AVAC

Global Advocacy for HIV Prevention

# HIV Prevention Research Process: The Basics . . . and more

Fellows Workshop 2018

# From the lab to you: the research process

- Preclinical research (concept, lab, animal studies)
- Clinical (human) research
  - Phase 1: smaller safety studies,
  - Phase 2: larger, longer, look at safety and immunogenicity
  - Phase 2b/3: even larger, look at safety and efficacy

**After effectiveness results……**

- Open-label, 3b, post-licensure Phase 4 marketing studies


**"Gold Standard": Randomized and controlled**

# How are clinical trials conducted?

- The “gold standard” in research is a randomized and controlled study (RCT)
- Three key concepts:
  - Controlled
  - Randomized
  - Double-blind

# Randomized **Controlled** Trial

- Looks at the effect of an intervention/product in a trial setting – factors are more controlled than in real life
- Involves a minimum of 2 arms (study groups)

**Intervention or Active Arm**

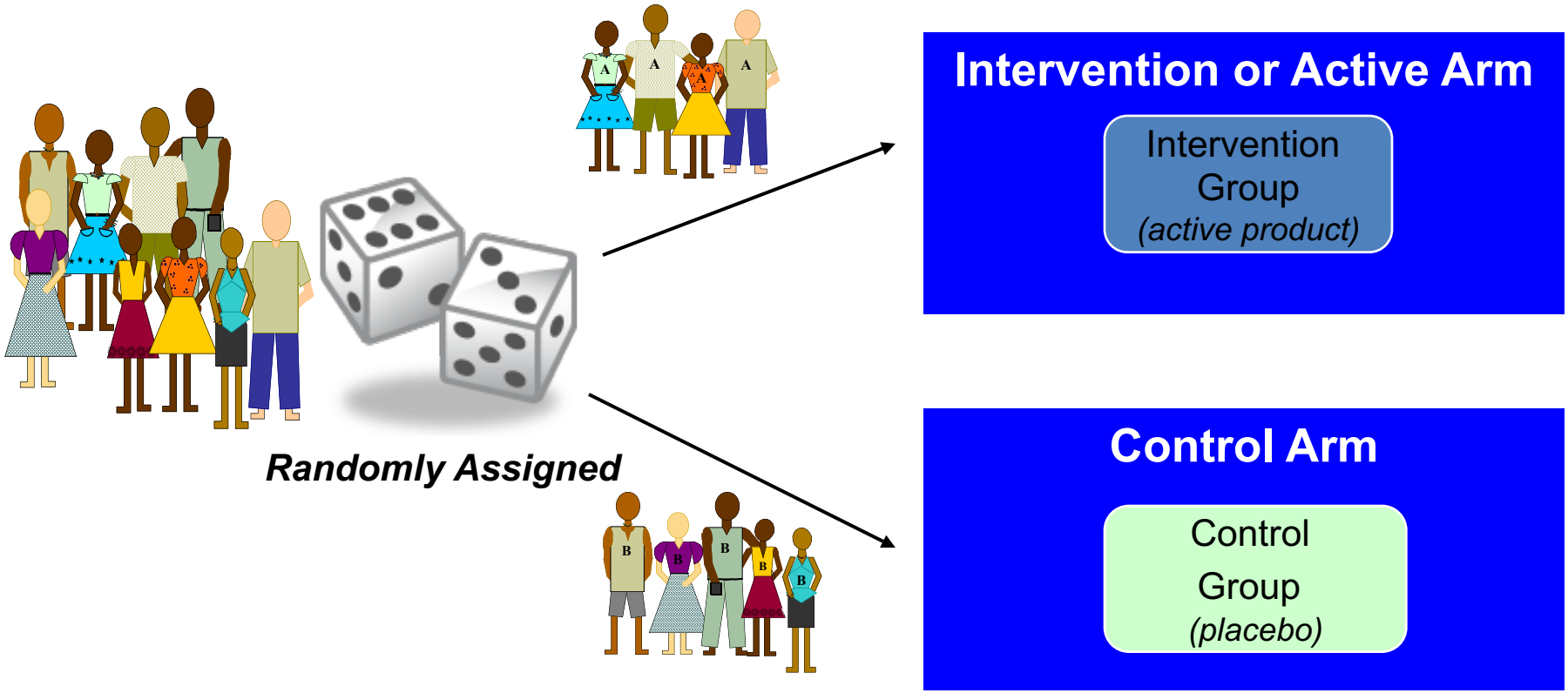
Intervention Group *(active product)*

**Control Arm**

Control Group *(placebo)*

# **Randomized** Controlled Trial

Participants are randomized



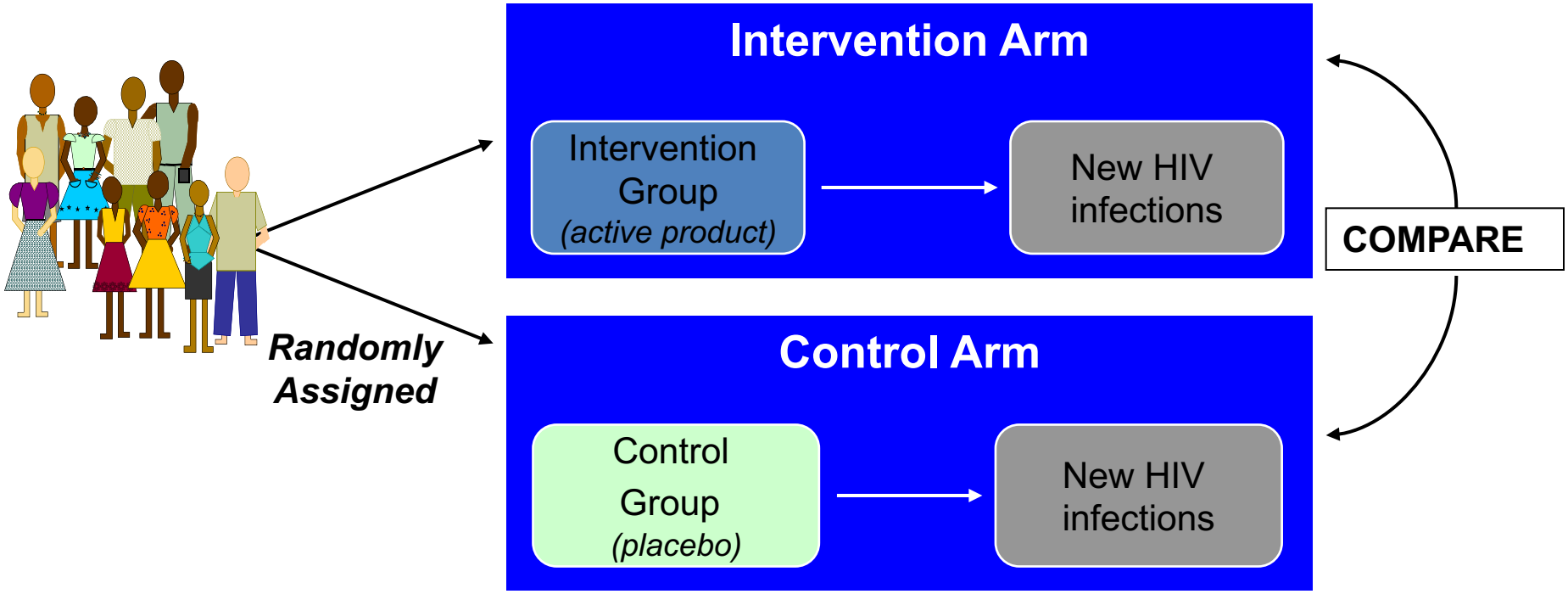
# Double-Blinded RCT

The trial is double-blinded:

