STUDY PROTOCOL WITH
STATISTICAL ANALYSIS PLAN

Impact of Community-Based Biofeedback Program on Drug Use and Mental Health Among People Experiencing Homelessness

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Document Type	Study Protocol with SAP and/or ICF

1. Protocol Synopsis

Protocol Element	Description
Official title	Impact of Community-Based Biofeedback Program on Drug Use and Mental Health Among People Experiencing Homelessness
Study type	Investigator-initiated, minimal-risk, randomized control pilot study
Purpose	Pilot test an 8-week HRV-BF intervention using an RN/CHW model of care among homeless and unstably housed people experiencing homelessness (PEH).
Population	Adults aged 18-75 years who self-reported residing in a homeless living condition during the previous night; English- or Spanish-speaking participants competent to provide informed consent; prior COVID-19 Study participants who meet eligibility criteria.
Planned sample	Planned enrollment N=50, with 25 participants per arm. Actual enrollment of 40; 36 participants who completed (HRV-BF n=17; Health Promotion n=19).
Study duration per participant	2 months (+/-14 days).
Allocation	Randomized 1:1 to HRV-BF or Health Promotion
Masking	None (Open Label).
Assessment time points	Baseline, weekly sessions during the 8-week program, and 8-week/2-month follow-up. Resting HRV was assessed at week 1 and week 8.
Locations	Amity Foundation, Downtown Women's Center, and Los Angeles Christian Health Centers, Los Angeles, California.
Outcomes	**Primary:** change in heart rate variability. **Secondary:** mental health status, anxiety symptoms, depression symptoms, posttraumatic stress disorder, drug and alcohol use, physical disease, and urine evidence of drug use. **Other:** social support.
Analysis	Descriptive analysis followed by regression analysis for continuous change outcomes; R v4.0.2; one-tailed alpha level of 0.05.

2. Background and Scientific Rationale

PEH are at high risk for COVID-19 and experience higher rates of chronic diseases than non-homeless populations. The supplied protocol describes Skid Row-Los Angeles as a critical COVID-19 epicenter and reports that stay-at-home orders limited social services, closed shelter doors, and increased social isolation, anxiety, stress, depression, and drug and alcohol use.

The protocol identifies a need for cost-effective strategies that target anxiety, stress, depression, and substance use and can be delivered in part remotely. Biofeedback is described as a process in which physiological processes and markers are measured and fed back to the individual. Heart Rate Variability-Biofeedback (HRV-BF) is described as cardiorespiratory biofeedback in which real-time heart-rate data are provided during guided slowed breathing to maximize respiratory sinus arrhythmia and produce a state of calm alertness.

The study builds on the COVID-19 Survey of 100 PEH (IRB 2021-6426). A Community Advisory Board of eight members from that study, including four COVID-19-recovered PEH and four not yet infected or not tested, was formed to assess the feasibility and acceptability of the HRV-BF program and to inform recruitment, retention, and delivery.

3. Study Objective, Specific Aim, and Hypotheses

3.1 Specific Aim

The objective was to compare the effectiveness of the HRV-BF intervention with the Health Promotion active control among PEH. The primary outcome was change in heart rate variability. Secondary outcomes were change in mental health status, anxiety symptoms, depression symptoms, posttraumatic stress disorder, drug and alcohol use, physical disease, and urine evidence of drug use. Social support was another prespecified outcome.

3.2 Research Hypotheses

Hypothesis	Statement
H0-2a	Participants enrolled in the HRV-BF program will demonstrate significantly greater increases in HRV indices at 8-week follow-up compared with the Health Promotion group.
H0-2b	Participants enrolled in the HRV-BF program will report significantly greater improvements in mental health status and reductions in anxiety, depression, and PTSD symptoms at 8-week follow-up compared with the Health Promotion group.
H0-2c	Participants enrolled in the HRV-BF program will demonstrate significantly greater decreases in drug and alcohol use at 8-week follow-up compared with the Health Promotion group.

4. Study Design

This randomized control pilot study was built upon the COVID-19 Survey. The planned enrollment was up to 50 homeless adults who met eligibility criteria, with randomization to the 8-week HRV-BF intervention or Health Promotion active control. Interested participants were randomized after informed consent was administered, followed by completion of the baseline questionnaire.

