# INFORMED CONSENT DOCUMENT

Project Title: **Associations of Adverse Childhood Experiences, Sleep Disruption, and Vascular Dysfunction in Young Adults: The Iowa ACEs and Sleep Cohort and Manipulating Sleep in Young Adults with ACEs Studies**

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This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

## WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you are a male or female between the ages of 18 and 29 years, with no known cardiovascular, metabolic, pulmonary, or autoimmune disease or inflammatory disorders, do not currently smoke or vape, are not pregnant or breastfeeding, and are willing to complete visit(s) to a research laboratory and at-home sleep monitoring, as well as potentially undergoing a sleep intervention.

The purpose of this research study is to examine the associations among Adverse Childhood Experiences (ACEs), sleep, and blood vessel health.

## HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 450 people will take part in this study conducted by investigators at the University of Iowa.

## HOW LONG WILL I BE IN THIS STUDY?

There are two parts to this study. If you agree to take part in this study, your involvement will last for at least a total of 2–3 weeks (Part 1 only) and potentially up to 8-9 weeks (Part 1+2). If you qualify for Part 1 of this study, you will complete one experimental visit in the laboratory followed by a 7-day in-home sleep monitoring period. The experimental visit will last about 3 hours. The in-home sleep monitoring period will require about 30 minutes of your time on a daily basis. Therefore, the projected total time commitment for this study is at least 6.5 hours.

If you qualify for Part 2 of the study, you will complete a 6-week intervention or control period, and then again complete a 7-day in-home sleep monitoring period and one experimental visit in the laboratory. If you are in the intervention group, you will complete a psychotherapy intervention for sleep known as cognitive behavioral therapy for insomnia (CBT-I). The CBT-I sessions will be delivered weekly via Zoom for 1 hour at a time (total ~6 hours). Therefore, if you complete both Part 1 and Part 2 of this study, we anticipate that your commitment for this study will be ~21 hours across an 8-9 week period.

## WHAT WILL HAPPEN DURING THIS STUDY?

The overall study design following consent and eligibility determination will be as follows:

**Eligible for Part 1 only:**

1. Physiological and Psychological Testing Visit in Integrative Laboratory of Applied Physiology: 4 hours
2. In Home Sleep Monitoring: Daily for a 7-day period followed by a 30-minute follow-up meeting in person or over Zoom

**Eligible for Parts 1 and 2:**

1. Physiological and Psychological Testing Visit in Integrative Laboratory of Applied Physiology: 4 hours
2. In Home Sleep Monitoring: Daily for a 7-day period
3. 6-week CBT-I intervention or Waitlist Control period
4. In Home Sleep Monitoring: Daily for a 7-day period
5. Physiological and Psychological Testing Visit in Integrative Laboratory of Applied Physiology: 4 hours

## 1. PHYSIOLOGIC AND PSYCHOLOGICAL TESTING VISIT

### A. Questionnaires

You will be asked to fill out several questionnaires following completion of the informed consent document. The first documents to be completed include a demographic and health history questionnaire, and questionnaires asking about medications, alcohol, tobacco and drug use, depression and anxiety symptoms, and physical activity. These documents and the information provided in them will be used to verify your eligibility (i.e., birth date and no pre-existing medical conditions). We will then measure your height and weight using a device and scale similar to what is used in a doctor's office to verify your eligibility based on body mass index and then, if you are a female, will collect a urine sample to perform a pregnancy test, verifying eligibility if you are not pregnant. Finally, we will collect two blood pressure readings to verify that your blood pressure is within the eligible range for this study.

After confirming eligibility, you will complete questionnaires that assess adverse childhood experiences and maltreatment and abuse chronology of exposure scales positive childhood experiences, childhood stress exposure and socioeconomic status, resilience, social support, emotional regulation, psychological distress, vigilance, cognitive flexibility, perceived stress, discrimination, psychological distress, coping for stress, stress disorder with life events checklist, COVID infection history, sleep timing, sleep environment, sleep behaviors and sleep quality. These questionnaires provide information to add additional context about psychosocial stress, mental and physical health, and protective factors in your life. All questionnaires will be performed online in REDCap. These are questionnaires that have been widely used previously. All responses will be associated directly only with your study identifier, and not your name such that a direct link cannot be made between your responses and answers. Further, an investigator who does not know your identity will score the surveys to help maintain privacy. The questionnaires will take approximately 45-60 minutes to complete in the laboratory.

