

# The HIV bnAb pipeline and feasibility as HIV PrEP

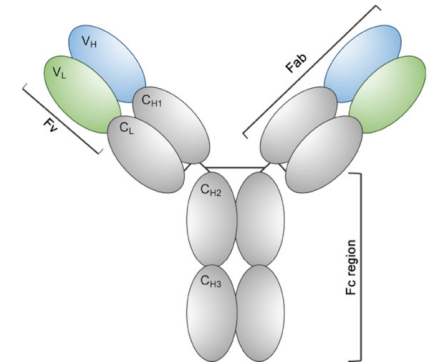
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HVTN



# > 100-year history of antibodies to prevent infections

INFECTION	INDICATION	PRODUCT DESCRIPTION
Measles	Prevention	Concentrated human gamma globulin
Polio	Prevention	Concentrated human gamma globulin
CMV	Prevention	Cytomegalovirus Immune Globulin
Hepatitis A	Prevention (travel)	Immune serum globulin (ISG)
Hepatitis B	Post Exposure	Hepatitis B Immune Globulin
Rabies	Post Exposure	Rabies Immune Globulin
RSV	Prevention (high-risk infants)	Monoclonal antibody
VZ	Post Exposure	Varicella Zoster Immune Globulin
SARS-CoV-2	Prevention, Treatment	Monoclonal antibodies
Malaria	Prevention	Monoclonal antibodies



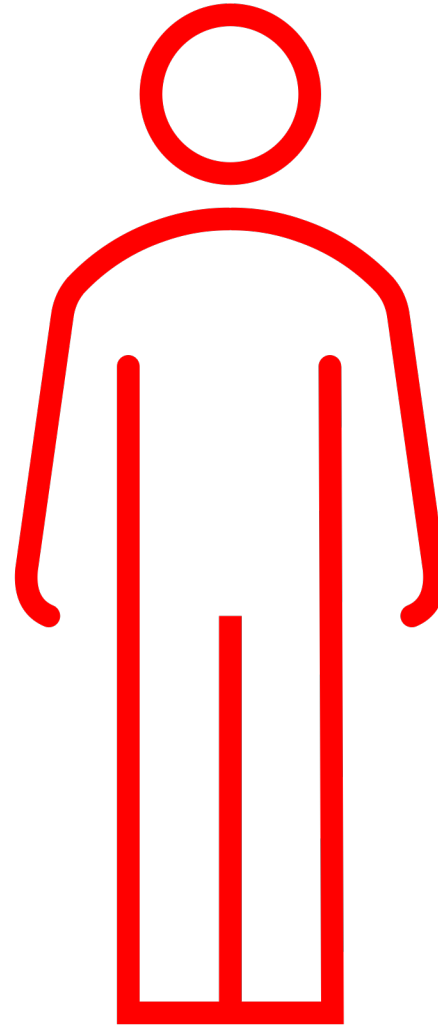
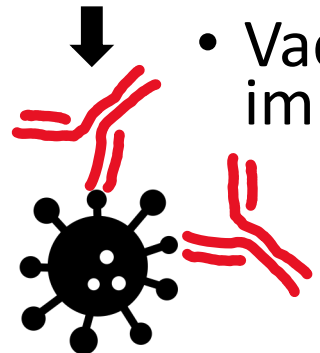
# Active and Passive Immunization Compared



## Active immunization

### Vaccination

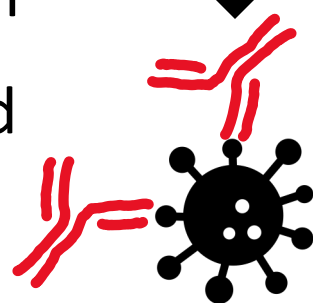
- Vaccines (antigen) stimulate the immune system to make antibodies
- No immediate protection – usually requires 2-3 immunizations to generate antibody response (weeks)
- Protection may last for years
- Vaccines may elicit other immune responses



