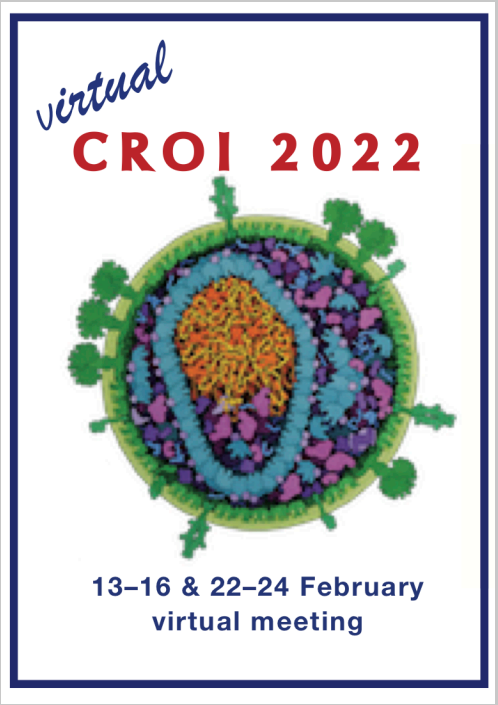
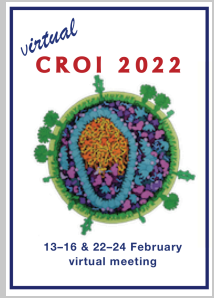
AfroCAB:
CROI 2022 update on CAB-LA PrEP

31 March 2022



CAB-LA at CROI 2022



PrEP: HPTN 083

- Landovitz RJ et al. CAB-LA vs TDF/FTC for PrEP, CROI 2022, Oral abs 96. https://www.croiconference.org/abstract/updated-efficacy-safety-and-case-studies-in-hptn-083-cab-la-vs-tdf-ftc-for-prep/
- Eshleman S et al. Early detection of HIV infection may reduce resistance. CROI 2022. Oral abs 95. https://www.croiconference.org/abstract/cab-la-prep-early-detection-of-hiv-infection-may-reduce-insti-resistance-risk/

Treatment: ATLAS 2M

- Overton et al. Three-year follow-up. CROI 2022. Poster abs 479. https://www.croiconference.org/abstract/long-acting-cabotegravir-rilpivirine-every-2-months-atlas-2m-week-152-results

CAB-LA: efficacy

CAB-LA is highly effective at preventing HIV.

Superior to daily oral TDF/FTC *(because of better adherence).*

CAB/RPV-LA is highly effective at treating HIV.

Rare breakthrough infections and viral failures can occur with perfect adherence.

CAB-LA PrEP breakthrough infections remain very rare, but unexplained

- HPTN 083 now reports a total of 7 cases of breakthrough despite on-time injections in 4660 person years of CAB-LA participant follow-up (0.15 per 100 PY)

Landovitz RJ et al. CROI 2022, Oral abs 96.

New infections in HPTN 083

Blinded = 51 new infections

CAB	TDF/FTC
12	39 T

4 occurred during the blinded phase (2 CAB, 2 TDF/FTC)

42 after unblinding (11 CAB, 31 TDF/FTC).

HR=0.33 95%CI (0.18-0.62) and HR=0.34 95%CI (0.17-0.67).

Unblinded = 48 wks FU = 46

13	33

2 newly-identified blinded CAB arm were both with on-time injections;