### B. Physiologic Testing

You will arrive to the laboratory following an 8-10 hour overnight fast. It is important that you come to the

lab normally hydrated, so you will be asked to consume at least 16 oz of **only** water before arrival. In addition, it is very important that you abstain from factors that can influence the physiologic outcomes we are measuring as they can confound our study findings. As a result, you will be asked to abstain from alcohol, heavy exercise, and non-steroidal anti-inflammatory medication (also known as NSAIDs such as Tylenol, Advil, Motrin, etc.) use for the 48 h prior to your visits in the laboratory.

***Pregnancy Test:*** All females who are physically able to become pregnant will be required to have a pregnancy test after enrollment but before completing study procedures. If the test shows that you are pregnant, you will not be able to continue in the study. This testing will occur in a private area without any of your family members with you. We will only tell you the results of the test.

***Dietary Intake Survey:*** You will be asked to report the type and quantity of all food that you consumed within the 24 hours preceding your laboratory visit. This will be done via an online survey on an iPad.

***Body Composition:***
You will remove your shoes and socks and have your height measured as in a doctor's office and then have your waist circumference measured using a flexible cloth tape. Then, you will stand on a specialized medical grade scale that measures your body composition by assessing the impedance to small electrical currents. This is similar conceptually to the scales that measure body composition that can be purchased at Walmart, except much more sophisticated in function. To complete the test, you will simply stand still while holding special hand grips on the scale for approximately 30 seconds. The total time necessary for this test will be about 5 minutes.

***Arterial Pressure Waveform:***
You will sit upright in a seated, resting position for 10 minutes in a quiet, darkened room prior to assessment. A blood pressure cuff will then placed on your upper arm and inflated and deflated twice automatically. Systolic and diastolic blood pressure and heart rate will be measured.

***Blood and Endothelial Cell Sample Collection:***
After assessment of body composition, a catheter will be placed in a vein in your forearm under aseptic (clean) conditions. Approximately 60 mL (or 4 tablespoons) of blood will then be collected into special tubes for various analyses. In addition, cells that line your vein (known as endothelial cells) will be collected using special surgical guide wires inserted through the catheter by an individual trained in this technique. These cells will be put on slides and saved for future analyses of proteins in your cells.

***Assessment of Blood Vessel Function:***
The flow-mediated dilation (FMD) technique will be used to assess your blood vessel function. You will rest in a quiet, dark room for 15 minutes, and then the main artery in your upper arm will be scanned and visualized using an ultrasound device. Two minutes of imaging will be captured at baseline. An automated blood pressure cuff will then be inflated rapidly to 230-240 mmHg on your forearm for 5 minutes, before being suddenly released to induce an increase in blood flow. Blood vessel imaging will continue during cuff inflation, and for 3 minutes after cuff deflation to determine FMD. The total procedure will take approximately 35 minutes, including the rest period and the time necessary to visually locate the artery.

All of the described Physiological Testing procedures will take a total of approximately 240 minutes.

**In Home Sleep Monitoring**

You will complete an in-home sleep monitoring period that includes 7 nights of sleep. To monitor your sleep you will complete what is known as the Consensus Sleep Diary where you will track your sleep each morning after you wake up for 7 nights. You will begin this diary starting the morning following the experimental visit (assuming that you qualify to continue in the study). During the same time period, you will also wear a special watch 24/7 that we provide to you that measures your sleep and activity. You will use a special button on the device to denote when you go to sleep and when you wake up, but otherwise all you will need to do is wear the device on the wrist just like a watch (and remove for bathing).

In addition to complete the sleep diary and wearing the watch on a daily basis for 7 nights, you will also complete 2 nights of in-home sleep monitoring with a specialized device known as polysomnography or PSG. This device goes on your head sort of like a sweatband and has specialized sensors that are placed on your forehead, as well as on your collarbones. It also has a device that is worn on your wrist and finger-tip to measure your blood oxygen levels, much like when you go the doctor and they measure blood oxygen with a finger-tip device. Finally, the device also has a nasal cannula (tubes) that insert just inside of your nostrils and a band that goes around your chest to measure your breathing. The device takes a little getting used to, so we will ask you to wear it for two nights in a row during the 7-day in home sleep monitoring period to allow you to adjust to wearing it (but you only will need to wear it for two, back-to-back nights). You will put the device on immediately prior to going to bed and then take the device off once you wake up in the morning.

