HIV Prevention Trial Terms
An Advocate's Guide

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AVAC
Global Advocacy for HIV Prevention

This fact sheet explains some of the terms used to talk about trials designed to test new HIV prevention tools.

The most basic plan for a clinical trial:

1. One group of participants uses the test product or strategy (active arm);
2. the other group does not use the test product or strategy at all (control arm);
3. all participants get standard prevention tools (like condoms and maybe PrEP);
4. and, at the end, the 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.

Not all trials use this approach. In fact, today's HIV prevention trials are using a range of different approaches. But this basic framework is a good starting point for understanding different types of trials. We hope you'll use this list of definitions when you are reading other AVAC resources focused on specific trials and products. To see the latest, visit ***www.avac.org***.

- **Active control arm** is when a group of trial participants uses an HIV prevention product (like oral PrEP) or strategy (like circumcision) already known to work. The other trial group uses a new tool that is being tested (like long-acting injectable PrEP). This way, researchers can compare a strategy already known to work to a new one—to find out if the new one is (1) better, (2) just as good or (3) not as good as the one that works.

- **Blinded trials** are ones in which no participant knows who is getting the test product and who is not. No matter what arm you are in, the product you are asked to use will look just like the one that everyone else in the trial is using. Some participants will be getting the test product and some will be getting a placebo (a fake product that looks like the test one).

  A blinded trial design protects against bias. If participants know whether they are getting the active test product or the placebo, it might affect how they act. Participants taking the test product, for example, might take more risks if they thought the test product would protect them. Participants who knew they had the placebo might use more condoms more often. "Blinding" the trial can prevent those behavior changes by making it impossible for people to know what they are getting. This keeps each group's level of risk-taking similar, making it possible to see whether the test product was effective or not.

- In **double-blinded trials**, neither the participants nor the trial staff know who is getting which product. This reduces the chance that trial staff will change how they treat participants based on what product they are receiving. For example, a counselor who knows for sure that one participant is getting the placebo might do more forceful HIV prevention counseling with that participant. This could affect the participant's behavior and that could affect the group's outcome.

- **Double-dummy double-blind trials** are a way to compare two strategies that clearly look different from each other, without participants or trial staff knowing who is getting what. Suppose there is a trial where some people will get an injection and others

will get a pill. Clearly, people will know which one they are getting. Given what they know or think about the pill or the injection, people could change their behaviors. This could change the trial result.

A double-dummy, double-blind trial design is one way to avoid this. In this kind of trial, all of the participants would get both a pill and an injection. One group would get an active pill and a dummy injection. The other group would get an active injection and a dummy pill. Dummy, like placebo, is just another word for a fake product. It looks exactly like the test product, but it doesn't have any active ingredient. A dummy pill can be a sugar pill, a dummy injection can just have saline (sterile salt water) in it, etc. By using these, neither the trial staff nor the participants would know who had which active strategy.

- **Non-inferiority trials** are designed to find out if a new method (Product A) is just as good as an already-existing method (Product B). Researchers who are testing new drugs to use as PrEP, for example, have to show that their new test product is at least not inferior to (just as good as) the PrEP that is already on the market. If A doesn't meet or exceed B's effectiveness, it is considered inferior. This doesn't mean that it isn't effective, just that it is not better than the existing product.

- **Open-label trial** is one where both the participants and trial staff know what participants are using. Medical male circumcision efficacy trials were open-label because it was clear who had undergone the procedure. In these trials, some men got circumcised immediately and some were assigned to the delayed group who got circumcised a few months later. Researchers measured rates of HIV in men who got circumcised immediately versus those who waited. They saw lower rates in the circumcision arm in three different trials. So they concluded that this strategy reduced HIV risk. All of the men were then offered circumcision. It is important to remember that all trial participants were provided with condoms and urged to use them to protect themselves—both before and after the circumcision.

  Some future trials of long-acting PrEP could be open-label. One group could receive daily oral PrEP while the other receives the test product which will be a form of injectable PrEP.

- **Open-label extension (OLE) trials** are usually done right after a trial shows that a new test product is effective. They are called "open-label" because all the participants in an OLE trial are offered the new, effective product. Usually, everyone who participated in the product's effectiveness trial is invited to join the OLE trial. Sometimes other community members are also invited to join. Everyone knows what they are getting and that the product worked in an efficacy trial. OLE trials collect information about how people's product use and risk behaviors may change when they know for sure that they are getting a product that can reduce HIV risk.

- A trial's **prevention package** is the set of tools and services offered to all trial participants, no matter what arm of the trial they are in. The prevention package in HIV prevention trials includes male and female condoms, counseling, testing for HIV and other STIs, and STI treatment, if necessary. It may also include other services such as harm-reduction assistance, referrals for voluntary medical male circumcision, PrEP, etc.

- **Superiority trials** are designed to show that a new method (product A) is more effective than a 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).

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