**Title of research study:** Association between low bone density, vertebral fractures, and pain in sickle cell disease: an observational study

**Lead Investigator:** Oyebimpe Adesina, MD, MS

## California Experimental Subjects Bill of Rights

- Someone will explain this research study to you, including:
  - The nature and purpose of the research study.
  - The procedures to be followed.
- Any common or important discomforts and risks.
- Any benefits you might expect.
- Whether or not you take part is up to you.
- You can choose without force, fraud, deceit, duress, coercion, or undue influence.
- You can choose not to take part.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- You can ask all the questions you want before you decide.
- If you agree to take part, you will be given a signed and dated copy of this document.

## Key Information about This Research Study

You are being invited to participate in a research study. The purpose of this research is to learn more about the level of pain in people with sickle cell disease (SCD) with and without low bone density (or weak bones) or fractures in their back bones. It is common for adults with SCD to have weak bones, which can happen when blood doesn't flow well to the bone. Low blood flow to the bone may cause weak bones to easily break.

You are invited to be in this study because you are at least 18 years of age and have SCD.

Your participation in this research will involve one visit and will last about an hour. We expect about 50 people from UC Davis Health and non-UC Davis facilities to join.

Participation in this study will involve filling out a pain questionnaire, collecting blood and urine samples, and getting a bone density scan to measure how strong your bones are. While in the bone density scanner, you will also get an X-ray of your back to look for any fractures in your back. All research studies involve some risk. Risks of this study are minimal. These risks are described in detail later in this document. You will not directly benefit from participation in this study.

Here are some reasons you may not want to participate in this research:

- It will take extra time for you to have the bone density scan and back X-ray.
- You might not want to complete the survey.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. You will not lose any services, benefits, or rights that you would normally have if you decide not to participate in the study.



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The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions you wish to help you decide whether to join this study.

Information to help you understand research is available online at http://www.research.ucdavis.edu/policiescompliance/irb-admin/for-research-participants.

## What if I have questions?

The person in charge of this study is Dr. Oyebimpe Adesina. If you have questions or concerns about this study, please contact Edward D. Lingayo Jr. at (916) 607-1729.

If you have any questions about your rights as a research subject or have complaints about the research study or study team, you may talk to a team member at the Institutional Review Board (IRB) at (916) 703-9158, hs-irbeducation@ucdavis.edu, or 2921 Stockton Blvd, Suite 1400, Room 1429, Sacramento, CA 95817. The IRB is a group of people who oversee research.

## How is this research funded?

This research is being funded by the National Institutes of Health and the Doris Duke Charitable Foundation. These funders are also called the Sponsors. Sponsors may change or be added.

## Why is this research being done?

The purpose of this study is to learn more about how bone problems cause pain in people with sickle cell disease (SCD). SCD alone may cause intense pain, but we are not sure if SCD pain is worse in people with weak bones or back fractures. We want to learn more about pain in patients like you.

## What happens if I say yes, I want to be in this research?

If you decide to participate in this research study, we will schedule you for a research visit. You will need to be fasting for this research visit. We also ask that you do not exercise 24-hours before your study visit. At the visit, you will have a bone scan and back X-ray, and complete a pain survey. The bone scan will measure your overall bone strength. We do this with a bone density machine called a dual X-ray absorptiometer or DXA scanner. The bone density machine can also be used to check an X-ray of your back, which can find fractures or breaks in your spine (or back bones). We will also collect a small amount of blood and urine from you for research purposes. The blood and urine samples must be collected first thing in the morning before you eat breakfast, ideally between 7:30am – 10am. If it is difficult for you to come to the research clinic in the morning, we can send an experienced research nurse to your home to collect the samples. All women who are still having menstrual periods will be asked to have a urine pregnancy test before the DXA scan. This is required for safety reasons. If the pregnancy test is positive, we will not do the bone scan or back X-ray. Any woman who has a positive pregnancy test will still receive full payment for coming for the research visit even though they won't get the bone density scan.

We will ask you questions about your pain and how it affects your life. We can do this in-person, over the phone, or virtually. The study team can meet with you for a video visit (through Study Pages video visit or Zoom). We will review your medical record so we can collect information about your past medical history. We will look at your older scans to see how sickle cell disease has affected your bones in the past. We will

ask you for more information if it is missing from your medical record.

