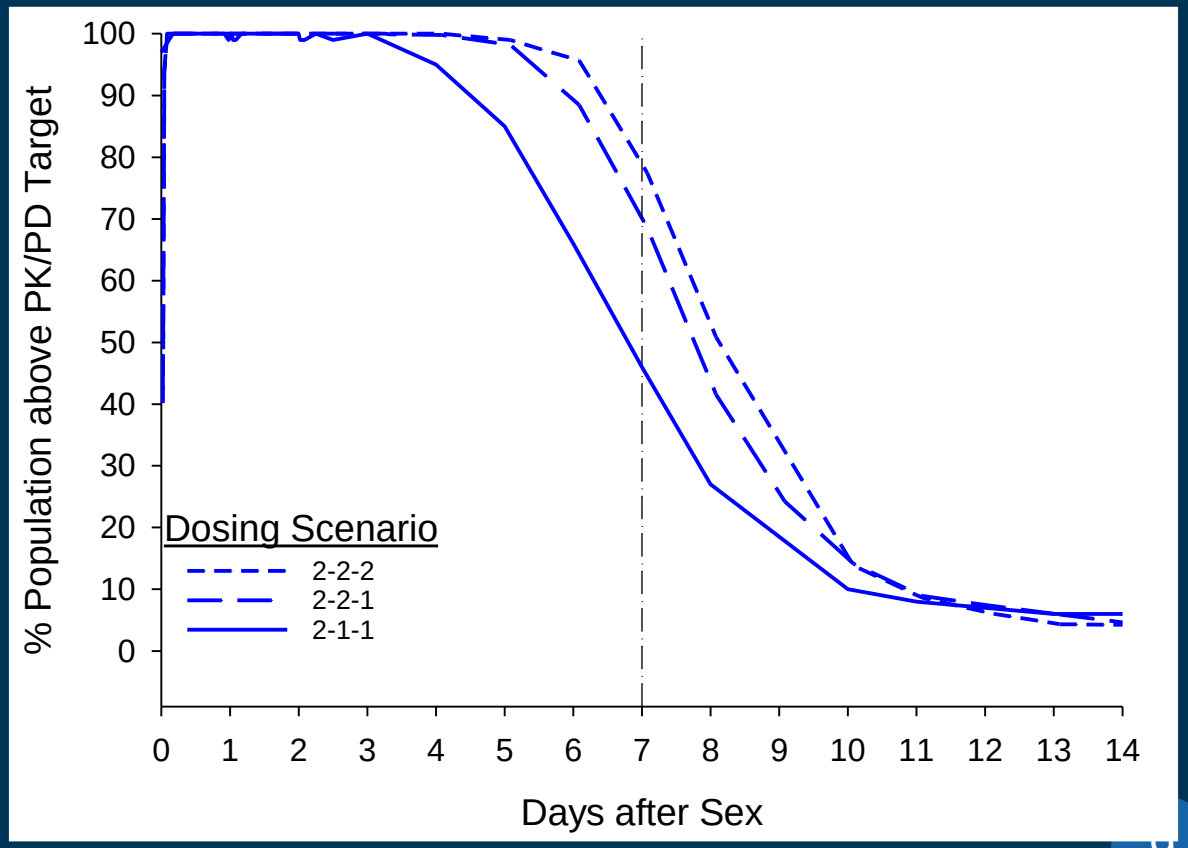
2-2-2 dosing increases predicted efficacy in FGT by >30%



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