



University of California, San Diego
Nonalcoholic Fatty Liver Disease (NAFLD) Adult Database 2
Informed Consent Statement
(Adult Consent)

STUDY INVESTIGATOR AND SPONSOR

Drs. Rohit Loomba and Heather Patton are conducting a research study to find out about liver problems in adults. They study Non-alcoholic Fatty Liver Disease (NAFLD) and Non-Alcoholic Steatohepatitis (NASH). This study is sponsored by the National Institutes of Health (NIH).

WHY IS THIS STUDY BEING DONE?

The purpose of the NAFLD Database is to better understand nonalcoholic fatty liver disease (NAFLD) by following and evaluating people yearly with this condition. NAFLD is a common liver disease in the United States. The causes of NAFLD are unknown, but are probably due to different reasons, from inherited characteristics to personal lifestyle. Some reasons may increase the chance of developing NAFLD (these are called “risk factors”) while other reasons may decrease the chance of developing NAFLD (“protective factors”). The factors that determine whether a patient progresses from NAFLD to more severe liver disease are unknown. The time it takes for a patient to progress to more severe disease is also uncertain.

NAFLD is usually discovered because of abnormal liver tests or from a liver ultrasound in persons with normal liver tests. The few known risk factors include high blood sugar and fat levels in the blood. Patients with NAFLD often have resistance to the normal action of insulin, a hormone which is important for processing sugar and fat. Increased resistance to insulin can lead to fat in the liver.

The term NAFLD covers a range of liver disease progression. When fatty liver disease moves on to a more severe level of liver injury, it is called nonalcoholic steatohepatitis (NASH). NAFLD/NASH is likely the most common liver disease in the United States and is thought to be related to obesity or diabetes. A liver biopsy (small amount of liver tissue removed by needle) is usually done to confirm liver disease. The biopsy results may show different amounts of fat, inflammation (swelling), and scarring in the liver. NASH can lead to severe liver disease in some patients. You have been asked to join this research study because one of the liver tests described above has shown you may have NAFLD, NASH, or NASH-related cirrhosis (scarred liver of unknown cause).

The main purpose of this study is to learn more about fatty liver disease by collecting information locally. The information collected will be stored locally in computer programs and may be sent to a national clinical research network in the future.

TYPE OF STUDY

The NAFLD Database study is an observational study. Treatment for NAFLD will not be provided by this study. This study is a nationwide study funded by the National Institutes of Health (NIH). Your participation could last up to five years or longer.

WHAT MAKES THIS DIFFERENT FROM THE USUAL TREATMENT?

This study will give you information about future studies and will not change your current treatment. There are no experimental treatments in this study. There will be a tissue bank for storing of some of your

blood, DNA, and liver specimens. These specimens will be taken at the same time as your clinical check-up so that there is no need to take extra tissue from you. Any available liver tissue will be obtained from your hospital, where it is usually kept after your liver biopsy, as part of your medical record.

Serum is a clear, yellowish liquid part of blood that appears when blood is separated into its solid and liquid parts after the blood has clotted. We will store some of your serum. We will also store DNA but only if you give us permission to do this in a separate consent form. We will use the stored serum and DNA (only with separate permission) to check for any characteristics that can be used as signs of NAFLD or NASH. The biological characteristics found in serum (called “biomarkers”) may be signs of inflammation, or fibrosis, or other kinds of damage. Fibrosis occurs when an organ is damaged and makes extra fibrous tissue, which is like a scar. If you have signed the consent to bank your DNA, your DNA will be used to check for “genetic markers” of NAFLD or NASH. Genetic markers are inherited characteristics that be be signs of NAFLD or NASH. By storing the serum and DNA which came from your blood, the researchers hope to do further scientific tests now and in the future (new tests may be developed which are not available yet) to find out what causes NAFLD/NASH and how to treat it better.

SELECTION OF PATIENTS

You may have previously participated in the NAFLD Database study or the Farnesoid X Receptor Ligand Obeticholic Acid in NASH Treatment (FLINT) Trial and we would like to invite you to continue your participation during the second phase of the study. In order to participate in this portion of the study, you must again read and sign the informed consent.

To be eligible for this study you must be at least 18 years old and must have NAFLD or NASH-related cirrhosis. You cannot have drunk significant amounts of alcohol within the past two years. We will ask you questions to check that you are not drinking significant amounts of alcohol during the study.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

There will be approximately 150 people locally who will take part in this study.

HOW LONG WILL I BE IN THE STUDY?

