# *Model comparison of the cost-effectiveness of long-acting cabotegravir for HIV PrEP in South Africa*

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## BACKGROUND

Long-acting injectable cabotegravir (CAB-LA) is superior to oral emtricitabine / tenofovir disoproxil fumarate (TDF/FTC) for HIV pre-exposure prophylaxis (PrEP) and has the potential to expand PrEP usage. Evaluation of its affordability and cost-effectiveness (CE) in sub-Saharan Africa is needed to optimize health resource allocation.

## METHODS

EPIDEMIOLOGICAL MODELING

- Three independent age- and risk-stratified HIV transmission models (EMOD-HIV, Synthesis, and Thembisa) were calibrated to South Africa epidemiological data. Models were not standardized across parameters, including independent risk strata, PrEP effectiveness, nor discontinuation. Expanding PrEP usage was simulated to:
  - cover 5, 10, or 15% of the sexually active population, with preferential uptake by higher-risk groups
  - scale-up within either 5 or 10 years
  - have either 0 or 100% of TDF/FTC users eventually switch to CAB-LA.

COSTING

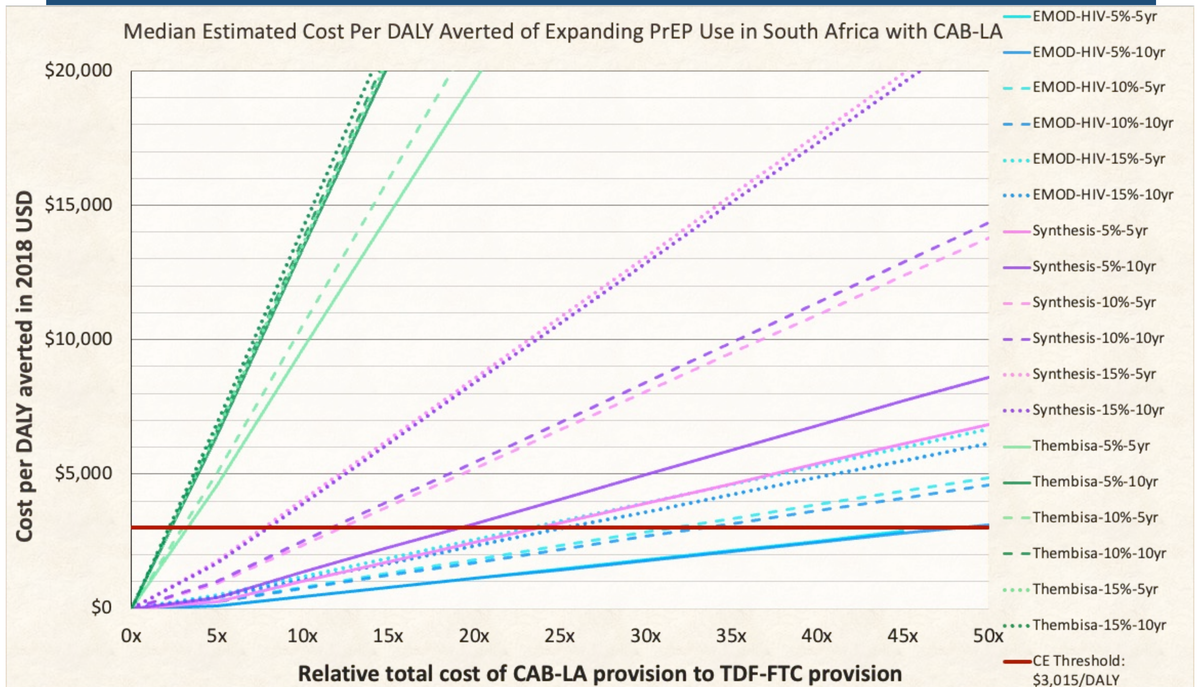
- Standardized across models; used government perspective
- Included 1) PrEP procurement & delivery services, 2) outpatient ART provision, and 3) HIV-related inpatient costs by CD4 count
- Potential annual total delivery cost of CAB-LA was varied from 1 to 50 times that of TDF/FTC ($124/yr).

ANALYSIS

- PrEP expansion modeled new initiations for 20 years, and projected effects (without further initiations) for 50 years.
- Scenarios were compared to model-determined baseline projected trends without expansion.
- Expansions solely with TDF/FTC were compared to expansions with CAB-LA.
- Both DALYs & costs were discounted at 3% annually.
- CE was defined at an empirically estimated threshold of $3,015 / DALY averted (from Edoka & Stacey, 2020).

Three independent models predict expanding PrEP coverage in South Africa with CAB-LA to be cost-effective if delivered at a cost at or below 2.4 times that of TDF-FTC.

CAB-LA may be cost-effective at much higher relative delivery cost with: greater risk-informed selection into PrEP, more modest coverage targets, lower TDF-FTC effectiveness, and projected higher baseline HIV incidence.




## RESULTS

- **Coverage:** All models showed diminishing CE with higher proportions of the population on PrEP. Diminishing average user risk with higher coverage was a key factor.
- **Model comparison:** Models differed substantially in CE predictions, with Thembisa predicting the worst, EMOD-HIV the best, and Synthesis in between. Given cost standardizing, differences reflect model epidemiology only.
- *All models predicted that expanding PrEP coverage with CAB-LA would be cost-effective under the $3,015 / DALY threshold if delivered at a combined procurement and delivery cost of 2.4 times that of TDF-FTC.*
- Synthesis and EMOD-HIV predicted potential cost-*savings* at CAB-LA total delivery costs of up to to 6.3 and 9.0 (respectively) times that of TDF-FTC.
- Compared to Thembisa, EMOD-HIV and Synthesis:
  - assumed more risk-informed PrEP delivery
  - predicted lower HIV incidence declines without CAB-LA
  - assumed gradual rather than immediate switching from TDF-FTC to CAB-LA within the expansion years.
- EMOD-HIV assumed lower TDF-FTC effectiveness (58%) than Thembisa (65-85%) or Synthesis (90-95%)
- Expansions with TDF-FTC alone were consistently projected to be cost effective under the $3,015 / DALY threshold.
- Expansions with CAB-LA and TDF-FTC were projected to be equivalently cost effective at the following cost ratios:

| Coverage (%) | Scale-up (yrs) | CAB-LA to TDF/FTC Cost Ratio | | |
|---|---|---|---|---|
| | | Thembisa | Synthesis | EMOD-HIV |
| 5 | 5 | **1.7** | **6.3** | **7.3** |
| 5 | 10 | **2.0** | **5.0** | **7.7** |
| 10 | 5 | **1.7** | **2.7** | **3.7** |
| 10 | 10 | **1.7** | **2.3** | **4.0** |
| 15 | 5 | **1.7** | **2.0** | **2.3** |
| 15 | 10 | **1.7** | **2.7** | **2.3** |

## CONCLUSIONS

Three independent models predict expanding PrEP coverage with CAB-LA up to 15% of the sexually active population would be cost-effective (ie, ≤ $3,015 / DALY) if delivered at a cost near that of TDF/FTC, and highlight the importance of primarily reaching people with high risk, especially at higher CAB-LA prices.