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### Authors

Nyamathi, Adeline

Salem, Benissa E

Lee, Darlene

et al.

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## Exploratory Assessment: Nurse-Led Community Health Worker Delivered HCV Intervention for Homeless Adults

**Adeline Nyamathi, ANP, PhD, FAAN [Distinguished Professor],**

University of California, Irvine, Sue & Bill Gross School of Nursing, Irvine, CA

**Benissa E. Salem, PhD, RN, MSN, PHN, CNL [Associate Adjunct Professor],**

University of California, Los Angeles, School of Nursing, Los Angeles, CA

**Darlene Lee, ND, MSW, BCB [Naturopathic Doctor],**

University of California, Irvine, Susan Samueli Integrative Health Institute

**Zhaoxia Yu, PhD [Professor],**

University of California, Irvine, Department of Statistics, School of Information and Computer Sciences

**Angela Hudson, RN, PhD., PMHNP [Associate Professor],**

Samuel Merritt University

**Sammy Saab, MD, MPH [Clinical Professor of Medicine and Surgery and Medical Director, Adult Liver Transplant Program],**

University of California, Los Angeles, David Geffen School of Medicine at UCLA, Los Angeles, CA

**Sanghyuk S. Shin, PhD [Associate Professor],**

University of California, Irvine, Sue & Bill Gross School of NursingIrvine, CA

**Alexandria Jones-Patten, MSN, RN [Graduate Student Researcher],**

University of California, Irvine, Sue & Bill Gross School of Nursing, Irvine, CA

**Kartik Yadav, MSCR, PGDPM, CRA [Research Director],**

University of California, Irvine, Sue & Bill Gross School of Nursing, Irvine, CA

**Mitra Alikhani [Research Assistant],**

University of California, Los Angeles, School of Nursing, Los Angeles, CA

**Richard Clarke, Lead Community Health Worker,**

University of California, Irvine, Sue & Bill Gross School of Nursing, Irvine, CA

**Alicia Chang, MD, MS [Regional Health Officer],**

Los Angeles County Department of Public Health, Community Field Services, Inglewood, CA

**Kathryn White, MD [Chief Medical Officer],**

Los Angeles Christian Health Centers, Los Angeles, CA

**Lillian Gelberg, MD, MSPH [Professor]**

\* **Corresponding Author:** Adeline Nyamathi, ANP, PhD, FAAN, 854 Health Sciences Quad, Office 4345, Irvine, California, 92697, anyamath@hs.uci.edu, (949)824-8932.

Exploratory Assessment: Nurse-Led Community Health Worker Delivered HCV Intervention for People Experiencing Homelessness

David Geffen School of Medicine at UCLA, UCLA Fielding School of Public Health, University of California, Los Angeles, Los Angeles, CA

## Abstract

**Background:** Getting and maintaining hepatitis C virus (HCV) cure is challenging among people experiencing homelessness (PEH) as a result of critical social determinants of health such as unstable housing, mental health disorders, and drug and alcohol use.

**Objectives:** The purpose of this exploratory pilot study was to compare a registered nurse-community health worker (RN/CHW)-led HCV intervention tailored for PEH, “I am HCV Free”, with a clinic-based standard of care (cbSOC) for treating HCV. Efficacy was measured by sustained virological response at 12 weeks after stopping antivirals (SVR12), and improvement in mental health, drug and alcohol use, and access to healthcare.

**Methods:** An exploratory randomized controlled trial design was used to assign PEH recruited from partner sites in the Skid Row Area of Los Angeles, California, to the RN/CHW or cbSOC programs. All received direct-acting antivirals. The RN/CHW group received directly observed therapy in community-based settings, incentives for taking HCV medications, and wrap-around services, including connection to additional healthcare services, housing support, and referral to other community services. For all PEH, drug and alcohol use and mental health symptoms were measured at month 2 to 3 and 5 or 6 follow-up, depending on HCV medication type, while SVR12 was measured at month 5 or 6 follow-up.

**Results:** Among PEH in the RN/CHW group, 75% (3 of 4) completed SVR12 and all three attained undetectable viral load. This was compared with 66.7% (n=4 of 6) of the cbSOC group who completed SVR12; all four attained undetectable viral load. The RN/CHW group, as compared to the cbSOC, also showed greater improvements in mental health, and significant improvement in drug use, and access to healthcare services.

**Discussion:** While this study shows significant improvements in drug use and health service access among the RN-CHW group, the sample size of the study limits the validity and generalizability of the results. Further studies using larger sample sizes are necessitated.

## Keywords

Hepatitis C Virus treatment; persons experiencing homelessness; RN-CHW intervention

## Introduction

Hepatitis C Virus (HCV) infection disproportionately impacts vulnerable populations including persons experiencing homelessness (PEH) (Beiser et al., 2019; Centers for Disease Control and Prevention [CDC], 2013; Khalili et al., 2022). The prevalence of HCV seropositivity among PEH in Southern California remains high, with recent rates ranging from 27% in Los Angeles (Gelberg et al., 2012) to 46% in San Francisco (Page et al., 2017). In the United States, the incidence rate of chronic hepatitis C was 40.7 cases per 100,000 people in 2020, with hepatitis C virus-associated deaths increasing by 4% from 2019 (CDC, 2020). Worldwide, it is estimated that greater than 3% of people are infected with HCV (Salari et al., 2022).

Among PEH, a significant risk factor associated with HCV infection is injection drug use (Khalili et al., 2022; Leach et al., 2021; Masson et al., 2020); other social determinants of health (SDoH) that predict poor HCV treatment outcomes include ongoing substance use (Khalili et al., 2022; Noska et al., 2017; Page et al., 2017), unstable housing (Arum et al., 2021; Nyamathi, Salem, et al., 2021; Stone et al., 2022), history of incarceration (Gelberg et al., 2012; Nyamathi et al., 2013); mental illness (Khalili et al., 2022; Leach et al., 2021; Page et al., 2017); being uninsured or supported by government-sponsored programs; and general mistrust of the health care system (Harris et al., 2016; Ward et al., 2021).

