A Guide to Participating in Clinical Trials for Patients with NAFLD/NASH

This is intended to be a brief guide for people at risk for or diagnosed with nonalcoholic fatty liver disease (NAFLD) or nonalcoholic steatohepatitis (NASH) to understand and assess clinical research opportunities.

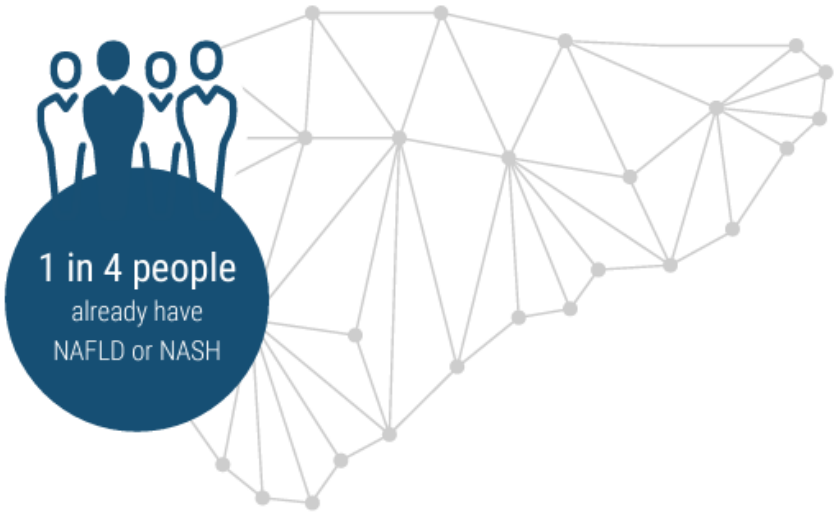
Questions Answered in this Guide:

1. What is NAFLD/NASH?
2. Why is there research in this field?
3. What questions are NASH research studies trying to answer?
4. How can my participation help answer those questions?
5. What should I consider when looking for a NASH trial?
6. Where can I learn more?

What is NAFLD/NASH?

NAFLD stands for nonalcoholic fatty liver disease. NASH or nonalcoholic steatohepatitis is the more severe form of NAFLD, which includes an accumulation of fat in the liver, inflammation and a type of injury called ballooning, with or without scarring (fibrosis). NASH can lead to cirrhosis, cancer, or the need for transplant.

Current estimates show that as many as one in four people already have NAFLD or NASH, yet these conditions are underrecognized, underdiagnosed, and undertreated. People who have type 2 diabetes, BMI over 30, and/or age over 50 are more likely to have NAFLD or NASH but this condition can affect anyone, even those of normal weight or children.



Why should I consider participating in research in NAFLD/NASH?

With the exception of India, no regulatory agency has approved medication specifically for NASH. Without patient participation in clinical research studies, from designing the trials to filling out surveys to providing biological samples, there would be no way to develop medications, devices, or other interventions to understand or treat this spectrum of disease.

Moreover, studies need volunteers with diverse characteristics and backgrounds to ensure that researchers understand the risks and outcomes for the different groups affected by a particular disease. Demographics that can affect risk, benefit, and outcomes for treatment include: race, ethnicity, age, gender, and concurrent diseases.[1]

What questions are NASH research studies trying to answer?

Trials are generally divided into: Interventional (actively doing something) and Observational (watching and monitoring over time). Observational trials are also sometimes called natural history studies.

Types of Interventional Trials:

- **Drug/medication** - those that may reduce inflammation and fat or resolve ballooning
- **Medications**
  - Effects of fat reduction
  - Effects of weight loss
  - Effects of stopping or regressing fibrosis
  - Effects of reducing inflammation
- **Device or diagnostic methods** (e.g. those that can analyze a person's liver using non-invasive methods)
- **Devices**
  - Device-based therapies as an alternative to invasive surgical procedures addressing obesity and gastrointestinal conditions

Types of Observational Trials:

- **Observational studies** - those that look at how NAFLD or NASH affects children over time
- **Natural History** - Genetic and other risk factors that predict progression

Questions

- Can a particular medication reduce the scarring associated with NASH?
- Can a particular medication or combination of medications reduce the inflammation associated with NASH?
- Are there certain genes or other drivers that predispose someone to progress to NASH faster than other people?
- Is there a specific diet that helps people with NASH?
- Is there a type, duration, or intensity of exercise that most helps people with NASH?