In summary, you will complete a sleep diary every morning and wear a specialized watch every day (all day) for 7 days/nights in a row. In addition, during the first 2 nights of the 7-day monitoring period, you will wear a specialized sleep monitoring device that is worn on your head. You will then return your sleep diary, specialized watch, and PSG device following the 7-day sleep monitoring period. At that time, you will meet with a member of the research team for up to 30 minutes to review your sleep diary data. This will occur over Zoom or in person, based on your ability to return to the lab.

*****PART 2 ONLY*****

Approximately 1/3 of participants that qualify for this Part 1 of the study will be eligible to proceed to Part 2, which is a randomized intervention study. If eligible and interested in completing Part 2 of the study, you will be randomized to either a 6-week Cognitive Behavioral Therapy for Insomnia (CBT-I) intervention or a Wait-List Control, and then complete a post-intervention in-home sleep monitoring protocol and a post-intervention experimental testing visit. The details regarding CBT-I are provided immediately below. If you are randomized to the Wait-List Control, you will receive no intervention for 6 weeks and will then complete the post-intervention period sleep monitoring and psychological and physiological testing. However, after completing the post-intervention experimental visit, you will receive the CBT-I intervention should you wish to receive it. You do have the ability to decline the intervention at this point if you decide you would rather not receive CBT-I. Randomization will occur in a 1:1 fashion (a 50-50 chance, like flipping a coin) using a randomization code that is generated by our study statistician. This means that neither you as the participant nor us as the investigators have the ability to select whether you receive the intervention immediately or after a 6 week waiting period.

**Cognitive Behavioral Therapy for Insomnia**

The CBT-i intervention will be delivered to you by trained clinical psychologists at the University of Iowa. CBT-i is the recommended first line treatment for those with poor sleep/insomnia. CBT-i will be delivered in 6, approximately 1 hour sessions across the course of 6-7 weeks and the topics covered in these sessions will include information about sleep, the regulation of sleep, reviewing your sleep schedule, techniques to improve your sleep and manage stress that may be impeding your sleep.

The CBT-I intervention sessions will be delivered using telehealth inside of the University of Iowa Zoom ecosystem using private links and will be recorded. The recording is not optional but will only be used by select members of the research team, and additional information about the purpose of these recordings is provided below.

**Tissue/Blood/Data Storage for Future Use**

As part of this study, we are obtaining blood samples and immune and endothelial cells from you. We would like to study your blood and immune and endothelial cells in the future, after this study is over without further consent. Your sample, information, and/or data may be placed in a central repository or other national repositories sponsored by the National Institutes of Health or other Federal agencies. If this happens, it may be stripped of identifiers (such as name, date of birth, address, etc.). Other qualified researchers who obtain proper permission may gain access to your sample and/or data for use in approved research studies that may or may not be related to in the purpose of this study.

The tests we might want to use to study your blood samples and immune and endothelial cells may not even exist at this time. Therefore, we are informing you that if you participate, your blood samples and immune and endothelial cells will be stored so that we can study them in the future. These future studies may provide additional information that will be helpful in understanding psychosocial stress and cardiovascular disease, but it is unlikely that what we learn from these studies will have a direct benefit to you. While unlikely, it is possible that your blood and immune and endothelial cells might be used to develop products tests, or discoveries that could be patented and licensed. In some instances, these may have potential commercial value and may be developed by the Investigators, University of Iowa, commercial companies, organizations funding this research, or others that may not be working directly with this research team. However, donors of blood and immune and endothelial cells do not retain any property rights to the materials. Therefore, there are no plans to provide financial compensation to you should this occur.

Your blood and immune cells will be stored *without* your name or any other kind of link that would enable us to directly identify which sample(s) are yours, other than with a participant ID and this link will be destroyed following completion of the study. Therefore, if you participate in this study, your blood and immune cells will be available for use in future research studies indefinitely and cannot be removed.

