HFSA
HEART FAILURE SOCIETY OF AMERICA

Module 11

CLINICAL TRIALS

Contents

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 The Heart Failure Society of America (HFSA) is a non-profit organization of healthcare profession als and researchers who are dedicated to enhancing quality and duration of life for patients with heart failure and preventing the condition in those at risk. HFSA developed these education mod ules to help patients, their families, and individuals at risk for heart failure understand and cope with the disease. For more information about the HFSA, please visit our website at www.hfsa.org This booklet was developed under the direction of the Heart Failure Society of America. The book let is designed as an aid to patients/physicians and sets forth current information and opinions on the subject of heart failure. The information in this booklet does not dictate an exclusive regimen of treatments or procedures to be followed and should not be construed as excluding other acceptable methods of practice. Variations taking into account the needs of the individual patient, resources, and limitations unique to the institution or type of practice may be appropriate.

Module 11

CLINICAL TRIALS

Know Who to Contact

Please write down important contact information in the space below. You may also want to share this information with family members and friends.

Health Care Provider Treating Me for Heart Failure:

Name _____

Address _____

City _____ State ____ ZIP _____

Phone _____

Fax _____

E-mail _____

Other Important Phone Numbers:

Ambulance, fire department, or emergency services: **911**

Pharmacy _____

Other healthcare providers:

_____

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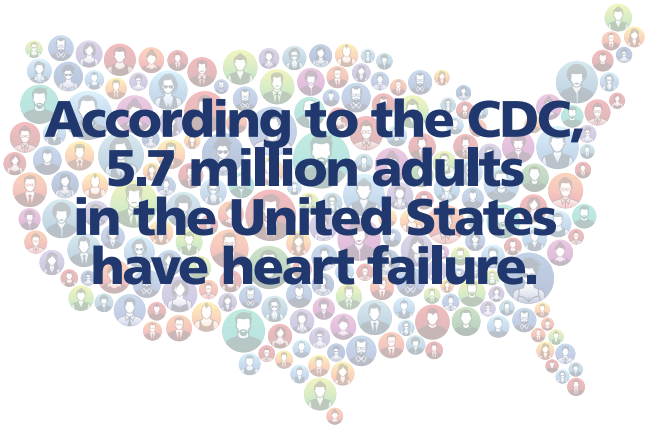
Introduction to Clinical Trials

The term "clinical trial," refers to a research study in which information (data) is collected about people with a specific medical condition to learn more about that condition, or to determine whether a new treatment can help people suffering from that problem. Information gained from clinical trials therefore helps us understand more about diseases and how best to treat them. For the management of heart failure, for example, numerous clinical trials performed over the past three (3) decades or more have helped guide your doctor on how best to treat your condition.

There are different types of clinical trials. Broadly, clinical trials fall in to two basic categories: observational and therapeutic trials. We'll discuss each of these in more detail on the pages that follow.

Within a given trial, the ***investigator*** is the medical provider who is in charge of that study at a given hospital or institution. The ***subject*** is the person who has agreed to participate in the trial. Within many interventional trials, there is a control group or a comparison group that receives standard therapy but not the new treatment being tested. The ***treatment*** group refers to that group receiving the new treatment, either in addition to standard therapy or compared directly to standard treatment. The majority of trials choose which subject or participant will be placed into the treatment group or the control group at random (like the flip of a coin) to help ensure a fair comparison.



Types of Clinical Trials

Observational Studies

An investigator conducts observational studies by gathering specific information on the subjects who decide to participate in the study to help define the course of a given disease. The purpose of an observational study is to explore how specific variables (such as gender or race) affects the course of a disease.

In these studies, the investigator will collect patient-specific information (such as age, gender, race, height, weight, and routine blood test results) and then follow their course over time. For example, we have learned from several heart failure registries that patients with kidney disease are at higher risk for readmission to the hospital after an initial hospitalization for heart failure. We have also learned from observational studies that the incidence of heart failure in the United States and elsewhere increases sharply with age, and that hypertension is an important risk factor for the development of heart failure later in life. These are just a few examples of how observational studies have increased our knowledge of heart failure and how it is influenced by other conditions or variables such as hypertension and age.

Therapeutic Trials

Therapeutic trials study the effect of an intervention on a specific condition. Therapies can vary widely and may include devices (such as pacemakers), medications, or other non-medical interventions. For example, non-medical interventions might include dietary changes (such as a low versus a high salt diet) or exercise. A therapeutic trial might even include teaching sessions to help patients with heart failure better understand their own disease.

Therapeutic trials fall into different categories, described on the pages that follow.

