# The relative cost-effectiveness of long-acting injectable cabotegravir versus oral pre-exposure prophylaxis

## A modelled economic evaluation and threshold analysis in South Africa based on the HPTN 083 and 084 trials

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# Background

- Oral pre-exposure prophylaxis (PrEP), in the combination drug tenofovir (TDF) and emtricitabine (FTC), is 65%-85% effective in preventing HIV infection *(Hansom 2016, Fonner 2016, Baeten 2012)*
- Compared to TDF/FTC, long-acting injectable cabotegravir (CAB-LA) reduced risk of HIV infection by 66% in gay men and other men who have sex with men and transgender women *(HPTN 083: Landovitz 2021)*, and 89% young cisgender women *(HPTN 084: Delany-Moretlwe 2022)*
- CAB-LA removes the need for users to take daily pills, allowing for persistent use and improving adherence in the short term
- Acceptability studies have found a higher stated preference for long-acting injectable products compared to daily pills *(Tolley 2019, 2020; Cheng 2019; Gill 2020)*
- Limited studies on the cost and impact of injectable PrEP in sub-Saharan Africa, and no studies comparing injectable PrEP to oral PrEP

# Methods

- Model the **impact and cost-effectiveness of CAB-LA compared to TDF/FTC** over a 20-year time horizon (2022-2041) **in South Africa**
- We estimate the **threshold cost of CAB-LA**, per injection, that makes it similarly or more cost-effective compared to TDF/FTC
- Model used: **Thembisa**, a deterministic compartmental HIV transmission model of the South African HIV epidemic (https://thembisa.org)
- We model **two coverage scenarios** (medium/high) and, for CAB-LA, **two duration scenarios** (minimum: average duration on PrEP same as oral PrEP, maximum: longer than oral PrEP)
- **Baseline**: current TDF/FTC roll-out programme (low coverage 0.5-3% of target populations)
- We target adolescent girls and young women (AGYW), female sex workers (FSW), adolescent boys and young men (ABYM), gay men and other men who have sex with men (MSM)