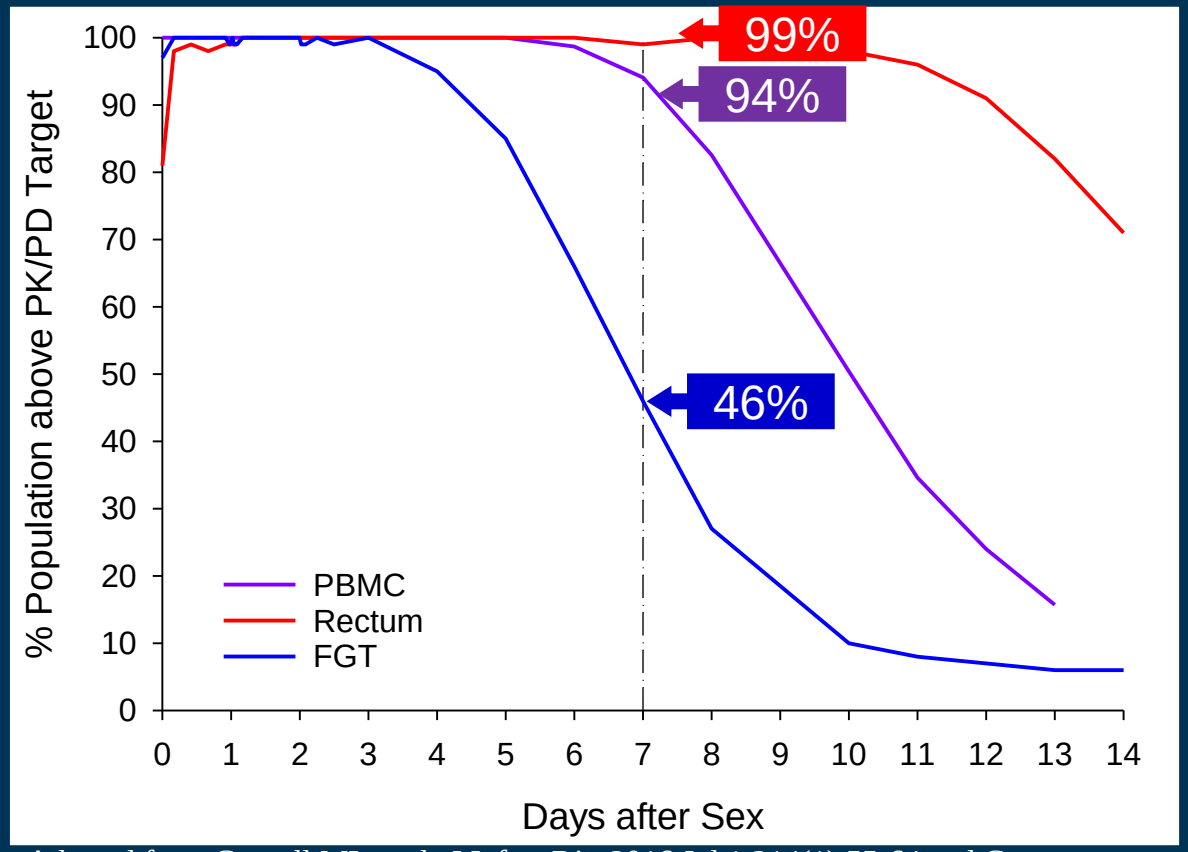

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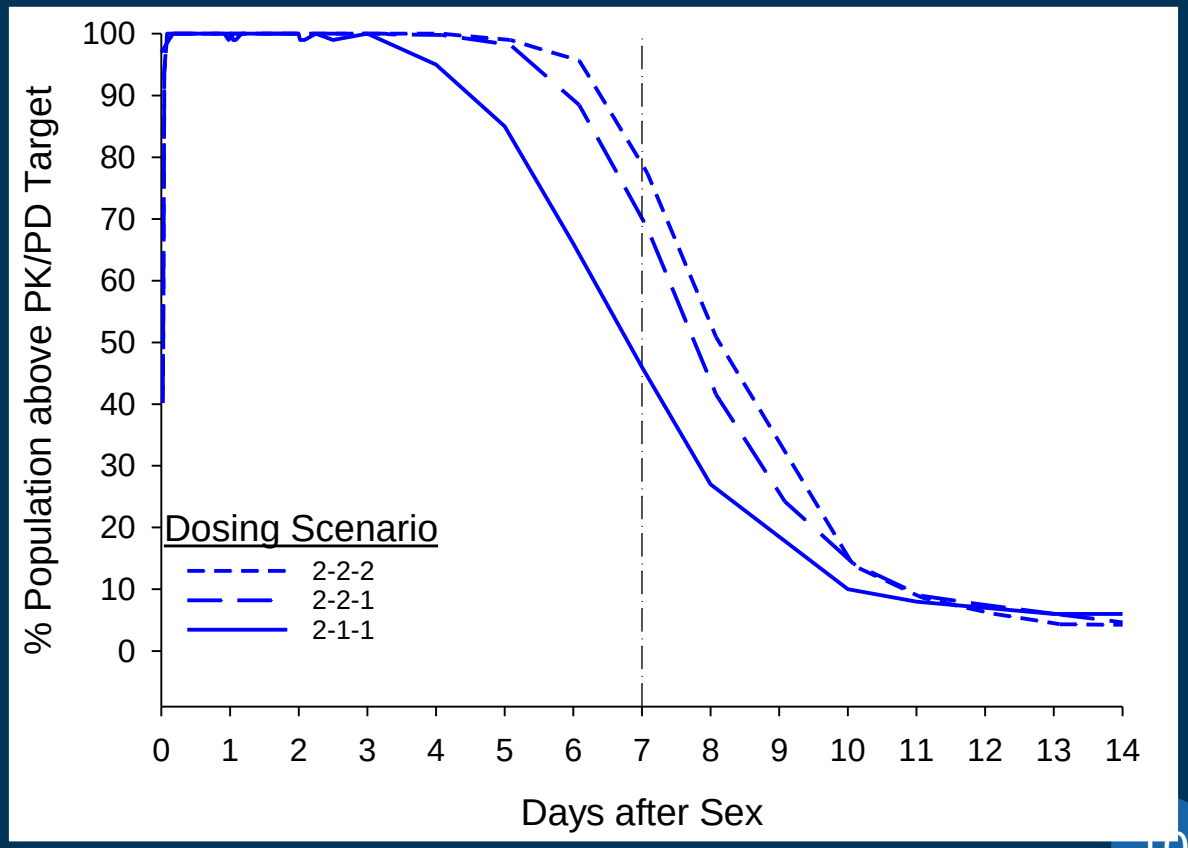