How can my participation help answer those questions?

Currently, only India has a medication approved specifically for NASH. Several medications, however, are being tested in clinical trials for approval. Specific areas of study needed for further research include treating patients who have both NASH and diabetes, Hispanic patients with certain genetic factors, as well as individuals who are lean and have NASH.[2]

Will I be accepted into the trial automatically?

Acceptance and enrollment into a study are not automatic. Studies have both **inclusion criteria** as well as **exclusion criteria**. Furthermore, not every person who meets the criteria will be accepted into a trial.[3]

Studies need volunteers with diverse characteristics and backgrounds.

How can I tell if a specific NASH trial is right for me? What should I consider when looking for a NASH trial? What can I expect when participating in a NASH clinical trial?

Consult with your physician on whether a clinical trial would be appropriate for you and if they would suggest clinical trials available in your area. The location of the study could be a hospital, university, physician's office, community clinic, or another location, depending on the organization conducting the study.[4] The length of a trial may also range from six months to five years or longer.

In addition, take time to carefully assess whether you can complete the activities involved in a particular NASH drug or device trial. Potential activities may include fasting, lifestyle modifications (e.g. nutrition, exercise), completing blood work (e.g. ALT, AST levels), undergoing imaging tests (e.g. ultrasound, MRI), and even having one or more biopsies, a procedure in which a sample of tissue is taken from the body for further examination.

You should ask the research team any questions you have about participating in the trial, such as:

- How do the possible risks, side effects, and benefits of this trial compare with those of my current treatment?
- What tests and procedures would I undergo?
- How long will the study last?
- If I benefit from the intervention, can I continue receiving it after the trial ends?
- Who will oversee my medical care during the trial?
- Where do I have to go to participate in this trial? Is there travel involved?

View additional possible questions to ask, as shared by the National Institutes of Health in the U.S.

Visit NIH

Additional Specific Considerations for Participating in a Clinical Trial

Pregnancy: The guidelines for studies of certain treatments may prohibit participants from conceiving during the trial and for a period of time following the study due to safety concerns for the baby. If you are interested in conceiving, speak with your provider about how long you would need to wait to conceive as well as for advice on contraception.

Vacations: Studies may prohibit travel abroad if participants must be monitored regularly. Speak with your provider first about any travel plans before enrolling in a study.

Informed Consent

Through the process of **informed consent,** researchers communicate to potential and enrolled participants about the risks and potential benefits of participating in a clinical study, allowing possible participants and those already enrolled to make informed decisions.[5] The process may involve multiple aspects, such as recruitment materials, instructions given verbally, question-and-answers sessions, and additional opportunities to ask questions. In general, volunteers must sign an informed consent document before enrolling in a study, though they may still leave the study at any time if they choose to.

How a Clinical Trial Works

Clinical trials follow a rigorous process. Before researchers can begin a clinical trial and test a drug in people, they must assess whether the drug could cause serious harm. To accomplish this, they conduct either **in vitro** or **in vivo** preclinical research. Preclinical studies are usually not large in size.[6]

Once a clinical trial begins, it may normally take several years to be completed. Biomedical clinical trials have four phases: I, II, III, and IV. In Phase II, the goal is to determine the appropriate dose and treatment regimen. Sometimes Phase II trials are further divided into Phase 2A and 2B. Phase 2A focuses specifically on the dosing requirements while Phase 2B tests the efficacy of the drug in terms of how successful it is in treating or preventing the disease. In Phase III, participants are randomly placed into treatment groups, also called trial arms.[7] At this point in research development, a NASH patient will most likely be asked to participate in a clinical trial currently in stage 2B or III. A control group would receive the standard-of-care treatment or a **placebo**; the other group(s) would receive the new treatment. Trials can also have more than two groups, with each group receiving different dosages of the new drug.[8]

How To Find Trials for NAFLD and NASH Treatments

European Union

In the European Union (EU), the EU Clinical Trials Register lists protocol and results information on interventional clinical trials conducted in the EU and the European Economic Area (EEA) as well as clinical trials conducted outside the EU and EEA that are linked to European pediatric-medicine development.