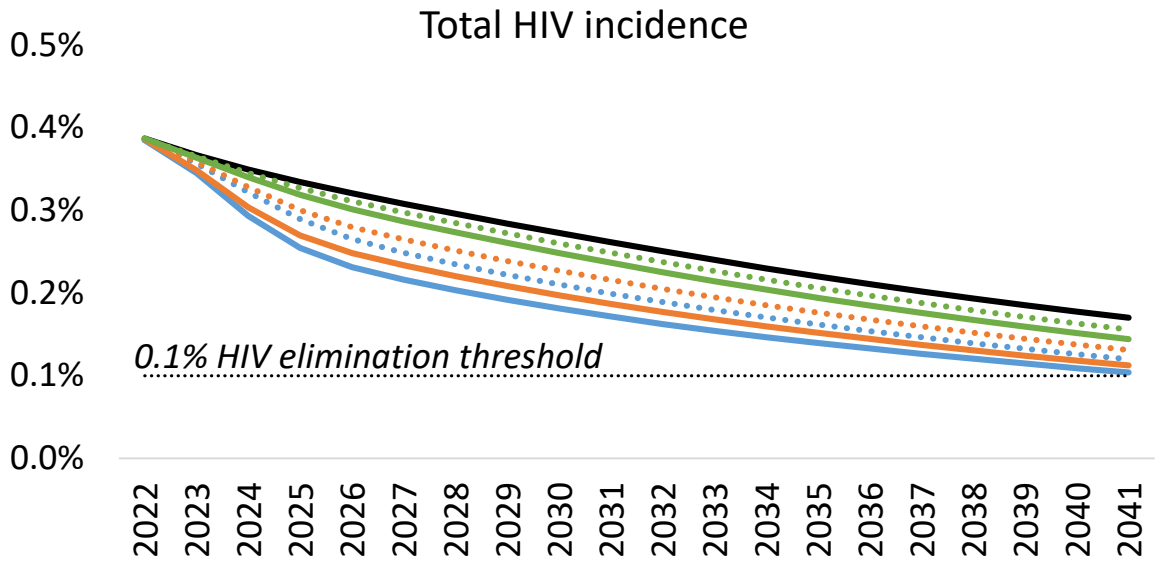
# Methods: Cost analysis

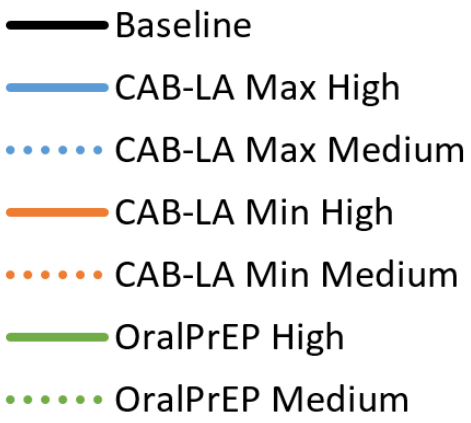
- Ingredients-based costing from the **provider's perspective**
- Resource use data:
  - Oral PrEP: guidelines, implementation and demonstration projects
  - CAB-LA: trial protocols, adjusted for public sector implementation
- Cost includes lowest staff cadre, demand creation and training
- Drug prices:
  - Oral PrEP: current generic drug prices
  - CAB-LA: **range between 1-5x** that of oral PrEP
- CAB-LA costs include staff time for injections, excludes creatinine
- Costs in 2021 USD, undiscounted

