Indiana University Informed Consent Statement and Authorization for Research

A Randomized Controlled Trial Assessing the Effects of Cognitive Behavioral Therapy to Prevent Worsening Insulin Resistance in Depressed, Virologically Suppressed, Antiretroviral-Treated Adults with HIV
Protocol#28855
ClinicalTrials.gov NCT07226128
Supported by a grant from the National Institutes of Health (Grant # 1R01DK141366)

You are being asked to participate in a research study. This consent and Authorization form will give you information about this study to help you decide whether you want to participate. It is your choice whether or not you want to be in this research study. Please read this form, and ask any questions you have, before agreeing to be in this study.

Important Things to Know:

- Purpose: This study will test whether treating depression in people with HIV can lower their risk of developing diabetes by improving how the body uses insulin (called insulin resistance).

- What You Will Do: If you choose to participate, you will attend several study visits over about one year. You will complete surveys, have blood drawn, and provide urine and stool samples. You will also be randomly assigned, like the flip of a coin, to one of two groups:

    - Group A: participants receive an internet-based program for depression with therapist support called Good Days Ahead (GDA), which teaches skills to manage depression; or
    - Group B: participants receive current care for depression in their healthcare system along with depression education and symptom monitoring by the study team.

- Duration: Your participation will last about one year and include up to four in-person visits (Screening, Entry, Week 24, and Week 48).

- Risks: The main risks are mild emotional discomfort during surveys or depression sessions, minor pain or bruising from blood draws, and possible embarrassment when providing urine or stool samples. Some participants may also experience thoughts of self-harm due to depression, and the study has a safety plan to respond right away if that happens.

- Benefits: You may or may not personally benefit. The information gained may help improve depression care and diabetes prevention in people with HIV.

- Voluntary Participation: Taking part is your choice. You may decide not to join or to leave the study at any time without penalty or loss of care or benefits**.**

Please review the rest of this document for more details about this study and the things you should know before deciding whether to participate.

Why is This Study Being Done?

This study will test whether treating depression in people with HIV can lower the risk of developing diabetes by reducing insulin resistance. Insulin resistance occurs when the body does not use insulin effectively to control blood sugar.

You are being asked to take part because you are at least 18 years old, have depression, do not have diabetes, and are receiving HIV treatment with well-controlled viral levels (below 75 copies per milliliter). People who are pregnant or breastfeeding cannot join this study.

The study is led by Drs. Samir Gupta and Tuan Tran from the IU School of Medicine and Dr. Jesse Stewart from IU Indianapolis. It is funded by the National Institutes of Health.

How Many People Will Be in the Study?
If you agree to participate, you will be one of 150 people in Indianapolis to enter the trial.

What Will Happen During the Study?
If you agree to take part in this study, you will attend several study visits over about one year. Each visit will include different activities, described below.

Screening Visit
We may first call you on the phone to see if you might qualify for the study. With your permission, we will ask you a few questions about your mood and medical history to see if you are eligible and if it is safe for you to participate.

If you qualify, we will schedule an in-person Screening Visit. This visit will take about one hour at one of the following locations:

- The Infectious Diseases Research Clinic (Fifth Third Office Building, Eskenazi Health Campus), or
- The Clinical Research Center at University Hospital.

<u>At this visit:</u>

- We will ask more questions about your depression symptoms and review your medical records.
- If you can become pregnant, we will do a urine pregnancy test. If you are pregnant, you will not be able to take part in this study.
- We will take a small blood sample (about half a tablespoon) to check your HIV levels and blood sugar.
- If your results show that you qualify and it is safe for you to continue, we will schedule your next visit, called the Entry Visit.
- You will receive a Fitbit to wear for 7 days before your Entry Visit to track your usual physical activity. We will show you how to use it, and you will return it at your next visit.

Entry Visit
Your Entry Visit will take place within 30 days of the Screening Visit and will last about two hours. It will occur at the same clinic locations listed above.

<u>At this visit:</u>

- We will review any changes in your health or medications and measure your height, weight, temperature, blood pressure, and heart rate.
- You will complete surveys about your mood, sleep, fatigue, quality of life, alcohol use, tobacco use, and dietary habits.
- If you can become pregnant, we will repeat the pregnancy test. If you are pregnant, you will not be able to continue in the study.
- We will take about 4 tablespoons of blood to measure blood sugar, inflammation, gut health, HIV viral load, and immune system levels (CD4 count).