4.1 Randomization

After potential participants were identified and eligibility was confirmed, participants were randomly allocated to one of the two study arms in a 1:1 ratio. The project biostatistician created a randomization table before study initiation. The table was uploaded to the REDCap Randomization Module and used to assign participants to a study arm.

4.2 Blinding

Masking was none (open label).

4.3 Sample Size

The planned overall study sample size was 50, with 25 participants expected to complete in each arm. The IRB enrollment table also listed a maximum of 29 participants to be consented or collected in each arm and 25 expected to complete in each arm. Actual 40 participants were enrolled and 36 completed the study in their assigned group: 17 in HRV-BF and 19 in Health Promotion.

5. Study Population

5.1 Inclusion Criteria

- Participant in the COVID-19 study.
- Age 18-75 years.

- Self-reported residing in a homeless living condition during the previous night.
- History of substance use, including heroin, crack/cocaine, and alcohol use in the past year.
- History of depressive symptomatology.
- Willing to provide informed consent.

5.2 Exclusion Criteria

- Exclusively speaking languages other than English or Spanish.
- Actively hallucinating or cognitively impaired, as assessed by inability to understand informed consent.
- Any history of severe paranoia, delusional disorder, or severe obsessive-compulsive disorder, as assessed by self-report.
- History of structural heart disease, cardiac deficiency, rhythm abnormalities or arrhythmias, pacemaker use, or use of medications affecting autonomic function, as assessed by self-report, because these conditions affect HRV.

5.3 Eligibility Rationale

The protocol limits enrollment to adults aged 18-75 years because children differ developmentally in substance-use patterns, counseling and social-service referrals, and social-isolation patterns.

6. Recruitment and Informed Consent

Prior or continuing COVID-19 Study participants were informed of the HRV-BF study by phone, in person, or through an IRB-approved flyer. Recruitment occurred at Amity Foundation, Downtown Women's Center, and Los Angeles Christian Health Centers in Los Angeles, California.

The consent process used paper-based signed informed consent and signed HIPAA authorization. Study staff provided an oral explanation, allowed questions, and permitted up to 72 hours for a considered decision. Consent could occur in a private room or an isolated space while maintaining privacy.

7. Study Interventions

7.1 Arm 1: HRV-BF Intervention (n=25)

A nurse-led Community Health Worker team delivered HRV-BF for 30 minutes weekly for eight weeks: a 10-minute video and 20-minute EmWave Pro practice. Participants practiced for 10 minutes twice daily; the CHW collected logs and provided referrals.

Week	Topic	Key Points	Homework
1	Stress and Your Body	Basic stress physiology; awareness of the impact and somatic experience of stress.	Keep an awareness log.
2	Belly Breathing	Diaphragmatic breathing.	Belly breathing twice daily; 20 minutes total per day.
3	Paced Breathing	Paced diaphragmatic breathing.	Paced breathing twice daily; 20 minutes total per day.
4	Introduction to Self-Regulation	Concept of self-regulation and orientation to the HRV-BF device.	Paced breathing twice daily; 20 minutes total per day.
5	Heart Rate Variability	HRV-BF and Heartfelt Breathing.	Paced breathing twice daily; integrate skills throughout the week.

Week	Topic	Key Points	Homework
6	Self-Regulation Strategies, Part 2	HRV-BF and application of tools in real-life situations.	Paced breathing twice daily; integrate skills throughout the week.
7	Self-Regulation Strategies, Part 3	HRV-BF and application of tools in real-life situations.	Paced breathing twice daily; integrate skills throughout the week.
8	Final Session	Exit questionnaires and a plan for continued practice.	

7.2 Arm 2: Attention Control Health Promotion (n=25)

The Health Promotion active control group received weekly 30-minute visits for eight weeks from the nurse-led Community Health Worker team. The manualized program addressed chronic health conditions highly prevalent among PEH, using the module topics listed below, with discussion and referrals based on participants' expressed needs.

