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Effect of a Nurse-Led Community Health Worker Intervention on Latent Tuberculosis Medication Completion Among Homeless Adults

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Clinical Trial Registration: The protocol is registered with [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT03702049) at <https://clinicaltrials.gov/ct2/show/NCT03702049?id=NCT03702049&draw=2&rank=1>. The trial was registered October 10, 2018, and began on January 24, 2019.

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Abstract

Background: Tuberculosis (TB) disproportionately affects marginalized and impoverished homeless adults. While active TB can be prevented by treating latent TB infection (LTBI), individual factors, such as high prevalence of depression and anxiety, drug and alcohol use, and unstable housing, lead to poor LTBI treatment adherence and completion among homeless adults.

Objectives: We hypothesized that delivery of a tailored nurse-led, community health worker (RN/CHW) program across the LTBI continuum of care (e.g., screening, diagnosis, treatment) that delivers 3HP treatment³ (3HP; rifapentine plus isoniazid) for homeless adults (e.g., sheltered and unsheltered), and is tailored to their health and social service needs, will overcome existing treatment completion barriers. We also hypothesized that mental health symptoms (e.g., depression and anxiety), drug use score, and problematic alcohol use will decline over time among clients receiving this treatment.

Methods: We assessed the effect of delivering a theoretically guided, RN/CHW-based, single-arm study among eligible LTBI-positive homeless adults ($N=50$) on completion of a weekly, directly observed, 12-dose 3HP LTBI treatment in Central City East (Skid Row). Completing 3HP treatment was compared to the only known historical, clinic-based control that obtained 65% completion among homeless adults. Secondary outcomes included drug and alcohol use, depression, and anxiety.

Results: The RN/CHW program achieved a 91.8% 3HP treatment completion rate among homeless adults. Younger homeless adults (< 50 years old) were less likely to complete 3HP treatment compared to those who were older. Neither drug use, depression, nor anxiety was associated with 3HP treatment completion. Decrease in anxiety was observed at 3 months, but not at 6 months, compared to baseline.

Discussion: To our knowledge, the pilot study is the first to evaluate an effective RN/CHW delivered, community-based intervention, which can reduce the burden of active TB for homeless adults.

Keywords

LTBI medication; nurse-led community health worker; vulnerable population

Mycobacterium Tuberculosis (TB) is an infectious disease that can be fatal (National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, 2018). While the incidence and prevalence of TB have been on a decline for nearly the last 3 decades (Centers for Disease Control and Prevention [CDC], 2020d), current data show that in 2019 there were 8,916 new cases of TB and an estimated 13 million people were living with latent TB infection (LTBI) (CDC, 2020e). This decline is due in part to current strategies to manage TB in the population (Schwartz et al., 2020).

In the United States, there are two promising approaches to eradicate TB. One approach targets LTBI before it develops into the transmittable, symptomatic, and deadlier active TB disease. The other approach focuses on treating one of the high-risk groups: homeless adults

(Diel et al., 2013). Homeless people are disproportionately affected by TB. In 2019, 4.5% of individuals with new cases of TB were experiencing homelessness despite just 1% of the U.S. population experiencing homelessness in a given year (CDC, 2020a; CDC, 2020b). A previous study demonstrated that homeless adults are more likely to contract TB and spread it to others due to their high contact rates with other homeless adults (Dowdy et al., 2014). Therefore, focusing on this specific group rather than the larger general population may be an efficient and cost-effective approach likely to significantly affect the TB incidence and prevalence rates (Dowdy et al., 2014).

Notably, there are significant barriers to effectively lowering TB rates among homeless populations; one such barrier is low treatment adherence. Homelessness is significantly associated with an increased likelihood of discontinuation of treatment (Sandul et al., 2017). Compared with the general population, homeless adults are 2.3 times more likely not to complete treatment (Bamrah et al., 2013).

Substance use and mental health disorders, such as depression and anxiety, are possible significant contributors to low adherence (Franke et al., 2008; Pachi et al., 2013; Ugarte-Gil et al., 2013; Volkmann et al., 2015). Similarly, social support has been noted to be a significant factor in substance use recovery (Majer et al., 2020) and may contribute to LTBI treatment adherence and completion. While rates vary among homeless subpopulations (e.g., veterans, men who have sex with men) and homeless adults in separate studies, about 28% (Fletcher et al., 2014) to 37.2% of homeless adults have co-occurring substance use and mental health disorders (Ding et al., 2018).