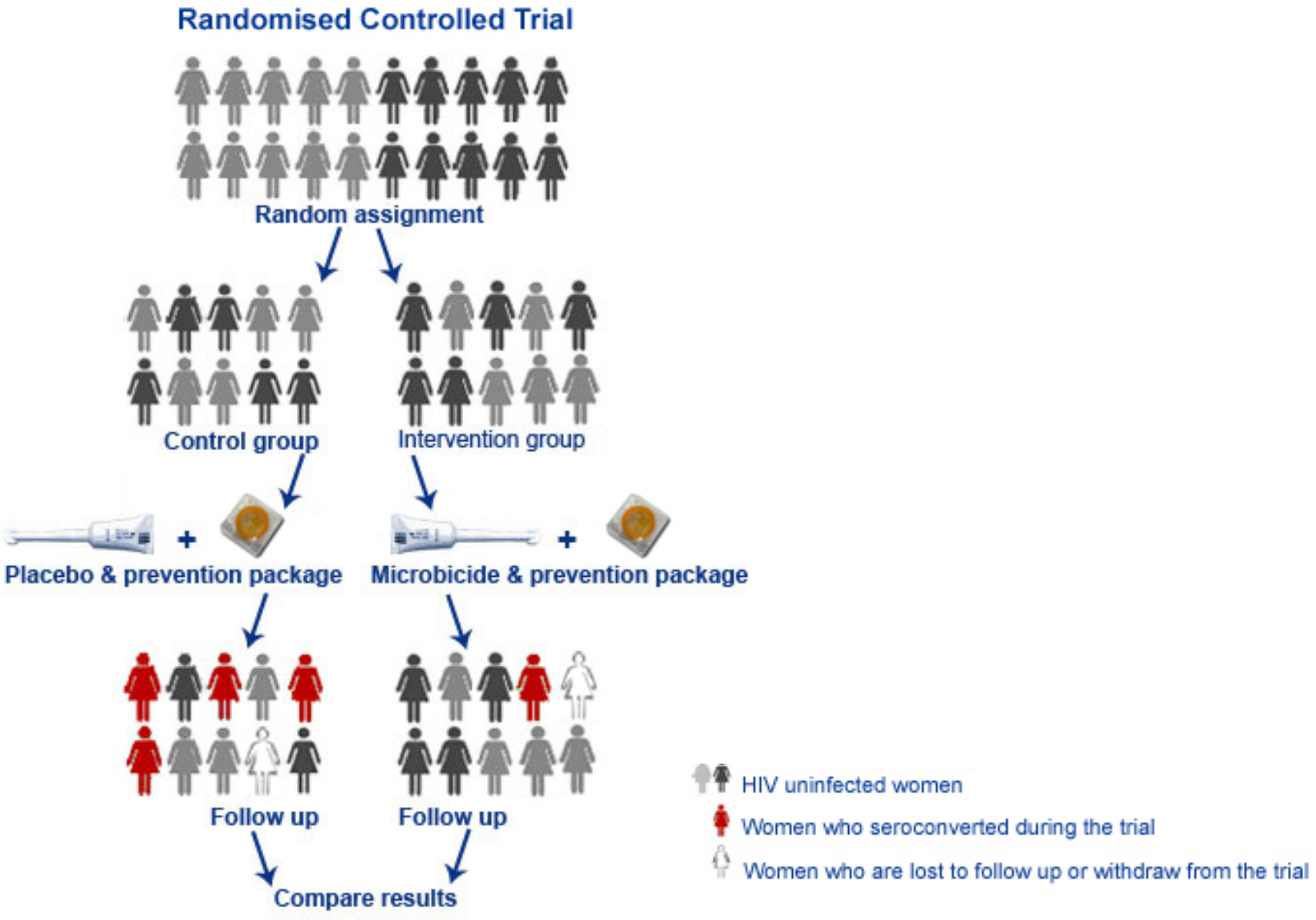
- Neither participants nor researchers know whether each participant is in the active or control arm(s)
- Less potential for bias
- Data unblinded at the end of study to compare between groups

# Randomized Controlled **Trial**

- Goal is to assess if the active study product really works, by comparing to the control
- HIV prevention research: compare new HIV infections in the study arms to determine if the intervention prevented infection and/or progression to disease



# Measuring effectiveness



# RCT Summary

1. One group of participants uses the test product or strategy (active arm)
2. Other group does not use the test product or strategy at all (control arm)
3. All participants get standard prevention tools
4. At the end, researchers compare outcomes (such as numbers of new HIV infections) in each group
5. If fewer people got HIV in the active arm than in the control arm, that would suggest that the test strategy reduced HIV risk