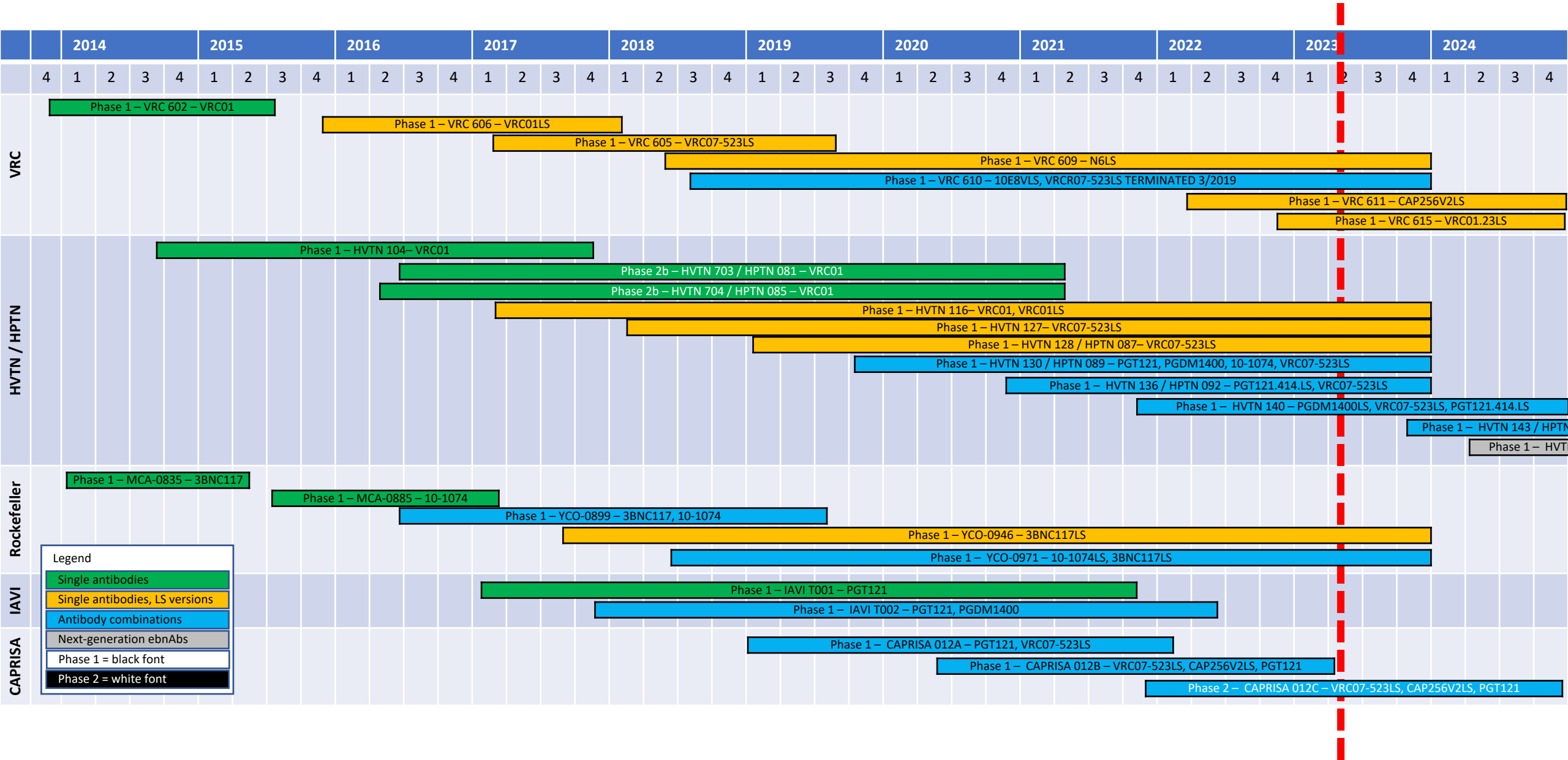
## Passive immunization

### bnAb administration

- Direct administration of antibodies – no need for immune system to make
- Immediate protection – Antibody response starts right after administration (hours)
- Protection lasts for months
- Repeated administration (for example every 6 months) will be required



# HIV bnAb clinical trials in HIV-uninfected adults – 2013-2024



> 4900 participants  
> 40,000 infusions  
> 50 sites  
11 countries

# HIV bnAbs are generally safe and well tolerated

- Key safety results from AMP studies HVTN 703/HPTN 081 and HVTN 704/HPTN 085
  - 41,116 IV infusions in 4,625 participants
  - Most participants have no solicited AEs
  - AE rates active product ~ placebo

Most common solicited AEs	Placebo	Dosage	
		Low	High
Mild (grade 2) pain and/or tenderness at infusion site	22%	21%	20%
Mild (grade 2) maximum systemic symptom severity	35%	33%	33%