Despite the introduction of well-tolerated, direct-acting antiviral drug regimens designed to cure HCV infection (CDC, 2013; Grebely et al., 2018), PEH continue to experience significant delays in being screened and in progressing along the HCV care continuum, the steps along the pathway from identifying a person as infected with HCV to cure (Bush et al., 2019; Coyle et al., 2019; Hanlon et al., 2018). Since 2000, chronic liver disease or liver cancer has risen sharply (CDC, 2020). Although current guidelines recommend that persons who use drugs should receive HCV treatment (World Health Organization, 2016), a study of HCV-positive people who inject drugs in Maryland found 23% had ever been evaluated for HCV treatment by a provider and only 17% had ever started HCV treatment (Falade-Nwulia et al., 2019).

In a systematic review of barriers to HCV screening and treatment among PEH, Paisi et al. (2022) revealed factors which limited HCV screening among this population, including limited advocacy by shelter staff for HCV services and fear of testing HCV positive. In a qualitative study of factors impacting successful HCV screening and treatment completion among PEH, critical barriers to overcome included: 1) limited knowledge and misperceptions regarding HCV; 2) mistrust of healthcare providers; 3) active substance use, mental illness and chronic health conditions; 4) limited advocacy for HCV services by shelter staff; 5) social stigma against homeless persons; 6) decreased personal motivation to complete treatment; and 7) lack of financial incentives (Masson et al., 2020).

Moreover, once screened, initiation into HCV treatment has been low; ranging from 10–15% of PEH (Benitez et al., 2020; Coyle et al., 2019; Hawks et al., 2016). Barriers to HCV care have included factors such as lack of awareness of being HCV infected (Norton et al., 2014; Skeer et al., 2018), challenges in accessing health care (Fokuo et al., 2020; Nyamathi, Wall, et al., 2021), ongoing drug and alcohol use (Crowley et al., 2017), and limited HCV treatment availability (Norton et al., 2014). Further, SVR12 has ranged from 81% (Khalili et al., 2022) to 87.5% (Benitez et al., 2020).

In a shelter-based study located in San Francisco and Minnesota, 64% (n = 772) of PEH approached for HCV screening were screened; 21.1% (n=162) of the 762 eligible PEH were found to be HCV infected (Khalili et al., 2022), and of these, 66% had detectable HCV RNA. Among this group, 61.7% initiated treatment, and 81% achieved SVR12 (Khalili et al., 2022). However, as this study was shelter-based, it eliminated the non-sheltered PEH who are at even greater risk for being HCV infected (Fuster & Gelberg, 2019).

In an HCV screening and treatment study conducted in federally qualified health centers located in the high prevalence area of Skid Row, Central East Los Angeles, PEH who were both sheltered and non-sheltered were approached. While the percentages of people approached and screened were not disclosed, during this nearly 1.5-year study period, 6,767 PEH were screened for HCV. Among this group, 11.4% had detectable HCV antibodies, among whom 57.6% were viremic. Initiation into care was accepted by 13.3% (n = 59); with 87.5% having SVR12, revealing undetectable virus (Benitez et al., 2020).

Previous studies have also examined nurse-led, community health worker interventions on their impact on mental health, substance use, and access to healthcare (Nyamathi et al., 2022; Nyamathi, Salem, et al., 2021). In a single-arm, trial which tested a nurse-led, CHW trial to improve latent tuberculosis infection, Nyamathi and colleagues (Nyamathi, Salem, et al., 2021) found that anxiety decreased at three months. However, neither drug use, depression, or anxiety was associated with medication completion. Interestingly, there was significant and ongoing drug use decrease at 6-month follow up (Nyamathi et al., 2022). For instance, amphetamine, cannabis, methamphetamine significantly decreased at six-month follow up (Nyamathi et al., 2022). While healthcare access remained unreported, it's important to note that the intervention linked PEH with mental and physical health resources.

## Purpose

To our knowledge, no experimental study has been found which has evaluated the effect of a nurse-guided community health worker (RN/CHW) program to improve HCV treatment rates for PEH as compared to a typical standard of care program. Community health workers are effective, frontline, lay health leaders who can successfully link clients to vital health and social services (Perez & Martinez, 2008) and assist them through the HCV Care Continuum. In light of these strengths, we developed the RN/CHW intervention, "I am HCV Free", delivered to PEH who resided both in shelters and in unsheltered conditions (e.g., on the streets) aimed at attaining cure for HCV by SVR12, an indication of treatment success. Given the complex factors that affect HCV treatment adherence among PEH, particularly those who are unsheltered, we report an exploratory assessment of the intervention in terms of SVR12, as well as improvement in drug and alcohol use and mental health as compared with a clinic-based standard of care (cbSOC) program in a pilot RCT. The Community Health Seeking and Coping Paradigm (CHSCP) (Nyamathi, 1989) underpins the intervention model and the conceptual basis and design of the intervention as briefly described in the next section.

## Theoretical Health Seeking and Coping Framework

The Comprehensive Health Seeking and Coping Model (Nyamathi, 1989) served as the theoretical framework for this pilot study. It has been well utilized by the research team for decades, focused on promoting the health of PEH with chronic health conditions (Nyamathi, Salem, et al., 2021; Nyamathi et al., 2007; Nyamathi, Wall, et al., 2021; Nyamathi et al., 2006). Based on the CHSCP, several factors should be considered in the implementation of an intervention that will positively impact health outcomes (in this case, HCV treatment

completion). These include demographic, situational, social, behavioral, and psychological factors.

Demographic Factors include age, race/ethnicity, history of drug and alcohol use and current use status, county of origin, hepatitis status (all genotypes), HIV, and history of mental illness and incarceration. Situational Factors: Sheltered and unsheltered housing (i.e., homeless shelters, single residence occupancy dwellings, living in tents or under bridges, etc.). Social Factors: Social support by the CHW is thought to act as a resource by providing encouragement for health promotion. Behavioral Responses, such as drug and alcohol use are critical to address to promote HCV treatment completion and reduce risk for cirrhosis (Osna et al., 2017; Pateria et al., 2013). In addition, adherence is known to be impacted by a positive relationship between individuals and their healthcare providers (Masson et al., 2020; Nyamathi, Wall, et al., 2021).