There will be up to 6 visits that are each about 1 hour long. The study duration is up to 5 years. All participants will complete a minimum of one year of follow-up. The follow up visits are annual visits after the initial screening visit. The study visits are based on the following weeks: 48, 96, 144 and 192. All of your information will be included in a computer program. You will be called or mailed to let you know about new studies. At the end of the study your data will be sent to the Nonalcoholic Steatohepatitis Clinical Research Network (NASHCRN) where it will be included in a bigger multicenter study. Other materials collected during the study will be sent as well (e.g., serum, plasma, slides, stool samples)

WHAT IS INVOLVED IN THE STUDY?

Screening visit(s): We will ask you to come to this visit in a fasting state (nothing but water for 12 hours before the visit). We will interview you and give you a physical examination. We will ask you about any medicines that you are taking or that you have taken in the past. We will



draw about six tablespoonfuls of your blood for laboratory testing and for specimen banking. The specimens that we will bank will include your blood serum and plasma – (serum is the clear yellowish fluid after the separation of blood cells that have been allowed to clot first. Plasma is the liquid part after the separation of blood cells, but the blood was put in a tube with chemicals that don't allow it to clot). We will also take your blood pressure, temperature, pulse, height, weight, waist, and hip measurements. We will also ask you to fill out questionnaires about your alcohol use. We will check your medical records for information that will help us determine if you are eligible for the study, such as results of prior liver biopsies, including a liver biopsy obtained during participation in the FLINT trial, laboratory tests for other liver disease, and imaging studies of your liver.

During this visit you may be asked if you will be willing to have an optional magnetic resonance imaging (MRI) or magnetic resonance spectroscopy (MRS) scan, which takes about 60 minutes. During the MRI or MRS scan, you will lie down on a narrow bed. The bed will be rolled slowly into a tunnel that is 6 feet long, 22 inches wide, and open at each end. You will lie there for about one hour. At times during the scan, you will be asked to hold your breath and keep still. During these times you will hear a loud tapping noise and you may feel warm during this procedure.

It may not be possible to complete all the screening procedures on the same day, therefore you may be asked to return to the clinic for an additional screening visit to complete study testing.

Follow-up visits: After enrollment, we will ask you to return to the clinic for annual visits for up to a four-year period. We will schedule your first visit at about 1 year after enrollment. We will ask you to come to each of the annual follow-up visits in a fasting state (nothing but water for 12 hours before the visit). At each of these visits, after an overnight fast, we will draw about four tablespoonfuls of blood for laboratory testing and specimen banking. These visits will also include a physical examination.

Liver tissue: If you have a liver biopsy as part of your regular care of your liver disease at any time during this study, we ask your permission to use a piece of the tissue. Slides will be made from this piece of tissue, and the slides will be examined by the study doctors and will become part of your study records. A portion of the tissue will be stored for future studies. If the study cannot be provided with a piece of tissue (for example, the sample obtained is too small to be divided), we ask that you let the study doctors review the slides made for your regular care.

WHAT ARE THE RISKS OF THE STUDY?

Risks and Discomforts

MRI/MRS: The magnetic resonance scanner is a long narrow tube that is open on both ends. A small number of individuals experience claustrophobia once inside. You will be able to signal the investigators with a squeeze ball device at any time to pause or stop the study or simply to ask questions. The potential risks of MRI are very small. The scanning procedure does not involve the use of X-rays. However, since the MRI pictures are obtained using a strong magnet, metal objects containing iron in the MRI room could move and harm you during the exam. Precautions will be taken to prevent such an event from happening; loose metal objects are not allowed in the MRI room. Certain metal objects, which may be in your body, could also move or not function properly during the exam and harm you. You will be asked questions before the MRI/MRS to be certain that you do not have any of these objects nor devices in or on your body. Temporary hearing loss has been reported from noise the machine makes. The scanner produces loud banging noises while acquiring images. You will be given a set of earplugs to protect your ears and to help with the noise. It can be uncomfortable to lie in the scanner for 60 minutes, and you may be bothered by staying in a closed chamber.



There are no known effects from exposure to magnetic fields. However, some patients might become anxious during scanning. If this happens to you, you can stop the procedure at any time. You can also experience some discomfort and fatigue from lying in a confined space during the imaging.

If you have any metal clips, plates or a pacemaker in your body, you should tell the investigator. MRI may not be appropriate under some of these conditions: a cardiac pacemaker; metal fragments in the eyes, skin or body; heart valve replacement, brain clips, venous filter, history of sheet metal work or welding, aneurysm surgery, intracranial bypass, renal or aortic vascular clips; prosthetic devices such as middle ear, eye, penile implants or joint replacements; hearing aide, neurostimulator, insulin pump, IUD, pregnancy; vascular shunts or stents; metallic implants, plates, pins, wires or screws; permanent eyeliner or eyebrows, or tattoos.

Unforeseeable risks:

Although serious injury to organs or death have never been attributed to MRI, it is possible that currently unforeseen side effects, including serious injury to organs or death may occur. Also, because this is an investigational study, there may be some other unknown risks that are currently unforeseeable. The subject will be informed of any significant new findings.