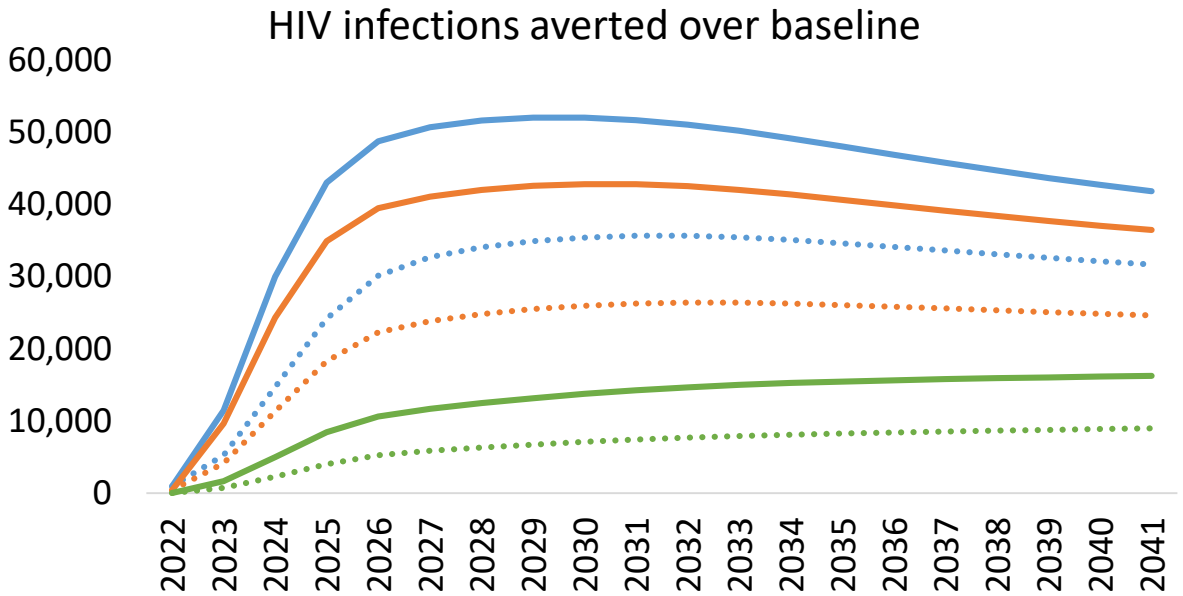
# Methods: Scenarios

| | Oral PrEP (TDF/FTC) | | CAB-LA | | | |
|---|---|---|---|---|---|---|
| | | | *Minimum duration* | | *Maximum duration* | |
| | **Medium coverage** | **High coverage** | **Medium coverage** | **High coverage** | **Medium coverage** | **High coverage** |
| **Duration** | 5 mo (AGYW, FSW, ABYM); 11 mo (MSM) | | *Same as for TDF/FTC* | | 12 mo (AGYW, FSW, ABYM); 24 mo (MSM) | |
| **Coverage** | 5% (AGYW, ABYM); 15% (FSW, MSM) | 10% (AGYW, ABYM); 30% (FSW, MSM) | 10% (ABYM); 20% (AGYW); 25% (FSW, MSM) | 20% (ABYM); 40% (AGYW); 50% (FSW, MSM) | 20% (ABYM); 35% (AGYW); 40% (FSW, MSM) | 35% (ABYM); 60% (AGYW); 67% (FSW, MSM) |
| **Effectiveness** | 65% (AGYW, FSW); 85% (ABYM, MSM) | | 95% (all populations) | | | |
| **Annual cost per person initiated** | $76-78 (AGYW, FSW, ABYM); $116 (MSM) | | $78-81 (AGYW, FSW, ABYM); $122 (MSM) | | $131-137 (AGYW, FSW, ABYM, MSM 1st year); $105 (MSM 2nd year) | |