We would also like to keep your name, email address, phone number, participant ID, and ACE score in a password-protected excel sheet on a secure server managed by the University of Iowa for future reference so that we can follow-up with you in future years should we have the opportunity to do so. Providing this information does not guarantee that you will be contacted in the future. Providing this information also does not obligate you to participate in a future study and a separate consent document would be signed for future studies.

**WILL I BE NOTIFIED IF MY [DATA\BIOSPECIMENS\IMAGES] RESULT(S) IN AN UNEXPECTED FINDING?**

The results from the biospecimens/data we collect in this research study are not the same quality as what you would receive as part of your routine health care. However, some of our biospecimen/data results will be reviewed by a physician who normally reads such results and will inform us if there are any unexpected findings, such as the at-home sleep tests. If we detect likely moderate-to-severe obstructive sleep apnea (AHI ≥ 15), we will provide a letter to you with the measured values, the device used to measure these values, the date and time of the measurement, so that you can follow up with your health care provider. In addition, we will be measuring aspects of mental health and blood pressure that have clear diagnostic criteria. If you endorse symptoms consistent with clinically significant depressive or anxiety disorder, we will also provide a letter defining the scale information and ratings to follow up with your health care provider. Resources for health care providers in the area will also be provided. Should you endorse suicidality, we will administer the suicide severity scale and contact crisis services if necessary. Finally, if you have a blood pressure that is greater than stage 1 hypertensive range (systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 90 mmHg) we will provide a letter to you with the measured values, the device used to measure these values, the date and time of the blood pressure measurement so that you can follow up with your health care provider.

*****PART 2 ONLY*****

**Audio Recording/Video Recording**

One aspect of this study involves making audio/video recordings of you during the CBT-I intervention sessions. These recordings of the intervention are to ensure that all interviewers are administering the intervention in a standardized manner, and sessions will be coded to ensure the accuracy of the treatment. The recordings will be destroyed after coding. Up until the point that the recordings are destroyed, recordings will be stored on a password-protected drive so that only key members of the research team can access them.

## WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

1. Several questionnaires will be administered to assess adverse childhood experiences, mood, anxiety, stress, distress, and trauma symptoms. These instruments may evoke discomfort and occasionally distress in some participants.
2. Given the nature of this study, there is potential that we may discover incidental findings that alert us to the potential that a participant has a potentially undiagnosed clinically-relevant mental health disorder, or is in distress and/or exhibiting signs of suicidality.
3. Measurement of blood pressure: Participants may experience brief discomfort while the arm is squeezed by the blood pressure cuff.
4. Flow-mediated dilation (FMD) assessment: The FMD technique requires that a special pressurized cuff is inflated to 230 mmHg (a supra-systolic pressure) for 5 minutes. The purpose is to induce mild tissue ischemia and therefore this technique is uncomfortable. Participants typically experience tingling sensations, 'cold' fingers, a loss of sensation, and/or general discomfort.
5. Fasted blood draw: There are no major risks associated with fasted blood draws. Some discomfort or a

brief sensation of pain may occur from needle insertion. Swelling and redness occasionally, but infrequently, occur. In some instances, participants may also feel light-headed. There is a small risk of the needle insertion site becoming infected.

6. Endothelial cell collection: There are minor risks of inserting the J-wire for endothelial cell collection that include potential insertion through a valve, which are flaps in your veins that help to regulate blood flow.
7. Completing study questionnaires: Some survey questions may be potentially uncomfortable for participants.
8. At-home Sleep Assessment: Participants will wear a special device on their head and wrist and bands and wires on their chest. This may interfere with sleep.
9. There is a risk of loss of confidentiality of data

*****PART 2 ONLY*****

Cognitive-Behavioral Therapy: The CBT-I intervention may make participants uncomfortable, as the cognitive therapy includes identifying potentially difficult thoughts and emotions that impede sleep. In addition, CBT-I employs methods such as sleep restriction, which may cause participants to experience sleepiness during the initial sleep restriction period.

## WHAT ARE THE BENEFITS OF THIS STUDY?

We don't know if you will benefit from being in this study. However, in the future, there may be considerable general benefit to society based on information that will be gained from this study. Data may help identify a potential, modifiable bio-behavioral mechanism that links Adverse Childhood Experiences with vascular endothelial dysfunction – an important causal factor in CVD development. These data will help to inform actionable targets to reduce cardiovascular and sleep health disparities.