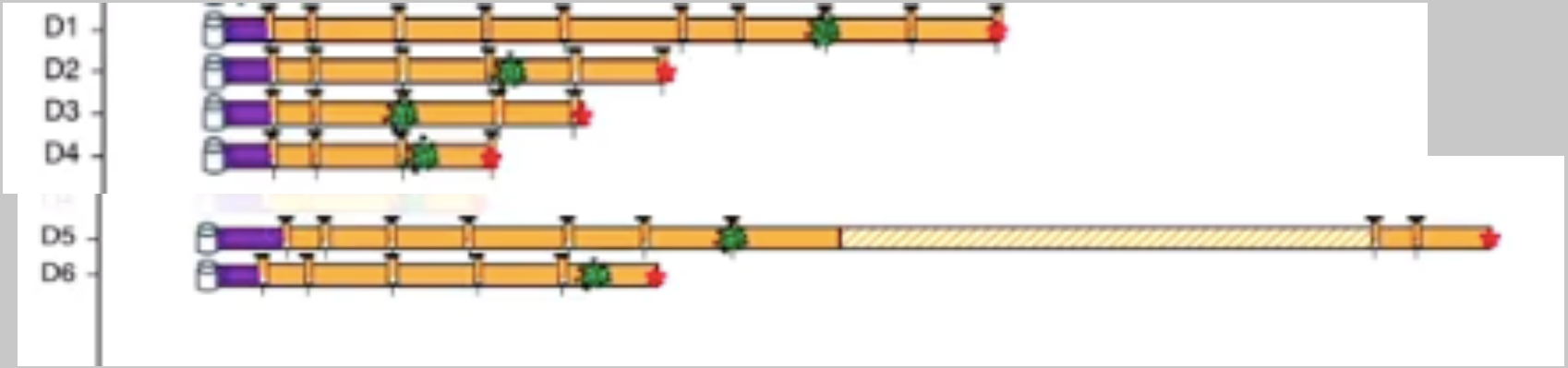
The 11 newly-identified unblinded CAB arm infections included:

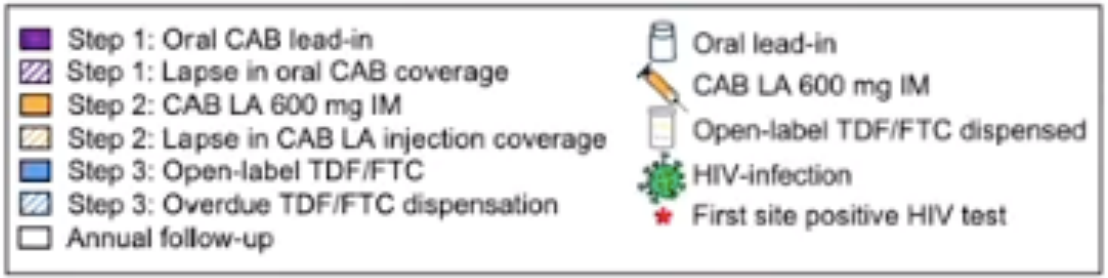
1 with on-time injections.

3 with delayed injections.

7 that occurred ≥6 months after the last CAB exposure (2 of these 7 never received a CAB injection).

Landovitz RJ et al. CROI 2022. Oral abs 96.





Overton et al. Three-year follow-up. CROI 2022. Poster abs 479.

Table 3. Participants With CVF Since the Week 96 Analysis

Participants With CVF Since Week 96					
#, arm	Sex at birth, BMI (kg/m^2), country	HIV-1 subtype at baseline	Viral load at failure (copies/mL)	RPV RAMs observed at failure	INI RAMs observed at failure
1, Q8W	Male, <30, Germany	B	24,221	E138A+M230M/L	Q148R
2, Q8W	Male, <30, Russia	A6*	59,467	E138A+Y181Y/C	Q148R

*This participant was originally classified as subtype A1 but, upon reanalysis, was later reclassified as subtype A6.
BMI, body mass index; CVF, confirmed virologic failure; INI, integrase inhibitor; Q8W, every 8 weeks; RAM, resistance-associated mutation; RPV, rilpivirine.

- The characteristics of the two participants (Q8W arm) who met the CVF criterion between Week 96 and 152 (Week 112 and Week 120) are shown in **Table 3**.
  - Neither had RAMs at baseline; however, the participant with subtype A6 had L74I integrase (IN) polymorphism at baseline.
  - Both had treatment-emergent RAMs to CAB (Q148R) and RPV (E138A+Y181Y/C; E138A+M230M/L).
- In total, through Week 152, 13 participants had CVF (Q8W, n=11 [2%]; Q4W, n=2 [<1%]).

Cautions.1

CAB-LA has a VERY long half life.

Risk of drug resistance if someone becomes HIV positive with CAB-LA drug levels.

(i) Missed infection when starting.

(ii) PrEP failures with good injections.

(iii) Becoming positive after stopping.

Phase 3 studies required daily oral PrEP for 1 year after stopping injections.

Cautions.2

Risk of drug resistance increases with time.

Resistance to CAB-LA will limit use of dolutegravir.