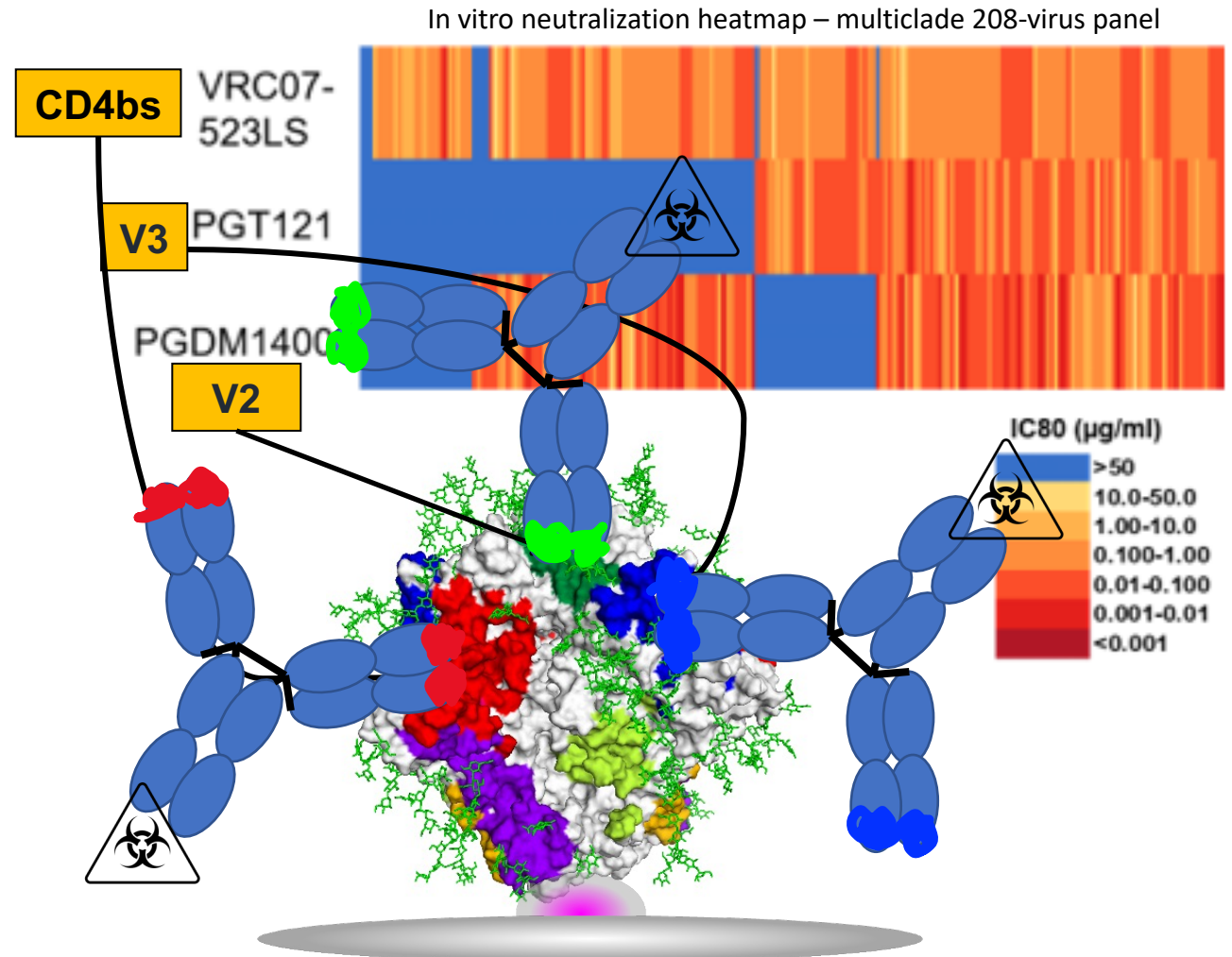
- HIV bnAbs are human antibodies with a pathogen as the target (non-self), different mechanism of action (target) compared to oncology and anti-inflammatory mAbs (anti-self)