Blood drawing: Blood drawing can be painful and may cause bruising and rarely, fainting, blood clots or an infection at the site. During the entire study period (lasting up to 5 years), you will have up to 23 tablespoonfuls of blood drawn (350 mL). If numbing cream is used for blood draws, it may cause pain, skin irritation, or the skin temporarily turning red, white or developing a rash. This usually doesn't last very long.

General risks: Your condition may not get better or may get worse while you are in the study. You will be made aware of any new findings that may change your decision to remain in this study.

There is a potential risk to your confidentiality. While every effort will be made to maintain your confidentiality, it is possible that others may learn about your health information and such a breach might lead to problems with getting insurance or a job. Your medical records will be kept private but research staff will look at this information. This information will be included in computer programs kept private by password protection. Written information will be stored in locked areas. Research records will be kept confidential to the extent provided by law. It is however, always possible that the information in the research records could become known outside of the research setting.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You may benefit from health information obtained during the physical exams, laboratory tests, and other study procedures. You may help future patients by providing important information about the progress of NAFLD NASH-related cirrhosis. The doctors may learn more about liver disease and how to better treat people with it later.

At your direction, we will provide the results of any procedures done to screen you for this study to your liver care provider.

WHAT OTHER OPTIONS ARE THERE?

You can choose to not participate. If you do not participate, your treatment will be unchanged. Slow weight loss through regular exercise and a low-fat, low-refined carbohydrate diet may improve NAFLD. There are no proven drug treatments for NAFLD, NASH or NASH-related cirrhosis.



If you are found to be ineligible to continue with the study, we will keep your data in the Database.

WHAT ABOUT CONFIDENTIALITY?

Every reasonable effort will be made to keep your records confidential. However, while you are in this study all related hospital and office records may be made available to:

- The NASHCRN-NIH (sponsor of the study)
- The UCSD Institutional Review Board (for the protection of human subjects in research)
- Other regulatory entities responsible for overseeing research, such as the Federal Office for Human Research Protections

Your records will not be released without your consent to the extent the law allows. The study doctors can use the study results as long as you cannot be identified. This information will be included in computer programs kept private by password protection and encryption. Written information will be stored in locked areas accessible to study staff only.

Your participation in this study will be kept confidential and your name, address, and other personal identifying information will not be made known to anyone other than study personnel at this site. Your health and medical information will be sent to the Data Coordinating Center currently located at The Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. The information will be labeled with only an identifying number and code that cannot be linked to your name or other personal identifiers except at the clinical center where you complete visits. When results from this study are published in medical literature, you will not be identified by name. Representatives of the National Institutes of Health, Data Coordinating Center, or other experts may review your records at visits to the clinic as part of the ongoing monitoring of the progress of the study. In addition, representatives from the United States Food and Drug Administration (FDA) or the Institutional Review Board at this clinic may review your records, including your medical records.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health, which will allow us to resist any demands for your health information, with a few exceptions as explained below. The Certificate protects us from being forced to disclose information that may identify you, even if by a court subpoena. We are also protected from demands for your information made by federal, state, local civil, criminal, administrative, legislative, or other sources. However, the Certificate cannot be used to resist a demand from the U.S. Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the U.S. Food and Drug Administration. The Certificate does not prevent you or a member of your family from voluntarily releasing information about you or your involvement in the research. If an insurer, employer, or other person obtains your written consent to receive research information, then we may not use the Certificate to withhold that information. Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse or neglect or a risk of harm to yourself or others, we are required to notify the proper authorities.

During this study we may inform you if we know that you are eligible to participate in any other studies that are being done for people with NAFLD, or NASH. At that time we will give you information about those other studies if you wish. Participation in this study does not signify an obligation to participate in any other study.

WHAT ARE THE COSTS?

You will not be billed for any part of this study and there are no costs to you.



WHAT IF I AM INJURED IN THE STUDY?

If you are injured as a direct result of participation in this research, the University of California will provide any medical care needed to treat those injuries. The University will not provide any other form of compensation to you if you are injured.

You may call the Human Research Protections Program Office at (858) 455-5050 for more information about this, to inquire about your rights as a research subject or to report research-related problems.

WILL I GET COMPENSATED TO BE IN THIS STUDY?

You will be compensated \$50.00 for your time after each completed visit.

WHO DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

Drs. Loomba or Patton or _____ have explained this study to you and answered your questions. If you have other questions or research-related problems, please call: Thu Nguyen 619-543-5459

After Hours:

UCSD Hospital Operator at 619-543-6737 – Ask the operator to page Drs. Loomba or Patton. Let the operator know that you are a research participant.

