Published on *The Well Project* (http://www.thewellproject.org)

Understanding Clinical Trials [1]

Submitted on Nov 11, 2016

Table of Contents

What Are Clinical Trials?

The term clinical trial is used to describe many different types of research studies on human subjects. There are five main types of clinical trials:

- **Treatment trials**
  Study new medications, new combinations of existing medications, or new types of therapies
- **Prevention trials**
  Look for better ways to prevent disease?sometimes with medicines, sometimes with behavior changes
- **Diagnostic trials**
  Test the best way to detect disease or changes within the body
- **Natural History trials**
  Study the natural course of disease in the human body
- **Quality of Life trials**
  Study ways to improve aspects of life for people living with illnesses

*Click above to view or download this fact sheet as a **PDF slide presentation** [2]*

The Basic Components of Clinical Trials

The scientists and health care providers who manage clinical trials are usually called investigators. The people who join clinical trials are usually called participants, but may be referred to as volunteers or study subjects. ALL clinical trials are voluntary ? you never have to participate in a clinical trial unless you want to; this is a human right protected by international laws.

In 2002, the World Health Organization (WHO) released a Handbook for Good Clinical Research Practice [3], which was intended as a guide for each country to develop its own laws governing clinical trials. The WHO's handbook is based in part on the recommendations for good clinical practice set forth by the International Conference on Harmonisation (ICH) in 1996. In the US, for example, the Food and Drug Administration (FDA), which approves drugs for public use, has adopted the ICH's guidance on good clinical practice for clinical trials.

Each clinical trial has a written plan, or study protocol, that describes the goals of the study, how long the study will last, who is eligible to participate (also called inclusion and exclusion criteria), and what tests and procedures are required of each participant.

Inclusion and exclusion criteria are the guidelines used to determine who can and cannot participate in a specific clinical trial. Inclusion criteria are requirements that a person must meet to participate (such as HIV drug-naïve, or never having taken HIV drugs, CD4 cell [4] count, viral load [5], age, or many others). Exclusion criteria are factors that prevent a person from participating either for his or her safety or to make it easier to understand the study results. For example, people might be excluded for having liver problems, or if they have already taken a drug that is being studied.

Each participant in a clinical trial must sign an informed consent. When you sign this document it means that you understand the details of the study and you agree to participate. You may want to take the document with you and talk about the study with your health care provider, family, or friends before you decide to participate. If your native language is not the language spoken by the people describing the study, you should ask if translation is available. It is important that you truly understand the study and what you will be asked to do. If you have any questions, be sure to ask the study staff. It is their job to make sure that, when you sign, you are making an informed choice and understand what you are agreeing to do in signing the document.

You may be paid for travel expenses to and from the study site and for your time; this payment is sometimes called compensation. Childcare may also be provided. You can choose to drop out of a study at any time and for any reason.

The Stages of Treatment Trials

The most common type of clinical trial in HIV is a treatment or drug study. There are four stages, or phases, of clinical trials for new treatments. With each phase, a little more is known about the treatment being studied. Each phase has a different purpose and helps researchers answer specific questions about the drug in trial.

- **Phase I: Is the drug safe?**
  A Phase I trial tests a drug in a small number of participants (usually fewer than 100) to find a safe dose and to document the side effects [6] of the drug. Phase I trials are usually short, lasting a few days to a few weeks.
- **Phase II: Is the drug effective?**
  A Phase II trial tests a drug in a larger number of participants (on average 100 to 300) to see if the drug works. Phase II trials may also test different doses of the drug to find which dose works best. The safety of the drug also continues to be evaluated. A Phase II trial usually lasts six months to one year.
- **Phase III: Is the drug safe and effective in larger groups of people for longer periods of time?**
  A Phase III trial tests a drug in a very large group of participants (typically 1,000 to 3,000). Phase III trials gather more information about the safety and effectiveness of the drug by comparing it to an existing medication or treatment. Phase III trials generally last two to three years.
- **Phase IV or Post-Marketing studies:**
  What are the long-term results of using the drug? These trials are done after US Food and Drug Administration (FDA) approval to get more information about the drug's best use and to further examine long-term side effects [6].

Once a drug trial has completed the first three phases of research, the company that makes the drug submits the study data to the organization that regulates drugs in that country (e.g., the FDA in the US) for approval. Because the need for treatments for HIV is so great, a drug company can apply for something called accelerated, or quicker, approval if the drug offers something new or meets a need for people living with HIV (HIV+).

Accelerated approval may put special restrictions on how the drug can be used. However, even if a drug gets accelerated approval, the drug company must continue doing long-term research on the drug for it to get full approval.

