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https://hptnmodelling.org/
Motivation

- Two clinical studies (HPTN 083 and HPTN 084) have shown that long-acting injectable cabotegravir (LA PrEP) is highly efficacious at preventing HIV among cisgender MSM and transgender women in North and South America, South Africa and Thailand and Vietnam and women in Sub-Saharan Africa, respectively.

- 66% lower risk of HIV infection in participants receiving CAB compared to TDF/FTC in HPTN 083
- 89% lower risk of HIV infection in participants receiving CAB compared to TDF/FTC in HPTN 084

- Currently approved for use as PrEP in US. WHO discussed their recommendations on a guidance meeting in March. Expected soon.
What is the importance of these results?

- Efficacy demonstrated against highly effective competitor
- Completely different delivery route which may appeal to new users
- It brings us a step closer to HIV vaccine
Outline of the analysis

• Joint project of the HPTN Modelling Center and the HIV Modelling Consortium

• Other key stakeholders:
  • the HIV prevention team at WHO and
  • Gates Foundation

• Main objective: Conduct a model comparison analysis of the population-level impact of expanding PrEP coverage by offering LA PrEP, over different time horizons, derived from transmission-dynamic models of HIV in different geographic areas and selected risk populations.
Participating models

**HPTN modeling center**
Team: Kate Mitchell
Romain Silhol
Mia Moore
Marie-Claude Boily
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Simulated Epidemic: MSM, Atlanta

**McGill University**
Team: Carla M Doyle
Rachael M Milwid
Mathieu Maheu-Giroux
Yiqing Xia
Simulated Epidemic: MSM, Montreal

**Thembisa**
Team: Lise Jamieson
Gesine Meyer-Rath
Leigh Johnson
Simulated Epidemic: Generalized, South Africa

**HIV Synthesis model**
Team: Jennifer Smith
Loveleen Bansi-Matharu
Valentina Cambiano
Andrew Philips
Simulated Epidemic: Generalized, Southern & Eastern Africa

**Erasmus University**
Team: Marjolein van Vliet, Brooke E Nichols, Remco Peters
D.A.M.C. van de Vijver
Simulated Epidemic: MSM, Amsterdam

**EMOD**
Team: Anna Bershteyn, David Kaftan
Simulated Epidemic: Generalized, Sub-Saharan Africa
Metrics of impact

- **Population-level effectiveness**: Cumulative fractions of new HIV infections averted over 20 years for different intervention scenarios compared to base-case scenarios.

- **Population-level efficiency**: Additional person-years on PrEP needed to prevent one HIV infection for different intervention scenarios compared to base-case scenarios.

- **Cost-effectiveness**: The additional cost per disability-adjusted life year (DALY) averted over 20 years for different intervention scenarios compared to base-case scenarios.
PrEP expansion – 80+ scenarios

1) **Overall PrEP coverage target** (oral and LA PrEP users combined)
   - 15%, 30%, 40%, 50%

2) **Time to achieve targeted PrEP coverage**
   - 5 years, 10 years

3) **Proportion of current/projected oral PrEP users switching to LA PrEP**
   - 0%, 15%, 30%, 50%, 100%

4) **Distribution of LA PrEP** (excluding those who switch from oral PrEP)
   - based on current PrEP eligibility criteria at each setting
   - proportionally across risk and age groups

5) **Assumptions about LA PrEP** *(same for all teams)*
   - Per act efficacy – 91% (MSM, North America) and 95% (generalized, South Africa)
   - Discontinuation rates – 16.8% (MSM, North America), 8.4% (generalized, South Africa)
Base-case scenario:
- Oral PrEP introduced in 2018
- 18.8% oral PrEP coverage in 2022
- 25.6% expected oral PrEP coverage in 2032

Expansion scenarios:
- 30% overall PrEP coverage target
- Achieved in **10 years** (2032)
- 0% of current/potential oral PrEP users choose LA PrEP instead when available