WHAT ARE MY RIGHTS AS A RESEARCH SUBJECT?

Participation in research is entirely voluntary. You may refuse to participate or decide to stop participating at any time without jeopardy to the medical care you receive. If you do participate, you may freely withdraw from the study at any time. Your decision will not change your future medical care at this site or institution. The study doctor or the sponsor may stop your participation in this study at any time without your consent. The reasons may include: the study doctor thinks it is necessary for your health and safety, you have not followed study instructions, the sponsor has stopped the study, or administrative reasons require your withdrawal. If you decide that you no longer wish to continue in this study, you will be required to sign a document stating your intent. Please contact the study coordinator or the Investigators to express your intent. We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

If you have questions about your rights, or to report research related problems, please contact:

University of California, San Diego
Human Research Protections Program
(858) 455-5050

**SPECIMEN BANKING AND DATA REPOSITORY**

Dr. Loomba will be responsible for deciding how your specimens will be used. The specimens collected from you and the DNA that they contain may also be used in additional research to be conducted by the University of California personnel collaborating in this research. These specimens, DNA, and their derivatives may have significant therapeutic or commercial value. You consent to such uses.

Your specimens (serum, plasma, and liver tissue) collected as part of this study will be sent to the NIDDK Biosample Repository. At the end of the study, the data collected on you will be sent to the NIDDK Data Repository.

The Repositories are a research resource supported by the NIH. The Repositories collect, store, and distribute biological samples and study data from people with many kinds of disorders, from unaffected family members, and from other healthy people. The purpose of this collection is to make samples and data available for use in health research. Your samples and data will be used by the researchers carrying out the NAFLD Database, but they also may be used by other researchers, both during the study and after it ends. Your samples and data may be stored indefinitely.

Your samples and data will be labeled with a code number before they are sent to the Repositories. Your name, address, social security number, date of birth and other personal identifiers will not be sent to the Repositories, and the Repositories will not be able to give out your name or other information that identifies you to the researchers who use your samples and data.

If you do not agree to have your samples and data sent to the Repositories, you may not participate in the NAFLD Database. If you agree now but change your mind later about having your samples and data sent to the Repositories, you may withdraw unused samples during the study. No additional samples will be sent to the Repositories and no further data will be collected on you, but samples and data already collected will continue to be used.

Because researchers will not have access to your identity, you will not get the results of any studies that might be performed on your samples. Sometimes research results in findings or inventions that have value if they are made or sold. These findings or inventions may be patented or licensed, which could give a company the sole right to make and sell products or offer testing based on the discovery. Some of the profits may be paid back to the researchers and the organizations doing this study, but you will not receive any financial benefits.

SIGNATURE AND CONSENT TO BE IN THE STUDY

Your signature below means that you have read the above information about this study and have had a chance to ask questions to help you be informed about what you will do in this study. Your signature also means that you have been told that you can change your mind later if you want to. You will be given a copy of this consent form and a copy of the "Subject's Bill of Rights" to keep. By signing this consent form you are not giving up any of your legal rights.

You agree to be contacted in the future for other related studies Yes No
Initials _____

You agree to participate.

NAME OF SUBJECT

SIGNATURE OF SUBJECT

DATE

SIGNATURE OF PERSON WHO EXPLAINED THIS FORM

DATE



SUBJECT BILL OF RIGHTS

As a subject in a research study or as someone who is asked to give consent on behalf of another person for such participation, you have certain rights and responsibilities. It is important that you fully understand the nature and purpose of the research and that your consent be offered willingly and with complete understanding. To help you understand, you have the following specific rights:

1. To be informed of the nature and purpose of the research in which you are participating.
2. To be given an explanation of all procedures to be followed and of any drug or device to be Used.
3. To be given a description of any risks or discomforts, which can be reasonably, expected to occur.
4. To be given an explanation of any benefits which may be expected to the subject as a result of this research.
5. To be informed of any appropriate alternative procedures, drugs, or devices that may be advantageous and of their relative risks and discomforts.
6. To be informed of any medical treatment which will be made available to the subject if complications should arise from this research.
7. To be given an opportunity and encouraged to ask any questions concerning the study or the procedures involved in this research.
8. To be made aware that consent to participate in the research may be withdrawn and that participation may be discontinued at any time without affecting continuity or quality of your medical care.
9. To be given a copy of the signed and dated written consent form.
10. To not be subjected to any element of force, fraud, deceit, duress, coercion, or any influence in reaching your decision to consent or to not consent to participate in the research.

If you have questions regarding a research study, the researcher or his/her assistant will be glad to answer them. You may seek information from the Human Research Protections Program - established for the protection of volunteers in research projects - by calling (858) 455-5050 from 7:30 AM to 4:00 PM, Monday through Friday, or by writing to the above address.