Why It's Important to Participate in a Clinical Trial

To date, women have been drastically underrepresented in HIV clinical trials. This means that many decisions about women's HIV care and treatment are based on research studies of men. Women are not simply smaller versions of men. Women's bodies are different; consequently, we need women's participation in clinical research to help us understand how HIV acts in the female body.

What are the correct HIV drug dosages for women? How do opportunistic infections [7] and gynecologic problems [8] affect women living with HIV? What side effects [6] are more likely to occur in women than men? Women who participate in clinical trials can help answer many questions specific to women living with HIV while also benefiting the field of HIV research as a whole.

There are many good reasons to participate in a clinical trial. You may:

- Gain access to new treatments not available to the public
- Receive expert medical care at leading healthcare facilities
- Gain access to new experimental medications
- Have a chance to help others by contributing to medical research

Should I Participate in a Clinical Trial?

Choosing to participate in a clinical trial is a big decision. There are risks and benefits to consider when making the choice.

Risks

- You may experience unpleasant or serious side effects
- You may have to stop all current medications, including any HIV medications
- You may receive a placebo (a pill containing no medication)
- There is no guarantee that the experimental drug will be an effective treatment for you

Benefits

- You may experience health benefits from a new treatment that is not yet available to the general public
- Most trials provide free laboratory tests, expert medical care, and drugs at no cost, for the purpose of the study
- You are contributing to the development of a new medication or increasing understanding of HIV disease

Important Lessons from Clinical Trials

Over the past several decades, we have gained important knowledge about the treatment and prevention of HIV through clinical trials research. Here are some of the highlights:

- A combination of HIV drugs (combined antiretroviral therapy) is much more effective at controlling HIV and maintaining good health
- Giving pregnant women [9] HIV drugs can reduce the chances that they will pass HIV on to their babies to as low as one in 100
- Treatment as prevention [10]: For people living with HIV, taking HIV drugs can reduce their viral load, thus making them much less likely to spread HIV to others. For people who are HIV-negative, taking HIV drugs can protect them against becoming infected if they are exposed to HIV (e.g, PrEP [11] or pre-exposure prophylaxis).
- The results of a recent study (the START trial) have definitively shown that people living with HIV who start treatment earlier, while their CD4 counts are still high, have a much lower risk of illness and death. This includes people living with HIV who may have no outward signs of ill health.

Clinical Trials and Women Living with HIV

Worldwide, women represent over half of all those living with HIV. In the past, women were excluded from participating in many types of clinical trials. Now, despite being able to participate freely, the number of women participating in HIV treatment trials remains low. A study from 2012 reported that women represented, on average, only one in five participants in clinical trials of antiretroviral drugs approved by the FDA from 2000 to 2008. The good news is that, globally, women's participation in prevention studies, including vaccine studies and behavioral methods, appears higher.

It is important to participate in research because HIV and some of the HIV drugs act differently in women's bodies. The only way to discover these differences is for more women living with HIV to join clinical trials. For information on a clinical drug trial in the US that was successful in recruiting large numbers of women and people in color, see our fact sheet Lessons from GRACE [12].

To find clinical trials that might be of interest or benefit to you, you can search the following registries:

- ClinicalTrials.gov [13] from the US National Institutes of Health (NIH)
- HIV/AIDS Clinical Trials at AIDSinfo [14]
- AIDS Clinical Trials Group (ACTG) [15]
- HIV Prevention Trials Network (HPTN) [16]
- HIV Vaccine Trials Network [17]
- Microbicide Trials Network (MTN) [18]
- International Clinical Trials Registry Platform [19] from the World Health Organization

Tags:

- Clinical trials HIV [20]
- Research HIV [21]
- Human subjects [22]
- Treatment trials [23]
- Prevention trials [24]
- Drug trials [25]
- Informed consent [26]
- Phase 1 trial [27]
- Phase 2 trial [28]
- Phase 3 trial [29]
- Clinical trials women [30]
- Inclusion criteria [31]
- Exclusion criteria [32]
- HIV studies [33]
- HIV studies women [34]