# What's next: Combine 3 HIV bnAbs to increase prevention efficacy

## ■ Combination:

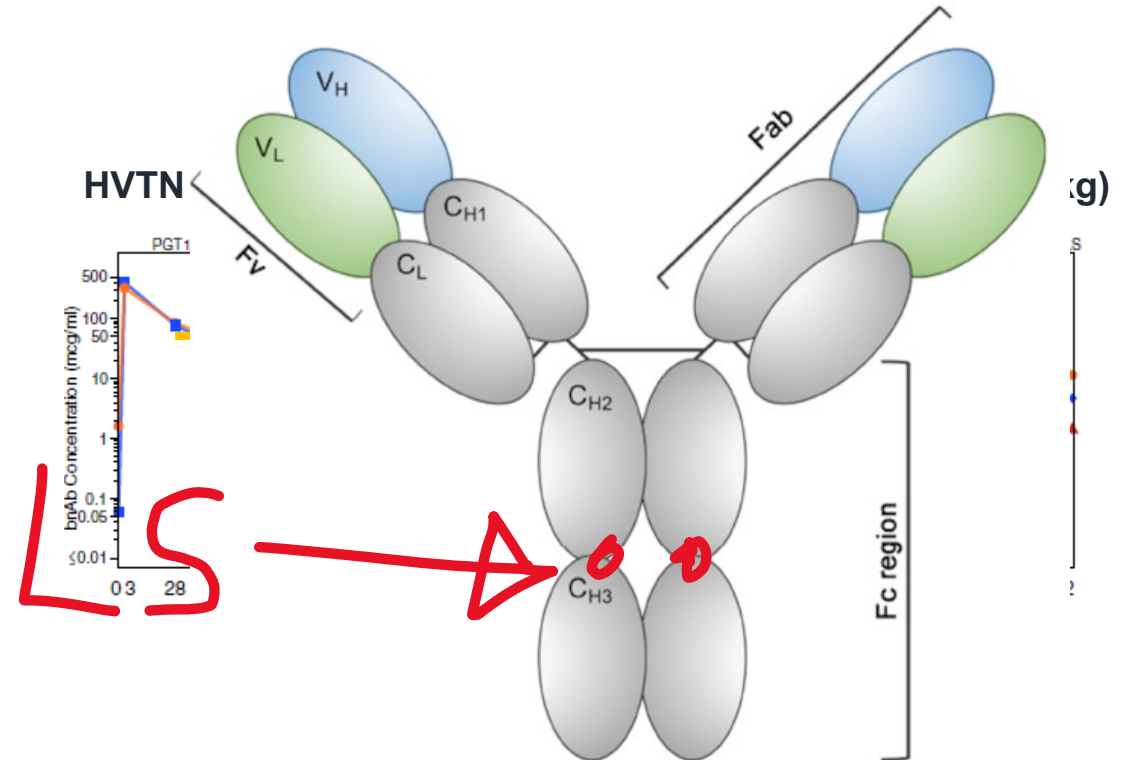
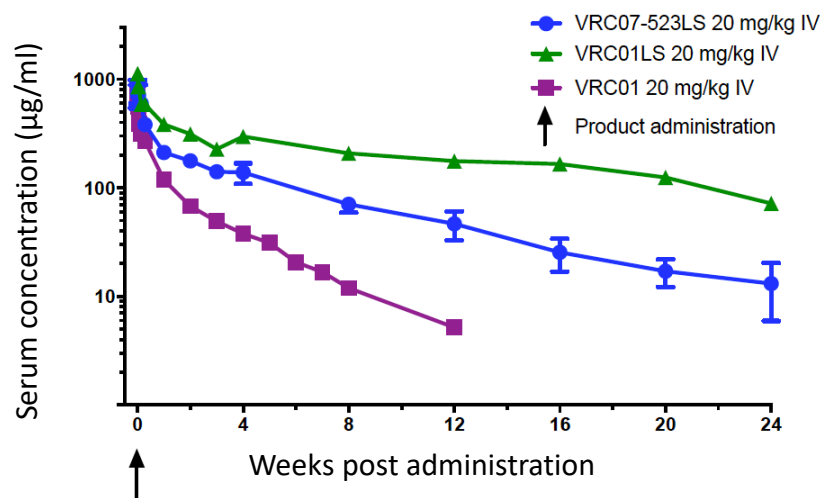
- Each HIV bnAb targets a different part of the HIV envelope
- Potency & breadth greater than with single HIV bnAbs alone
- Double or triple coverage may limit early viral escape
- Reduced levels of incomplete neutralization
- CD4bs, V2, and V3 mix considered most promising



# What's next: Combinations and LS

- 3 bnAbs can be combined
- LS mutation in Fc part of antibodies allows Q6m dosing: serum half-life extends from ~20 to ~70 days and concentration in mucosa increases

