Coordinating Implementation Science for CAB for PrEP: Linking Modellers with the Latest Implementation Science Evidence

AVAC/BioPIC and WHO

29 September 2023, 9am- 11am EDT

Background/Rationale

As more countries approve injectable cabotegravir (CAB) for PrEP and introduction plans take shape, there remain many evidence gaps, particularly around testing and risk of HIV drug resistance, safety during pregnancy, implementation in diverse populations, patterns of use, optimum service delivery strategies, and cost and cost-effectiveness. While data gathered through the Open Label Extensions and implementation science (IS) studies will help to fill these gaps, the sample sizes for these studies are relatively small, with the majority featuring fewer than 5,000 participants, which can limit the generalisability of the findings.

Modelling can support evidence generation by extrapolating from this data to estimate the impact of wider scale-up, which can then aid Ministries of Health to make decisions on issues such as cost and price, target populations, and testing strategies. To improve the quality of the model outputs, it is critical that they are built using the latest evidence from real-world use of CAB for PrEP- therefore a continued open dialogue between modellers and implementation science study leads is needed.

Meeting Objectives:

1. Align on data and evidence needs to fill CAB for PrEP evidence gaps
2. Agree on a framework for implementation science study leads and modellers sharing results of analyses, including gaining input from IS leads into how results are used in models

Key Takeaways and Actions

- IS study leads agreed to share study results with modellers ahead of publication.
- Modellers and IS study leads agreed to meet biannually to share study updates and remain aligned on evidence needs.
- AVAC will use the modelling summary presented at this meeting to develop a modelling brief to be shared publicly on avac.org and via other channels.
- AVAC will create and share a tracker to track which key modelling inputs are being collected by which studies.
- The PrEP Choice Investigators group will begin engaging modellers as they work on defining indicators around patterns of use.
- All participants to continue support keeping the study dashboard up to date by alerting Catherine Verde Hashim of any changes.

Modelling Overview

Modelling exercises are currently exploring the following questions:

- What is the predicted realistic effect on HIV incidence of CAB for PrEP introduction in different populations in different settings?
- What would be the maximum price for CAB for PrEP to be cost-effective, and what factors, such as delivery channel and setting, influence cost and cost-effectiveness?
- What is the potential for increased resistance to dolutegravir for those exposed to CAB for PrEP?
- What is the appropriate HIV testing approach for those on CAB for PrEP?

The HIV Synthesis model found that use of antibody-only rapid HIV testing with CAB for PrEP only has a small increase on integrase strand transfer inhibitor resistance compared to use of nucleic acid-based tests, and thus rapid testing should be sufficient. The other questions have not yet been fully answered. A summary of key modelling findings to date can be found in the modelling summary brief.

Implementation Studies Overview

For details on all implementation studies, see the Implementation Study Dashboard. For further details on specific indicators being collected by studies, see the CAB for PrEP Implementation Study Data Tracker.

Areas Requiring Further Inquiry

HIV Drug Resistance

The potential impact of low CAB for PrEP continuation rates on integrase strand transfer inhibitor (INSTI) resistance is currently unknown. INSTI resistance amongst dolutegravir (DTG) users is growing, though documented transmission is rare. INSTI resistance has been detected at higher rates amongst CAB users than DTG users.

A challenge for implementers will be detecting INSTI resistance in CAB for PrEP users who seroconvert during the pharmacokinetic tail. This is complicated by the fact that users who seroconvert in this stage have an undetectable viral load, meaning resistance tests cannot be performed. An effective method for screening those who seroconvert for prior PrEP use will need to be developed and adopted widely. If implementers can perform routine viral load testing, it may be possible to test whether there is an association between CAB exposure and virologic failure.

Diagnostic dilemmas may occur, where implementers see individuals they are fairly certain are HIV+, but undetectable. There may be a need to revise diagnostic guidance to ensure those who have seroconverted can be identified as HIV+.

Providers need practical solutions to potential INSTI resistance acquired through CAB usage, such as starting former CAB users who have seroconverted on tenofovir, lamivudine, and dolutegravir (TLD) and monitoring how they progress.

Patterns of Use

Though the oral CAB lead-in is not required in the African countries where CAB for PrEP has so far been approved, it's possible CAB users may at times struggle to access injectable CAB and temporarily switch to oral CAB or TDF/FTC until injectable CAB is available. The impact of this "bridging" on outcomes like HIV

incidence or drug resistance is not yet known. For the purposes of implementation studies, this type of behaviour is not considered method switching.

A subset of the PrEP Choice Investigators group is looking into harmonising indicators around patterns of use; engaging modellers in these conversations will be important as how indicators are defined will impact how modellers can use them.

Cost Effectiveness

The degree to which PrEP use corresponds with times of risk will have a significant impact on cost-effectiveness- if implementation studies are able to collect this information, it would improve the quality of cost-effectiveness models, though this requires following up with those who are no longer coming in for clinical care which is challenging. The HPTN modelling centre is examining how patterns of use correspond to efficacy.

HIV Testing

While the US Centres for Disease Control have mandated that CAB users should receive a PCR test with each dose, the WHO supports countries following their national testing strategy, which commonly involves use of rapid tests only. The CATALYST study will be collecting blood samples at each CAB injection to batch test for viral load and see if rapid testing has missed any positive cases.

Additional Resources:

- WHO Guidelines on Long-Acting Injectable Cabotegravir for HIV Prevention, July 2022
- A Plan for accelerating access and introduction of injectable CAB for PrEP, June 2022
- CAB for PrEP Integrated Study Tracker, November 2023
- BioPIC Think Tank Notes