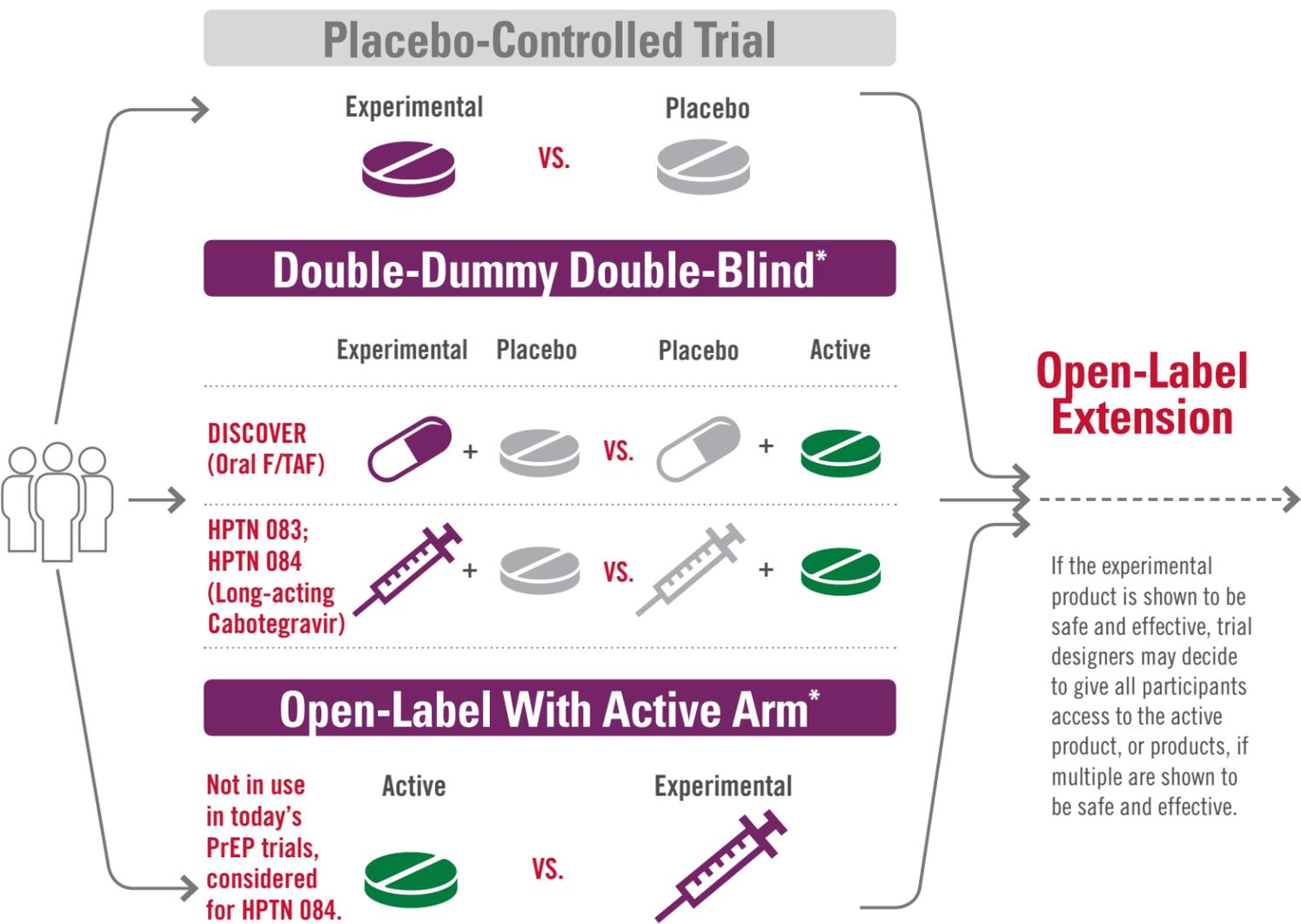


There are more biomedical strategies available for HIV prevention than ever before. Daily oral PrEP is rolling out in countries around the world. Voluntary medical male circumcision continues to be scaled up. And antiretroviral treatment (ART) for people living with HIV is available “on demand” in many countries. Effective ART is good for people’s health and can help reduce the risk of passing on the virus.