- 50% of current/potential oral PrEP users choose LA PrEP instead when available
Base-case scenario with oral PrEP only

Atlanta Model

- Higher HIV prevalence & HIV incidence
- Low ART coverage & high oral PrEP coverage
- High oral PrEP effectiveness: 82% (range 75%-87%)
- PrEP eligible are at ~3 times higher risk to acquire HIV

Montreal Model

- Low HIV prevalence & HIV incidence
- High ART coverage & low oral PrEP coverage
- High oral PrEP effectiveness: 86%
- PrEP eligible are > 10 times higher risk to acquire HIV
Expanded PrEP coverage among eligible: Population effectiveness

**Atlanta:** Increasing overall PrEP coverage by 8-10 pp led to averting 35-40% of new infections.

Meeting coverage targets 5 years earlier led to averting 7-10 percentage points more infections in Atlanta compared to 2-5 percentage points more in Montreal.

Montreal: PrEP coverage must be increased by ~20 pp to avert close to 40% of new infections.

15% and 30% coverage levels not applicable as baseline PrEP coverage in Atlanta is 30%.

Notches in boxplot show 95% CI for the median. Dotted lines show maximum/minimum without outliers.
Expanded PrEP coverage among eligible: Effect of switching to LA PrEP

Switching existing users from oral to LA PrEP has a small positive effect (up to 3 pp)

Notches in boxplot show 95% CI for the median.
Dotted lines show maximum/minimum without outliers
Expanded PrEP coverage among eligible: Population efficiency

**Atlanta: Population Efficiency**

- Increasing overall PrEP coverage by 8-10 percentage points resulted in ~20 NNT
- More efficient than IPREX & Partners PrEP, comparable with interventions among black adolescents
- Switching oral PrEP users to LA PrEP improves efficiency by ~10%

**Montreal: Population Efficiency**

- NNT extremely high because of very low HIV incidence (note different scale on y-axis)
- Switching to LA PrEP did not change NNT when expanded among PrEP eligible

For comparison:
- NNT = 62 iPrEx
- = 78 Partners PrEP
- = 25-32 Black adolescents
- = 150-250 White adolescents
Expanded PrEP coverage among eligible: Cost-effectiveness analysis CEA by Jesse Heitner (UW)

Cost parameters represent US National averages

Cost effectiveness shown for coverage achieved in a 5 year timeline.
Neither costs nor effects discounted in this model (to be updated in future, which will worsen cost-effectiveness).

Not particularly cost effective compared to generic oral PrEP, but can be cost-effective compared to branded oral PrEP (not shown)

Though price point is unknown, LA-PrEP is not expected to be cost effective for this population at even the price of oral PrEP
Targeting by adherence to oral PrEP

Alternative scenarios in Atlanta with 50% of oral PrEP users switching to LA PrEP:

- **Poor adherers** switch to LA PrEP, Oral PrEP effectiveness **increases** to 90%

- **Good adherers** switch to LA PrEP, Oral PrEP effectiveness **decreases** to 60%

Up to 20% difference in effectiveness
Summary

• Adding LA-PrEP may avert a significant proportion (35-40%) of expected new HIV infections over 20 years in settings with already high oral PrEP (like Atlanta, USA) if it results in ~10 pp increase in overall coverage among PrEP eligible population.

• Substantially larger increase in overall PrEP coverage (~20 pp) is needed to achieve comparable reduction in settings with low current PrEP use (like Montreal, Canada).

• If PrEP coverage is expanded among PrEP eligible MSM, switching existing users from oral to LA PrEP is predicted to have only a small positive effect due to the high efficacy and adherence to oral PrEP assumed in the models. Much stronger effect if expanded proportionally.

• Expanding the PrEP toolbox with LA-PrEP could be a highly efficient and possibly cost-effective intervention in places with high HIV incidence (like Atlanta) but unlikely to be cost-effective in settings with low HIV incidence (like Montreal).
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