# Results: Impact on HIV

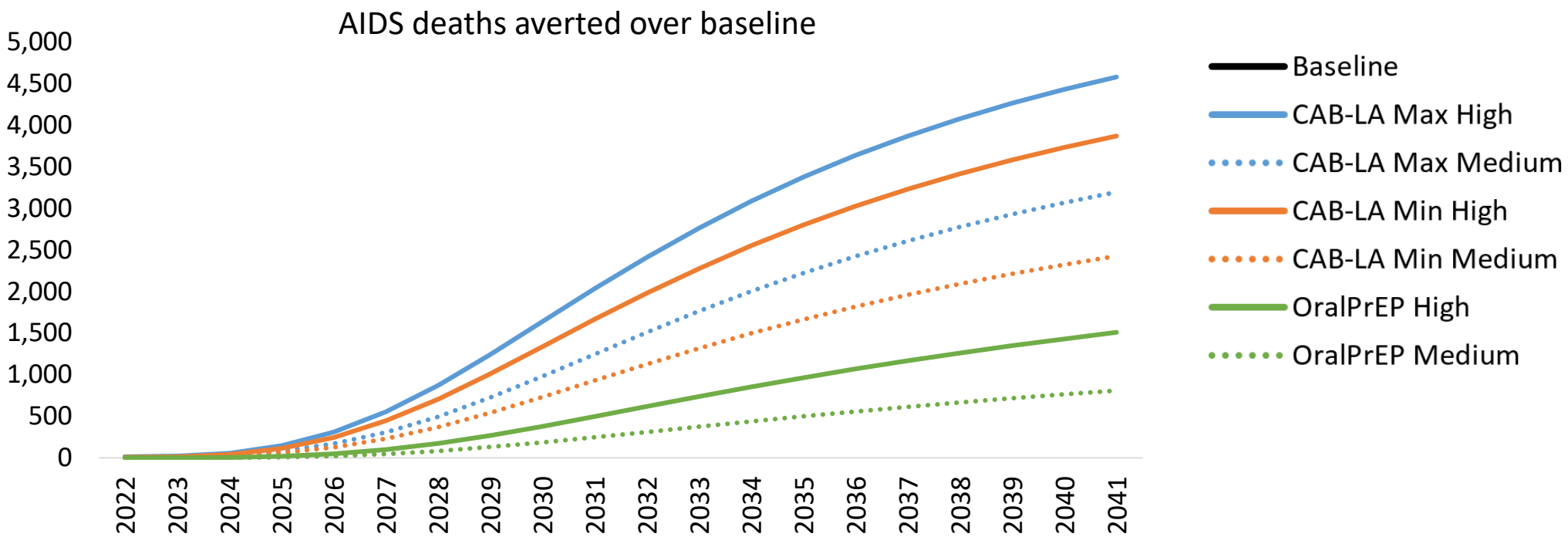


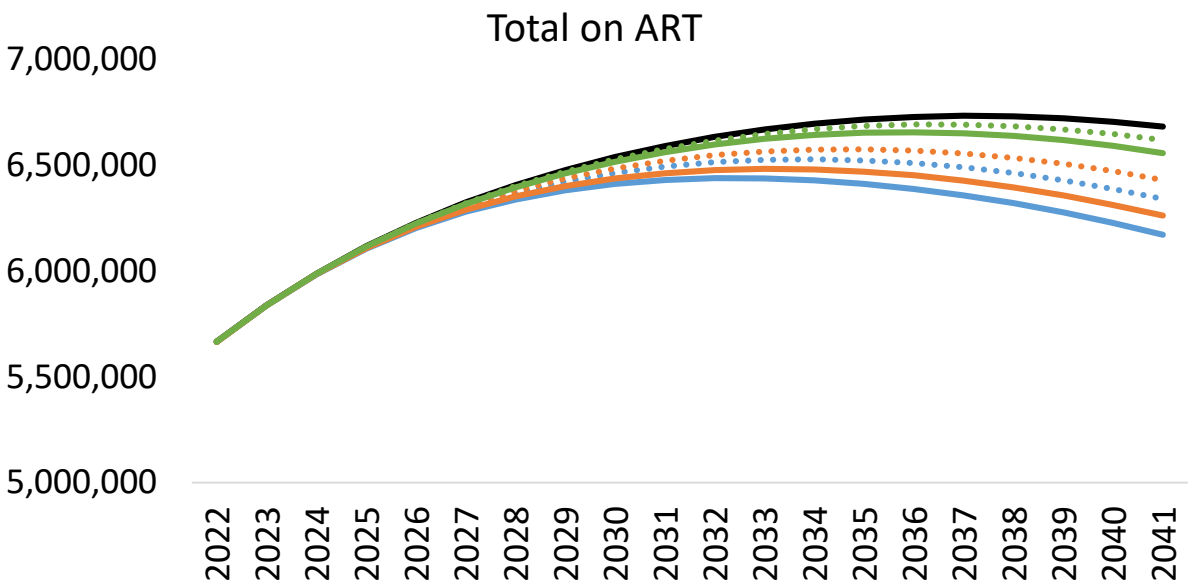

- At baseline, HIV incidence is declining from 0.39% to 0.17%
- By 2041, incidence decreased to:
  - 0.15%-0.16% (TDF/FTC)
  - 0.10%-0.13% (CAB-LA)
- HIV infections averted:
  - max. 8,900-16,300 infections/yr (TDF/FTC)
  - max. 26,400-52,000 infections/yr (CAB-LA)