Earlier studies have administered 12-dose 3HP LTBI treatment (3HP; rifapentine [RPT] plus isoniazid [INH]) to homeless populations of men, women, and children without the use of a nurse-led, community health worker (RN/CHW)-based model with some success (completion rates of 76.6% and 81.2%; Nwana et al., 2019; Sandul et al., 2017). However, little is known about the barriers to treatment completion when engaging an RN/CHW treatment model. Thus, it may be essential to address co-occurring substance use and mental health symptoms in LTBI treatment to improve LTBI treatment adherence and completion.

The primary goal of this study was to assess the effect of a community-based RN/CHW intervention on 3HP treatment completion, as compared with local historical community health, Skid Row clinic control group. We hypothesized that the delivery of the RN/CHW program across the LTBI continuum of care (e.g., screening, diagnosis, treatment) that delivers 3HP treatment for homeless adults (e.g., sheltered and unsheltered) and is tailored to their health and social service needs will overcome existing LTBI treatment completion barriers. We also hypothesize that mental health symptoms (e.g., depression and anxiety) and drug use, and problematic alcohol use, will decline over time among clients receiving the treatment.

Comprehensive Health Seeking and Coping Paradigm Guiding Theoretical Framework

The Comprehensive Health Seeking and Coping Paradigm (Nyamathi, 1989), which served as the theoretical guide for this study, has been utilized most recently among populations with significant health disparities (Garfin et al., 2020; Nyamathi et al., 2014, 2017; Nyamathi, Shin, Salem et al., 2018; Nyamathi, Shin, Smeltzer et al., 2018). Based on the framework, health behaviors are influenced by behavioral, psychosocial, and environmental factors (Nyamathi, 1989) and promote community-engaged research to strengthen social support, decision-making and problem-solving skills, reduction of substance use, and stable housing.

Addressing these underlying factors can inform individualized treatment that leads to improved adherence. **Behavioral Factors:** As substance use is a significant barrier to adherence, we have assessed the effect of drugs and alcohol on completion of LTBI treatment (Noel et al., 2008; Rehm et al., 2009). **Psychosocial Factors:** Emotional distress is likewise associated with substance use behaviors in homeless adults (Ibabe et al., 2014), and improvement in this area may affect completion of 3HP treatment. **Environmental Factors:** Unstable housing among homeless adults (Onwubiko et al., 2019; Zhang et al., 2020) can be a major barrier to LTBI treatment completion and necessitates intervention during LTBI treatment; the less chaotic an individual's lifestyle, the more likely health needs will become a priority. Understanding and addressing these underlying factors can inform individualized treatment that leads to improved access to care by improving communication stability to access health services as well stable transportation and adherence processes.

Methods

A single-arm study was used to assess the effect of a community-based, RN/CHW intervention on completion of 3HP treatment among homeless adults diagnosed with LTBI compared to a clinic-based, historical control group. The control group had attained a 66% 3HP LTBI treatment completion rate among homeless adults administered treatment in Skid Row (Chang, 2016). The single-arm trial was appropriate because the purpose of this pilot study was to obtain preliminary evidence of the efficacy of the intervention. Follow-up was conducted at 3- and 6-months posttreatment initiation. In total, 416 homeless adults were screened. Of these, 48 were determined as ineligible as determined during the screening process as ineligible criteria (previous LTBI treatment completion, not homeless, not interested, no history of mental illness, substance use, and medical care while homeless, not willing to take a blood test, and not willing to take medication). In addition, 153 were lost to follow-up after the screen. A further 215 were ineligible after the screen due to negative Purified Protein Derivative (PPD), negative (Quantiferon TB Blood Test (QFT), found to have been previously treated for LTBI, not interested in continuing, moved out of state, chest X-ray (CXR) positive, and HIV positive (Figure 1). The follow-up completion rate for both 3- and 6-month follow-up was 94%. The University of California, Irvine, Institutional Review Board (IRB) Human Subjects Protection Committee approved the

study, and the protocol is registered with [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT03702049) (NCT03702049). The data were collected between January 24, 2019, and May 29, 2020.