HIV bnAb pharmacokinetics in VRC 602, VRC 605, VRC 606 clinical trials



HVTN 116 extended half-life of VRC01LS in rectum (IHC)

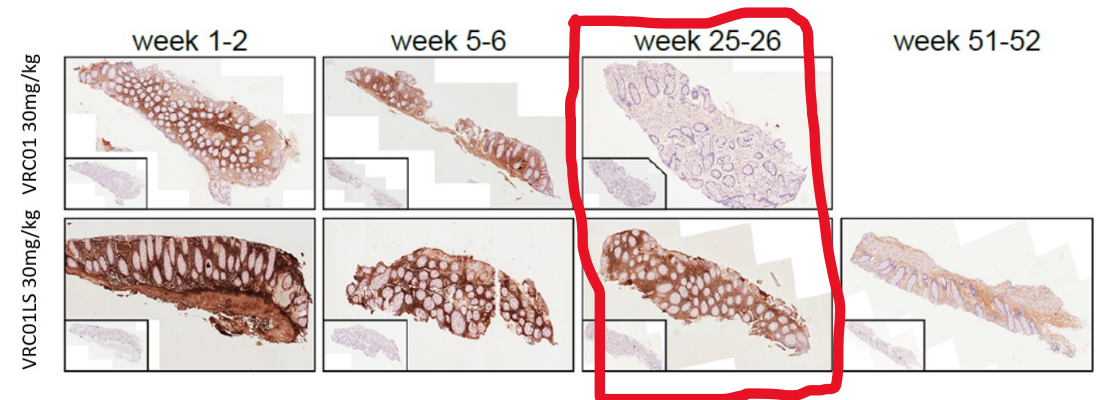


Image: M. Lemos, R. Astronomo, HVTN 116 Study Team.

# Summary: HIV bnAbs in HIV-uninfected adults

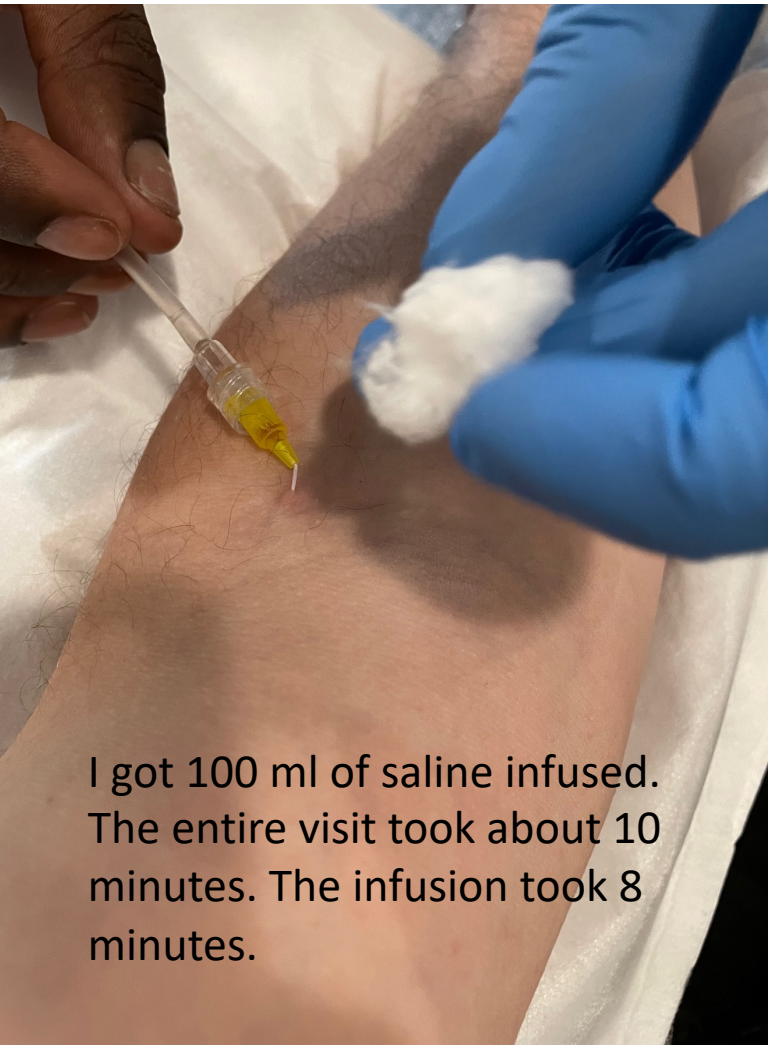
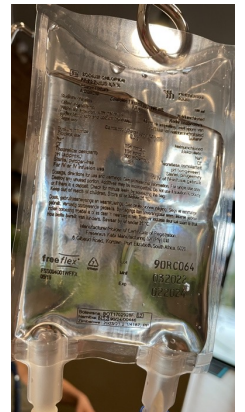
- Administration of antibodies is an old (> 100 years) technique to prevent and treat infections
- HIV broadly neutralizing antibodies (bnAbs) are safe
- 3 HIV bnAbs can be combined
- LS modified HIV bnAbs allow dosing every 6 months
- AMP trials: HIV prevention with 1 bnAb is possible, but combination of 3 bnAbs needed to increase prevention efficacy
- We hope to start AMP follow up 'triple combo AMP' efficacy clinical trials in next 2 years
  - 3 bnAbs administered at the same time, fixed dosage, LS versions, IV
  - 3 doses, every 24 weeks, week 0, week 24, week 48
  - Determine prevention efficacy and correlates of protection