Open Label Trials

In open label trials, subjects receive the treatment under investigation in an "open label" manner. That means that both the patient and the investigator know that the patient is receiving the specific therapy being studied. This type of trial has the advantage of studying the safety of a given treatment or intervention. However, there is concern that enthusiasm for a newer treatment could lead to better outcomes being reported in the treated patients, regardless of any true treatment-related benefit.

The outcomes of patients participating in such a study can be compared to "historical controls," referring to patients treated with standard treatment whose outcomes were studied in other trials or observational studies. However, the conclusions that can be drawn from this type of study are limited because the patients receiving the treatment may not be well matched to the controls used for comparison.

Randomized Trials

As mentioned previously, randomized trials do exactly that: they randomly assign a subject to be included in the **treatment group** or the **control group**. Participants assigned to the treatment group receive the new treatment or intervention being tested while those in the control group typically receive standard treatment. Control groups are necessary because without them, there is no way to determine if the treatment being studied actually helps a given condition.

The control group serves as an important comparison group. This group will receive standard treatment in addition to a pill or treatment that might look similar to the new therapy being tested. However, in the case of a pill or capsule, the control group will take one containing inactive materials (a sugar pill or "placebo") rather than that containing the new treatment. In a device trial, the control group might undergo implantation of a new device in question but the device will not be activated or turned on. The treatment group is that which receives the new therapy being tested, most often added on top of standard therapy.

Most randomized trials are **double blind**. This means that neither the participant nor the investigator knows which group the participant is in (control or treatment group). This makes the results of a study more reliable as this approach tends to eliminate the influence of "bias" on the part of the subject or investigator. For example, if the patient knows they are receiving the real treatment, they may feel better just because they expect to, rather than their improvement being a true effect of the treatment. Eliminating bias is therefore important to ensure that the effect seen is real.

In the same way, if the investigator knows the patient is receiving the real medication rather than placebo, he or she may interpret the information pertaining to a given patient in a way that leans toward benefit. The best type of clinical trial is therefore one that is both randomized and double blind. The Food and Drug Administration usually requires this type of vigorous testing before a new drug or device can be approved and used.

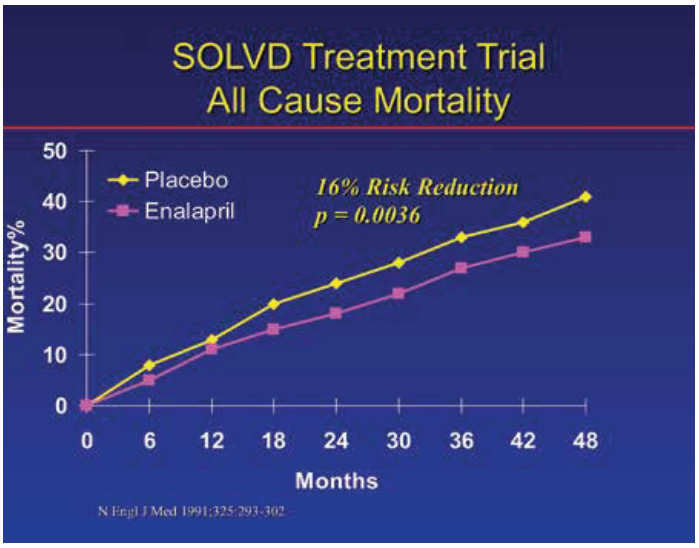
Example of an Observational Trial or Registry

The OPTIMIZE-HF registry entered data from patients admitted to participating US hospitals (259 total) with heart failure from 2003 to 2004. The investigators gathered important clinical Information on more than 48,000 patients. Investigators followed some of the patients in this registry after that initial hospitalization for 60-90 days, which was important to define what variables were related to better or worse outcomes. This study unveiled numerous important variables that identified patients at higher risk for re-hospitalization or early death. For physicians caring for patients with acute or chronic heart failure, results such as these can heighten the awareness of risk.

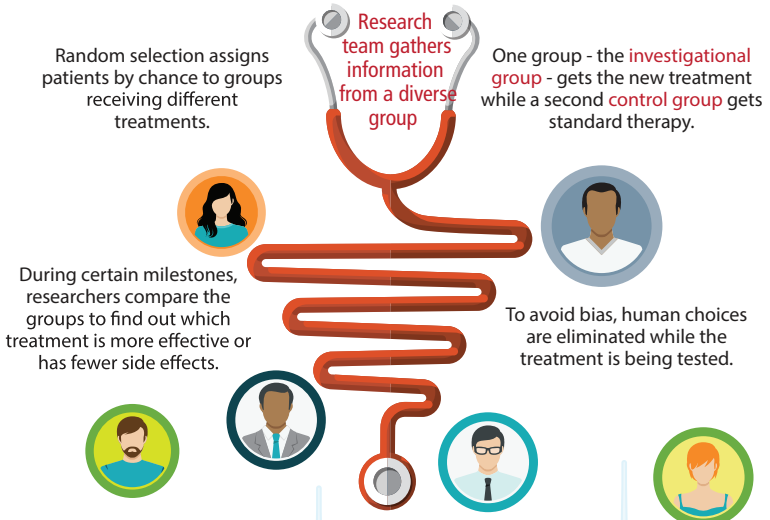
Example of a Key Therapeutic Clinical Trial in Heart Failure