Sample and Setting

The sample included homeless adults ($N=50$) diagnosed with LTBI who were screened and cleared for active TB disease and resided in the Skid Row area of Los Angeles, Service Planning Area 4. Participants were included if they met the following inclusion criteria: (a) self-reported homeless adults, (b) ages 18–60, (c) willing to provide informed consent, and (d) reported current or recent substance use within the last 12 months. A homeless person was defined as anyone who spent the previous night in a public or private shelter or on the streets (Hoben, 1995). Participants were recruited from at least 10 shelters and unsheltered sites (e.g., tents).

Participants were excluded if they met the following criteria: (a) screened as having active TB or currently treated for TBI, as they would either need to be treated more aggressively with TB medications if diagnosed with active TB, or they would currently be treated for LTBI; (b) history of treatment for active TB or TBI; (c) a serum aspartate aminotransferase (AST) level of five times the upper limit of normal, a contraindication for current LTBI medications; (d) HIV infected and not receiving antiretroviral therapy; (e) pregnant; and (e) judged to be cognitively impaired. The CDC guidelines state that HIV-infected persons can receive 3HP if the person is taking antiretroviral medications with acceptable drug–drug interactions with rifapentine (CDC, 2016). Based on CDC recommendation, 3HP is not recommended during pregnancy because its safety during pregnancy has not been studied (CDC, 2020c).

Development of RN/CHW 3HP LTBI Intervention, Protocol and Manuals, Tailoring Intervention to PEH

Prior to implementing the RN/CHW intervention, a community advisory board (CAB) of persons experiencing homelessness (PEH) was established to identify perspectives of homeless adults, who had undergone LTBI treatment, and integrate those perspectives in the development of a multicomponent intervention to increase LTBI acceptance and treatment completion. After that, focus groups were held with PEH ($n=11$) to evaluate acceptability and feasibility of the 3HP LTBI intervention (Salem et al., 2020). Based on the CAB and focus group sessions, an intervention manual was developed that incorporated focus-shared areas (i.e., comprehensive health and social services approach, medication side effects, inclusion of goal setting, use of incentives, knowledge of homeless community).

Procedures

Recruitment, Informed Consent, and Compensation—A well-trained RN and CHWs visited shelters and informed residents frequenting the sites about the study. Approved flyers were posted, and informational session presentations were given by the staff in the lobbies of the shelters where residents and visiting homeless awaited services. After informed consent was administered, a brief 2-min structured questionnaire, which assessed TB history, followed. All potentially eligible participants were escorted to our community-based partner clinic in Skid Row and were tested with a blood assay using

QuantiFERON-TB Gold Plus (QFT-Plus), a Tuberculin Skin Test alone, or a combination of screening with the Tuberculin Skin Test followed by the QFT-Plus, as well as other routine testing (i.e., liver function and HIV tests). LTBI positive homeless adults were escorted back to the clinic and completed a CXR to rule out active TB.

Following a subsequent clinic visit, all eligible participants were cleared for 3HP treatment for LTBI and were administered a second informed consent, followed by a 60-min questionnaire that assessed general health and psychosocial and behavioral variables. All participants were paid \$3 for the screening questionnaire, and if eligible, \$5 for further laboratory tests at the clinic and \$20 for the completion of baseline measures.

RN/CHW LTBI Program Training and Competency Evaluation

Upon development of the intervention protocol, the RN/CHW team was trained to deliver the 3HP LTBI intervention. The team was composed of a research RN and four part-time CHWs. CHWs were selected because they were formerly homeless adults who had transitioned out of homelessness, had excellent social skills, were positive role models, and had knowledge of the community and culture of homelessness. During the research team training, each member completed human subjects and HIPAA training, quizzes evaluating knowledge, baseline and follow-up questionnaire administration and mock training, and case studies of PEH with corresponding discussions. After the research leadership team introduced all content and knowledge that was assessed verbally using discussions, role play, and teach-back methods, the RN/CHW team was evaluated by the primary investigator and research investigators using a comprehensive competency checklist.

Development of RN/CHW 3HP LTBI Weekly Operations, Fidelity Monitoring, and Oversight

During the study implementation, a weekly operations and fidelity report on Research Electronic Data Capture was used to track outreach (e.g., flyer distribution, recruitment, information sessions, screening), participant clinic appointments (e.g., lab tests, CXRs, PPD test/CXR test result), physician clearance, daily monitoring, weekly activities, and sessions. On a daily basis, the RN/CHW team reported to the research investigators and project coordinator. Every week, the research team went over the weekly operations, discussed, and evaluated research study progress. Based on these reports, concerns that arose during intervention implementation were addressed using constant evaluation, brainstorming, and creative approach to mitigating further challenges were discussed.