- You will also provide a urine sample and a stool sample for future research on kidney and gut health.
- You will return your first Fitbit and receive a new one to wear for 7 days before your next visit.

You will then be randomly assigned, like the flip of a coin, to one of two groups:

1. Group A: participants receive an internet-based program for depression with therapist support called Good Days Ahead (GDA)
2. Group B: participants receive current care for depression in their healthcare system along with depression education and symptom monitoring

We will let your HIV care provider know which group you are assigned to and share information about your depression symptoms. Your provider will continue to help you manage your depression as needed.

Group A

If you are assigned to Group A:

- You will complete nine 45-minute online sessions over 6 months, ideally in the first 3 months.
- GDA uses cognitive behavioral therapy (CBT), an approach that helps you recognize and change unhelpful thoughts and behaviors.
- Sessions include videos, exercises, and activities. You can do them at home, on your own schedule, about one session per week.
- A study assistant will call you before you begin and after each session for a 20-minute support call to answer questions, review lessons, and provide encouragement.
- You may borrow a tablet with internet access for up to 6 months to complete the sessions, and we will show you how to use it. The tablet will be returned at the Week 24 Visit.
- You may continue to receive any usual depression care, such as medications or counseling, recommended by your provider during this study.

Group B

If you are assigned to Group B:

- You and your usual healthcare provider(s) will decide how best to treat your depression.
- You will receive a 30-minute call to review depression education materials, including your provider's role in managing depression and depression treatment options. You will also receive a list of local mental health services. The study assistant will share your initial depression score with your provider and encourage follow-up.
- A study assistant will call you each month for about 10 minutes to check your depression symptoms.
- The study assistant will share your depression scores with your provider every two months and encourage follow-up if your symptoms remain high.
- You may continue to receive any usual depression care, such as medications or counseling, recommended by your provider during this study.

Week 24 Visit

About 24 weeks after your Entry Visit, you will return for a Week 24 Visit lasting about two hours.

<u>At this visit:</u>

- We will review your health, medications, and any new depression treatments.
- We will measure your blood pressure, heart rate, temperature, and weight.
- You will complete the same surveys as before.
- If you can become pregnant, we will do another pregnancy test.
- We will take about 4 tablespoons of blood, a urine sample, and a stool sample.
- You will return your Fitbit and receive another one to wear for 7 days before your final visit.

Week 48 Visit (Final Visit)
About 48 weeks after your Entry Visit, you will complete your final visit, which will last about two hours.

At this visit:

- We will again review your health, medications, and any new depression treatments.
- We will measure your blood pressure, heart rate, temperature, and weight.
- You will complete the same surveys as before.
- If you can become pregnant, we will do a final pregnancy test.
- We will collect about 4 tablespoons of blood, a urine sample, and a stool sample.
- You will return your Fitbit at this visit, and your participation in the study will be complete.

In total, you will provide about 12-13 tablespoons of blood during the entire study.
We may learn things about you from the study activities which could be important to your health or to your treatment. If this happens, this information will be provided to you, especially if we find your blood sugar levels are increasing, thereby leading to a diagnosis of diabetes. We might learn about how well your HIV is responding to HIV medications. We will provide you these results if they are abnormal or worrisome. If you wish to see these results even if normal, we will provide you a copy. You may need to meet with professionals with expertise to help you learn more about your results. However, the study team/study will not cover the costs of any follow-up consultations or actions.

What Are the Risks of Taking Part in the Study?
While participating in the study, the risks, side effects, and/or discomforts include:

- Risks of possibly experiencing emotional discomfort when completing surveys: The surveys will be given in private settings. You may choose not to answer any questions that make you feel uncomfortable.

- Risks for Urine and Stool Collection: You may feel mild embarrassment or discomfort when providing urine or stool samples. These will be collected in private, and you will receive clear instructions and materials to collect them safely and discreetly,

- The risks of possible loss of confidentiality: We will not tell anyone other than your main HIV provider that you are taking part in this study. All your information will be identified with a coded number and without any personal identifying information. All test results will be locked in a cabinet and restricted.

  Please note that if you choose to undergo the Good Days Ahead treatment sessions in a public location, others around you may see that you are viewing an online depression treatment program.

- The risks of drawing blood: There are small risks in blood draws as part of this study, which include pain, bruising, infection, and damage to the veins in your arm.

