**Official Title**: Daily Stress Processes and Sympathetic Reactivity in Depression

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# The University of Texas at Arlington (UTA)

# Informed Consent for Biomedical Studies with Adults

**TITLE OF RESEARCH PROJECT**
Stress Reactivity in Human Depression

**RESEARCH TEAM**
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**CONCISE SUMMARY**
The purpose of this research study is to better understand cardiovascular system function in response to stress in people with depression. People with and without depression are being asked to participate.

**Inclusion Criteria**: You must be between the ages of 18-55 years. Healthy adults will not have a history of depression. Adults with depressive symptoms will be confirmed by diagnostic interview. You must be able to access and complete an online survey using a smartphone, tablet, computer, or any other device with internet connection capabilities. During the screening visit, we will check to ensure that you meet all of these requirements.

**Exclusion Criteria**: You will not be allowed to participate in the study if you have a mental illness aside from depression; if you are treated with any medication for depression; if you have active suicidal/homicidal intent; if you have active alcohol or drug dependence; if you have an eating disorder; if you are treated with a medication that could alter how your brain or cardiovascular system functions; if you make any changes or alterations in medication status; if you have cardiovascular, kidney, lung, or metabolic disease (e.g., diabetes); tobacco use; pregnancy; latex allergy; no reliable way to access and complete an online survey. During the screening visit, we will confirm that you do not meet any of these exclusion criteria.

**FOR RESEARCH TEAM ONLY**

*Does the volunteer identify with any of the exclusion criteria (check appropriate box)?*
*YES_____ NO_____*

_____
*Signature of Research Team Member Documenting Explanation of Exclusion Criteria*

If you choose to take part in the study, you will first be asked to attend an initial screening visit to make sure you qualify to participate. You will be asked to answer a series of questions about your physical and mental health, you will have your height, weight, heart rate, and blood pressure measured, and you will complete an assessment of your brain's thinking ability and speed. We will collect a blood sample. This visit takes about 2 hours.

We also ask you to complete an online survey that assesses your daily stress. You will complete this survey once per day for 8 consecutive days. The survey takes ~10-15 minutes to complete each day. You will be asked to return for the experimental visit on the last day of the daily stress assessment.

During the visit, we will measure how reactive your cardiovascular system is to acute physiological (cold water test, handgrip exercise) and psychological (emotional images, mental arithmetic) stress. We measure sympathetic nervous system activity with a technique called microneurography. This technique involves the placement of a small microelectrode into one of the nerves near the surface of your skin in your lower leg. We continuously measure blood pressure and heart rate throughout the visit. The research visit will take place at the UTA Science and Engineering Research & Innovation Building, and will take about 4-5 hours. You will be paid for your participation.

People who are depressed are at a greater risk of hurting or killing themselves. However, the research team will provide you with resources and referrals for counseling and/or suicide prevention support depending upon your needs. There are also physical risks associated with the blood draws, including discomfort/bruising, possible infection, or fainting. However, throughout the tests you will be closely monitored, and you can stop at any time.

You might want to participate in this study if you if you want to potentially help others with depression by contributing to scientific knowledge about how depression impacts blood vessel function. However, you might not want to participate in this study if you are uncomfortable with sharing your medical or mental health history with researchers, if you are uncomfortable with the psychological stress procedures, if you are afraid of blood draws or needles, or if you do not have the time to attend multiple study visits on the UT Arlington campus.

If you are interested in learning more about this study, please continue to read this document.

This study has been reviewed and approved by an Institutional Review Board (IRB). An IRB is an ethics committee that reviews research with the goal of protecting the rights and welfare of human research subjects. Your most important right as a human subject is informed consent. You should take your time to consider the information provided by this form and the research team, and ask questions about anything you do not fully understand before making your decision about participating.

**TIME COMMITMENT**

You will visit the laboratory for an initial screening and familiarization visit, which lasts approximately 2 hours. You will complete an online survey once per day for 8-consecutive days. Each survey takes ~10-15 minutes to complete (~2 hours in total across all 8 days). You will visit the lab for one experimental visit, which will last approximately 4-5 hours.