People want options so they can make choices

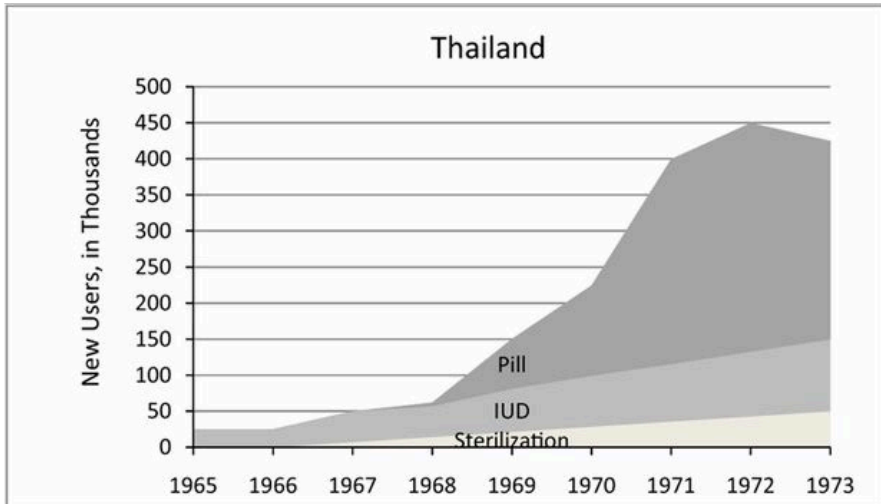
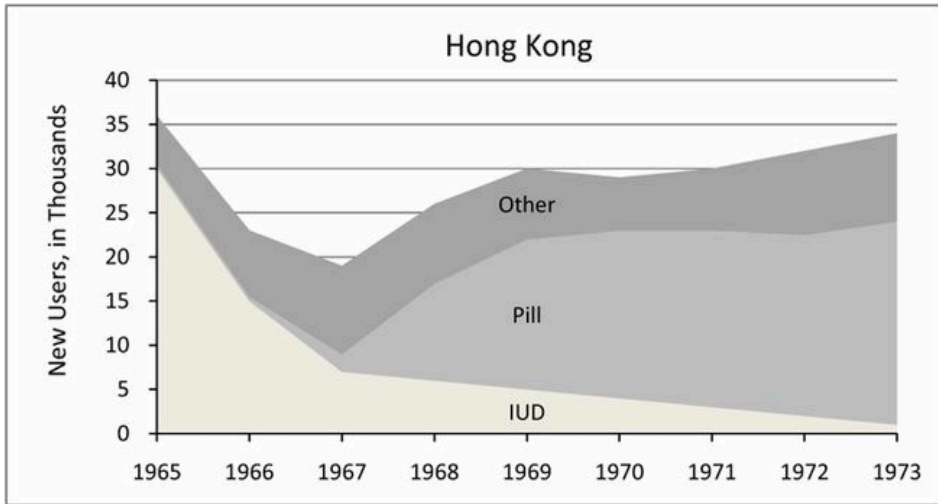
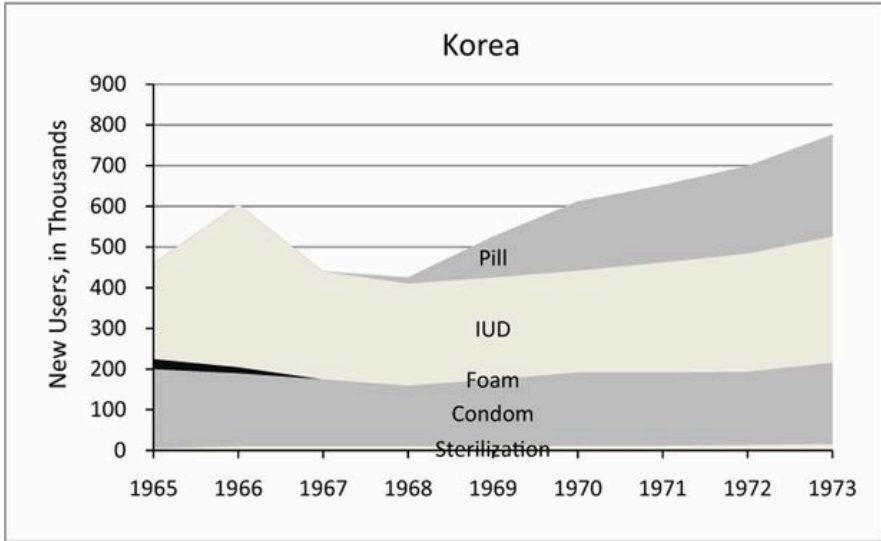
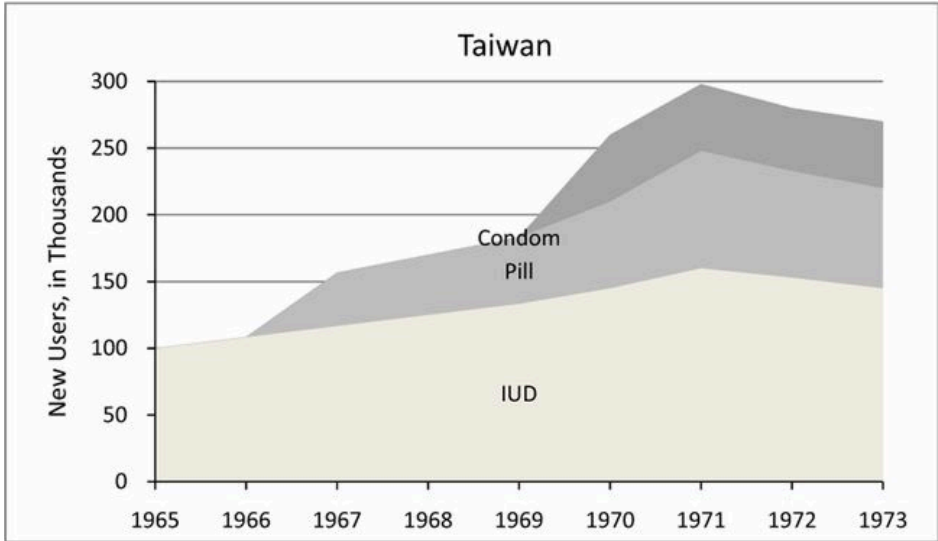
# 5 February 2023: A brief visit to the IV Bar in Benmore Centre Mall, Sandton, Johannesburg, South Africa