Psychological Factors: Depression is correlated with reduced drug use (Jaffe et al., 2007). Guided by our community-based model, the RN/CHW intervention focuses on improving social support, coping skills, problem-solving, self-management, physical and mental health, drug and alcohol use, and stable housing.

## Methods

### Design

Following a formative phase of our study wherein a Community Advisory Board was formed to provide perspectives from PEH and health care providers of PEH regarding the intervention, we refined our RN/CHW HCV intervention, as reported elsewhere (Nyamathi, Wall, et al., 2021). Subsequently, a pilot randomized controlled trial was planned with 108 eligible PEH to assess initial efficacy data of the intervention on SVR12 and improvement in drug and alcohol use and mental health as compared with the clinic-based Standard of Care (cbSOC) program. The University of California, Irvine Institutional Review Board Human Subjects Protection Committee approved the study, and the University of California, Los Angeles relied on the UCI agreement. Data collection for Phase II was initiated on October 5, 2020.

### Sample and Setting

This pilot RCT took place in one of the largest geographical areas where PEH are concentrated in Los Angeles, a 54-block area called Skid Row, in which a 2022 point-in-time count revealed 9,204 PEH residing in both sheltered and unsheltered dwellings on any given night (Los Angeles Homeless Services Authority, 2022). Recruitment occurred between 10/05/2020 to 10/5/2022 in two community-based shelters, a needle exchange site, two community-based clinic settings serving PEH, and in outdoor areas. The inclusion/exclusion data are presented in Table 1.

### Consenting, Recruitment and Screening Procedure.

The CHWs visited the sites and posted approved flyers and conducted presentations in the lobbies of the sites where residents and visiting non-sheltered homeless adults awaited

services. After reading the initial informed consent with potential participants in a private area, a brief 2-minute structured questionnaire was administered by the CHWs to assess sociodemographic factors and HCV-related health history as well as month and day of birth and the first three letters of the mother's first name to identify repeaters. Subsequently, the CHWs conducted a preliminary HCV antibody assessment using the OraQuick HCV Rapid Antibody Test (OraSure Technologies, 2010).

Among those presumptive positive, a confirmatory HCV confirmation was conducted by the clinic staff, using HCV PCR. Once HCV was confirmed, the CHW and RN contacted the potential participants, and then escorted the potential participants back to the clinic for liver function tests and rapid HIV tests. Potential participants were also screened for hepatitis B virus infection by measuring HBsAg. Pretest and posttest counseling for HCV, HBV and HIV were performed by the RN for all participants. In addition, blood specimens from participants were assessed for liver disease severity using the aspartate aminotransferase to platelet ratio index (APRI) and/or FIB4 scores, which are noninvasive, accurate indicators of liver fibrosis (Loaeza-del-Castillo et al., 2008; Vallet-Pichard et al., 2007). As individuals with cirrhosis are at risk of decompensation and development of hepatocellular carcinoma, they were excluded from the study and referred for further care to the clinics' referral Gastrointestinal/Hepatologist. A positive rapid HIV test was also sent to the Los Angeles County Public Health Lab for confirmatory testing. The CHWs also collected data using a detailed locator guide to eligible participants to assure follow-up.

CHWs then brought the participants to the selected clinic physician (MD) or nurse practitioner for final clearance, based upon all test results. All those found to have HCV and successfully completed diagnostic testing were offered second level informed consent. Thereafter, trained research staff administered a 60-minute questionnaire, with periods of breaks and nourishing snacks. The health care providers at the study clinics (MDs or NPs under standardized protocols supervised by the clinic physician) provided the direct acting antiviral medication doses to the RN and CHWs which were then delivered by either the nurse-guided CHW in the community (daily directly observed therapy) or in the clinic setting (in one month supply) by the cbSOC MD/RN. The MDs also provided clinical support to the research team.

Tracking for follow-up and actual administration of the baseline and follow-up questionnaires (at 2/3, and 5/6 months) was conducted by the research staff. The variation of 2 versus 3 months and 5 versus 6 months relates to the varying indicated duration of treatment of different DAAs; that being Mavyret (glecaprevir/pibrentasvir) are prescribed for 2 months while Harvoni (ledipasvir/sofosbuvir) and Epclusa (sofosbuvir/velpatasvir) are prescribed for 3 months. Follow-ups then followed 3 months later. All participants were paid \$3 for the screening questionnaire, \$5 for the lab test for screening HCV and liver function tests, \$20 for the baseline assessment, \$25 for the 2/3 months follow up, and \$30 for the 5/6-month follow up completed. Completers of all aspects of the study received up to \$168 in cash over the 5 months. The RN/CHW group participants receive an additional \$1 incentive for each daily dose taken (56 to 84 doses x \$1= \$56 - \$84) as well as \$3 per session for a total of 8 sessions (\$24). The Research Electronic Data Capture (REDCap) randomization module enabled randomization by site (sheltered vs non-



sheltered) with allocation concealment, preventing alteration of the group membership once the participation was assigned.

### **RN/CHW Intervention – “I am HCV Free”**

A team of two CHWs and a research RN comprised the RN/CHW team. In the RN/CHW group, each participant was assigned to a CHW, who delivered all components of the program and assessed HCV side effects under the guidance of the RN. As designed, each CHW could be assigned up to 7–8 participants per cohort until the study enrollment was achieved.

See Table 2 for an outline of the RN/CHW HCV intervention and the cbSOC programs. Over the eight week program, the RN/CHW team delivered provided detailed information about HCV, reviewed the barriers to completion and assessed the needs of the participant in relation to the goals of completing treatment. Over the weeks, impact of using drugs and alcohol was discussed as a risk factor to treatment completion, and best coping scenarios were discussed in relation to treatment completion as well as reducing drug and alcohol use and improving mental health. Resources in the community were also facilitated.

The RN oversaw all components of the program, including assessing HCV side effects, referrals, and supported the CHWs in counseling with complex health-related issues. The RN also ensured the medication was picked up from the pharmacy and the correct dosage was provided for each participant, as administered by the CHW. Finally, the RN supported the CHW in selecting appropriate referrals for community services as needed. The CHW role included the following: After the first dose of the medication, the CHWs ran a brief (20 min) weekly in person, 1:1 education and 20 min case management session over the 8 weeks (see details of weekly elements below).