**RESEARCH PROCEDURES**

*This study involves up to two total visits to the laboratory. Please read the descriptions of the indicated lab visits/experimental measurements/procedures, then write your initials.*

We may ask you to repeat a trial, procedure, or test. This could happen for many reasons, such as equipment failure, power outage, inconclusive test results, etc. You do not have to repeat a trial, procedure, or test if you do not wish to do so.

**Initial:**

Screening Visit (~2 hours)

1. The staff measures your height, weight, waist circumference, blood pressure (BP), heart rate (HR), and temperature.

2. You complete a health history form. The staff reviews your medical history.
3. If you are a woman who is not post-menopausal, you will have a urine pregnancy test.
4. Dr. Greaney gives you the Mini-International Neuropsychiatric Interview (MINI). The MINI has 16 sections. This interview helps us look for signs of depression.
5. You will be asked to practice the techniques to be performed at the experimental visit so that you are familiar with them and know what to expect.

The following procedures may be conducted at either the screening visit or the experimental visit.

Initial:
1. Blood Draw: The staff draws 100 ml (6.7 tablespoons) of blood from a vein in your arm. We send the blood to a lab to see if the proteins, blood cells, electrolytes, etc. are within normal levels. The researchers do not perform genetic analyses on the blood or look for presence of disease (e.g. HIV). Some of this blood will be stored in a freezer and may be tested for substances of interest (NOx metabolites, inflammatory cytokines, indices of oxidative stress, and peripheral blood mononuclear cells).

Initial:
2. Brain Function Test: You complete an assessment of your brain's thinking ability and speed on an iPad. This assessment takes ~45 minutes. You will take several different tests that assess memory, language, decision-making, and processing speed. Many of these tests are similar to "games." In one task, you will be asked to stop paying attention to parts of the task that are not necessary. In another, you will be asked to match a target to two different choices based on shape or color. In another, you will be asked to repeat a series of items in the order of size, from smallest to largest. You will also be asked to read a series of words out loud. In another task, you will have to pick a picture that matches a word spoken out loud by the investigator.

Initial:
3. Emotional Health Test: You complete an assessment of your current emotional state on an iPad. This assessment takes ~10 minutes. You will take several different surveys that assess positive and negative mood, friendship, loneliness, stress, anger, and general life satisfaction. You will be asked to rate your "feelings" on a scale from "not at all" to "very much" or from "strongly disagree" to "strongly agree."

Initial:
4. Ambulatory Blood Pressure Monitoring: The staff assesses blood pressure over a 24-hour period using Ambulatory Blood Pressure Monitoring. We provide the blood pressure monitor, teach you how to use it, and provide a handout with instructions. We ask you to return the blood pressure monitor at your experimental visit.

Initial:
5. Flow-Mediated Dilation: We place a small blood pressure cuff around your forearm. We place gel on your upper arm just above the elbow. We place a Doppler ultrasound probe on the gel. The ultrasound makes sound waves to measure the size of blood vessels and the speed of the blood. We make a "resting" measurement before we inflate the blood pressure cuff. Then we inflate the cuff for 5 minutes to stop blood flow to and from the forearm. We deflate the cuff and continue measuring for 3 minutes. We may repeat this measurement several times.

Initial:
6. Applanation Tonometry: A pen-like probe will be placed over your skin to detect a pulse from the artery. At the same time, a blood pressure cuff on your upper leg will inflate and then deflate. These pulses will be used to assess the speed of the pulse in the artery.

Initial:

Assessment of Daily Stress (~2 hours in total)

1. For 8 consecutive days, you will be asked to complete the Daily Inventory of Stressful Events (DISE). This assessment will occur using an online survey tool called Qualtrics. It can be completed on any device that has internet connection capabilities (smartphone, tablet, laptop, desktop computer, etc.).

2. This survey takes ~10-15 minutes to complete and consists of ~100 questions. The main types of information that will be obtained using the DISE include questions about the types of daily stressors (e.g., argument with a friend, work/school deadlines, malfunctioning computer), how the stressor made you feel (e.g., angry, nervous), feelings of psychological distress (e.g., anxiety, irritability), and daily physical symptoms. You will also be asked questions about stress related to the COVID-19 pandemic. You are free to skip any questions that you prefer not to answer.
3. A laboratory team member will send you a text message and an email every day for the 8 consecutive days of the assessment, and these reminders will contain information on how to access the DISE.
4. On the last day of the DISE (i.e., Day 8), you will be asked to return to the lab for the experimental visit.