SOLVD (Studies of Left Ventricular Dysfunction) Trial was a double blind, randomized, placebo-controlled trial sponsored by the National Institutes of Health. Its purpose was to study the effect of a class of drugs known as angiotensin converting enzyme (ACE) inhibitors in patients with left ventricular dysfunction (weakened heart muscle). The purpose of this study, published in 1991, was to explore whether the ACE-inhibitor, enalapril, could help heart failure patients live longer and do better.

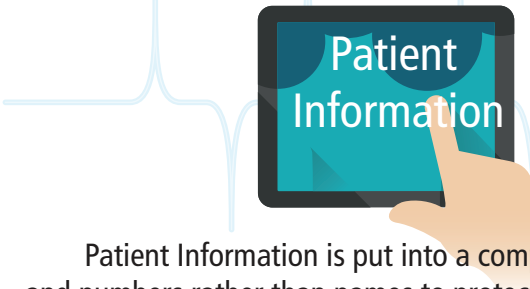
After an average follow-up period of approximately three (3) years, subjects treated with enalapril did better than those patients treated with the placebo with improved survival and fewer hospitalizations for heart failure. As a result of this study and several others, ACE-inhibitors became a key component of therapy for patients with reduced heart function. The graph below displays the mortality curves from the SOLVD trial.



Random Selection or Sampling Prevents Bias



Random sampling helps prevent bias



Patient Information is put into a computer using acrostics and numbers rather than names to protect the participant's identity.

Control group gets standard therapy

Investigational group gets new treatment

Possible Advantages to Participating in a Clinical Trial

There are several advantages to participating in a research trial. First, people are living longer lives from successful heart failure treatments that are the results of past clinical trials. Secondly, if you decide to participate, you can be proud that you will be contributing to advances in a specific field of medicine, and you will be helping generations to come. Many patients participate in trials for this very reason. Lastly, patients who participate in clinical trials can be assured that they will be cared for by very well trained experts in a given medical field (such as a heart failure specialist). As such, you can be sure that you will receive the best treatment by the research team and have regular, careful follow up.

It is has been well established that in clinical trials, the group receiving standard therapy (control or placebo group) will often do surprisingly better than what was expected as a result of this careful management. They will also have access to the latest medical advances in the field of research. One other potential advantage to participating in a research study is that most trials will actually cover the cost of the study medication and may compensate you for the time you devote to participating in the study.

Potential Risks of Participating in a Clinical Trial

All investigators must follow ethical principles or rules whereby patient safety is the primary focus. One thing that you can be sure about is that all investi-gators that conduct clinical trials have taken a course on research ethics that emphasize that the primary goal of any study is to keep participants safe. Nevertheless, there are times when clinical trials demonstrate no benefit of a new treatment. Some new treatments have been disappointing, in that they may worsen, rather than help, a specific condition. There are also times in which a drug may not influence the survival time for a condition, but still help some patients feel better. Such situations may cause an investigator to ask the company sponsoring a study whether the study drug could be continued on a "compassionate use" basis if an individual patient appears to have a striking response and feels better on that therapy they received during the study.

Maintaining Safety

A clinical trial is made up of few groups that make important decisions regarding how a trial is conducted, which type of patients are enrolled, and how to keep the study and its participants safe. In each trial, there is a group of experts that form the data safety monitoring board (DSMB). This board meets every three to six months to review all of the pertinent information about the outcomes of patients treated with the study medications versus those who are treated with placebo or an inert pill (the control group). The DSMB sees information that the investigators are not allowed to see and thus has a unique knowledge to help make the study safer.

If the DSMB feels as though the study treatment offers overwhelming benefit, they may halt the trial earlier than planned to report the results and to encourage faster acceptance or approval of that new therapy. Alternatively, if the DSMB board feels that the new treatment may be causing harm rather than benefit, they may choose to halt the trial so that this information can be studied more fully. When considering participating in a trial, always address questions of safety to the principal investigator or a their representative.

