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OFFICIAL STUDY TITLE:
Effects of GPS Tracking on Patient Adherence to Hepatitis C Treatment Among People Experiencing Unsheltered Homelessness

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Research Proposal

Study Title: Effects of GPS Tracking on Patient Adherence to Hepatitis C Treatment Among People Experiencing Unsheltered Homelessness

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Study Procedures

1. **Background/Rationale**
    a. Previous research on Hepatitis C infection has found positivity rates between 12% and 27% among people experiencing homelessness; far exceeding typical rates found among a general housed population (1%). The usual course of Hepatitis C in the healthcare system is screening and diagnosis in primary care, then referral to specialty care (such as Hepatology or Gastroenterology) for treatment. All of this takes place within the confines of traditional "brick and mortar" clinics. This screen, refer and treat model presents a multitude of person- and systems-level barriers for individuals experiencing homelessness.
    b. Street Medicine was developed as an alternative healthcare delivery model to better account for the unique circumstances of the unsheltered homeless population and better meet their healthcare needs. It is defined as the delivery of individually tailored health and social services to people experiencing unsheltered homelessness directly in their own environment. Street Medicine clinicians are ideally positioned to screen, diagnose and treat patients for Hepatitis C. Treatment of uncomplicated Hepatitis C requires daily medication for 8 to 12 weeks. While our preliminary pilot data have shown Street Medicine teams have had success in completing treatment of Hepatitis C on the street for many patients, attaining adequate follow-up for effective treatment has been a problem for others.
    c. Innovative, practical, and ethical solutions to help locate patients experiencing homelessness who require follow-up for medical treatment are needed. One such potential solution is the use of discreet GPS tracking devices that may be activated when providers are in the field to locate and care for patients. GPS tracking devices have been used by other Street Medicine programs caring for patients experiencing homelessness. However, no research has used GPS devices for treatment of Hepatitis C amongst people experiencing unsheltered homelessness or elicited the patient perspective on it.

    d. This study seeks to evaluate the impact of using a GPS tracker among patients engaged in street-based treatment for Hepatitis C on medication adherence.
    e. A randomized-controlled study design and qualitative interviews to explore the perspective of unsheltered homeless patients engaged in both study arms are proposed.

2. **Purpose/Objectives/Aims/Research Questions**
    a. The purpose of this study is to evaluate the impact of a GPS tracker among patients engaged in street-based treatment for Hepatitis C on medication adherence.

    b. This study's primary objective is to measure the effects of GPS tracking on patient adherence to medication compared to usual care (no tracker).

    c. Another primary objective is to understand the experience of unsheltered homeless individuals who participated in both study arms (GPS tracker and no tracker).

    d. We aim to answer the following questions:
        i. Does using a GPS tracker improve medication adherence at eight-weeks or twelve-weeks for the treatment of Hepatitis C among patients experiencing unsheltered homelessness?
        ii. Are patients with a GPS tracker able to be successfully located for treatment compared to patients who do not have a GPS tracker?
        iii. What is the Hepatitis C positivity rate among patients with a GPS tracker compared to those without a GPS tracker at the end of their treatment course, in other words, what is the cure rate or Sustained Virologic Response at 12 weeks (SVR12)?
        iv. What is the subjective experience of unsheltered homeless individuals with active HCV infection who do or do not have a GPS tracker?
        v. Is using a GPS tracker to deliver Hepatitis C medications to the unsheltered homeless population more cost effective than the traditional model?