The CHWs had a case management role, for which they facilitated medical, mental health, drug and alcohol use, social service, and legal appointments for participants, as well as housing referrals, and accompanied the participants to the appointments as requested. The CHWs rigorously tracked participants who missed a dose, and promoted the building of effective coping skills, personal assertiveness, self-management, communication, and self-esteem. In the sessions, CHWs also educated PEH about HCV and prevention of hepatitis B Virus and HIV during individual appointments using educational tools such as anatomical models of the liver and Hepatitis flipcharts. Participants in the RN/CHW intervention were brought back to the clinic monthly for liver function tests. In the cbSOC group, all program delivery components were conducted by clinic staff as described in Table 2.

### **Fidelity of Program Implementation.**

During Phase 1, after the intervention was refined, together with the CAB, the study team developed the protocols, manuals, and process measures to strengthen the fidelity of the program and outlined study constructs, measures, and timeframes for data collection, recruitment, and randomization. **Process Measures.** Process logs were designed to ensure fidelity and included: 1) participant attendance and content log of educational sessions



delivered by the CHWs; 2) medication completion log; 3) lab results log; 4) medical/housing/social service referrals made; and 5) referral attendance.

### **Training of RN/CHWs.**

The RNs and CHWs underwent specific training to conduct the research study assessments and the RN/CHW HCV intervention. This included training by the investigative team on HCV, HBV, drug and alcohol addiction and mental health, key resources in the community, and training to become competent facilitators of HCV risk reduction. Our CHWs were also trained to deal with reactions of individuals who are determined to be HCV, HIV or HBV positive, in communication skills, and in providing psychosocial support.

Mock sessions were held with the two CHWs and RN by the investigators and the Project Coordinator to assess their skills in presenting the intervention. The CHWs met with the RN twice weekly and received support with the education sessions, implementing the program, delivering the medication, and in organizing the paperwork. Although it was expected that adverse events with the hepatitis medication would be quite low ( 5%), and may include fatigue, headache, nausea, diarrhea, and insomnia (Gilead Sciences, 2015), CHWs were trained to fill out logs that recorded any side effects relative to the medication doses received and monitoring any medication side effects on REDCap. All medical concerns were reported to the HCV treating physician at the clinic.

**Documentation** of notes on referrals made for clients and appointments kept were captured on REDCap (Harris et al., 2009) by enabling signatures on the tablets for both the participant as well as CHW. This process not only captured signatures but also date / time stamped the process, thereby maintaining the fidelity of the program.

### **Medication Adherence.**

For the RN/CHW group, the daily directly observed therapy delivery of hepatitis medication (Mavyret - glecaprevir-pibrentasvir; Epclusa - sofosbuvir-velpatasvir; or Harvoni - ledipasvir-sofosbuvir) were administered by CHWs and were documented on REDCap on a computer tablet each time the CHW observed the participant swallow a pill. The RN/CHW also took a photograph to record the consumption of the medication by taking a selfie with participants consuming the medication, signed the tablet, and recorded all responses and events so that the research nurse could verify the picture in the record and confirm that the dose was taken. This process was important since the nurse was not always together with the CHW. The photo/selfie was deleted once the research nurse matched it to the picture in the record and confirmed that the dose was taken.

For the cbSOC group, the clinic-based physician/nurse practitioner conducted a pill count monthly, based on the medications left in the pill bottle; each month, or at greater periods of time, the participant was scheduled to pick up the next monthly supply.

### **Missed Doses.**

For the RN/CHW group, any interruptions in HCV dosing were assessed individually with a focus on resuming the schedule in consultation with the overseeing clinician.

## Clinic-based Standard of Care

As an active control arm, two collaborating medical clinics cleared participants for both groups medically and prescribed the direct acting antiviral medication. These clinics were equipped with staff who conduct HCV screening in the community. In general, the clinics were fully functioning, and included nurses, physicians, case managers, pharmacy, and mental health services. HCV patients were provided education, supply of medication, generally for one month and return appointments every month. In addition, an HCV facilitator assisted their HCV patients throughout the HCV care continuum.

## Measures

Data were obtained at screening, baseline, and 2/3 and 5/6 month assessments.

**HCV Positivity Screening**—Positivity was assessed by the RN or the CHW using the OraQuick HCV Rapid Antibody Test (OraSure Tech.), a rapid assay for the presumptive detection of HCV antibody in fingerstick capillary blood, with sensitivity and specificity similar to FDA-approved assays. A reactive result was confirmed by collecting blood at the clinic from a subsequent venipuncture for testing for HCV RNA in blood, by polymerase chain reaction as a marker for HCV viremia (CDC, 2013).

**Primary Outcome: SVR12**—Sustained virological response (SVR12) was tested at 5/6-month follow up (12 weeks after treatment completion) via quantitative PCR testing for HCV RNA. A sample was determined to be undetectable if no HCV was detected in the blood sample. SVR at 12 weeks post-treatment has been concordant with SVR24, and is a reliable indicator of patient response to HCV treatment (Burgess et al., 2016).

## Secondary Outcomes

**Drug and Alcohol Use:** Texas Christian University Screen II (Knight et al., 2002; Simpson & Knight, 1998) was assessed during the past 3 months. Yes/No to each drug was assessed for use versus dependency. The total score ranged from 0 – 9; higher scores (> 3) correspond to the DSM drug dependence diagnosis.

**Mental Health:** Mental Health was assessed by the Mental Health Inventory-5, which has well-demonstrated reliability for detecting psychological disorders within the past month (Berwick et al., 1991). Reliabilities of .77 and .71 were found for women/men, respectively (Leake et al., 1997).

**Access to Physical and Mental Health Services:** Assessed during each session by asking PEH if they need any assistance with health and/or social services including, but, not limited to federal benefits assistance, birth certificates and identification, clothing, dental care, drop-in services, emergency shelter, faith/religious services, food, mental health, reentry programs, drug and/or alcohol use treatment, tattoo removal, and other. Responses include yes or no.