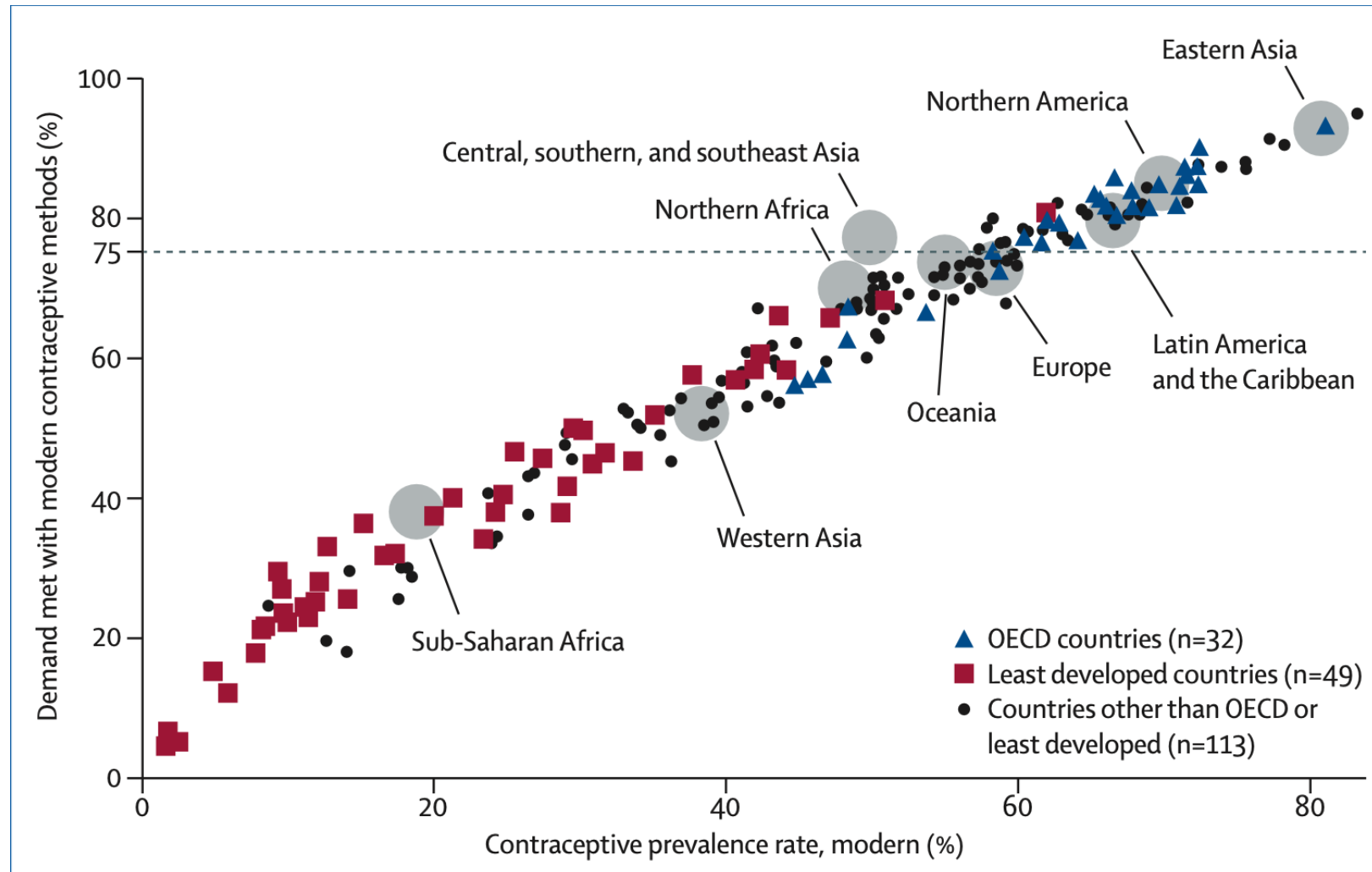
I got 100 ml of saline infused. The entire visit took about 10 minutes. The infusion took 8 minutes.