**Transportation options:**

All transportation costs to and from the study visit will be reimbursed. If you drive your own vehicle to the research visit, we will reimburse you for mileage (distance traveled to and from the research clinic) and parking fees. Please submit parking receipts for reimbursement. If you prefer to take a ride share (Uber or Lyft) or taxi to the research visit instead, please provide your receipt so we can reimburse you fully.

**Meals:** Since you'll be fasting for the study, we will provide you a meal voucher after the study visit that can be used for 1 person's meal at the main hospital cafeteria.

## How is being in this study different from my regular health care?

If you take part in this study, the main difference between your regular care and the study is the research visit. This visit includes the pain survey, the bone density scan, and the back X-ray. This study is not part of your regular health care.

## What are my responsibilities if I take part in this research?

If you take part in this study, you will be responsible for coming in for the research visit. We can collect the blood and urine samples from you at home, but we will still need you to come in for the DXA scan and back X-ray on the day of your study visit. Some of the blood work can be collected up to 7 days before or after your study visit, but the fasting labs must be collected in the morning of your study visit.

## Do I have to be in this study? What if I say "yes" now and change my mind later?

No, you do not have to be in this study. Taking part in research is voluntary. If you decide to be in the study, you can choose to leave the study at any time.

If you decide not to take part in the study, or if you choose to leave the study, your choice will not affect your relationship with your doctors or medical team here at UC Davis Health or any services you receive from them. No matter what you decide, and even if your decision changes, there will be no negative effects to you. You will not lose medical care or any legal rights.

If you decide not to be in this research study, you do not need to come in for the research visit. Please let the researchers know if you choose to leave the study so they can cancel your research visit.

## What are my other choices if I do not take part in this study?

You do not have to be in this research study to get care for your sickle cell disease. If you decide not to be in this research study, you do not need to come in for the research visit. The research visit includes the pain survey, blood and urine sample collection, bone density scan and back X-ray. You may choose to take part in a different study if one is available. These options may have risks. Please discuss the possible risks and benefits with your study doctor.

We will tell you if we find any new information that may affect your health, welfare, or choice to stay in the research study. If we find out any new information about your health during this study, we will contact you as soon as possible.



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## Can I be removed from the research without my OK?

The researchers may take you out of the study, even if you want to continue, if:

- your health changes and staying on the study is no longer in your best interest;
- you no longer meet the requirements to be in the study; or
- the study is stopped by the sponsor or researchers.

## Is there anyway being in this study could be bad for me?

There are risks to participating in this research. The study doctor and study team will monitor you to see if you are experiencing any harm related to your participation. If you experience any pain or discomfort, you must inform the study team as soon as possible.

Potential risks of this study are as follows:

- Dual energy X-ray absorptiometry (DXA): Using the DXA scanner for the bone scan and back X-ray has some risks. DXA scans use very low doses of ionizing radiation. This level of radiation does not significantly increase the risk of cancer. You may feel uncomfortable on the DXA scanner. The technician who does the scan is very well trained to position patients. They will do their best to help you feel comfortable.

- We will collect a blood and urine sample from you: Blood will be drawn by putting a needle in your arm or your port. About 30cc (6 teaspoons) of blood will be taken. We will also collect about 10cc (2 teaspoons) of urine. Collecting the blood and urine samples will take about 20 minutes in total.

- Risks to a pregnancy: There may be risks to a fetus (unborn baby still developing in the womb) due to the low dose radiation from the bone density scan. The potential risks to a fetus are not known. If you are of childbearing age you will have a pregnancy test to minimize risk. If you have a positive pregnancy test you will not have a bone density scan.

- Privacy risks: As with all research, there is a chance that confidentiality could be compromised. To minimize the risks of breach of confidentiality, we will not include any information that directly identifies you on the information we collect, and on the data resulting from the research. Instead, we will record a code on the data we collect from you, and we will keep a link between the code and your identity in a different and secure location.

## What about Birth Control?

### Contraception Requirements for Subjects Able to Become Pregnant

The bone density scan and back X-ray may harm a fetus. If you are pregnant, you cannot take part in this study. If you think you may be pregnant, you should not volunteer for this study. If you can become pregnant, you must have a pregnancy test before the bone scan.