## Statistical Analyses

Basic demographic information was tabulated, and proportions were reported. The association between the treatment type and a categorical outcome was tested using Fisher's exact test; the association between the treatment type and a continuous outcome was tested using Wilcoxon's rank sum test. SVR12 was assessed for the entire enrolled sample, both those who completed SVR12 and those who did not in the intent-to-treat analysis. Missing/non-completed SVR12 data were labeled as treatment failure (Asselah et al., 2016).

We hypothesized that the "I am HCV Free" arm would lead to improved outcomes (SVR12) compared with the cbSOC arm; as a result, all p-values are one-sided.

## Socio-Demographics

Sociodemographics were measured at baseline: site, age, birthdate, gender, race/ethnicity, education, religion, employment, relationship status, country of birth, history of incarceration, homelessness history, drug and alcohol use history, and pregnancy status (if female).

## Data Management.

Interview data were captured electronically using REDCap (Harris et al., 2009), a secure, web-based application designed to support data entry and storage for research studies. Laboratory data were entered in separate REDCap electronic forms and merged with the interview data. Study data were then exported into SAS data files.

## Results

### Sociodemographics

In total, over 24 months (October 2020 to October 2022), 1,384 PEH were approached, and consented to screening; revealing 173 (12.5%) screened as presumptive HCV positive. Of 68 (39.3%) presumptive positive PEH who returned to the clinic for a confirmatory test for HCV, 68 (100%) were confirmed as HCV positive. Among these 68 eligible for further testing, 36 (52.9%) were determined as not eligible, due to either low viral count ( $n = 25$ ) or APRI scores  $>0.7$  ( $n = 11$ ). In total, 10 (14.7%) of all those determined to be HCV positive enrolled in the trial. Among presumptive HCV positive individuals (173), 69 (39.9%) were lost to follow-up, another 40 (23.1%) declined to continue consideration of treatment, and 28 (16.2%) were unable to complete clinic appointments to ensure meeting all criteria for enrollment due to moving out of town, incarceration, etc. See Consort diagram (Figure 1).

Among the 10 participants enrolled in the study, 4 were randomized to the intervention (aka RN/CHW "I am HCV free") group and 6 were randomized to the cbSOC group. Eight out of ten (3 intervention group, 5 cbSOC group) participants completed the 5/6 month follow up assessment. Overall, patients were predominantly male (80%), mean age 53.3 (SD 9.0), while 40% were Black and 30% White. 40% had no more than a tenth-grade education, including 20% with no more than an eighth-grade education. There was no significant difference between the arms in age, gender, race/ethnicity, and education.

### Sustained Virologic Response (SVR 12) at 12 Weeks

In the total sample, 7/10 (70%) of participants completed the SVR12 measure, our primary outcome. In total, 100% of participants who completed SVR12 demonstrated undetectable viral loads. Based upon intent-to-treat analysis, SVR12 was 75% for the intervention group (3/4) and 66% (4/6) for the cbSOC group ( $p = 0.667$ ). While completion of treatment was not considered a primary outcome due to its subjective nature, it was documented that all 6 cbSOC participants self-reported completion of treatment; while 3 or 4 RN/CHW participants completed HCV treatment based on DOT assessment.

### Mental Health

No statistically significant differences were found in improvement in mental health between the RN/CHW and the cbSOC+ programs. However, the cbSOC+ participants demonstrated a significant decrease in mental health wellbeing (mean=18, sd=18.8, one-side  $p=0.03$  for both paired t-test and Wilcoxon signed rank test). As a comparison, there is no noticeable decrease in the RN/CHW “I am HCV Free” arm (mean=1.3, sd= 20.5). These results suggest that the RN/CHW program is likely to show significant improvement in mental health with a larger sample size. See Figure 2 for the plot for all 10 participants.

### Drug and Alcohol Use

PEH enrolled in the intervention arm had statistically significant improvements in drug use as compared with the cbSOC group ( $p=0.046$ ) over the two month period. While a decrease in alcohol use was found among PEH enrolled in the intervention arm as compared with the cbSOC arm, it did not reach statistical significance ( $p=0.078$ ). See Figures 3 and 4.

### Access to Physical and Mental Health Services

At the final 5/6-month follow-up, we assessed whether PEH reported access to both physical and mental health services. A statistically significant difference was found among PEH enrolled in the intervention versus cbSOC programs ( $p=0.018$ ) in receipt of physical healthcare over the two-month period. In particular, at month 5/6 visit, 0 out of 5 (0%) cbSOC participants reported having access to care for physical health conditions while 3 out of 3 (100%) of the intervention participants had physical health access.

At the final 5/6-month follow-up, a statistically significant difference in access to mental health services was found among PEH enrolled in the intervention versus cbSOC programs ( $p=0.11$ ): 0 out of 5 (0%) cbSOC PEH reported having access to mental health services, while 2 out of 3 (66.7%) of the RN/CHW participants reported having mental health access.

### Discussion

In this pilot trial, we found that implementation of the RN/CHW “I am HCV Free” intervention program, delivered by a RN-CHW team in the community, was feasible for delivering DAA to PEH who are sheltered as well as unsheltered. SVR12 results were improved in the RN/CHW intervention arm compared with standard clinic-based delivery of care (75% vs 67%). Of participants who completed SVR12 testing, 100% reached SVR in both the intervention and cbSOC groups. Furthermore, participation in the

intervention group significantly decreased drug use, and increased access to physical and mental health services as compared to the cbSOC group. In addition, while not significant, participants in the RN/CHW program improved in mental health scores as compared to the cbSOC participants. In total, of the number screened for HCV, 12.5% were found to be presumptively positive; and among the 68 who selected to return for confirmatory testing, all screened HCV positive. However, over half, 52.9%, were excluded due to low HCV viral loads and high APRI scores. Among the eligible sample of 32 PEH, 10 (31.13%) were actually enrolled.