- Suicidal thoughts: Because this study involves people with depression, some participants may report thoughts of being better off dead or of hurting themselves. This could happen during a phone call or an in-person visit. If this occurs, our protection plan will be used. You will first be asked a series of questions. If it is determined that immediate care is needed, the study team will contact Dr. Stewart or Dr. Gupta to determine the right course of action. If we believe that you are in imminent danger of harm, we will have to report it, potentially to authorities, including the police, for your own protection. We may contact your primary doctor, your primary HIV provider, and your HIV social worker or care coordinator. We may also consult with the LifeCare

clinic psychiatrist or with the Sandra Eskenazi Mental Health Center and escort you to the Crisis Intervention Unit at Eskenazi Health Hospital.

If you prematurely terminate a phone call after reporting suicidal thoughts, the study doctors will be notified to determine the right course of action. We will try to contact you back to obtain additional information. If it is determined that immediate care is needed and that you are in imminent danger of harm, we will have to report it, potentially to authorities, including the police, for your own protection. We may contact your primary doctor, your primary HIV provider, and your HIV social worker or care coordinator. We may also consult with the LifeCare clinic psychiatrist or with Midtown Community Mental Health Center and refer you to the Crisis Intervention Unit at Eskenazi Health Hospital.

We may also then decide in this situation that it is important for your own safety to end your participation in this trial.

Are there risks if I get pregnant during the study?
No. But if you do become pregnant, then we will remove you from further study participation as pregnancy affects the way we measure blood glucose and insulin levels in this trial.

Who Will Pay for my Treatment if I am Injured?
In the event of physical injury resulting from your participation in this study, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled.

What Are the Benefits of Taking Part in the Study?
You may receive no direct benefit from participating in this study. However, you may receive benefits if the depression treatment program improves your depression symptoms and reduces your diabetes risk. Information learned from this study may help others who have HIV.

Will I be Paid for Participating?
You will be compensated $25 after completing the Screening Visit and $150 after completing each of the Entry, Week 24, and Week 48 visits. If you complete all visits for the trial, you may receive a total of $475. Payment will be in the form of a pre-paid gift card or by a refillable gift card.

For any in-person visit (Screening, Entry, Week 24, and Week 48), you may be eligible for no-cost transportation from your home to and from the clinic via Uber Health or bus passes that we will provide you. If you require parking passes, we will also provide these to you. Please discuss this with the study staff to make travel arrangements.

What Are the Other Treatment Options?
Instead of being in the study, you have the option not to participate and choose to seek other types of depression treatment through your HIV provider. The most common alternative treatments for depression are medications and counseling. If you choose not to participate, your decision will not affect your regular medical care or your relationship with the study doctor.

How Will My Information and Specimens be Used?
The study team will collect information about you from your medical records. This may include information that can identify you, such as your name, contact information, and medical record number. Information from your medical records will be used to make sure you meet the criteria to be in this study, review results of your medical tests for safety purposes, and check on your health in the future to help answer our research question, etc.

The information released and used for this research will include all of your medical records. This may include information about mental health, alcohol or substance abuse, HIV/AIDS, sexually transmitted diseases, and/or results of genetic testing.

If you agree to participate, you authorize the following to disclose your medical record information:

- Indiana University Health
- Indiana University Health Physicians
- IUMG – Primary Care Physicians
- Eskenazi Health

The following individuals and organizations may receive or use your identifiable health information:

- The researchers and research staff conducting the study
- The Institutional Review Boards (IRB) or its designees that review this study
- Indiana University
- State and Federal government agencies as permitted by law, including but not limited to:
    - Office for Human Research Protections (OHRP)
    - National Institutes of Health (NIH)
- Data safety monitoring boards and others authorized to monitor the conduct of the study

After your medical record information is released for purposes of this research study, your information may no longer be protected under federal privacy laws, such as HIPAA. However, your identifiable information will still be stored securely and only used as described in this consent.

Information and specimens collected for this study may be used for other research studies or shared with other researchers who are conducting their own research studies. This may include sharing with researchers outside Indiana University and sharing with private companies. It may also include making the information available in public and private databases of research data so that other researchers can use the information to answer research questions.

If we share your information or specimens in this way, we will remove information that could identify you, such as your name and contact information, before any information or specimens are shared. Since identifying information will be removed, we will not ask for your additional consent for this sharing.

A description of this clinical trial is available on ClinicalTrials.gov under the number NCT07226128, 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 website at any time.