# Safeguards in clinical trials

- International Ethical Standards
- National Regulatory Bodies
- Institutional Review Boards (IRBs)/Ethics Review Committees
- Community/stakeholder input – governed by Good Participatory Practice (GPP) guidelines
- Informed Consent
- Adverse event monitoring
- Data Safety and Monitoring Boards (DSMBs/IDMC)
- Community Involvement

## From Research to Rollout: Evaluations that move a product to the "real world"


*AVAC Report 2013: Research & Reality*
www.avac.org/report2013

Times they are a changin’

(for trial design now that there’s PrEP)

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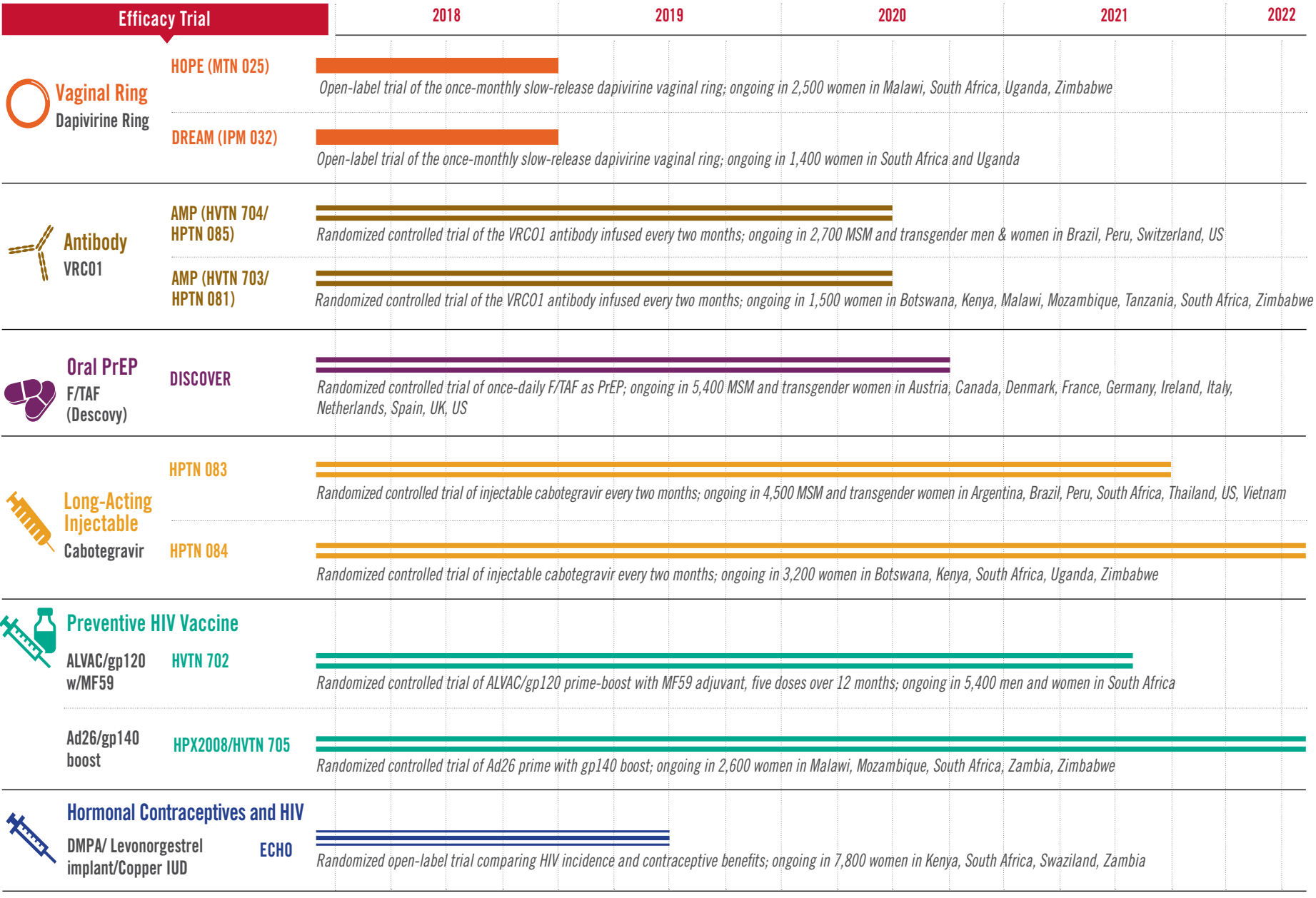
# The Years Ahead in Biomedical HIV Prevention Research