**Initial:**

Assessment of Physical Activity and Sleep

1. During the same 8-day timeframe that you are completing the assessment of daily stress, you will be asked to wear an accelerometer on your hip during the day, and on your non-dominant wrist during the night. You may take off the accelerometer during aquatic activities such as showering or swimming.
2. You will return the accelerometer on the last day of the DISE (i.e., Day 8) when you return to the lab for the experimental visit.

**Initial:**

Experimental Visit to Assess Cardiovascular Reactivity (~4 hours)

*Experimental Measures*

1. Vital Signs: When you arrive to the lab, we measure your heart rate, blood pressure, and oral temperature. Women who are not post-menopausal submit urine for a pregnancy test.
2. Self-Report Assessments: You will be asked to complete the Patient Health Questionnaire (PHQ-9) form to assess depressive symptom severity, the International Physical Activity Questionnaire (IPAQ) to assess regular physical activity, and a Daily Inventory of Stressful Events to assess chronic stress.
3. Heart Rate: We tape 3-5 sticky ECG tabs to your skin to measure heart rate continuously throughout the experiment.
4. Respiration: We place an elastic band around your abdomen to measure respiration throughout the experiment.
5. Blood Pressure: We may use up to three methods to measure blood pressure. Two methods use a cuff that inflates on your upper arm. In one, we listen with a stethoscope at the inside of your elbow. Another automated method also uses an upper arm cuff. The third method uses a small cuff that fits on your finger. Blood pressure is measured continuously throughout the experiment.
6. Blood Flow: Blood flow to the arm, leg, or neck may also be measured by placing a probe on the skin over the femoral artery of your leg or the brachial artery of your arm (alternatively in the instance of carotid artery, a blood vessel located at the side of your neck). This probe will provide a measure of the speed at which your blood is traveling through your artery and will allow for the calculation of blood flow. For these measurements, you can request an individual of the same sex as you be present to perform these measures.
7. Sympathetic Nerve Activity: We prepare your lower leg for the measurement of nerve activity. A nerve lies close to the surface of the skin on your lower leg, just below the knee. We touch a wand-like probe to the skin on your leg near the knee. The probe applies a mild electric stimulus. This allows us to locate the nerve. Then we insert a fine wire needle through the skin to record signals from the nerve. This needle is a “microelectrode.” We insert a second fine wire needle about 3 cm (about 1 inch) away. The second wire is the “reference needle.” In this way, we measure nerve signals to the leg muscle

throughout the experiment. To check the placement of the fine wire, we may ask you to hold your breath for several seconds. Also, we may ask you to hold your breath and "bear down."

*Experimental Protocol*

We collect baseline data during quiet rest for ~30 minutes. After this, you will be asked to perform three-to-four of the following stressful tasks:

- Cold Pressor Test: During this test, you immerse one of your hands (up to the wrist) in ice water for 2 minutes. After your hand is removed from the ice water, recovery data is collected for an additional 2 minutes. You will be asked to rate perceived discomfort using a numbered scale ranging from 1-11.
- Stroop Color Word Test: During this test, you will be asked to name the ink color of a color word. For some, there will be a mismatch between the ink color and the word (e.g., the word 'green' will be printed in red ink). You will be encouraged to respond as quickly as possible. You will perform this test for 3 minutes. You will be asked to rate perceived stress using a numbered scale ranging from 0-4.
- N-Back Test: During this test, you will be shown a sequence of letters/geometric shapes one at a time on a computer screen. You will be asked to indicate if the letter/geometric shape that you are currently viewing matches the letter shown 1 ("1-back") or 2 screens previously ("2-back"). You will be encouraged to respond as quickly as possible. You will perform this test for 3 minutes. You will be asked to rate perceived stress using a numbered scale ranging from 0-4.
- Emotional Stress: During this test, you will be shown a picture slide show of neutral (e.g., table lamp) and negative (e.g., wounded child) images. Each image will be viewed for 3 seconds, for a total of 3 minutes. You will be asked to rate perceived stress using a numbered scale ranging from 0-4.
- Mental Arithmetic: During this test, you will be asked to subtract the number 7 or the number 13 from a three-digit number. A new three-digit number will be provided every ~15 seconds. You will be encouraged to respond as quickly as possible. You will perform this test for 3 minutes. You will be asked to rate perceived stress using a numbered scale ranging from 0-4.
- Isometric Handgrip and Post-Exercise Ischemia: We determine your maximal grip strength in your dominant arm. You will squeeze the handgrip exercise device at the target workload for 2 minutes. You will be asked to rate how hard you are working using a numbered scale ranging from 6-20. During the last 5 seconds of exercise, we inflate a cuff on your upper arm. The cuff prevents blood flow into and out of your arm. After 3 minutes, we deflate the duff on your upper arm. You will be asked to rate perceived discomfort of the cuff using a numbered scale ranging from 1-11.