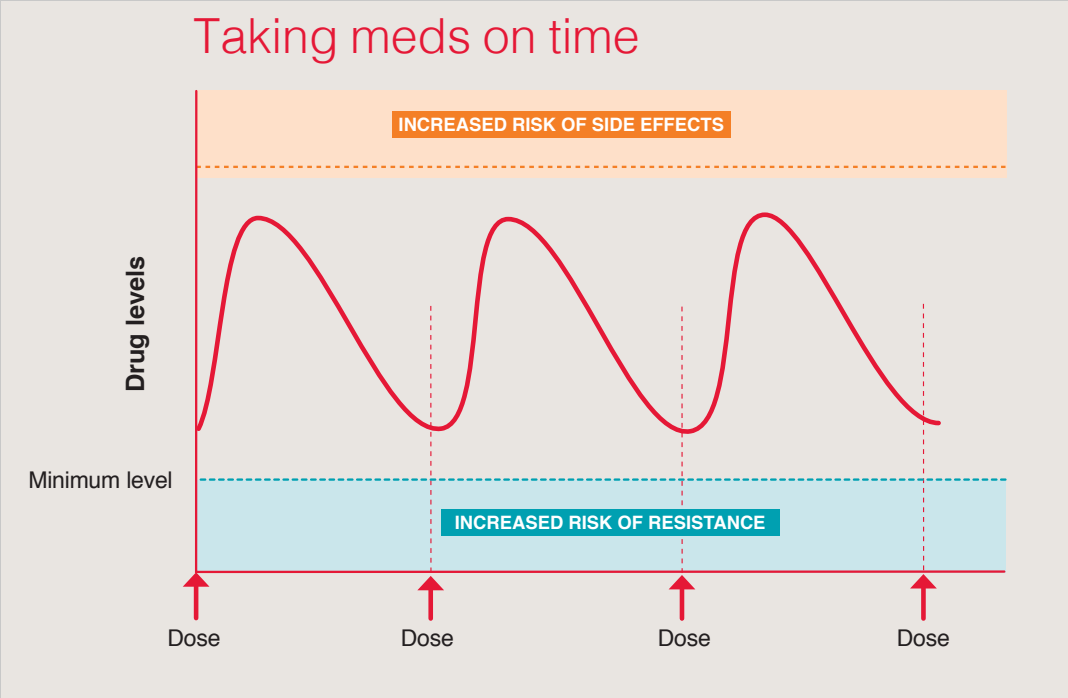
Resistance is usually lifelong.

Treatment: Two new cases of viral failure with perfect 2-monthly adherence.

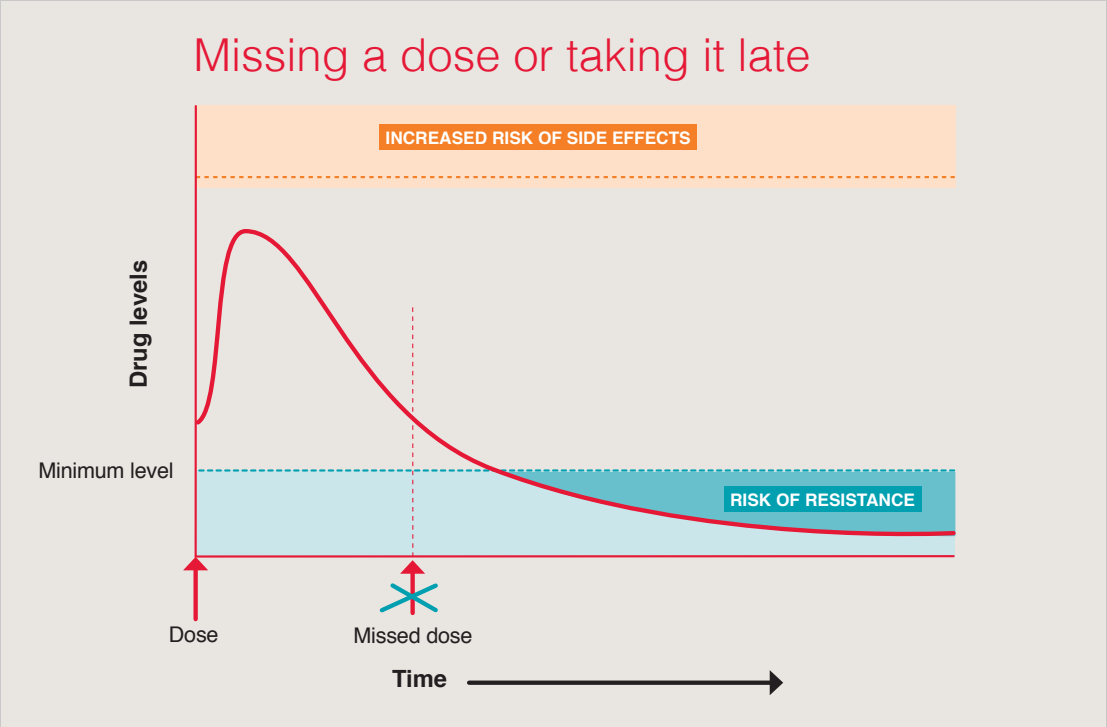
Viral load was 24,000 and 60,000 within 2 months.