Module	Topic
1	Orientation
2	Basics of High Blood Pressure
3	Basics of High Blood Pressure - Continued
4	Basics of Diabetes
5	Basics of Diabetes - Continued
6	Basics of Arthritis
7	Basics of High Cholesterol
8	Basics of High Cholesterol - Continued

8. Study Procedures and Schedule

Time Point	Procedures
Pre-screening and enrollment	Eligibility confirmation; recruitment information; signed informed consent and HIPAA authorization; randomization.
Baseline/week 1	30-minute REDCap questionnaire; structured measures; resting 5-minute HRV assessment; urine sample for recent drug use.
Weeks 1-8	Weekly 30-minute HRV-BF or Health Promotion session.
Daily between sessions	HRV-BF participants practiced 10 minutes twice daily without the device.
Week 8/2-month follow-up	Follow-up questionnaire; repeat resting 5-minute HRV assessment; repeat urine sample for recent drug use. Telephone follow-up could be used with permission if the participant could not meet in person.

8.1 Baseline and Follow-Up Questionnaire

The electronic REDCap questionnaire included sociodemographic characteristics, social support, substance use, physical disease, and psychological factors. Structured instruments included the Texas Christian University Drug History Form, Patient Health Questionnaire-9, Generalized Anxiety Disorder-7, Mental Health Inventory-5, Posttraumatic Stress Disorder Checklist-Civilian Version, Self-Administered Comorbidity Questionnaire, and Medical Outcomes Study Social Support Survey. Measures were repeated at follow-up where applicable.

8.2 Heart Rate Variability Measurement

For both groups, HRV was assessed during a resting 5-minute period at week 1 and week 8 using a medical-grade photo-detector sensor and HeartMath EmWave Pro Plus software. Standard HRV measures included SDNN and RMSSD, measured in milliseconds. RMSSD was the primary outcome measure.

8.3 Urinalysis

Participants provided urine samples at baseline and 8-week follow-up. A five-panel urine test cup screened for amphetamines, cocaine, methamphetamines, opiates, and cannabis. Results were reported as participant counts with a positive result for one or more drug classes or a negative result for all tested drug classes.

9. Outcomes and Measures

Outcome Classification & Title	Measure/Timing
Primary: Change in Heart Rate Variability	HeartMath EmWave Pro Plus; resting 5-minute assessment at week 1 and week 8; SDNN and RMSSD in milliseconds, with RMSSD identified as the primary outcome measure.
Secondary: Change in Mental Health Status	Mental Health Inventory-5; baseline and 8 weeks.
Secondary: Change in Anxiety Symptoms	Generalized Anxiety Disorder-7; baseline and 8 weeks.
Secondary: Change in Depression Symptoms	Patient Health Questionnaire-9; baseline and 8 weeks.
Secondary: Change in Posttraumatic Stress Disorder	Posttraumatic Stress Disorder Checklist-Civilian Version; baseline and 8 weeks.
Secondary: Change in Drug and Alcohol Use	Texas Christian University Drug History Form; baseline and 8 weeks.
Secondary: Physical Disease	Self-Administered Comorbidity Questionnaire; baseline.
Secondary: Evidence of Drug Use in Urine	Five-panel urinalysis reported as positive for one or more tested drug classes or negative for all tested drug classes; baseline and 8 weeks.
Other Prespecified: Change in Social Support	Medical Outcomes Study Social Support Survey; baseline and 8 weeks.

10. Risks, Risk Minimization, and Benefits

10.1 Risks and Discomforts

- Potential breach of confidentiality: rare; seriousness moderate.

- Anxiety or fear of stigma from possible disclosure of COVID-19 status or substance-use history, or concern that others will learn of study participation: rare; seriousness moderate.
- Emotional and mental distress from discussions of COVID-19, substance and alcohol use, and homelessness: rare; seriousness moderate.
- Relaxation-induced anxiety: unlikely; 10%.
- Drowsiness: less common; 40%.
- Mild lightheadedness: less common; 30%.