At the end of the experiment, we remove all equipment. We measure blood pressure and heart rate before you leave the lab.

**POSSIBLE BENEFITS**

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include a screening that informs you about your health such as your current blood pressure and blood cholesterol levels. There will be no charge for any tests required for the study. You could gain knowledge about how your body works. The information that we obtain will help us to understand the link between depression and increased cardiovascular risk.

Please note that UT Arlington is not a healthcare provider, and the procedures involved in this research study are not intended to provide medical treatment. There is no expectation or guarantee of

improvement or benefit for your health or any medical condition as a result of this research. If you are hoping to receive medical care, you should go to a medical doctor or other healthcare provider.

**POSSIBLE RISKS/DISCOMFORTS**

Individually, each procedure should not cause you much discomfort. However, it is possible that you may experience discomfort due to the sum of these procedures. The protocol is designed to reduce the likelihood of this occurring by minimizing the duration of each procedure. Nevertheless, if you experience a degree of discomfort which is greater than your expectations, we will stop the procedure(s) at your request. All tests that are to be performed have safely been used in both healthy and depressed individuals. Throughout the tests you will be closely monitored. Any new information developed during the study that may affect your willingness to continue participation will be communicated to you.

Although such events are extremely unlikely, the investigators are prepared to immediately stop experiments and seek medical assistance if you should experience a medical emergency. In this case, campus police will be contacted.

It is important that you report any illness or injury to the research team listed in this form immediately. Compensation for an injury resulting from your participation in this research is NOT available from The University of Texas at Arlington. In the event that you suffer a research-related injury, your medical expenses will be your responsibility or that of your third-party payer, although you retain your legal rights during your participation in this research.

MINI, PROMIS, PHQ9: These tools help us to sort people into the groups for this study. You may feel shy or disturbed by the questions. You may choose not to answer the questions and decline to be in the study. You may feel that these tools lead us to put you into the wrong group. We do not use these tools to diagnose depression. We do not use the tools to decide a recommendation for healthcare. The tools help us to find people who may have certain experiences useful for the purposes of this study. The tools help us to find those who have forms of psychological distress that are useful for this study. If you indicate a "high" level of suicidality, MHMR Tarrant County Crisis Relief will be called for an external evaluation. We keep the completed forms confidential and secure. Only approved staff may access the results. We treat all groups in the same way throughout the study. No one other than you and the approved staff know the group to which you have been assigned. If you have concerns about the results, we suggest that you seek follow-up with a healthcare or mental healthcare provider. If you do not have access to one or the other, we can provide you with contact information including:

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| UTA Counseling and Psychological Services | 817.272.3671 |
| MHMR Tarrant Country | 817.355.3022 |

Flow-Mediated Dilation/Doppler Ultrasound: There is a small chance the probe could irritate the skin. Minor redness may occur where the researchers place the probe against the arm. This is temporary. The gel is the same as that used with medical ultrasound tests. The gel may feel cool or cold on the skin. A bad reaction to the gel is highly unlikely.