3. **Participants (sample)**
    a. The target population for this study is: unsheltered homeless adults (age 18+); English- and Spanish-speaking; patients receiving care from a Street Medicine team; undergoing street-based treatment for positive Hepatitis C infection with active viral load, and meet the American Association for the Study of Liver Diseases (AASLD) criteria for simplified treatment of Hepatitis C: (Patients who do NOT have decompensated cirrhosis, have concurrent Hepatitis B or HIV infection, are pregnant, and have NOT previously received Hepatitis C treatment).

    b. Patients must be experiencing unsheltered homelessness at some point during their treatment course (this includes tent, encampment, on street, or in car, RV). Patients will NOT be excluded if they are temporarily or permanently housed at some point during their treatment.

    c. Exclusion criteria includes patients who do not meet the AASLD criteria for simplified treatment of Hepatitis C:
        i. Prior Hepatitis C treatment
        ii. Decompensated cirrhosis

iii. HBsAg positive
iv. Current pregnancy (pregnancy will be asked about during screening. If someone thinks they may be pregnant but is not sure, we can draw a HCG quantitative lab before the patient enrolls in the study).
v. Known or suspected hepatocellular carcinoma
vi. Prior liver transplantation

d. Participants who opt out during the screening process due to not wanting to wear a GPS tracker will be excluded, as the assignment of tracker will be random.

e. Children under 18 will not be included.

f. Note: If a patient becomes pregnant during the course of the study, we will not stop or change treatment because the medications can used for Hepatitis C treatment can be used in pregnancy. If this happens, we will identify in our discussion that a participant became pregnant during the study.

4. **Recruitment/Screening Process (sampling strategy)**
   a. Potential study participants will be identified and pre-screened for eligibility by the individual Street Medicine clinical team. When a patient tests positive for HCV with active viral load, their case will be further reviewed by a researcher involved in the study before treatment initiation to check that the patient meets all inclusion criteria and has none of the exclusion criteria characteristics as indicated above.

   f. Potential participants meeting eligibility criteria during pre-screening will be invited to participate in the study during their regularly scheduled medical encounter (usual care) with the Street Medicine team. The individual Street Medicine site will determine at what interval they will follow up with patient during treatment of Hepatitis C and make note of this. The potential participant will be informed that their participation is completely voluntary and their usual medical care from the Street Medicine team will not be affected if they choose to participate.

   g. The study will be conducted by their normal care team or study personnel affiliated with the Street Medicine team. Study personnel accompany the Street Medicine team at usual medical encounters with potential participants identified during the pre-screen. If different from the patient's typical care team, the medical team will introduce the patient/potential participant to study personnel at the conclusion of their usual medical encounter. Study personnel will explain the study, review the informed consent document, and answer questions.

h. An IRB-approved written informed consent document will be used to help guide study personnel during explanation of the study. A copy of the informed consent will be given to all potential participants to retain so that they may spend more time reviewing it before they make their decision. At the request of potential study participants, study personnel may accompany the medical team on a subsequent visit with that particular patient if they would like more time to decide.

i. To allow for randomization of groups, study personnel will explain that in this study, a GPS tracker may be used to find a patient for their Hepatitis C treatment and that to participate, they must be willing to keep a GPS tracker on them. Study personnel will explain that the patient may be selected to wear the GPS tracker at random and that if not, they will still receive the Hepatitis C treatment, but without the tracker. The study personnel will present a document to the patient explaining the specific GPS tracker, what information will be tracked, and details of when and how the tracker will be turned on to locate the patient. If the patient allows for the GPS tracker to be used, they will be eligible to participate in the study. If they do not want to wear a GPS tracker, they will not be eligible for the study. However, they will still receive Hepatitis C treatment, outside of the study parameters.

j. If eligible for the study, the patient will be presented with another informed consent document, explaining the details of the GPS tracker and that they consent to being tracked in this way.

k. Based on a power calculation performed by Wendy Mack, PhD, Director of the Biostatistics Core of the Southern California Clinical Translational Science Institute (CTSI), we aim to enroll N=124 participants in this study (n=62 intervention/tracker arm; n=62 usual care arm).