While the study sample size was not sufficient for statistically meaningful comparison of the primary outcome between the two study arms, we found that the intervention may be useful for achieving high HCV treatment success (75%). This was attributed to the CHWs' ability to bring the HCV medications to the PEH living in shelters or outdoor areas, providing the medications with supervision under daily DOT (vs traditional delivery of a determined portioned supply in the cbSOC arm), and/or providing a weekly incentive for each CHW session attended. While both groups received patient education that addressed the causes and risk factors of HCV (e.g., injection drug use, needle sticks) and the effects of alcohol and drug use on the body, CHWs were also more frequently involved in the client's care, with daily visits (vs possibly monthly visits in the cbSOC arm) and provision of supportive care and facilitation of linkage to health and housing services. PEH in the intervention group received social support in the form of accompaniment to appointments by CHWs and case management. Care provided by CHWs who come from the same community as the PEH may create strong provider-patient relationships which increase patient-reported quality of care and reduce health disparities (Barnett et al., 2018; Kangovi et al., 2018).

The finding of improvements in drug use and mental health within the RN/CHW intervention arm as compared with the cbSOC arm is promising, as mental illness and drug and alcohol use have been identified as significant barriers to HCV treatment (Khalili et al., 2022; Leach et al., 2021; Masson et al., 2020; Page et al., 2017). Within the general population, HCV infection has been linked to depression, with people infected with HCV showing 1.5–4.0 times the prevalence of depression as compared to the general population (Adinolfi et al., 2017). Cure of HCV infection with antiviral agents has also been associated with decreased symptoms of depression (Adinolfi et al., 2017); however, this does not explain the significant improvement in drug use and improvement in mental health between the intervention arm and the cbSOC. This difference may be explained by the intervention team connecting clients to auxiliary health services, such as mental health and substance use treatment. Due to the inverse relationship between housing access and mental health symptoms (Singh et al., 2019), linkage to housing services may also facilitate improvement in mental health symptoms.

Decreased drug use among both the intervention and cbSOC groups may be due to provision of HCV education regarding modes of transmission and risks of drug use and drug injection. The significant improvement in drug use within the intervention group may be attributable to linkage to drug treatment services and social support from CHWs. Indeed CHWs have specialized knowledge and language that allows them to build trust and transparency with clients who use drugs. CHWs may serve as an intermediary between the client who uses

substances and healthcare providers (Morgan et al., 2015). The intervention group also showed greater access to physical health and mental health services. This finding was surprising due to the control group receiving care in a clinic, where one would assume access to care was available. While greater access to health services may occur for a variety of reasons, study factors that may have contributed are CHW support in exploring health issues and areas of health need, CHW assistance with finding providers, making and keeping healthcare appointments and accompaniment to appointments. PEH in the intervention group may also have had increased motivation to utilize additional resources and services due to the education provided in the intervention teaching sessions regarding local health and social services resources.

This preliminary efficacy study has several major limitations. The first limitation is the small sample size, which was in part due to low enrollment of PEH testing presumptive positive in the study (12.5%) as well as low numbers of PEH testing HCV positive 68 (4.9%). In our study, 10 out of 68 eligible HCV positive (14.7%) were enrolled. Low enrollment may have been due to the COVID-19 pandemic as providers were overwhelmed with COVID-19 testing and vaccination and often unable to see potential participants and complete HCV testing in a timely manner. Delays were also due to difficulty in getting the DAAs approved by insurance companies using medicare or Medicaid. Low enrollment was likewise supported in the literature in terms of decreased screening and treatment of HCV (Kaufman et al., 2021; Nguyen et al., 2022). In the Benitez et al (2020) study, enrollment among eligible people living with HCV was 13.3%, during non-COVID-19 conditions, which confirms the general challenges of enrolling HCV positive PEH into treatment.

Secondly, among the HCV presumptive positive who did not proceed to enrollment, a significant number either did not respond to phone calls or attend arranged meetings. It is possible that a good number were concerned about going to a clinic setting during the COVID-19 pandemic due to fear of COVID-19 transmission. Further, as a number of shelters were in lock-down during the enrollment periods of the study (beginning in March 2020), screened participants were being relocated to many other areas in an effort to reduce numbers of PEH in sheltered areas.

The small enrollment may also relate to PEHs' existing knowledge of their HCV status and the desire to collect the screening incentive. Moreover, lack of knowledge regarding HCV may have also resulted in PEHs' aversion to be screened. While space and severe limitations on clinic resources is a reality, future studies might consider better integration of the community-based recruitment into the clinic logistics so that as eligible PEH are encountered, a smooth flow into the clinic operations might more readily be available.

Another limitation is the use of self-report indicators and the potential for social desirability bias, particularly regarding substance use, mental health, and access to care measures. However, our primary outcome was obtained from objective data, SVR12. Finally, another limitation is the lack of generalizability of the study to other settings, such as urban settings outside of Skid Row and rural areas.



Strategies for improving recruitment of a significantly larger sample will be critical to fully test the RN/CHW team model with “I am HCV Free”. This will include conducting additional focus groups and one-on-one interviews with medical and nursing providers in the community and evaluate collaborative recruitment models where clinic staff and CHW recruit side by side. We will also aim to understand ways to overcome insurance delays. Furthermore, anytime PEH had to wait longer than 30 minutes for an appointment, interest in continuing the recruitment process dwindled. Thus mitigating long wait times for PEH to undergo medical clearance will be of significant interest.

## Conclusions

This protocol and preliminary findings of the pilot RCT of “I am HCV Free”, an RN-CHW community-based delivery of HCV treatment to PEH, shows promise for delivering HCV treatment to untreated PEH, a most difficult-to-treat group who remain without HCV treatment despite the ease of administration and low side effect profile of DAAs. This community-based model of care utilizing RN/CHW teams might also help to address physical health, mental health, and drug and alcohol use among PEH, and improve their access to physical and mental health care. Future research will include testing this RN/CHW community-based care delivery model for delivering HCV in a larger sample and in other settings as well as delivery of other chronic disease treatments to PEH.