Additional Resources

Select the links below for additional material related to clinical trials.
Women in Clinical Trials (FDA Office of Women's Health) [35]
Las Mujeres en los estudios clínicos (La Oficina de Salud de la Mujer de la FDA) [36]
Clinical Trials: What Patients Need to Know (FDA) [37]
Kit de herramientas de Redes Sociales para Socio (La Oficina de Salud de la Mujer de la FDA) [38]
Women Who Make a Difference (YouTube) [39]
Women-Only HIV Trial Hailed as Landmark (Medpage Today) [40]
Women Are Focus of Recruiting Efforts for Local HIV-Related Clinical Trials (Cleveland.com) [41]
The Inclusion of Women in Clinical Trials (FDA) [42]
Inclusion of Women and Minorities in Clinical Research (NIH) [43]
Learn about Clinical Studies (NIH) [44]
NIH Clinical Research Trials and You [45]
Understanding Informed Consent (CenterWatch) [46]
Research and Clinical Trials in HIV/AIDS (womenshealth.gov) [47]
HIV-Positive Women in Clinical Trials (AIDSmap) [48]
International Clinical Trials Registry Platform (WHO) [49]

Links:
[1] http://www.thewellproject.org/hiv-information/understanding-clinical-trials
[2] http://www.thewellproject.org/sites/default/files/understanding%20clinical%20trials%20final.pdf
[3] http://apps.who.int/prequal/info_general/documents/gcp/gcp1.pdf
[4] http://www.thewellproject.org/hiv-information/understanding-cd4-cells-and-cd4-cell-tests
[5] http://www.thewellproject.org/hiv-information/women-and-viral-load
[6] http://www.thewellproject.org/hiv-information/side-effects
[7] http://www.thewellproject.org/hiv-information/what-are-opportunistic-infections

[8] http://www.thewellproject.org/hiv-information/caring-womans-body-care-and-prevention-gyn-problems
[9] http://www.thewellproject.org/hiv-information/pregnancy-and-hiv
[10] http://www.thewellproject.org/hiv-information/hiv-treatment-prevention-tasp
[11] http://www.thewellproject.org/hiv-information/prep-women
[12] http://www.thewellproject.org/hiv-information/lessons-grace-us-study-focused-women-living-hiv
[13] https://clinicaltrials.gov/
[14] https://aidsinfo.nih.gov/clinical-trials
[15] https://actgnetwork.org/trials_open_enrollment
[16] https://www.hptn.org/research/studies
[17] http://www.hvtn.org/en/participants.html
[18] http://www.mtnstopshiv.org/
[19] http://apps.who.int/trialsearch/
[20] http://www.thewellproject.org/tags/clinical-trials-hiv
[21] http://www.thewellproject.org/tags/research-hiv
[22] http://www.thewellproject.org/tags/human-subjects
[23] http://www.thewellproject.org/tags/treatment-trials
[24] http://www.thewellproject.org/tags/prevention-trials
[25] http://www.thewellproject.org/tags/drug-trials
[26] http://www.thewellproject.org/tags/informed-consent
[27] http://www.thewellproject.org/tags/phase-1-trial
[28] http://www.thewellproject.org/tags/phase-2-trial
[29] http://www.thewellproject.org/tags/phase-3-trial
[30] http://www.thewellproject.org/tags/clinical-trials-women
[31] http://www.thewellproject.org/tags/inclusion-criteria
[32] http://www.thewellproject.org/tags/exclusion-criteria
[33] http://www.thewellproject.org/tags/hiv-studies
[34] http://www.thewellproject.org/tags/hiv-studies-women
[35] http://www.fda.gov/downloads/ForConsumers/ByAudience/ForWomen/UCM488248.pdf
[36]
http://www.fda.gov/downloads/ForConsumers/ByAudience/ForWomen/FreePublications/UCM488255.pdf
[37] http://www.fda.gov/ForPatients/ClinicalTrials/default.htm
[38] http://www.fda.gov/downloads/ForConsumers/ByAudience/ForWomen/UCM489597.docx
[39] https://www.youtube.com/watch?v=DKJQALIz8hE
[40] http://www.medpagetoday.com/MeetingCoverage/ICAAC/53647
[41]
http://www.cleveland.com/healthfit/index.ssf/2015/01/women_are_focus_of_recruiting_efforts_for_local_hiv-related_clinical_trials_video.html
[42] http://www.fda.gov/ScienceResearch/SpecialTopics/WomensHealthResearch/ucm131731.htm
[43] http://orwh.od.nih.gov/research/inclusion/
[44] http://clinicaltrials.gov/ct2/info/understand
[45] http://www.nih.gov/health/clinicaltrials/index.htm
[46] http://www.centerwatch.com/clinical-trials/understanding-informed-consent.aspx
[47] http://www.womenshealth.gov/hiv-aids/research-clinical-trials-hiv-aids/
[48] http://www.aidsmap.com/HIV-positive-women-in-clinical-trials-A-gap-in-the-facts/page/1497093/
[49] http://www.who.int/ictrp/en/