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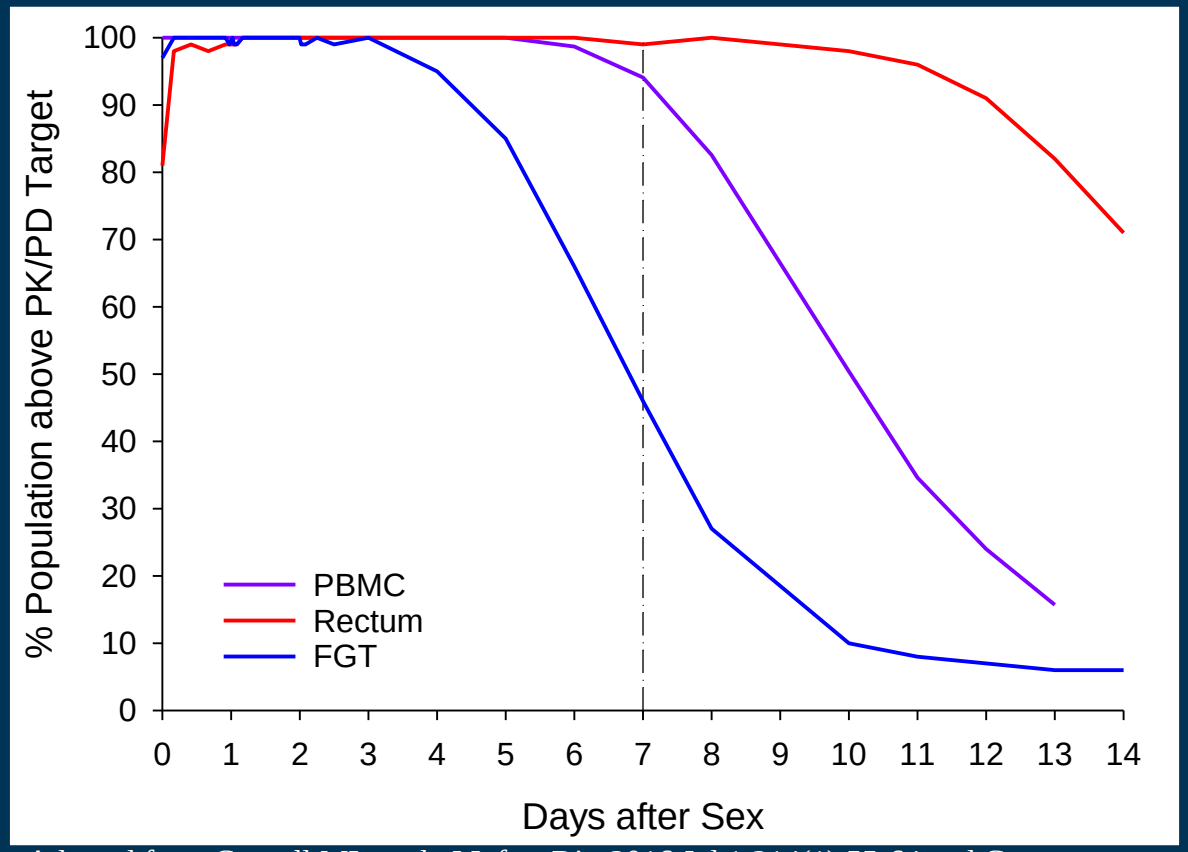

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