HIV prevention clinical trials

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# Research pipeline (not efficacy)

- Rectal microbicides
- MPTs (Multi-Prevention Technologies)
- Implants
- Long-acting injectables
- Cure
- Vaccines
- Broadly neutralizing antibodies

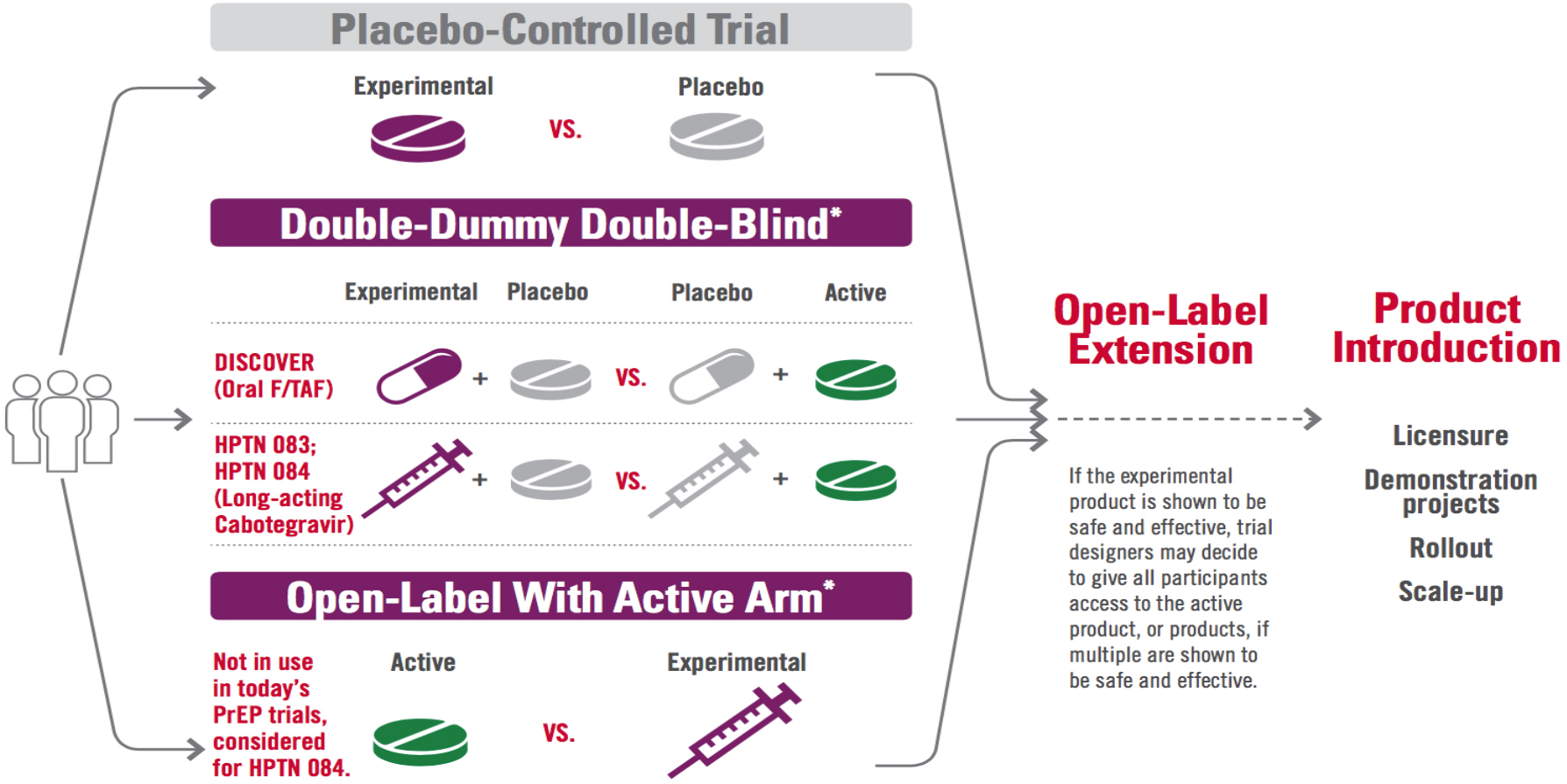
"In clinical trials, PrEP should be provided on-site (as part of SoC) to all participants only in countries with national guidelines on PrEP."