Intervention: RN/CHW Intervention Delivery

Each CHW was assigned seven to eight participants. At a mutually convenient time, the RN/CHW team met weekly with participants, under the direction of the RN, and assessed any side effects before the next dose. If none, the CHW provided directly observed treatment in a screened and private area. After the first dose of 3HP treatment, CHW conducted weekly one-on-one, 20-min case management sessions over 12 weeks, where detailed information was provided about the program, along with coaching support to identify personal values and goals participants set for themselves. Education about TB and LTBI, its dangers, and the need for support to counteract the barriers of drug and alcohol use and mental health issues to 3HP medication completion was provided. Participants were

encouraged to apply the problem-solving model to different hypothetical situations that served as triggers to engage in substance use, etc. Progress was reviewed in overcoming barriers to medication adherence and appointment keeping.

The team also provided health and social service referrals (e.g., physical, mental health, substance treatment, housing, etc.) and regularly tracked (detailed searching) participants who missed a 3HP dose. This tracking process was explained during the consenting process. If the participant failed to meet the team for the next dose, the team would begin making calls to reconnect based upon locator information provided by the participant. This process occurred when a dose was missed on a specific date, or a follow-up appointment was missed. Based on guidelines, participants who received 11 of 12 doses over 16 weeks were considered completers (Curry International Tuberculosis Center, 2012). Those who had a gap of > 4 weeks between doses were noncompleters and were encouraged to restart the treatment.

Historical Control Group—In our comparison group, the historical control was provided the 3HP LTBI treatment to PEH attending a clinic (Chang, 2016). As a result of an outbreak in the Skid Row area of Los Angeles in 2014, the county investigated and screened 727 homeless adults. Over two thirds of the sample were between the ages of 35–54, while the remainder were 55 and older. Three quarters of the sample were equally distributed as Black or Hispanic, while 13% were White and 2% were Asian. Among the 727 screened, 159 (21.8%) were LTBI positive, and 107 (67.3%) were recommended for 3HP treatment. Among the 56 who initiated treatment, 37(66%) completed treatment (Chang, 2016).

Instruments

In this study, the primary dependent variable was completion of a 12-dose 3HP LTBI treatment compared to a historical, clinic-based control group that obtained 66% completion among homeless adults. Secondary outcome variables included an assessment of decline over time of the mental health symptoms of depression and anxiety and the drug use score and problematic alcohol use.

Independent Variables

Sociodemographic Factors included age, gender, race/ethnicity, country of birth, and housing history (e.g., own/living with family or friends; shelter, street, living with family, friends).

General Health was measured using five items from the general health perceptions subscale of the RAND 36–Item Short-Form Health Survey (SF–36; Ware & Sherbourne, 1992). Participants responded to five statements, such as “my health is excellent” or “I expect my health to get worse,” with response options ranging from “true” to “definitely false,” and end points 100, 75, 50, 25, and 0, with several items reverse scored. A total score was determined by calculating the average, where higher scores of 80+ were termed as “a more favorable,” followed by a score of 60–80 as “favorable,” and scores of < 60 as “less favorable” perception of health. For this measure, Cronbach’s $\alpha = 0.78$.

Social Support was measured using the Medical Outcome Study (MOS) Social Support Survey (Sherbourne & Stewart, 1991); a 19-item instrument that assesses availability of social support and includes four subscales: emotional/informational support (eight items, $\alpha = 0.95$), tangible support (four items, $\alpha = 0.94$), positive support (three items, $\alpha = 0.98$), and affectionate support (three items, $\alpha = 0.96$). Participants respond on a 5-point Likert scale, ranging from 1 (*none of the time*) to 5 (*all of the time*), with higher scores indicating more social support. We have thus labeled the scores as *high* (75+), *moderate* (25–74), and *low* (< 25) social support. An overall support index was also calculated ($\alpha = 0.98$).

Primary Dependent Variables

3HP Treatment Completion.—As further clarified in the data analysis section, treatment completion was calculated by totaling the number of doses completed by each individual, with completion defined as 11 of 12 doses. The percent of treatment completion was calculated using 95% confidence intervals (CIs).