5. **Methods**
   a. A researcher team member at participating Street Medicine sites will conduct a pre-screening for potential study participants so that we may target those meeting eligibility criteria (see above).

   b. The researcher will use the electronic medical record to check the charts of potential study participants for the study eligibility criteria and speak with clinical team members that routinely care for the patient to gather any missing information. A pre-screening data collection form will be used for the researcher to input information about the potential study participants. We will use the patient's first name and first initial of their last name, the name of their lead clinician, and the date of the patient's next appointment to dispatch study personnel to accompany the clinical team and approach the potential participant about the study.

c. Study personnel will accompany the Street Medicine team at the next usual medical encounter for potential participants identified during the pre-screen. The lead clinician will introduce the patient/potential participant to study personnel at the conclusion of the usual medical encounter. Study personnel will explain the study, review the informed consent document, review the HIPAA authorization document, and answer questions. Potential participants will be given a copy of the informed consent and HIPAA authorization documents to retain and review; taking as much time as needed/requested. At the request of potential study participants, study personnel may accompany the Street Medicine team on subsequent usual care visits with that individual to answer questions and conduct study-related activities.

d. Study personnel trained in the responsible conduct of human subjects research will review a physical copy of an informed consent document with potential participants to explain the study and answer questions. Written consent and signed HIPAA authorization will be obtained from those volunteering to participate. A physical, printed copy of the informed consent and HIPAA authorization documents will be given to all participants (including those who would like more time to consider their choice). Then, the study personnel will also explain the potential of having a GPS tracker that must be worn by the participant, as outlined in the above section.

e. After a patient has agreed to participate and is enrolled in the study (i.e. signed informed consent provided), participants will be randomized to either the usual care or GPS tracker study arm. Randomization assignment will be determined by a random number list generated by SPSS statistical software version 22.0. Study personnel will explain to the participant specific information about the GPS tracker, including what information the study personnel will be using from the tracker and the purpose of the GPS tracking device. If the participant consents to wearing the GPS tracker, another written consent for the specific GPS tracker will be obtained by the participant, explaining all information that was verbally explained about the GPS tracking device.

f. GPS trackers will be Trak-4 brand. They will be given to the patient at the beginning of the study. Study personnel will recommend that the patient affix the tracker to a lanyard to be worn around their neck, under their shirt, although the patient will be encouraged to keep it on their body in whichever way they choose. It will be thoroughly emphasized to the patient that they should have the GPS tracker on them and always charged.
    i. A label with the specific Street Medicine program will be affixed to the tracker, including contact information of the program.
    ii. The GPS tracker will be fully charged at the initial encounter. At each subsequent encounter, the study team will bring a fully charged GPS tracker and exchange it for the patient's old tracker. GPS trackers will be charged at the office of the Street Medicine team. A solar charger will also be provided to the patient, in the instance that they want to charge the GPS tracker on their own.

iii. Lost GPS tracker: In the case of a lost GPS tracker at a subsequent follow up visit, the patient will be given another GPS tracker. The GPS tracker may be lost up to 3 times during the study. After the third time of losing the tracker, the patient will not be given another tracker. However, their Hepatitis C treatment will continue in the traditional model through the Street Medicine clinical team. In this instance, the participant will be labeled as "lost tracker," but they will continue to be followed in the study.

iv. Information that will be tracked by the Trak-4: The patient's location in real time when the Street Medicine team is looking for the patient for their medical visit. The patient's location will not be tracked at any other time. No other information will be gathered by the Trak-4.

g. Study participants will meet with the clinical team, including researchers from that specific Street Medicine team during regular intervals. The individual Street Medicine team may decide at what time intervals they will follow up with the patient and document this in the study notes. At these visits, the clinical team and study personnel will count how many pills were missed each week and keep a specific record of missed doses per week. A lab draw will be completed at 12 weeks post treatment. Between end of treatment and 12 weeks post treatment, the clinical team, including the researcher, will meet with the study participant at least twice to continue normal clinical care. The patient will continue to wear the GPS tracker until their 12-week post treatment lab draw. After this lab draw, the patient will be asked to continue to wear the tracker until the results are known and the clinical team can meet with them to discuss the results (approximately 1-2 weeks). After this visit, the patient will remove the GPS tracker and return it to the Street Medicine clinical team.