### Contraception Requirements for Subjects Able to Cause a Pregnancy

There is no known risk to sperm with the bone density scan or back X-ray. The low dose of radiation exposure from the bone density scan and back X-ray is below the levels that can cause any harmful effects to the sperm. A DXA scan is considered less harmful than a standard X-ray.

## Will being in this study help me in any way?

Being in this study will not help you directly. But your participation in the study may benefit other people in the future by helping us learn more about pain in people like you.

This study is not a substitute for your regular medical care. You should continue to see your regular medical providers.

## Will being in this study cost me anything?

There will be no cost to you for the research visit. The research visit is for research purposes only and is not part of your regular care. You will not have to pay for the bone density scan that is done for research purposes only.

You or your insurance company will have to pay for all costs for your regular medical care, including co-payments and deductibles. If you do not have health insurance, you will have to pay all the costs for your regular medical care just as you would if you did not take part in this study.

If you need treatment for side effects while you are on the study will be covered by the study sponsors.

For more information about possible costs, please contact the research team. The research team can follow UC Davis Uninsured Non-Emergency Estimate Policy (Policy ID 1883) to work with their department and Decision Support Services to get you a cost estimate.

## Will I be paid or receive anything for being in this study?

We will pay you $100 for the study visit. Payment will be provided after your research visit in the form of a Visa gift card. We will also reimburse you for mileage (distance traveled to and from the study visit) and parking fees. If you prefer to use a rideshare or taxi service, we will reimburse for transportation costs. We will also provide you a meal voucher to use at the main hospital cafeteria after your study visit.

You may be asked for your social security number for payment purposes. It will not be used for any other purpose without your permission.

If you receive $600 or more during a calendar year from the University for participating in research, you may receive a 1099 for tax reporting purposes. Reimbursements for travel and other expenses are not included in this amount.

Biospecimens (such as blood, tissue, or saliva) collected from you for this study and/or information obtained from your biospecimens may be used in this research or other research and shared with other organizations. You will not share in any commercial value or profit derived from the use of your biospecimens and/or information obtained from them.

## What happens if I am injured or get sick because of this study?

If you are injured because of this study, the University of California will provide the necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by the University or the study sponsor or may be billed to your insurance company just like other medical costs. The University and the study sponsor do not normally provide any other form of compensation for injury.



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For more information about compensation, you may contact the IRB Administration at (916) 703-9151 or HS-IRBAdmin@ucdavis.edu.

## What happens to the information collected for the research?

We will do our best to limit the use or disclosure of your personal information, including information from this research study and from your medical records to people who have a need to review this information. We cannot promise complete confidentiality. Some organizations may be required to inspect and copy your information including the IRB and other University of California representatives responsible for the management or oversight of this study.

We have strict rules to protect your personal information and protected health information (PHI). We will limit who has access to your name, address, phone number, and other information that can identify you. We will remove identifiable information from the data we collect about you. After we remove all the identifiers, we will place a code on the information. The code will be linked to your identity, but the link will be kept in a location that is separate from your study data. We will maintain your study data on encrypted computers and access to the information will be limited to only members of the research team who need the access to properly conduct the study. The information we send to the sponsor will not include information that directly identifies you. Instead, a code will be applied to the data and link between the code and your identity will be kept at the research site.

Any identifiable information we collect from you (e.g., your name, medical record number, date of birth, blood or urine samples) may be stored for future use. We may still use your data to answer additional research questions or share them with other investigators for additional research. If we do so, we will remove all identifiable information before use or sharing. Once identifiers have been removed, we will not ask your consent for the use of sharing of your data in additional research.

However, we cannot promise complete confidentiality. If you agree to be in this study, Federal or state laws may permit or require us to show information to university or government officials and to study sponsors responsible for monitoring this study. We may also show your medical records to study monitors, auditors, the IRB, and the FDA. These groups are obligated to maintain your confidentiality.

