BILL & MELINDA GATES foundation

DEEP DIVE REVIEW OF MODELING LONG-ACTING PREP

March 2023

MEETING OBJECTIVES

1. Detailed review of the current set of models with a focus on sub-Saharan Africa, including:
   - How model outputs map to priority questions regarding implementation and impact
   - The models' underlying structure (e.g., how they model population and transmission dynamics)
   - Model flexibility to incorporate multiple current and future PrEP products and evolve with the changing context

2. Identification of barriers and gaps associated with this work

This meeting took place among 29 participants in London and virtually on March 2-3, 2023

FINDINGS ABOUT HETEROGENEITY OF MODELS

We identified 11* models which can provide relevant insights into the impact, costs, and/or cost-effectiveness of CAB-LA in low- and middle-income countries. These models varied by:

- **Geography/geographic scope:** South Africa and the US were main countries of interest; most models focused on less than 3 priority countries (n=10), but a few (n=3) had 4+ countries included
- **Risk categorization/populations covered:** Most models included MSM (n=8), but heterosexual individuals, FSW, and AGYW also well-represented
- **Model type:** Most models were individual (n=8), but a few were compartmentalized (n=5)
- **Products:** The majority (n=10) models only included CAB-LA and oral PrEP, but a few included other products, including LEN, ISL, and dapivirine ring
- **Oral PrEP effectiveness:** Among eight models that reported oral PrEP effectiveness assumptions, assumptions ranged from 58-95%
- **INSTI resistance:** Only four models included INSTI resistance, but a few groups discussed its possible inclusion in the future given additional resources/interest
- **CAB-LA:** 11 models included CAB-LA and the remaining two models will have incorporate CAB-LA in the future

* Three different groups presented their work using the EMOD model, but it only accounts for one model in this count.

SUMMARY OF MODELS (1 OF 3)

Model	Participants	INSTI DR	CAB-LA	Model type	Populations	Geography	Time horizon	Oral PrEP effectiveness	PrEP types included	Objective and output(s)
CEPAC	Anne Neilan Andrea Ciaranello	Yes	Yes	Individual	AGYW, MSM, trans women, youth & adults, pregnant/ lactating people, children	US & South Africa	10 years	Not reported	Oral PrEP, CAB-LA	**Objective**: Model highest price premium that CAB-LA could command relative to oral PrEP **Outputs:** averted HIV transmission, QALYs, costs, incremental cost-effectiveness ratio
DRIVE	Jesse Heitner	No	Yes	N/A– uses other models as inputs	MSM	US, Benin, South Africa (initial stages)	Annual compared to current market	Not reported	Oral PrEP, CAB-LA	**Objective:** Model cost effectiveness of introducing CAB-LA **Outputs**: annual cost of offering injectable PrEP in a specific geography compared to oral PrEP
EMOD-UNISA	Edinah Mudimu Zviiteyi Chazuka	No	Yes	Individual	Heterosexuals; mother-to-child transmission	eSwatini, Kenya, Malawi, South Africa, Zambia, Zimbabwe	20-40 years	58%	Oral PrEP, CAB-LA, LEN, ISL	**Objective**: Model population transmission dynamics **Outputs**: ”standard HIV model outputs”, individual-level # of partners, partnership history, differences in disease and intervention use across partners
EMOD-HIV	Anna Bershteyn Dani Resar	No	Yes	Individual	CSW, CSW clients, AGYW	Nyanza (Kenya), South Africa, Zimbabwe	To 2060	58%	Oral PrEP, CAB-LA, LEN, ISL	**Objective**: Model the impact and cost-effectiveness of CAB-LA versus oral PrEP, i.e., calculate maximum per-dose cost for incremental cost effectiveness to be <=500 USD per DALY averted **Outputs:** cost per dose, cost per year, scenarios to reach epidemic control

SUMMARY OF MODELS (2 OF 3)

Model	Participants	INSTI DR	CAB-LA	Model type	Populations	Geography	Time horizon	Oral PrEP effectiveness	PrEP types included	Objective and output(s)
EMOD-UW	Linxuan Wu Monisha Sharma	Yes	Planned	Individual	CSW, CSW clients, otherwise stratified as high, medium, or low risk	Kenya	20 years	Not reported	Oral PrEP, CAB-LA, LEN, dapivirine ring	**Objective:** Model HIV self-testing for oral PrEP scale-up in Kenya and understand impact on drug resistance and HIV outcomes **Outputs:** HIV infections and related deaths averted, drug resistance, cost
Goals RSM and ASM	Matt Hamilton Katherine Kripke	No	Yes	Compart m-ental	MSM, IDU, FSW, H/M/L risk, 18-49 year-olds	RSM- 106 countries in all regions ASM: 38 countries in SSA	Customizable for any time period	90%	Oral PrEP, CAB-LA	**Objective:** evaluate the impact and cost-effectiveness of different scenarios for scaling up HIV interventions, including any forms of PrEP **Outputs:** HIV incidence, prevalence, mortality, side and CD4 status of HIV+ population, vertical transmission, costs
HIV synthesis	Andrew Philips	Yes	Yes	Individual	Heterosexual adults	sub-Saharan Africa	To 2070	95%, sometimes 90%	Oral PrEP, CAB-LA	**Objective**: Model HIV incidence with and without CAB-LA introduction **Outputs:** HIV incidence, prevalence, cost effectiveness
HPTN Model	Marie-Claude Boily Romain Silhol	No	Yes	Compart m-ental	MSM, female partners of MSM	US & Benin	Flexible time period	82%	Oral PrEP, CAB-LA	**Objective:** Model PrEP coverage, HIV transmission/infection **Outputs:** HIV incidence, prevalence, & deaths; HIV cases and deaths averted; life years lived; DALYs