h. Additionally, participants will be asked to agree to a retrospective chart review for existing demographic and clinical blood value data. A member of the study team will use the electronic medical records to review the patient chart, extract, and record the items (outlined on the data collection form) directing into Qualtrics for two time periods: lab values at time of blood draw yielding positive HCV infection with active viral load (T1) and lab values from blood draw collected 12 weeks post treatment (T2). Demographic characteristics will be recorded at baseline only and skip logic is included in the Qualtrics datasheet for simplicity and to ensure minimum necessary data are reviewed/recorded. In lieu of patient names, study identification numbers will be used. A single password-protected crosswalk (Excel file) linking participant names to study identification numbers will be maintained by the study PI. The coded data entered into Qualtrics will be downloaded as a single dataset (Excel and SPSS files) for analysis.

i. Adherence to treatment will be measured by the number of pills taken vs missed for each study participant at regular intervals, depending on the individual Street Medicine team (Research Questions 1 and 2). Additionally, completion of treatment will be measured by whether the participant completed the full 8 or 12-weeks. The

participant's lab data, showing whether they achieved SVR, will be used to determine success of treatment (Research Question 4). This will be compared to the adherence rate (# of pills), completion rate, and whether the participant wore the GPS tracker to understand if the GPS tracker had a significant effect on these data points (Research question 3).

i. Intervention: GPS tracker vs usual care Street Medicine
ii. Participant groups:
    1. Control: usual care Street-based Hep C treatment
    2. Intervention group: receives GPS tracker and usual care Street-based Hep C treatment
iii. Data points:
    1. Adherence to treatment: # of pills taken vs missed per week
    2. Completion of treatment: Did the participant finish the full 8- or 12-week course?
    3. Success of treatment: Did the patient achieve SVR at 12-weeks post treatment?
    4. Success rate of locating the patient

j. After completion of the study, a random convenience sample/subset (N=40) of patients from each study arm (n=20 tracker group; n=20 usual care) will be invited for a one-time, in-person interview during a usual patient encounter post treatment. The convenience sample will be chosen at random from each study arm, as we would like to understand the experience of patients in both groups. We are not interviewing all patients involved in the study, as the interview section of the study is an addition to the main study. Additionally, the interviews can be very lengthy and we may not have the personnel to complete interviews with 124 participants. Study personnel will be deployed to conduct an interview after a clinical team's encounter with the participant. Individual interviews are expected to last approximately 10-15 minutes, will be guided by a six-item semi-structured research protocol, facilitated by a study team member trained in the conduct of qualitative interviewing, and will be audio-recorded (with additional verbal consent by the participant). If a participant declines to be audio-recorded, field notes will be recorded by the interviewer. Audio files will be transcribed verbatim, cleaned to ensure they are de-identified, and transcripts (or field notes) will be analyzed. Electronic audio files will be destroyed once the transcript is complete. Participants will be given a physical printed copy of the transcript from their interview upon request.

k. Participant identity and confidentiality will be handled in numerous ways and include physical and electronic safeguards. First, prior to consent, access to personal health information and identifiers for potential participants is limited as much as possible. Secondly, we have established multiple ways for individuals to participate that allow them to decide which information, and how much, is included in the study. For example, participants may decline participation in some aspects of the study, such as audio

recording and/or retrospective chart review. All data will be coded with study identification numbers in lieu of participant names. We have also established electronic de-identified data collection sheets via Qualtrics. We will also use password protection on study documents (crosswalk) and hospital network computers which contain duo-authentication and cyber security software. Note: Participants can deny answering the questions during the interview if they choose. Additionally, investigators can end the interview if they see signs of discomfort in the participant. This is reiterated in the introductory portion of the interview script (see script).

l. We intend to disseminate study findings at academic and clinical conferences related to public health, hepatitis, street medicine, and homelessness. Additionally, we intend to develop a peer-reviewed journal article. If/when this research is published, we will provide a physical printed copy of the publication to the study participants.