*****PART 2 ONLY*****

We don't know if you will benefit from being in this study. You may experience certain benefits from the intervention.

*****PART 2 ONLY*****

## WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, you may discuss treatment options with your doctor. Instead of being in this study, you could receive the same treatment (CBT-i) outside the context of this study should you be eligible clinically. However, the costs of such treatment will be your responsibility.

## WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study. You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses.

## WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will need to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. You will also need to provide your address so a check can be mailed to you. If your social security number is obtained for payment purposes only, it will not be retained for research purposes. Individuals who enroll but do not complete any experimental testing procedures (e.g., experimental testing) will not be compensated.

**PART 1:** Total compensation for completion of Part 1 of this study will be $200. Compensation will be pro-rated, such that $125 will be paid for completion of experimental testing and an additional $75 will be paid for at-home sleep monitoring. The at-home sleep monitoring compensation will be split up as follows: $50 for 2 nights of polysomnography device wear, plus $25 for 7 days of wrist device wear. If it is determined that a third night of polysomnography data is needed, you will be offered an additional $50 for this additional night.

**PARTS 1 and 2:** Total compensation for completion of both Part 1 and Part 2 of this study (for those participants who are eligible) will be $400. Compensation will be pro-rated, such that $125 will be paid for completion of each experimental testing visit (i.e., $125 x 2) and an additional $75 will be paid for each at-home sleep monitoring period (i.e., $75 x 2). The at-home sleep monitoring compensation will be split up as follows: $50 for 2 nights of polysomnography device wear, plus $25 for 7 days of wrist device wear. If it is determined that a third night of polysomnography data is needed, you will be offered an additional $50 for this additional night.

## WHO IS FUNDING THIS STUDY?

The National Institutes of Health (NIH) are funding this research study. This means that the University of Iowa is receiving payments from the NIH to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from the NIH for conducting this study.

## WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

## WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- federal government regulatory agencies,
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

To help protect your confidentiality, we will give you a participant ID. Before the screening process, your ID will begin with 'IC' (e.g., IC01). Once you are enrolled and determined to be eligible, you will be given a subject number (e.g., S01) and will be referred to using this number. IDs will be stored in a data log and matched to your contact information in this log (and this log only) so that you can be contacted if needed. This log will be stored in a password protected Excel file shared only with key research staff on a secure

server (Iowa OneDrive) which requires dual authentication of U. Iowa personnel. Deidentified information from paperwork will be transferred to a password protected Excel Document on OneDrive, which only researchers will have access to. All other electronic data collected (i.e. physiological signals) will be identified using only your participant ID. Hard copies (i.e. paper logs) will be stored in a filing cabinet in a locked room, which only the researchers have access to. Blood samples will be labelled using your participants ID, and will be stored in a locked freezer at -80°C. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

The University of Iowa Hospitals and Clinics generally requires that we document your participation in research occurring in a University of Iowa Health Care facility. This documentation will be in either your medical record or a database maintained on behalf of the institution reflecting that you are participating in this study. The information included will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

## IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

### What if I Decide to Drop Out of the Study?

You are under no obligation to participate in the study and there will be no negative consequences if you do not wish to enroll or if you drop out of the study.

If you decide to leave the study early, we will ask you to come to a close-out visit to return your sleep diaries and sleep watch device, as well as to provide an overview of reasons for your dropout such that these can be quantified and reported in future communications to the IRB and in research communications.

### Will I Receive New Information About the Study while Participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information. We do not anticipate this scenario.

### Can Someone Else End my Participation in this Study?

Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned. This might happen because in our judgment it would not be safe for you to continue, or because you are not completing the intervention as expected.

## WHAT IF I HAVE QUESTIONS?

*We encourage you to ask questions*. If you have any questions about the research study itself, please contact Dr. Nathaniel Jenkins at 319-467-3091. If you experience a research-related injury, please contact Dr. Nathaniel Jenkins at 319-467-3091 or 267-987-9208.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, http://hso.research.uiowa.edu/. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed): _____

_____ _____
(Signature of Subject) (Date)

**Statement of Person Who Obtained Consent**

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)