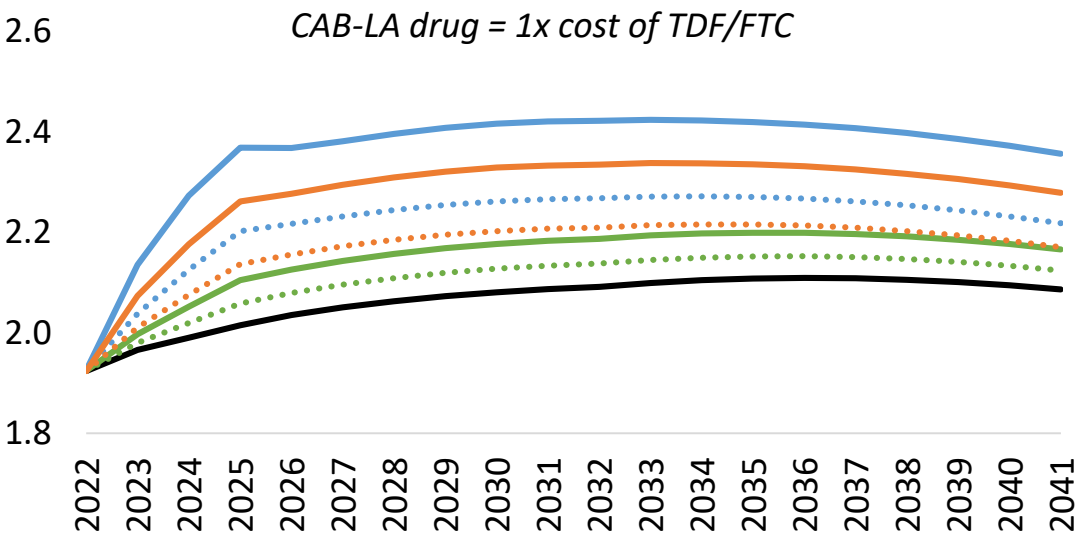
# Results: Impact on AIDS deaths

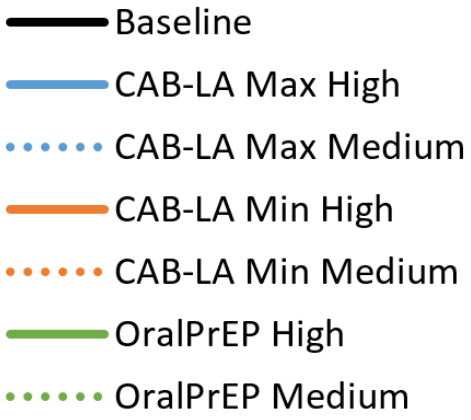



- Under CAB-LA, more AIDS deaths are averted annually
- Over 20 years, AIDS deaths averted:
  - 6,500 (0.6%) – 12,400 (1.2%) (TDF/FTC)
  - 21,500 (2%) – 43,400 (4%) (CAB-LA)

# Results: Impact on cost of the HIV programme




- By 2041, the number of people on ART, compared to baseline:
  - reduced by 1%-2% (TDF/FTC)
  - reduced by 4%-8% (CAB-LA)
- Total HIV programme cost higher with CAB-LA
  - despite less need for ART
  - due to assumed higher uptake compared to TDF/FTC

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# Cost effectiveness over 20 years

## ***Medium coverage*** *scale-up for PrEP interventions*

| Scenario | New HIV infections | | Life years lost due to AIDS | | CAB-LA drug cost relative to oral PrEP | Total cost of the HIV programme (billions 2021 USD) | | Incremental cost effectiveness (2021 USD) | |
|---|---|---|---|---|---|---|---|---|---|
| | *Number [millions]* | *% averted over BL* | *Number [millions]* | *% saved over BL* | | *Cost* | *Incremental cost over BL* | *Cost/ infection averted* | *Cost/ life year saved* |
| **Baseline** | 3.02 | | 37.34 | | | 41.29 | | | |
| Oral PrEP | 2.90 | 4% | 37.02 | 1% | - | 42.08 | 2% | **6,053** | **2,309** |
| CAB-LA minimum duration | 2.58 | 15% | 36.19 | 3% | 1x | 43.25 | 5% | 4,471 | 1,705 |
| | | | | | 2x | 44.46 | 8% | 7,211 | 2,751 |
| | | | | | 3x | 45.66 | 11% | 9,952 | 3,796 |
| | | | | | 4x | 46.86 | 13% | 12,692 | 4,842 |
| | | | | | 5x | 48.07 | 16% | 15,433 | 5,887 |
| CAB-LA maximum duration | 2.44 | 19% | 35.81 | 4% | 1x | 44.31 | 7% | 5,157 | 1,978 |
| | | | | | 2x | 46.24 | 12% | 8,447 | 3,240 |
| | | | | | 3x | 48.16 | 17% | 11,737 | 4,501 |
| | | | | | 4x | 50.09 | 21% | 15,027 | 5,763 |
| | | | | | 5x | 52.02 | 26% | 18,317 | 7,025 |

# Cost effectiveness over 20 years

## *High coverage scale-up for PrEP interventions*

| Scenario | New HIV infections | | Life years lost due to AIDS | | CAB-LA drug cost relative to oral PrEP | Total cost of the HIV programme (billions 2021 USD) | | Incremental cost effectiveness (2021 USD) | |
|---|---|---|---|---|---|---|---|---|---|
| | *Number [millions]* | *% averted over BL* | *Number [millions]* | *% saved over BL* | | *Cost* | *Incremental cost over BL* | *Cost/ infection averted* | *Cost/ life year saved* |
| **Baseline** | 3.02 | | 37.34 | | | 41.29 | | | |
| Oral PrEP | 2.79 | 8% | 36.72 | 2% | - | 42.92 | 4% | **6,610** | **2,498** |
| CAB-LA minimum duration | 2.31 | 24% | 35.41 | 5% | 1x | 45.42 | 10% | 5,779 | 2,145 |
| | | | | | 2x | 47.83 | 16% | 9,147 | 3,394 |
| | | | | | 3x | 50.24 | 22% | 12,515 | 4,644 |
| | | | | | 4x | 52.64 | 27% | 15,882 | 5,894 |
| | | | | | 5x | 55.05 | 33% | 19,250 | 7,144 |
| CAB-LA maximum duration | 2.17 | 28% | 35.03 | 6% | 1x | 47.10 | 14% | 6,785 | 2,510 |
| | | | | | 2x | 50.63 | 23% | 10,915 | 4,038 |
| | | | | | 3x | 54.16 | 31% | 15,045 | 5,566 |
| | | | | | 4x | 57.70 | 40% | 19,175 | 7,094 |
| | | | | | 5x | 61.23 | 48% | 23,305 | 8,622 |