m. There will be no additional cost to VCMC or affiliates for intervention. There will be no other administrative costs. The time that the study will take place will be during normal Street Medicine rounds or "backpack time."

n. Instrumentation:
    i. GPS Tracking Device
        1. Trak-4 GPS Tacker
        2. https://trak-4.com/
        3. See methods above (part F)
    ii. Hepatitis C medication treatment
        1. 8 or 12-week course of treatment will be administered to study participants
        2. Treatment type will be determined by the individual Street Medicine team clinician from the following options, based on the needs of the patient:
            a. glecaprevir / pibrentasvir (Mavyret) - 8-week course
            b. ledipasvir / sofosbuvir (Harvoni) - 8-week course
            c. sofosbuvir / velpatasvir (Epclusa) - 12-week course
        3. Medication will be distributed into a pill box and delivered at 1–2-week intervals on the same day every week.
    iii. Questionnaires/Survey Measures (names and citations):
        1. A brief survey will be administered to each patient at the start of treatment [see attached questionnaire]. This will be administered via Qualtrics.
        2. Existing chart data for 15-items will be extracted from the electronic medical record at three time points: at screening for Hepatitis C infection (T1) and at treatment conclusion (T2). The 15- items include:
            a. Age (T1)
            b. Gender identity (T1)

c. Racial/ethnic identity (T1)
d. Homeless history (years homeless) (T1)
e. Length of relationship with street medicine team (T1)
f. 10 laboratory (blood) values related to Hepatitis C
    i. Hepatitis C Ab (T1)
    ii. HCV RNA QN REAL TIME PCR (T1 and T2)
    iii. HCV Genotype (if possible) (T1)
    iv. Hepatitis B Surface Antigen (T1)
    v. ALT (T1)
    vi. AST (T1)
    vii. INR/PT (if applicable) (T1)
    viii. Platelet count (T1)
    ix. HIV AG/AB, 4^{th} Gen (T1)
    x. HCG quantitative for women of childbearing age (T1)

iv. Qualitative instruments
1. The interview protocol includes six open-ended questions with supplementary probes to elicit the patient's perspective on engaging in street-based treatment for Hepatitis C with or without the GPS tracker [see attached interview protocol].

o. Data Analysis

1. Quantitative Analyses: Data will be analyzed using SPSS statistical software version 28.0. Analyses will be analyzed by Co-I Coulourides Kogan in collaboration with biostatistical support from the USC Clinical Translational Science Institute, as needed.

ii.

1. <u>Primary data analysis</u> We will use univariate statistics to describe our sample, and bivariate and multivariate analyses to assess our primary and secondary research questions.
    a. Data points:
        i. Adherence to treatment: # of pills taken vs missed per week (univariate and bivariate statistics). Relationship between randomization assignment and adherence to treatment (bivariate and multivariate statistics).
        ii. Completion of treatment: Did the participant finish the full 8- or 12-week course?
    b. Success of treatment: Yes/No achieved SVR at 12 weeks post treatment (univariate and bivariate statistics). Relationship between randomization assignment and success of treatment (bivariate statistics).

2. <u>Secondary data analysis</u> of demographic and clinical blood value data extracted from the electronic medical record and entered into Qualtrics will be downloaded as a single SPSS statistical software file (and Excel

files as backups). Univariate statistics will be used to describe the sample (frequency and percent) and report blood values (mean, standard deviation, minimum value, and maximum value).

iii. Qualitative interview data will be analyzed by two or more independent coders/study team members following a modified grounded theory approach. They will upload the interview transcripts into NVivo qualitative research analysis software to guide their coding efforts. A final set of prominent themes, subthemes, and exemplary quotations will be compiled and reported. As needed, a clinical member of the study team will serve as an adjudicator to resolve any coding discrepancies. We will aim for 95% coding consensus.