Informed Consent

A consent form is a document that the investigator will give you to review as a basis for discussing all important information regarding the trial, the new treatment being studied, along with the known risks and benefits. This form will also cover the amount of time you will need to commit as a participant including the number of follow up visits during the study. You should read this document carefully before deciding whether you wish to participate. If you have any questions after reviewing the informed consent form, you can discuss them with the lead investigator or their representative.

It is important that you as the subject understands the information in the con-sent form and that you have any questions answered by the study team. Only you can decide if a trial is right for you.

Questions to Ask When Considering Clinical Trial Participation

What is being studied?

Why do the researchers believe the new treatment being tested might be helpful?

Has it been tested before?

What are the possible treatments that I might receive during the trial?

How will it be determined which interventions I receive (for example, by chance)?

Who will know which intervention I receive during the trial?

- **Will I know?**
- **Will members of the research team know?**

What are the possible risks, side effects, and benefits of this therapy compared with those of my current treatment?

How often will I have to visit the hospital or clinic?

How long will the study last?

Who will pay for my participation?

Will I be reimbursed for expenses?

What type of long-term follow-up care is part of this trial?

If I benefit from the new treatment, will I be allowed to continue receiving it after the trial ends?

Will results of the study be provided to me?

Who will oversee my medical care while I am participating in the trial?

What are my options if I am injured during the study?

The answers to many of these questions (and more) are typically available in the consent form, which you should read fully before agreeing to participate in a given study.

Where to Get Information About Clinical Trials for Heart Failure

On your own, you can learn more about trials that are being conducted in the United States. An especially valuable source of information is maintained by the U.S. National Institutes of Health and can be found at the website **www.clinicaltrials.gov**.

This site has links for patients and families to help them find studies and learn more about clinical studies in general. You can also find which centers are conducting specific trials on this website in order to contact specific centers and inquire about their availability, possibly arranging for a consultation to discuss a given research protocol.

Learn more about Heart Failure, Treatment, and Self-Management

You can learn more about how to take control of your heart failure by reading the other modules in this series. You can get copies of these modules from your doctor or nurse. Or you can visit the Heart Failure Society of America website at **www.hfsa.org**

The topics covered in the other modules include:

- **Introduction: Taking Control of Heart Failure**
- **How to Follow a Low-Sodium Diet**
- **Heart Failure Medications**
- **Self-Care: Following your Treatment Plan and Dealing with your Symptoms**
- **Exercise and Activity**
- **Managing Feelings about Heart Failure**
- **Tips for Family and Friends**
- **Lifestyle Changes: Managing other Chronic Conditions**
- **Advance Care Planning**
- **How to Evaluate Claims of New Heart Failure Treatments and Cures**
- **Heart Rhythm Problems**

These modules are not intended to replace regular medical care. You should see your doctor or nurse regularly. The information in these modules can help you work better with your healthcare provider.

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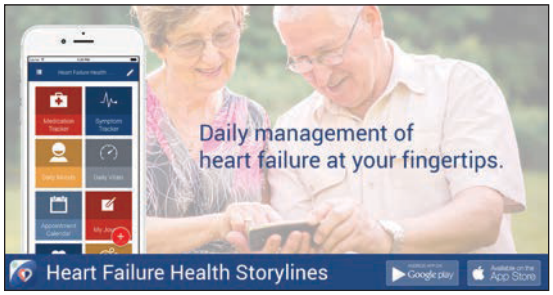
HEART FAILURE SOCIETY OF AMERICA

About the Heart Failure Society of America, Inc.

In the spring of 1994, a small group of academic cardiologists gathered in New York to discuss the formation of a society that would focus on heart failure. This group had long recognized that the disease was on the rise; yet there was no venue for researchers, trainees, and clinicians to gather to discuss new treatments, research results, and the rise in health care costs associated with heart failure. A society dedicated to heart failure would bring together health care professionals, including researchers, physicians, nurses, and other allied health care professionals, to learn more about the mechanisms of the disease, how best to treat patients, play a role in reducing health care costs, etc. The meeting led to the incorporation of the Heart Failure Society of America, Inc.

The Heart Failure Society of America, Inc. (HFSA) represents the first organized effort by heart failure experts from the Americas to provide a forum for all those interested in heart function, heart failure, and congestive heart failure (CHF) research and patient care.



Complimentary HFSA Patient Resource Available!

Heart Failure Storylines mobile app allows patients and caregivers to track appointments, mood, symptoms, and more on the same timeline as their treatment. It gives an accurate, shareable record of patient experiences between physician visits and helps care teams collaborate on treatment strategies. The app is useful for someone living with Heart Failure as well as a caregiver. Learn more today visit **www.hfsa.org.**

Made possible with support from Novartis

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