Dual resistance: both integrase (INSTI) and NNRTI.

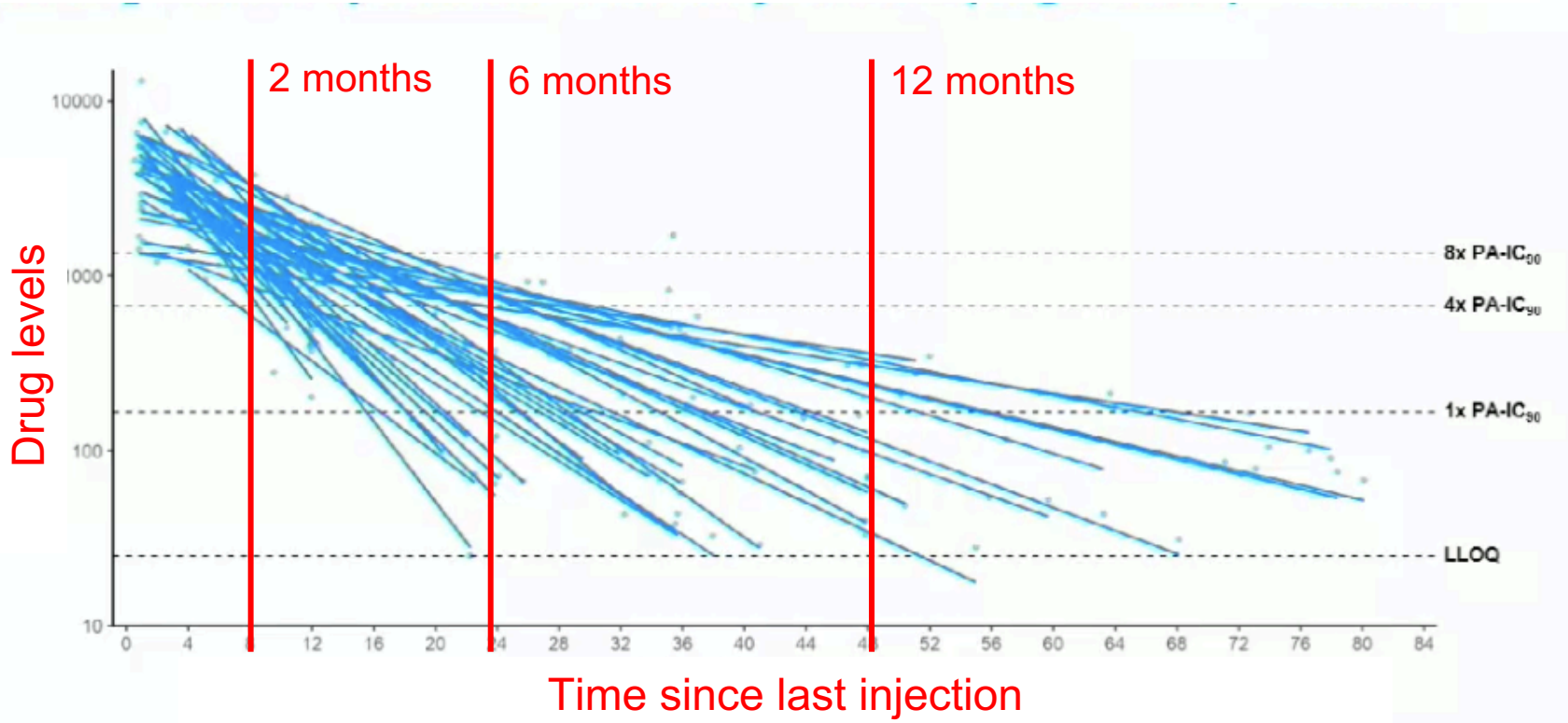
Drug resistance



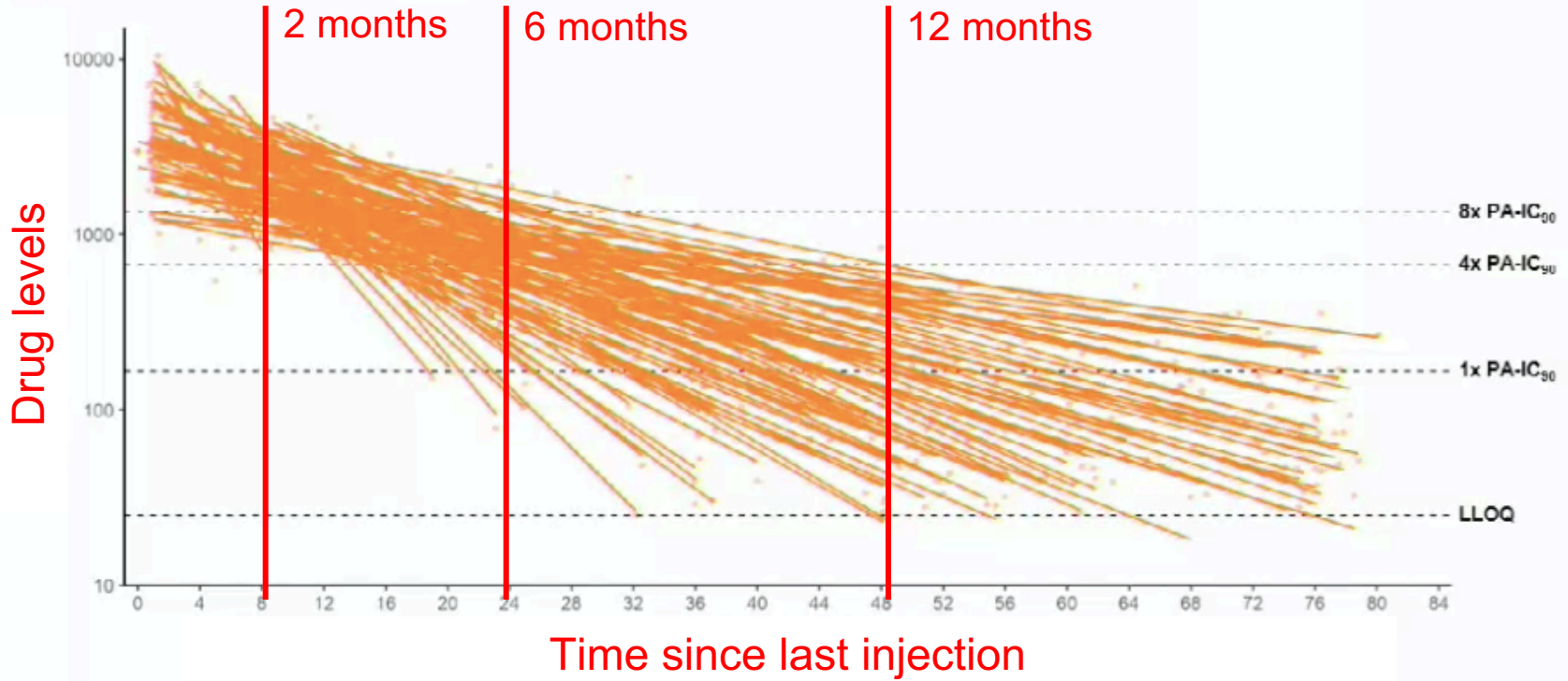
Drug resistance



Cabotegravir drug levels in men (after one injection)



Cabotegravir drug levels in women (after one injection)



Modelling.1

Modelling needs to predict safety/risk based on:

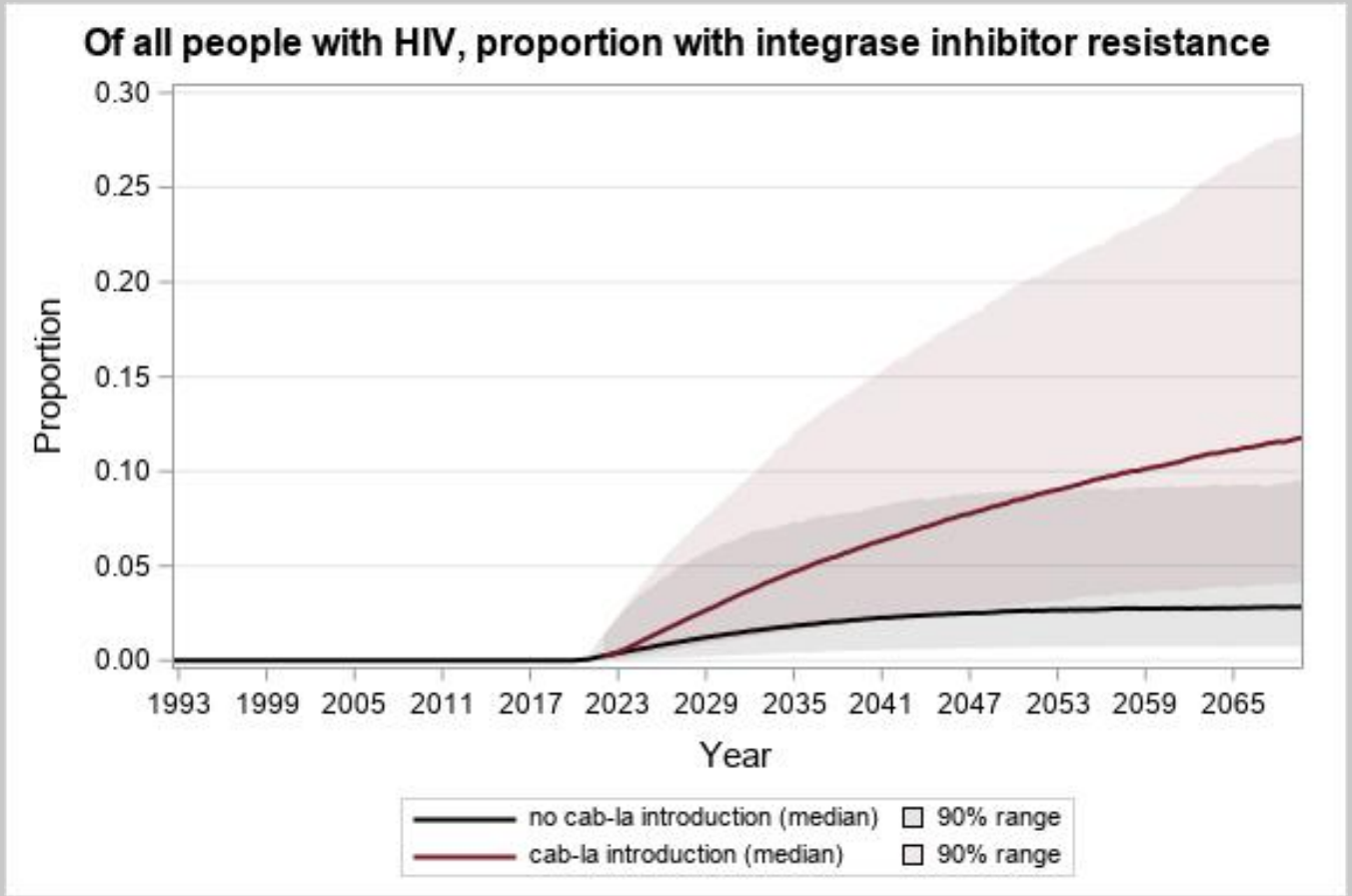
- PrEP uptake: 2%, 10%, 50% (in high risk groups).
- Loss to follow-up (5%, 10%, 50% etc). Stockouts?
- Background HIV incidence (allowing for decreasing and increasing).
- Impact of PrEP resistance on HIV treatment (limiting first-line and potential reinfection).

Modelling.2

Modelling should inform roll-out and pilot risks.

Ie if drop out is higher thanks predicted.

And changing care to match risk - ie design intensify programme for routine testing in all those lost to follow up etc



Phillips et al. unpublished