Secondary Outcome Variables

Drug use score and problematic alcohol use, as well as the mental health symptoms of depression and anxiety, were assessed to observe the effect on the primary outcome of treatment completion, as well as decline over time, and constitutes secondary outcomes of this study. These variables were of critical importance as they are historically considered significant barriers to treatment completion.

Drug Use Score and Problematic Alcohol Use was measured using the Texas Christian University (TCU) Drug Screen 5 (Institute of Behavioral Research, 2020), a 17-item measure that screens for mild to severe substance use disorder (SUD) per the Diagnostic and Statistical Manual for Mental Disorders 5 (DSM–5). Participants indicated either “yes” or “no” responses to substance dependency questions and frequency of drug use based on a 5-point scale from 1 (*never*) to 5 (*daily*). The TCU Drug Screen 5 is scored on a point system, ranging from 0–11. Participant scores correspond to the number of symptoms endorsed by the participant and the severity of SUD, including mild disorder (2–3 points), moderate disorder (4–5 points), or severe disorder (6 or more points). Problematic use of alcohol and specific drugs was defined as self-identified as being a problem (TCU Item #12) or daily consumption. For this measure, Cronbach’s $\alpha = 0.89$.

Depression was assessed using the Center for Epidemiological Studies Short Depression Scale-Revised (CESD–R-10): a 10-item measure used to screen for depression (Eaton et al., 2004). This scale assesses depressive symptoms using a 4-point Likert scale that reflects the frequency of a symptom in the past week, ranging from 0 (*rarely or none of the time*) to 3 (*most of the time*). Example items include, “I was bothered by things that don’t usually bother me,” “I felt depressed,” and “I felt fearful.” Responses are summed (range 0–30); a total score above 10 indicated depression. Reliability was good (Cronbach’s $\alpha = 0.79$).

Anxiety was measured using the Generalized Anxiety Disorder–7 (GAD–7), a seven-item self-report instrument used to screen and assess for anxiety, using a 4-point Likert scale ranging from 0 (*not at all*) to 3 (*nearly every day*; Spitzer et al., 2006). Example items

include, “worrying too much about different things,” “trouble relaxing,” and “not being able to control worrying.” Scores were summed and ranged from 0 to 21. The severity of anxiety was determined with cut-off scores 5 (*mild anxiety*), 10 (*moderate anxiety*), and 15 (*severe anxiety*). In this study, reliability was very good (Cronbach’s $\alpha = 0.87$).

Data Analysis

Descriptive statistics, including frequency and percentages, were computed for all variables. We assessed reliability of psychosocial scales used in our study by estimating Cronbach’s alpha. Our primary outcome was 3HP treatment completion, defined as completing 11 of 12 3HP doses. We estimated this outcome by dividing the number of participants with treatment completion by the total eligible participants and calculated the 95% CIs using the scoring method. The lower bound of the 95% confidence limit as compared to 66% historical completion to assess successful improvement. We used mixed-effects models to account for within-participant correlation across time for the secondary outcomes of changes in drug use severity, anxiety, and depression scores.

For each model, the secondary outcome was specified as the dependent variable, time point as an ordinal independent variable, and subject identification as the random variable. We also investigated the changes in problematic use of alcohol (binary outcome, yes vs. no) over time by fitting a generalized estimating equation to account for repeated measures over time for each subject. R v4.0.2 packages Hmisc, gee, and lme4 were used for analysis (R Core Team, 2020).

Results

Participant Characteristics

The baseline sample of eligible participants included 50 homeless adults who were diagnosed with LTBI. See Table 1 for baseline descriptive statistics of homeless adults. Among homeless participants, just over one third (38%) were over 60 years old, and about a third were equally divided among the group 50–59 years old or under 50 years old. Nearly three quarters ($n = 37$) were male, and 64% ($n = 32$) were born in the U.S. About two thirds (64.3%) lived in a shelter in terms of housing, while about 1 in 4 lived on the streets. Latinos comprised 42% of the sample, and almost half (46%) were Black. Self-report perception of general health varied among the participants. Drug use was relatively common: 22% reported mild/moderate drug use, and 14% ($n = 7$) reported severe drug use. Further, nearly one third (30%) reported problematic alcohol use.