# Threshold analysis:

## Solving the equation for the *exact* cost for CAB-LA (per injection) to be as cost-effective as oral PrEP

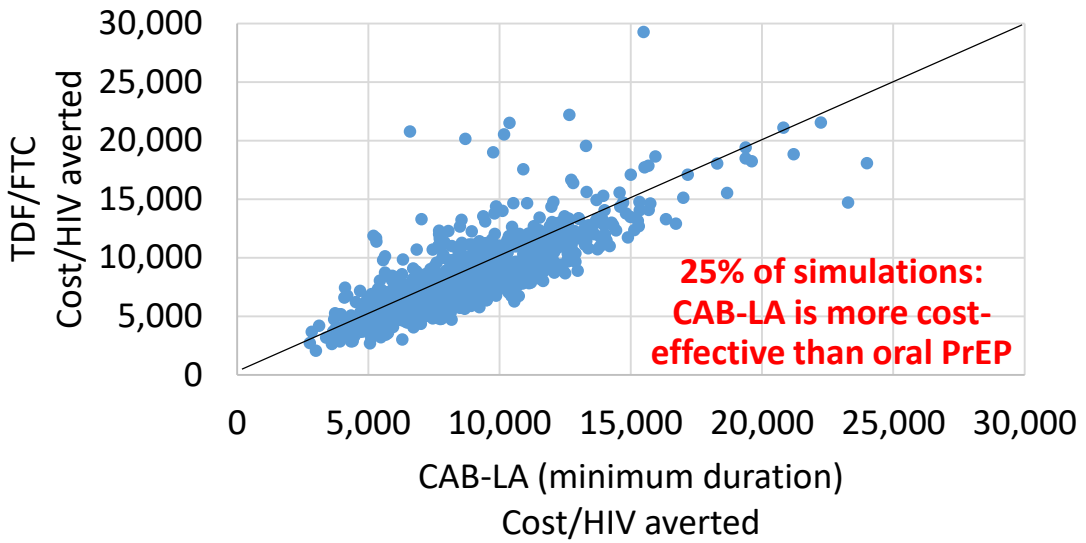
| | *Minimum duration scenario* | | *Maximum duration scenario* | |
|---|---|---|---|---|
| **Cost per CAB-LA injection (2021 USD)** | **Medium coverage** | **High coverage** | **Medium coverage** | **High coverage** |
| Equal ICERS for cost/HIV infection averted | $14.47 | $11.57 | $11.79 | $9.03 |
| Equal ICERS for cost/life year saved | $14.47 | $11.88 | $11.70 | $9.33 |