At the same time, research is continuing. Today’s ARV-based prevention tools require high levels of adherence (e.g., taking a pill every day). Additional tools like a vaccine or a long-acting form of PrEP would be important additions.

Today’s trials have to test these new tools—and meet ethical standards by providing participants with the best available prevention package. This means something different now that PrEP is rolling out. This graphic and the accompanying lexicon showcase some of the new trial designs and terms used to talk about trial design.



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

● Placebo ● Experimental product ● Safe and effective product * Trials with active control arm



HIV Prevention Trial Lexicon

- **Active arm [of a trial]** is the group of participants receiving a proven or experimental strategy. There can be one or more active arms in a trial. There can be an “active control” arm (see below) or an “active experimental arm”. The difference is whether the efficacy of the active strategy is known or not. Outcomes (like rates of HIV or rates of pregnancy) in people in the experimental active arm are compared to outcomes in people in the control arm.
- **Active control arm [of a trial]** is usually a group of trial participants who are receiving a known effective strategy or intervention that participants in the experimental arm are not receiving. For example, in trials of long-acting injectable PrEP, people in the active control arm are receiving daily oral PrEP, a known effective strategy.
- **Blinded trials** are ones in which the participants don't know what they are receiving. A **double-blinded** trial is one in which neither the participants nor the trial team know which participants are receiving the experimental product and which ones are receiving something else—either a placebo or another product. Blinding protects against bias. If participants or trial staff know who is getting the active experimental product they might act differently. Participants who know they got the experimental product might take more risks if they believe the experimental product provides protection; people who got the placebo might use more condoms.
- **Control arm [of a trial]** is the group of participants that are not receiving the experimental product or strategy. This group receives the same prevention package (see below) as the experimental arm.
 - **Double-dummy double-blind trials** are a way to compare two strategies that can't be made to look identical, without revealing who's receiving what. Imagine a trial seeking to compare an injection and a pill. They don't look alike, right? In a double-dummy double-blind trial design, all of the participants would get both a pill and an injection. One group of participants would get an active pill and a dummy injection; the others would get an active injection and a dummy pill. Neither the staff nor the participants would know who had which active strategy.
 - **Dummies** are the same thing as placebos. A dummy version of an experimental product looks exactly like that product (e.g., vaccine, injection, infusion, pill or ring) except that it doesn't have any active ingredient. Examples include a sugar pill or a saline injection or a ring without any drug inside it.
 - **Non-inferiority trials** are trials that are designed to show that a new method (Product A) works as well as a method that has previously been shown to work (Product B). If A doesn't meet or exceed B's effectiveness, it is considered inferior. This doesn't mean it isn't effective, just that it is not better than the existing product.
 - **Open-label [trial]** is a trial in which both participants and trial staff know who is receiving what. Trials of voluntary medical male circumcision were open-label in that trial staff and participants knew who had undergone the procedure immediately and who had been assigned to the delayed surgery arm.
 - **Open-label extension (OLE) trial** is a study that usually follows directly from an efficacy trial that showed the product was successful in reducing HIV risk. In OLEs, trial participants from both the active and placebo arm and, sometimes, members of their communities, get the chance to use the active product. Everyone knows what they are receiving and knows that the product worked in the efficacy trial.
- A trial's **prevention package** is the set of tools and services all participants receive, no matter which arm of the trial they are in. (In HIV prevention trials, all participants in both the control and active arms receive male and female condoms, counseling, HIV and STI testing and treatment and may receive other services like harm reduction, referrals for voluntary medical male circumcision, PrEP, etc.)
- **Superiority trials** are trials that are designed to show that a method (Product A) is more effective than placebo, or sometimes, to show that a new method (product A) is more effective than an already-existing method (Product B). A superiority trial is designed to find out whether Product A is more effective than placebo (or Product B) in enrolled participants, and the trial makes every effort to ensure the products are used correctly and consistently.