Microneurography: The wand-like device may cause minor discomfort. When we insert the fine wire needle through the skin, you may have minor discomfort. The wire's thinness helps to reduce discomfort. You may have a pins and needles feeling for a short time. You may have a cramping feeling for a short time. These feelings may occur while we search for the nerve. When we locate the nerve, the search is

over and the fine wire needle remains in place for the whole experiment (about 3 hours). You could have feelings of muscle weakness and/or pins and needles after the experiment. This has happened in only a few people. There is no treatment for these feelings. The feelings end by themselves. Most researchers think that using the wire needle less than 1 hour to search for the nerve minimizes the risks. Therefore, we strictly enforce this time limit. There is also a small risk of infection at the site where we inserted the fine wire needle.

Cold Pressor Test: Your hand is likely to feel cold during the time it is submerged in ice water. You may stop the test at any time. You are unlikely to have any long-lasting bad effects from this test.

Arterial Occlusion: This is a commonly utilized technique in research settings. You might feel slight temporary discomfort and possibly numbness and/or tingling at the fingertips or toes during and after cuff inflation. Symptoms subside within 30 seconds following cuff deflation.

Blood Pressure: We measure blood pressure with the method used in a doctor's office. A cuff inflates on the upper arm. As the cuff slowly deflates, we listen with a stethoscope at the bend in the elbow. During the short time we inflate the cuff, your arm may feel numb or tingly. The cuff could cause mild bruising. The cuff placed on your finger inflates. You can feel the cuff pulse as it follows your blood pressure. You finger may become numb or tingly in time. We can move the cuff to a different finger. The 24-hour blood pressure monitor may disrupt your sleep. You can turn the unit off and remove the cuff if it is too burdensome.

Blood Draw: Blood draws often cause mild pain, bruising, swelling, or bleeding. There is also a slight chance of infection or a small clot. If you are nervous about needles, blood pressure and heart rate may increase for a little while. You may also feel lightheaded, sick to your stomach, or may faint. Using the same techniques used in hospitals keeps the chance of infection minimal.

Tape and ECG Electrodes: Some people may have a skin irritation from the patches that connect the wires on your chest to the computer. Small amounts of skin and hair are pulled slightly when the patches are removed after the test. Research personnel will attach and remove the patches as carefully as possible.

Medical Screening: You may feel shy about giving health information. The staff collects the information in a private and professional manner. You may feel shy about being measured. You may request someone of the same sex to conduct parts of the screening.

Surveys and Cognitive/Emotion Function Assessment: These surveys help us learn of your experiences that are useful for the purposes of this study. The surveys help us to interpret the data we produce in the experiments. You may feel shy or disturbed by the questions. You may choose not to answer the questions and decline to be in the study. We do not use the tools to decide a recommendation for healthcare. We keep the completed forms confidential and secure. Only approved staff may access the results.

Latex: Some gloves and medical materials are made of latex rubber. Some people may be sensitive to latex. Screening finds and excludes subjects that have a known latex allergy.

Confidentiality: There is a risk of loss of confidentiality if your information or your identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening. The confidentiality of your electronic data created by you or by the researchers will be maintained to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

**COMPENSATION**

If you agree to take part in this research study, we will pay you for your time and effort. You will be compensated when you complete the study or choose to quit the study.

You will be compensated $30 if you qualify for study enrollment and complete the screening visit. You will be compensated $75 for the experimental. If you agree to repeat a visit, you will receive payment for the repeated visit as stated above. If you are asked to repeat a certain procedure or measurement, you will be compensated $15/hour.

You will be compensated $15 for completion of the DISE surveys. If you complete all 8 days of the DISE survey, you will receive a bonus of $5 ($20 for completion of all 8 days of the DISE surveys). You will receive this same compensation each time you complete an 8-day DISE assessment. Compensation for the DISE will be in the form of a gift card, distributed via email. You will be required to complete the UTA gift card release form before receiving the electronic gift card. For this, you will be required to include your full name, mailing address, phone number, and signature.

The Internal Revenue Service (IRS) considers all payments made to research subjects to be taxable income. Your personal information, including your name, address, and social security number, may be acquired from you and provided to UT Arlington's accounting office for the purpose of payment. If your total payments for the year exceed $600.00, UT Arlington will report this information to the IRS as income and you will receive a Form 1099 at the end of the year. If you receive less than $600.00 total for payments in a year, you are personally responsible for reporting the payments to the IRS.