SUMMARY OF MODELS (3 OF 3)

Model	Participants	INSTI	CAB-LA	Model type	Populations	Geography	Time horizon	Oral PrEP effectiveness	PrEP types included	Objective and output(s)
Optima HIV	Rowan Martin-Hughes	No	Planned	Compar-tmental	MSM, trans women, FSW, clients, PWID, PWUD, gen pop w/ age disagg.	60+ LMIC; 20+ include PrEP	Not reported	86% on demand, 95% for daily	Oral PrEP, CAB-LA	**Objective:** Model cost-efficiency and prioritization of HIV interventions **Outputs:** proportional PrEP coverage of at-risk sexual acts
PopART	Mike Pickles	No	Yes	Individual	14+ year-olds	Zambia, South Africa, Zim.	Adjustable – can be out as far as 2100	75%	Oral PrEP, CAB-LA	**Objective**: Model cost effectiveness **Outputs:** HIV prevalence, awareness of status, ART
SCHARP model	Dobromir Dimitrov Mia Moore	No	Yes	Individual	MSM, other men, AGYW	US & Thailand	A few years	Varied	Oral PrEP, CAB-LA	**Objective**: Model answers to key questions about new PrEP products **Outputs:** PrEP efficacy, PrEP assignment/adherence
TEAMS	David van de Vijver Shreoshee Mukherjee	Yes	Yes	Compar-tmental	MSM, transgender women	Thailand	Epidemiological impact: 15 years Cost effectiveness : 40 years	60%	Oral PrEP, CAB-LA	**Objective**: Model cost effectiveness and epidemiological impact of long-acting PrEP **Outputs**: number of method users, averted HIV infections, drug resistance, transmission of drug resistance
Thembisa	Lise Jamieson	No	Yes	Compar-tmental	AGYW, FSW, ABYM, MSM	South Africa	20 years	65% or 85% depending on population	CAB-LA, oral PrEP	**Objective**: Model cost effectiveness of long-acting injectable PrEP versus oral PrEP **Outputs**: provider-perspective cost effectiveness, HIV incidence, HIV infections averted, AIDS deaths averted

GLOBAL PERSPECTIVES AND FRAMING: WHO

- Globally, there are high expectations for CAB-LA, but its overall impact may be muted by increasingly limited funding and reductions in incidences in areas with the greatest HIV burden
- There remains critical information and data gaps on CAB-LA, including: “Real world” data, data for key populations, HIV testing and drug resistance, safety during pregnancy and breastfeeding, product switching and stopping, costs and cost effectiveness
- Modelling can help inform global and country decision-making by:
  - Modeling impact and effects of wider scale-up of CAB-LA
  - Sharing information about cost effectiveness and related price negotiations
  - Providing information about who to target for cost effectiveness and impact
  - Providing information about the costs and impact of drug resistance monitoring
- Looking ahead, we should consider modeling for aspirational versus realistic scenarios and modeling needed for diverse populations and geographies

GLOBAL PERSPECTIVES AND FRAMING: AVAC

- While initial studies showed efficacy, more data is needed to inform implementation among priority populations such as sex workers, gender non-conforming individuals, and people who use drugs.
- Unfortunately, few large implementation studies are currently planned, which limits learning on key topics such as demand creation.
- There are some current barriers to planning these studies and coordinating effectively among them, including:
  - National regulatory approvals of product
  - ViiV internal approvals of protocols
  - Product supply – manufacturing capacity, timing, shipping
  - Actual product delivery to participants

INITIAL EMERGING FINDINGS FROM THE STUDY OUTPUTS

Across these methods, there is some emerging preliminary alignment in key outputs

- **Impact:** CAB-LA can have a significant positive impact on the pandemic, but is not a panacea and, alone, is unlikely enough to achieve national goals. Most of this impact is projected to come from an expansion of coverage/use rather than increased effectiveness as compared to oral PrEP as models currently assume high levels of PrEP effectiveness.
- **Cost effectiveness:** CAB-LA may be cost effective in South Africa if its price is 1-2X of oral PrEP, though this may not be the case in all geographies. Cost effectiveness is highly dependent on overall level of incidence, the cost of treatment, and other factors.
- **INSTI drug resistance:** INSTI drug resistance may have effects at an individual clinical level, but is unlikely to have large effects on the epidemic based on what we currently know from studies. Widescale NAT testing could have a dramatic impact on cost effectiveness in LMICs
- **Policymaker engagement:** An emerging lesson from HICs, is that it may be hard to convince policymakers of the value of CAB-LA, depending on the final price of the product, especially as incidence continues to fall.

GAPS AND CHALLENGES EXIST FROM DEFINING QUESTIONS TO COMMUNICATING RESULTS

Defining priority questions from policymakers

- Understanding demand for CAB-LA modeling and priority questions
- Understanding how and when to engage ministry of health officials and other stakeholders at all levels
- Finding MIHPSA collaboration opportunities

Determining the right level of model complexity

- Defining and communicating key terms, such as adherence and coverage, which can vary study to study
- Finding key data inputs, like uptake, adherence, continuation, switching behavior/choice.
- Aligning how models describe coverage and targeting with programmatic realities (like defining types and level of risk in key populations, channels, reimbursements, access points)
- Capturing essential data from implementation studies amid limited product availability

Running the model

- Retaining key personnel and staffing to ensure smooth execution.
- Ensuring access to necessary computational resources.

Communicating methods and results

- Interpreting and using cost effectiveness analysis.
- Clarifying objectives and questions of interest regarding user preference and choice.