# Impact of Adding New Contraceptive Methods on the Number of Users, 1965–1973



# Meeting demand for family planning within a generation: the post-2015 agenda



People want options so they can make choices

# HIV Prevention Scorecard

	Condoms	PrEP					HIV Vaccine
		Oral ARV – Truvada, Descovy, Cimduo	Vaginal ARV ring – Dapivirine	Long acting injectable ARV – Cabotegravir	Long acting injectable ARV – Lenacapavir	Long acting injectable HIV bnAbs	
Frequency of administration	On demand	Every day or as needed	Every month	Every 2 months	Every 6 months	Every 6 months	1-2-3-4 shots, then protect for ≥ X years
Ease of administration	On demand	Oral	Vaginal	Intramuscular injection (IM)	Injection under the skin (SC)	Infusion in a vein (IV) or injection under the skin (SC)	Intramuscular injection (IM)
Compliance	Poor	Many users stop using	TBD	TBD	TBD	TBD	TBD
Available	Yes	Limited	Limited	Limited	Not yet	Not yet	Not yet



People want options so they can make choices

# Future HIV PrEP Landscape: Options

	Oral	Topical (ring, inserts, film)	Parenteral (IV, IM, SC, ID, implant)
ARV based	TDF/FTC TAF/FTC TDF/3TC	Dapivirine ring	Cabotegravir <b>Lenacapavir</b>
Passive Immunization			<b>bnAbs</b>
Active immunization			<b>Vaccine</b>

Variables:

- Prevention efficacy
- Dosing interval
- On demand option
- Ease of use
- Discretion
- Side effect profile
- 'natural' or 'artificial'
- Price
- Accessibility
- Availability
- User preference, understanding, familiarity, etc.
- Etc.