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## Data Availability Statement:

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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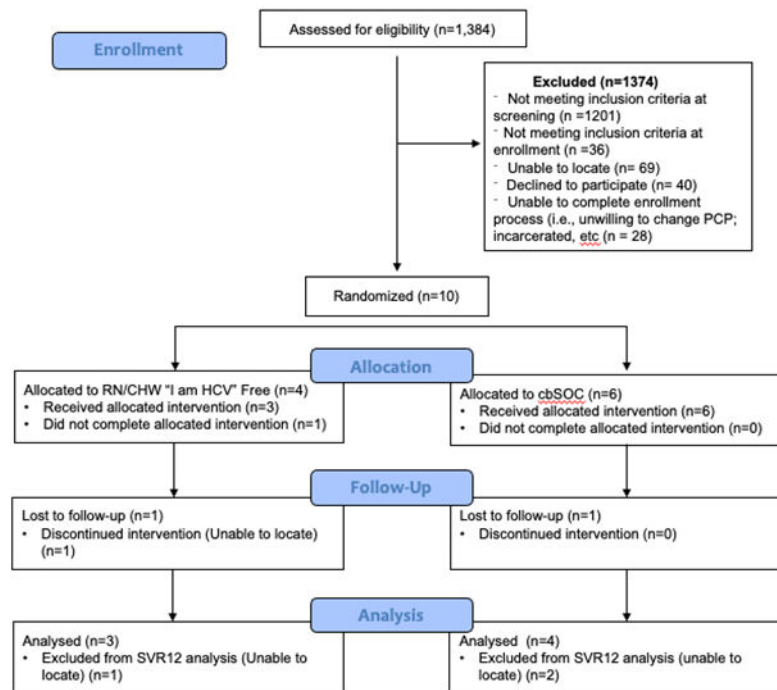
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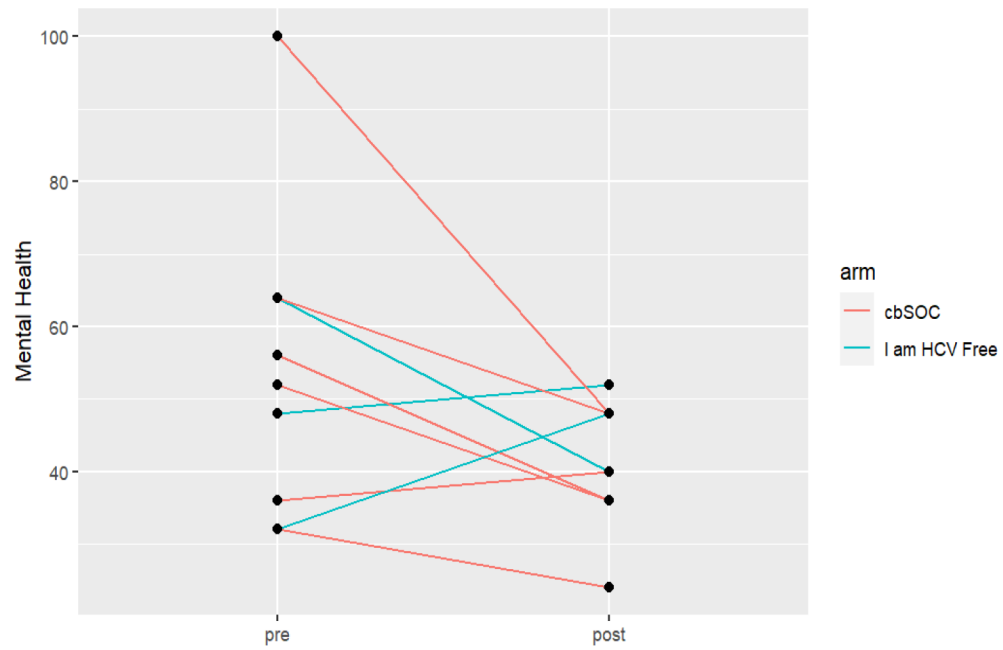


CONSORT 2010 Flow Diagram

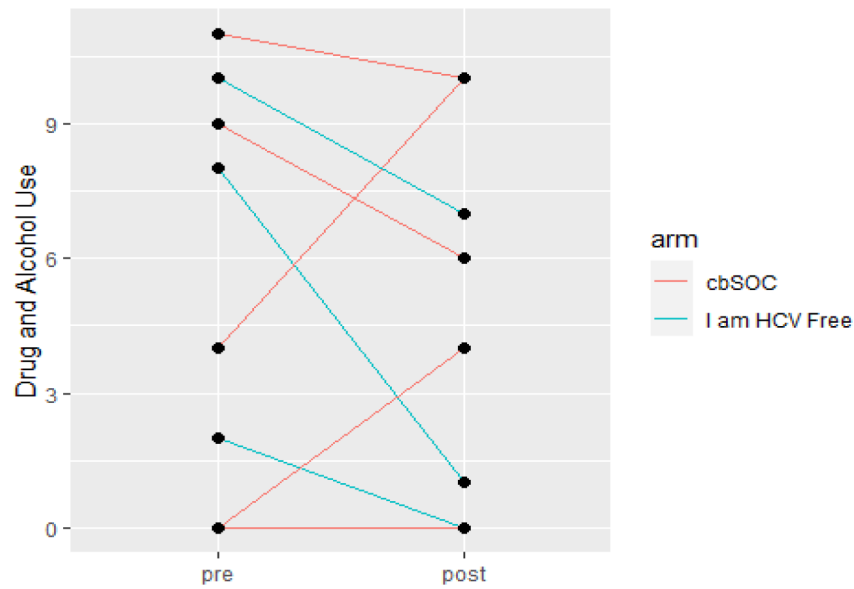
**Figure 1.**

Consort Diagram: Participant enrollment, allocation, and follow-up

Notes: Primary Care Physician, PCP; Registered Nurse/Community Health Worker, RN/CHW; Hepatitis C Virus, HCV; clinic-based standard of care, cbSOC; sustained virologic response-12, SVR12



**Figure 2.**  
Impact of RN/CHW “I am HCV Free” vs cbSOC on Mental Health as measured by MHI-5  
Notes: Registered nurse/community health worker, RN/CHW; hepatitis C virus, HCV;  
clinic-based standard of care, cbSOC; Mental Health Inventory-5, MHI-5.