The following is a list of individuals who may access your records:

- Members of the research team
- Offices and committees responsible for the oversight of research
- Personnel who schedule or perform medical tests or procedures, handle accounting and billing, or do other tasks related to this study
- U.S. Office for Human Research Protections
- The study sponsors, Doris Duke Charitable Foundation and NHLBI
- Companies or groups performing services for the research team, such as laboratories outside of UC Davis Health

If you agree to participate in this research study, a signed copy of this consent document and the privacy authorization form may be filed in your electronic medical record (EMR) and your study participation may be added to your EMR. This information will be used for your care and treatment and for healthcare operations, which may include billing and payment. Federal and state privacy laws give patients the right to access information about their care and treatment contained in their medical record. During this study, you may not be able to access certain information related to this study in your EMR until the study is

complete to ensure that the study remains unbiased. If needed for your care, this information will be provided to you or your physician.

If the research team uncovers abuse, neglect, or reportable diseases, we may need to disclose this sensitive information to the appropriate authorities.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this web site at any time.

We will access protected health information (e.g., your medical record) for this study and you will be asked to sign a separate form, commonly referred to as a HIPAA authorization, to give your permission. Your medical records may become part of the research record. If that happens, your medical records may be looked at by the sponsor of this study and government agencies or other groups associated with the study. They may not copy or take your personal health information from your medical records unless permitted or required by law.

Federal law provides additional protections of your medical records and related health information. These are described in the UC Davis Health System Notice of Privacy Practices (http://www.ucdmc.ucdavis.edu/legal/privacy/) and in an attached document.

This research is covered by a Certificate of Confidentiality (CoC) from the National Institutes of Health. The researchers with this CoC may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding. For example, the information collected in this research cannot be used as evidence in a proceeding unless you consent to this use. Information, documents, or biospecimens protected by this CoC cannot be disclosed to anyone else who is not connected with the research, except:

- To a federal agency sponsoring this research when information is needed for auditing or program evaluations;
- To meet the requirements of the U.S. FDA;
- If a federal, state or local law requires disclosure such as a requirement to report a communicable disease;
- If information about you must be disclosed to prevent serious harm to yourself or others such as child abuse, elder abuse, or spousal abuse;
- If you consent to the disclosure, including for your medical treatment, to an insurer or employer to obtain information about you; or
- If it is used for other scientific research, as allowed by federal regulations protecting research subjects.

This CoC also does not prevent you or a family member from voluntarily releasing information about yourself and your involvement in this research.

## Will information or leftover specimens be used for other research?

The data and/or specimens we collect with your identifiable information (e.g., your name, medical record number, or date of birth) as a part of this study may be used to answer other research questions or may



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be shared with other investigators for other research. If we do so, we will remove all identifiable information before use or sharing. Once identifiers have been removed, we will not ask your consent for the use or sharing of your data and/or specimens in other research.

## May we contact you by e-mail?

We are requesting your email address so we can communicate with you about your research visit. Email is generally not a secure way to communicate about your health, as there are many ways for unauthorized users to access email. You should avoid sending sensitive, detailed personal information by email. Email should also not be used to convey information of an urgent nature. If you need to talk to someone immediately, please contact Edward D. Lingayo Jr. at (916) 607-1729. You do not have to provide your email address to participate in this study.

Please initial one of the lines below.

_____ Yes, you may use email to contact me for this study.
My email address is: _____

_____ No, I do not want to be contacted by email.

## Are there other research opportunities?

If you are interested in being contacted for future research, please provide your phone number and/or email. <u>This is completely optional.</u>

_____(Initials) Yes, I am willing to be contacted for future research opportunities. My phone number

and/or email is: _____



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**What are my rights when providing electronic consent?**

- California law provides specific rights when you are asked to provide electronic consent:
  - You have the right to obtain a copy of the consent document in a non-electronic format.
  - You have the right to provide consent in a non-electronic format.
  - If you change your mind about electronic consent, you have the right to request your electronic consent to be withdrawn and you can then provide consent in a non-electronic format; however, a copy of your electronic consent will be maintained for regulatory purposes. If you wish to withdraw your electronic consent, please tell the study team.
- This agreement for electronic consent applies only to your consent to participate in this research study.

Your signature documents your permission to take part in this research.

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| Signature of subject | Date |
| Printed name of subject | |
| Signature of person obtaining consent | Date |
| Printed name of person obtaining consent | |



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