"Advocates cannot influence the products that are studied or trial designs."

# Research Complexity in Post-Placebo Era

- Active control (instead of placebo control)
- Double-dummy double-blind trials
- Open-label trial
- Non-inferiority trials
- Superiority trials

# Research in the Post-Placebo Era




*All of these designs are randomized, meaning that participants are assigned to a study arm by chance. This protects against bias, whether the particpant knows what he or she is receiving or not.*

# Percolating Pipeline in PrEP Era

| Strategy | Trial | # | Population | Status | Location | PrEP Status |
|---|---|---|---|---|---|---|
| Oral PrEP: Daily oral F/TAF | Discover | 5,000 | MSM & transgender | Fully enrolled | Canada, Denmark, Germany, Ireland, Italy, Netherlands, Spain, UK, US | Oral TDF/FTC as part of active control in double-dummy, double-blind design |
| bNAb: VRC01 infused every 2 months | HVTN 704/ HPTN 085 | 2,700 | MSM & transgender | Enrolling | Brazil, Peru, Switzerland, US | Access to oral FTC/TDF PrEP offered at no drug cost to every participant |
| | HVTN 703/ HPTN 081 | 1,500 | Sexually active women | Enrolling | Botswana, Kenya, Malawi, Mozambique, Tanzania, South Africa, Zimbabwe | Oral TDF/FTC discussed in IC, risk reduction counseling sessions, and referral systems |
| Vax: ALVAC/gp120 MF59 adjuvant boost, 5 doses in 12 months | HVTN 702 | 5,400 | Sexually active women & men | Enrolling | South Africa | |
| Vax: Ad26/Mosaic + gp140 boost, 4 doses in 12 months | HPX2008/ HVTN705 | 2,600 | Sexually active women | Enrolling | Malawi, Mozambique, South Africa, Zambia, Zimbabwe | |
| Long-acting injectable: cabotegravir every two months | HPTN 083 | 4,500 | MSM & transgender | Enrolling | Argentina, Brazil, Peru, South Africa, Thailand, US | Oral TDF/FTC as part of active control in double-dummy, double-blind design |
| | HPTN 084 | 3,200 | Sexually active women | Enrolling | Botswana, Kenya, Malawi, South Africa, Swaziland, Uganda, Zimbabwe | |
| HC/HIV: evaluating 3 contraceptives for possible increased risk | ECHO | 7,800 | Sexually active women | Enrolling | Kenya, South Africa, Swaziland, Zambia | Both PEP and PrEP will be offered, either onsite or by rererral, per local standard of care/national policy |
| Ring/PrEP: dapivirine ring and oral TDF/FTC | MTN 034/IPM 045/REACH | 300 | Sexually active women | Planned start early 2018 | Kenya, South Africa, Uganda, Zimbabwe | Open-label cross-over; all will try both ring and oral, then choose |

# Research in the Post-Placebo Era

- Advocate's Guide to Research Terms in the Post-Placebo Era
- HIV Prevention Trial Terms: An Advocate's Guide
- Px Pulse podcasts:
  - PrEP and Trial Design — A no brainer for some
  - Testing Long-Acting PrEP, Easier Said Than Done
  - Standard of Care in the Era of PrEP