10.2 Risk Minimization and Safety Monitoring

Confidentiality will be protected through subject codes, secured REDCap storage, and trained staff. Research nurses, CHWs, and research assistants will be trained in observation, communication, psychosocial support, and recognition of psychosocial distress and suicidal ideation or attempts. Staff will have referrals to acute-care institutions available. Ongoing dialogue during sessions will allow participants to report adverse effects and allow staff to address effects or halt the intervention if needed.

Participating community sites will notify the UCI research team of logistical challenges but are not involved in data safety monitoring, interim findings, adverse events, or unanticipated problems because they are not engaged in human-subjects research. Data and safety monitoring and modifications/amendments to the protocol or consent documents will be recorded and shared between participating sites.

10.3 Potential Benefits

HRV-BF participants may gain an understanding of how HRV-BF may improve psychological outcomes, increase HRV, and reduce drug and alcohol use. Participants may experience relaxation, lower muscle tension, improved sleep, and improved mental states. The scientific benefit is knowledge to inform future community-based interventions using an RN/CHW model.

11. Compensation

All participants received $15 for the baseline assessment and urinalysis, $10 for each weekly session for eight weeks ($80), and $20 for the completed 2-month follow-up and urine analysis. Participants were not reimbursed for out-of-pocket expenses and were not charged for study procedures.

12. Confidentiality, Data Management, and Retention

Category	Source-Specified Procedure
Electronic research data	Screeners and questionnaires were captured and stored in REDCap on a secured encrypted server maintained by UCI Irvine Health Information Services.
HRV data	Data could be stored on a UCI encrypted tablet or secure encrypted UCI servers. Data on the tablet were uploaded to the UCI Health server and deleted after successful upload.
Hard-copy data	Stored at the secured research-site office and accessible only to approved research personnel.
Identifiers	Kept separately from study information and linked by a code. Subject identifiers were not disclosed in presentations or publications.
Information sharing	Only de-identified information was shared with researchers outside the protocol team for purposes within the protocol scope.
Retention	Research information will be retained for 10 years after the end of the calendar year in which the research is completed.

Office 365 applications will be used for daily operations and sharing among approved team members. Zoom meetings will be invitation-only and temporary, with no data stored in Zoom. TheBox may be used for password-protected, de-identified project files. A Certificate of Confidentiality will be obtained; disclosures may occur as required by federal, state, or local law, including reporting of abuse, communicable disease, or threats of harm.

13. Statistical Analysis Plan

13.1 General Analytic Approach

Frequency distributions, measures of central tendency and variance for continuous measures, proportions for categorical variables, and graphical displays will be produced.

13.2 Primary Analyses

Descriptive analysis will be followed by regression analysis to determine associations between intervention group (1 = HRV-BF; 0 = Health Promotion) and continuous change outcomes for HRV, mental health status, anxiety, depression, PTSD, drug and alcohol use, and social support. Physical disease will be summarized at baseline. Urinalysis will be summarized using participant counts and proportions for positive and negative results at baseline and 8 weeks.

13.3 Statistical Software and Significance Level

R version 4.0.2 will be used for all analyses. Because this is a pilot study, statistical tests will use a one-tailed alpha level of 0.05. Positive findings will be verified in a future validation study.

13.4 Presentation of Results

Results will be presented using frequency distributions, measures of central tendency and variance, proportions, and graphical displays.

14. Administrative and Regulatory Information

Item	Description
IRB review	Minimal Risk (Expedited)
Initial approval date	August 19, 2021
Approved protocol narrative	APP# 16528; HS# 2021-6820
IRB submission type	Amended
IRB status in supplied record	Closed; administratively closed because the protocol was past six months since expiration
Coordinating center	UCI
Relying institution	UCLA
Community locations	Amity Foundation, Downtown Women's Center, and Los Angeles Christian Health Centers, Los Angeles, California.

15. Protocol Amendments

This consolidated Study Protocol with Statistical Analysis Plan incorporates the applicable amended IRB record and the UCI IRB-approved protocol narrative (APP# 16528; HS# 2021-6820).

IRB approvals timeline is as follows:

- Initial approval: Aug 19, 2021
- Study start date: Feb 22, 2022
- Amendment: Apr 05, 2022
- IRB record closure: Feb 25, 2025