**ALTERNATIVE OPTIONS**

There are no alternative procedures offered for this study. However, you can elect not to participate in the study or quit at any time at no consequence.

**VOLUNTARY PARTICIPATION**

Participation in this research study is voluntary. You have the right to decline participation in any or all study procedures or quit at any time with no consequences. Should you choose not to complete all study procedures, you will still receive compensation for the time spent participating in the experimental visits.

During the course of the study, you may decide not to participate in a particular experimental measurement or procedure and, therefore, this portion of the protocol will not be completed. However, all other measurements and procedures will be performed. This will not affect the scientific value of your participation as each experimental measurement and procedure provides important and, in most cases, independent information. In addition, the principal investigator and research staff may decide to re-enroll you in the study if previous testing was unsuccessful or certain experimental measurements and procedures were not initially performed. The re-enrollment has no additional safety risks other than those inherent to the protocol and this will assist in the scientific merit of the project by providing additional information. If there is a change to your medication status (e.g., if you start a new, additional, or different medication) during the course of the study, the principal investigator and research staff may decide to withdraw you from the study.

**CONFIDENTIALITY**

Every attempt will be made to see that your study information and results are kept confidential. All paper and electronic data collected from this study will be stored in the investigator's lab for at least three (3) years after the end of this research.

Qualtrics is a secure website and survey application designed to support data capture for research studies. All data is encrypted. Data are deleted from Qualtrics' servers within 24 hours. The data files are downloaded and stored on an external password-protected hard-drive. Only authorized personnel have access to these files.

The results of this study may be published and/or presented without naming you as a participant. Identifiers might be removed from the identifiable private information and, after such removal, the information could be used for future research studies or distributed to another investigator for future research studies without additional informed consent.

Although your rights and privacy will be maintained, the Secretary of the Department of Health and Human Services, the UTA Institutional Review Board (IRB), OHRP / FDA, study sponsors, and personnel particular to this research may have access to the study records. Although absolute confidentiality cannot be guaranteed, the research team will make every effort to maintain the confidentiality of your records according to current legal requirements and will not be revealed unless required by law, or as noted above. The IRB at UTA has reviewed and approved this study and the information within this consent form. If in the unlikely event it becomes necessary for the Institutional Review Board to review your research records, the University of Texas at Arlington will protect the confidentiality of those records to the extent permitted by law.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National

Institutes of Health (NIH). With this Certificate, we can't be forced by a court order or subpoena to disclose information that could identify you in any civil, criminal, administrative, legislative or other proceeding. However, there are circumstances where the Certificate does not protect against disclosure of your personally identifiable information:

- when the US government is inspecting or evaluating federally-funded studies;
- when information must be disclosed to meet FDA requirements;
- if you give someone written permission to receive research information, or if you voluntarily disclose your study information;
- if the researcher reports that you threatened to harm yourself or others;
- in cases of child abuse or elder abuse reported by the researcher;
- if the investigator reports cases of contagious disease (such as HIV) to the state.

**CONTACT FOR QUESTIONS**

Questions about this research study or reports regarding an injury or problem may be directed to Dr. Jody Greaney (817-272-7891; jody.greaney@uta.edu).

Any questions you may have about your rights as a research subject and complaints may be directed to the Office of Research Administration; Regulatory Services at 817-272-3723 or regulatoryservices@uta.edu.

**As a representative of this study, I have explained the purpose, the procedures, the benefits, and the risks that are involved in this research study:**

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**Signature & Name of Research Team Member Conducting Consent Process DATE**

**CONSENT**

By signing this form, you are confirming that you understand the study's purpose, procedures, potential risks, and your rights as a research subject. By agreeing to participate, you are not waiving any of your legal rights. You can refuse to participate or discontinue participation at any time, with no penalty or loss of benefits that you would ordinarily have. Please sign below if you are at least 18 years of age and voluntarily agree to participate in this study.

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**SIGNATURE OF VOLUNTEER DATE**

**If you agree to participate, please provide the signed copy of this consent form to the research team. They will provide you with a copy to keep for your records.*

| Initial: | I wish to be contacted by laboratories conducting other research studies for which I may qualify and be interested in participating. |
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