We may use your blood specimens to learn more about how depression affects HIV and blood sugar control. We will store all blood specimens using only your study code and keep them in the research freezers of Dr. Gupta. The research freezer is kept in a locked room in the R3 Research Building at Indiana University School of Medicine. Only Dr. Gupta and his study team have access to the research freezers in which your blood specimens will be stored. To protect you against the risks of loss of confidentiality, all samples will be marked with a unique code number. This information will be stored in an anonymous fashion in two different secured computer databases; one containing the sample codes

and the other with your information (such as age, sex, ethnic group, health conditions, etc.) to maximize confidentiality.

Making Your Choice
Blood and urine samples will be collected as part of your screening and/or during the study period. We will not obtain DNA or other kinds of genetic samples. Please read each sentence below and think about your choice. After reading each sentence, circle or check "Yes" or "No" and add your initials next to the choice. No matter what you decide it will not affect your care or your ability to participate in this study. If you have any questions, please talk to your doctor or nurse or call our Institutional Review Board, whose contact information can be found on the next page.

You retain (keep) the right to have any remaining sample material destroyed at any time by contacting the investigator. The investigator is responsible for the destruction of the sample at your request. However, any previously collected data from your sample cannot be destroyed.

Please initial next to the YES or NO to make your choices:

1. My sample(s) may be kept for a period of up to 20 years or more for use in future research to learn more about how to treat health problems.

   YES _____ NO _____

2. Someone can contact me in the future to ask me to take part in more research.

   YES _____ NO _____

How Will My Information be Protected?
We will do our best to keep your personal information private, but we cannot promise complete confidentiality. We won't share any information that we think could be used to identify you in publications about this study. However, your personal information may be shared outside the research study as described above and/or if required by law.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that information, documents, or specimens from this study that could identify you cannot be used in any legal action or lawsuit unless you say it is okay.

There are some types of sharing the Certificate does not apply to. The Certificate does not stop reporting required by federal, state, or local laws, such as reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate also does not stop sharing of information as described in the How Will My Information be Used section above.

Who Should I Call with Questions or Problems?
For questions about the study or a research-related injury, you may call the Infectious Diseases Research Clinic at 317-278-0255. You may also contact the researchers, Dr. Samir Gupta at 317-274-7926 or Dr. Jesse Stewart at 317-274-6761. After business hours (8:00 AM-4:00 PM from Monday-Friday), please call the on-call Infectious Diseases physician University Hospital at 317-944-5000.

For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or to offer input, please contact the IU Human Research Protection Program office at 800-696-2949 or at irb@iu.edu.

What if I Do Not Want to Participate or Change my Mind?
After reviewing this form and having your questions answered, you may decide to participate in the study. Or you may choose not to participate in the study. This decision is up to you. If you choose not to participate in this study or change your mind after signing this document, it will not affect your relationship with Indiana University or the medical care you receive from Eskenazi or IU Health.

If you change your mind and decide to leave the study in the future, the study team will help you withdraw from the study safely. If you decide to withdraw, please let the study team know.
If you choose to withdraw your authorization for use and disclosure of your protected health information, you must do so in writing by notifying Dr. Samir Gupta at sgupta1@iu.edu. If you withdraw your authorization, you will not be able to continue in this study. However, even if you cancel this authorization, the research team, research sponsors, and/or the research organizations may still use information about you that was collected as part of the research project between the date you signed this document and the date you cancelled this authorization. This is to protect the quality of the research results. Otherwise, this authorization remains valid until the research ends and required monitoring of the study has been completed.

Agreement to be Contacted by Text and/or Email
We would like to communicate with you about this study by text message and/or email. We might use text or email to send you reminders about upcoming visits or appointments, check on how you are doing, or tell you about the progress of the research.

Text messaging and email are not secure methods of communication. The information sent over text or email, which may include sensitive or personal information, such as protected health information, could be accessed or read by someone other than you. If you would like us to communicate with you via text or email, please initial the lines below and provide the phone number(s) and/or email address(es) you would like us to use.

_____ I authorize the researchers to send me emails related to this research study

Email address for this communication: _____

_____ I authorize the researchers to send me text messages related to this research study

Phone number for this communication: _____

You can still participate in this study even if you do not want us to contact you by text or email.

Participant's Consent and Authorization

I agree to participate in this research study.

Participant's Printed Name:_____

Participant's Signature:_____**Date:**_____

Participant's Address:_____

_____

(include street address, city, state, and zip code)

Printed Name of Person Obtaining Consent:_____

Signature of Person Obtaining Consent:

_____**Date:**_____