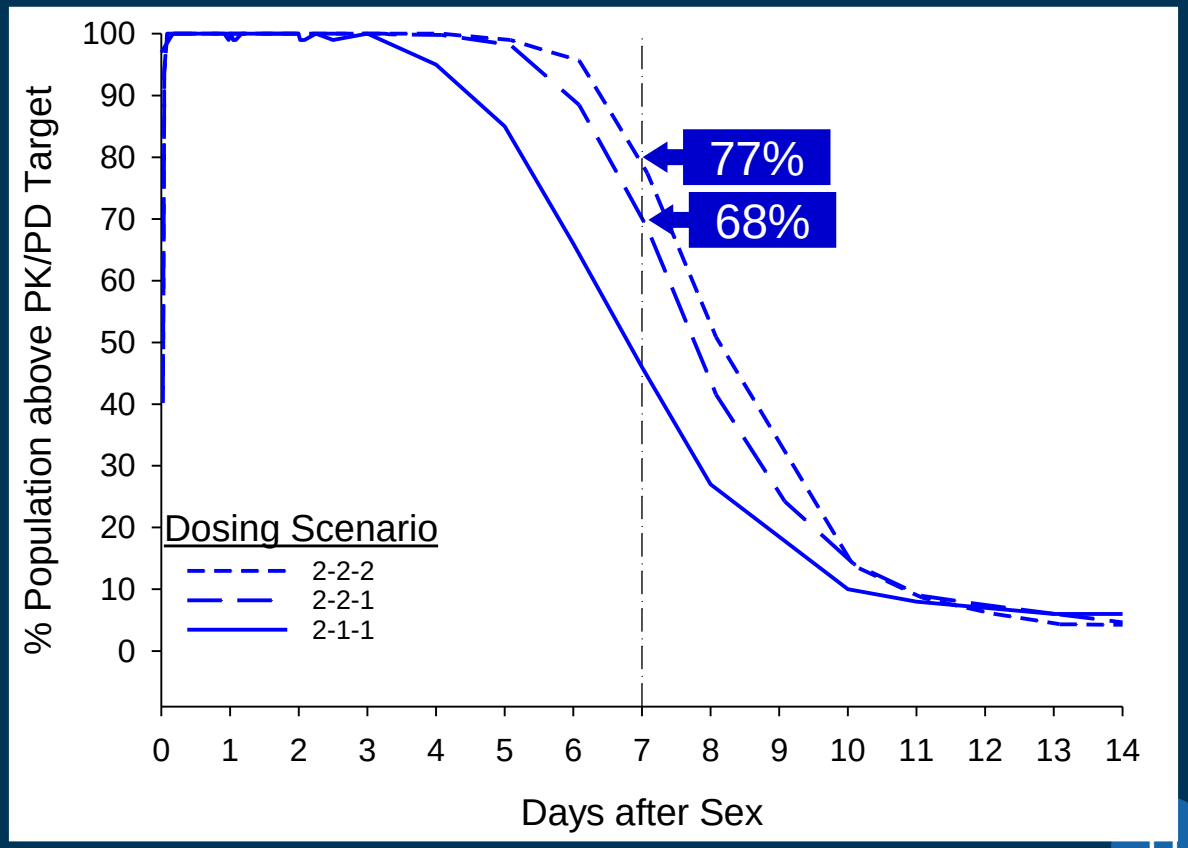

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Acknowledgments

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