Search EU Clinical Trials

OR

Search U.S. Clinical Trials

United States and Worldwide

The U.S. National Library of Medicine hosts a database of privately and publicly funded clinical studies conducted around the world, in all 50 states, and in 219 countries. (Note that being listed does not mean a study has been evaluated by the U.S. Federal Government). On the site, visitors can filter the list of studies by:

- Recruiting Status (e.g., “Recruiting”, “Enrolling by Invitation”, or “Completed”)
- Eligibility Criteria (e.g., Age and Sex)
- Key Words (e.g., fatty liver, NAFLD, NASH)
- Study Type (e.g., Interventional [Clinical Trial] or Observational)
- Study Results
- Study Phase
- Funder Type (e.g., Industry, Academic research institution, or Individual)
- Location (e.g., country, state, city)

World Health Organization Registry Network

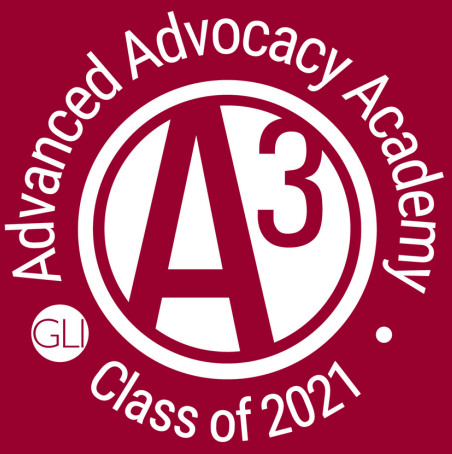
In addition, the World Health Organization (WHO) Registry Network includes registries from around the world that are specific to individual countries, such as the Australian New Zealand Clinical Trials Registry (ANZCTR), Clinical Trials Registry - India (CTRI), and the Clinical Research Information Service (CRiS) in the Republic of Korea.

Visit WHO

No matter how you learn about a clinical trial, it is imperative that you speak with your health care provider before participating in a study.

Are there other ways to support research other than by participating in a trial?

There are many opportunities for supporting NAFLD/NASH research and clinical trials. Patients are often included in clinical trial design advisory boards, asked to participate in observational trials, and needed for advocacy for better funding for research. Join Global Liver Institute's Advanced Advocacy Academy (A3) to learn more and support NASH/NAFLD research.



Learn About A3

Glossary of Clinical Trial Terms

Following are terms you may hear frequently as you navigate the clinical trial experience. Visit ***globalliver.org/liver-glossary*** for a full glossary of terms related to liver health.

Ballooning: a type of cell degeneration associated with cell swelling and enlargement.[9]

Biomarker: Measurable substance or physiological activity in the body that can be used as a sign of stable condition, an abnormal state, or disease; can be used to determine how well the body responds to new treatments.

Biopsy: An examination of tissue removed from the body to discover the presence, cause, or extent of a disease.

Blinding: Concealing how groups are allocated from one or more individuals involved in a clinical research study, most commonly a randomized controlled trial. Randomization minimizes the differences between treatment groups at the start of a trial; blinding helps prevent differential treatment or assessments.[10]

Exclusion criteria: Factors that prevent a person from participating.

Informed Consent: To give permission for something to happen or agree to do something.

Imaging Studies: Non-invasive tests that can produce detailed pictures of the body's organs and structures; include x-rays, computerized tomography (CT) scan, magnetic resonance imaging (MRI), and ultrasound.

Inclusion criteria: Factors that a participant must meet, such as age or sex.

Institutional Review Board (IRB): A group of people who review, approve, and monitor the clinical study's protocol. Their role is to protect the rights and welfare of people participating in a study (referred to as human research subjects), such as by reviewing the informed consent form. The group typically includes people with varying backgrounds, including a community member, to make sure that research activities conducted by an organization are completely and adequately reviewed. Also called a human subjects protection review board or an ethics committee.

In vitro: Outside of an organism.

In vivo: Within an entire organism.

Placebo: An inactive substance or treatment that looks the same as, and is given in the same way as, an active drug or intervention/treatment being studied.[11]

Principal Investigator: The person who is responsible for the scientific and technical direction of the entire clinical study.

Prohibited Drugs/Medications: Drugs that participants may not take during the clinical trial because they could affect the study.

Screening: Checking for disease when there are no symptoms with the hope of finding disease at early stages.

Sponsor/Study Sponsor: The organization or person who initiates the study and who has authority and control over the study.

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