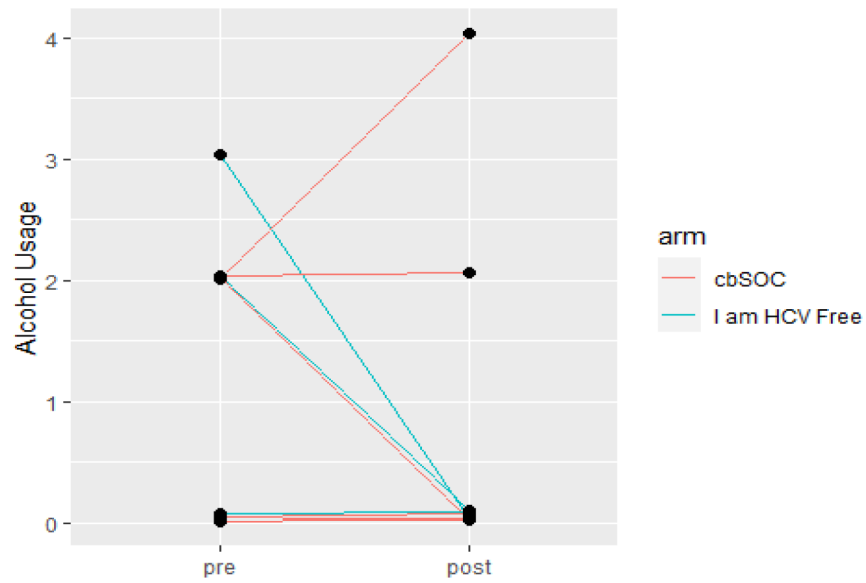


**Figure 3.**

Impact of the RN/CHW “I am HCV Free” and cbSOC on Drug and Alcohol Use as Measured by TCU Drug Screen 5

Notes: Registered nurse/community health worker, RN/CHW; hepatitis C virus, HCV; clinic-based standard of care, cbSOC; Texas Christian University, TCU.





**Figure 4.**

Impact of the RN/CHW “I am HCV Free” and cbSOC on Alcohol Use as Measured by the TCU Drug Screen 5

Notes: Alcohol use scores shown pre- and post-intervention for each participant in the “I am HCV Free” arm and cbSOC. Registered nurse/community health worker, RN/CHW; hepatitis C virus, HCV; clinic-based standard of care, cbSOC; Texas Christian University, TCU.

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Table 1

Inclusion and Exclusion Criteria for Enrollment

<u>Inclusion criteria:</u> includes PEH who report	
1) sleeping in the past night in a homeless shelter or place not meant for sleeping (e.g., car, abandoned building) or in outdoor areas (Housing and Community Development, 2022);	
2) HCV-positive as documented by laboratory results;	
3) 18 years of age; willing to have blood tests to be screened for HCV and testing HCV antibody positive;	
4) APRI 0.7, with no signs of advanced cirrhosis (jaundice, ascites, encephalopathy) and willing to undergo the abdominal ultrasound as the standard of care (at the clinic);	
5) History of substance use (past 5 years); and	
6) Able to provide informed consent and speak English or Spanish.	
<u>Exclusion Criteria:</u> PEH with	
1) History of past or current treatment for HCV;	
2) Current HBV infection;	
3) HIV infection and not receiving medications for HIV treatment;	
4) Testing pregnant; and	
5) Judged to be cognitively impaired.	

Notes: People experiencing homelessness, PEH; hepatitis C virus, HCV; Aspartate aminotransferase to platelet ratio index, APRI; hepatitis B virus, HBV; human immunodeficiency virus, HIV.

Table 2

Description of RN/CHW HCV Intervention and cbSOC Program

Week 1	Detailed information about the program is provided; personal values and goals are then delineated. Information is shared about HCV, its transmission, and risk reduction. Stigma associated with having HCV is discussed. Culturally-sensitive discussions are provided throughout about potential barriers to completing treatment, seeking healthcare access, etc. CHW works early on with their contacts in the community to facilitate securing stable housing.
Week 2-3	The impact of drug and alcohol use and its role as a risk factor for HCV, HBV and HIV is discussed, as well as gender-specific reasons why people use drugs. CHW actively works with participants to facilitate their attending outpatient drug and/or alcohol substance use programs, if actively using, and to continue their work in securing stable housing, job skills, and other goals, with support of the RN.
Weeks 4-6	CHW continues facilitating stable housing opportunities, reducing drug and alcohol use, and seeking health care access, etc. Basic problem solving in relation to reducing risk includes: a) identifying triggers that could increase use of substances; b) identifying a goal/outcome to reduce or avoid risk; c) identifying potential steps to reach the goal of reducing/avoiding risk; d) evaluation of usefulness of steps discussed; and e) planning how to act on the best solution. Coping scenarios provide examples of positively dealing with situations that place individuals at risk for on-going drug use. The importance of positive social relationships is discussed in supporting compliance with HCV treatment. The CHW also facilitates referrals to community agencies by making calls and walking participants to appointments. The intervention is gender-sensitive; for example, women may be engaged in discussing empowerment and the impact of depression on risk behaviors, while men may be engaged in discussions on risk behaviors.
Weeks 7-8	Continued discussions on problem-solving skills related to HCV/HIV risk reduction. Participants placed in stable housing are assessed to determine new needs relative to maintaining housing security, employment opportunities, etc.
Clinic-based Standard of Care (cbSOC) program	Delivered by a clinic-based MD or clinic-based NP at the clinic site. CHW conduct the interviewing/survey administration and follow-ups at the clinic-based site. The clinic NP conducts, per usual clinic-based-MD and/or NP, monthly visits over the 8 week program. Components include: 1) HCV pre-treatment education; 2) one-month supply of DAA; 3) monitoring adverse events; and 4) responding to questions on HCV. Referral to drug/alcohol and housing programs is provided as per standard of care. The cbSOC participants <b>do not receive the community delivery of the DAA, or accompaniment to needed services, but do receive case management as needed</b> . Outreach to find patients lost to follow-up is conducted by the clinics' outreach teams.

Notes: Registered nurse/community health worker, RN/CHW; hepatitis C virus, HCV; hepatitis B virus, HBV; human immunodeficiency virus, HIV.