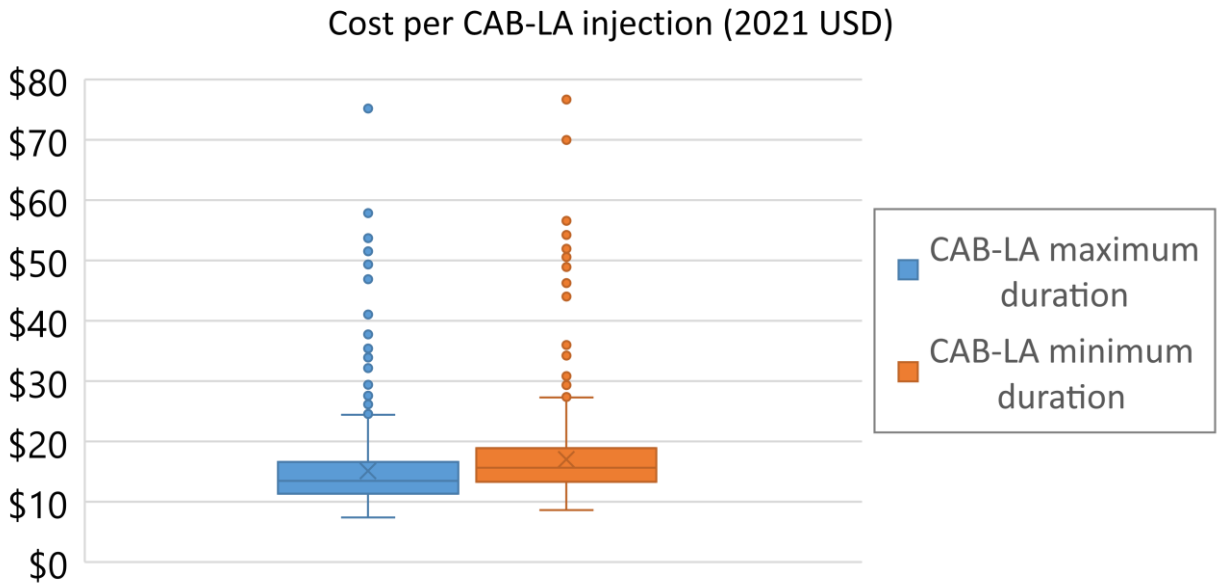
**→ Acceptable range of cost per injection $9-$15**

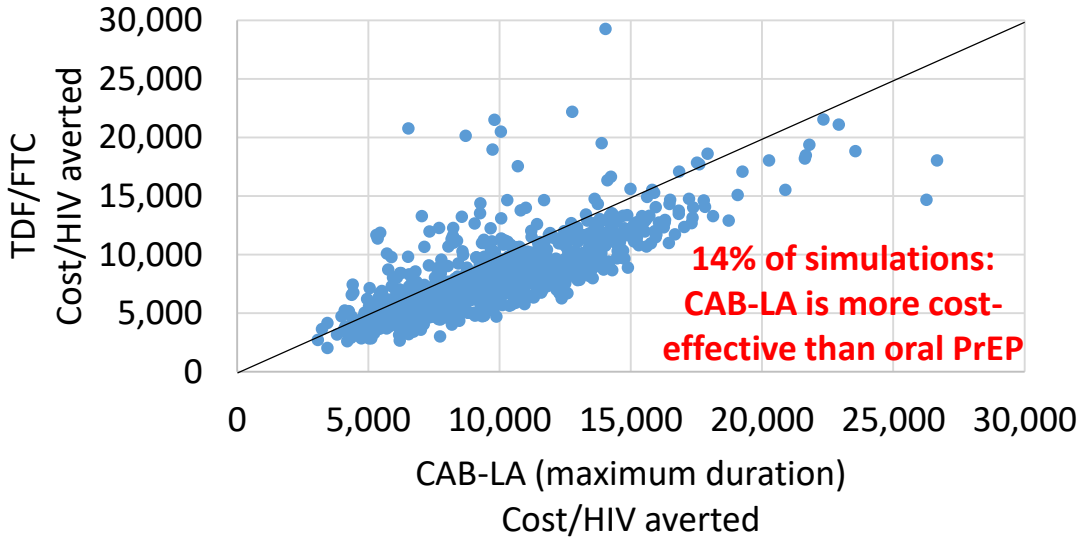
# Probabilistic sensitivity analysis

Cost of CAB-LA = 2x cost of oral PrEP

- We run 1,000 Monte Carlo simulations, sampling from distributions for key parameters (coverage, effectiveness, reduction in condom use while on PrEP, relative uptake rate in low HIV risk users, cost of PrEP provision)
- With uncertainty, **acceptable range of cost per injection $11-$19** (interquartile range)



# Conclusion

- CAB-LA is a highly effective in preventing HIV transmission
  - Estimated 3- to 5-fold increase in averting HIV infections and AIDS deaths over 20 years
- Cost of CAB-LA drug needs to be <$9/injection (high coverage) or <$15/injection (medium coverage) for it to be similarly or more cost-effective than TDF/FTC in South Africa
- Current US list price = $3,700/injection – unaffordable for low- and middle-income countries
- Manufacturer has very recently agreed to discussions on voluntary licensing terms with the Medicines Patent Pool
- The last of the 6 current patents on CAB-LA is due to expire in 2031