Completion of 3HP LTBI Treatment at 3 Months

One participant stopped 3HP treatment based on physician recommendation among the enrolled participants, as his QFT test came back negative after five doses. Thus, the follow-up sample size was 49. Among the 49 participants, almost all completed 3HP treatment (91.8%; $n = 45$). The lower bound of the 95% confidence limit was 80.8%—higher than the 66% treatment completion evidenced in the historical comparison control. At 3-month follow-up, younger age (< 50) was significantly associated with lower odds of 3HP treatment completion ($p = .005$; Table 2). While no significant differences were found in the

completion of 3HP in terms of other patient characteristics, it was noted that men were less likely to complete than women.

Completion of 3HP Treatment by Substance Use and Mental Health Symptoms

As illustrated in Table 3, we assessed the association of traditionally significant challenges that homeless adults experience when attempting to complete the 3HP medication treatment. There was no association of completion of 3HP treatment with any category of drug use disorder, alcohol use, or drug treatment motivation. Similarly, depression, anxiety, and knowledge did not have a statistically significant association with treatment completion.

Change in Substance Use and Mental Health Over 3 and 6 Months

To assess the effect of the RN/CHW treatment program on mental health, drug use symptoms (TCU score), and problematic alcohol use, we assessed change over time at 3- and 6-month follow-up. As illustrated in Table 4, only anxiety exhibited a statistically significant decline from baseline to 3 months ($b = 2.13, p = .007$) and a trend-level decrease from baseline to 6-month follow-up ($b = 1.38, p = .093$).

Discussion

LTBI is a critical issue among homeless populations due to the significant risk of developing active TB among this vulnerable population. We assessed the effect of a community-based, nurse-led CHW intervention on 3HP medication adherence compared to a clinic-based, historical control group on LTBI treatment completion (Chang, 2016). Our novel findings revealed that the use of the RN/CHW program achieved a 91.8% 3HP medication treatment completion rate, significantly surpassing the 66% historical, clinic-based control rate. While prior studies have noted the importance of addressing LTBI among homeless populations (Aldridge et al., 2018; Nyamathi et al., 2007), none have assessed the utility of an RN/CHW team on LTBI medication adherence.

Notably, there was no association between 3HP medication completion and substance use (i.e., drug or alcohol use) at 3- or 6-month follow-up. While this association has been reported with active TB (Franke et al., 2008) in other studies, further exploration in future studies will be critical as it relates to LTBI in larger samples. Our findings also indicated that depression and anxiety symptoms had little effect on 3HP completion.

Contrary to our hypothesis that mental health symptomology was a critical factor that typically would affect 3HP treatment completion among homeless adults diagnosed with LTBI. However, as just stated, our findings indicate that depression and anxiety symptoms had little effect on 3HP completion. A possible explanation is that the RN/CHW team regularly accompanied homeless adults to routine health care visits, as well as scheduled appointments for mental health symptomology (i.e., depression, anxiety). The present study raises the possibility that a comprehensive LTBI continuum of care approach (e.g., screening, diagnosis, linkage to treatment and care) by caring peers, such as that provided by this RN/CHW team, can successfully improve not only LTBI treatment adherence but other health and social service needs. Future research should be undertaken to quantify the health and social service referrals, along with the costs associated with this delivery model.

Surprisingly, while no significant differences emerged between completion of 3HP treatment and other participant characteristics, one unexpected finding at 3-month follow-up was that younger age (< 50) was significantly associated with less 3HP treatment completion. It can be argued that homeless adults less than 50 years of age may be employed and possibly experience more challenges with scheduling, along with lack of interest in consuming 3HP. To understand this area, future research necessitates applying the transtheoretical model of behavioral change (Prochaska et al., 2009; Prochaska & Velicer, 1997) to this intervention to assess the varying levels of readiness for behavior change (e.g., medication adherence, substance use).

Interestingly, men were less likely to complete 3HP as compared to women. These findings necessitate further examination of the differences in receptivity of a RN/CHW intervention among men compared to women. Our RN/CHW team was disproportionately composed of women ($n = 3$) compared to men ($n = 1$). Although in our preliminary Phase 1 findings, participants shared that participants would equally welcome both genders, it is plausible that the disproportionate gender composition of the team affected 3HP completion. This is an important issue for future research on the effect of the composition of research teams in LTBI Directly Observed Therapy.

While not significant, another finding was that there were differences in 3HP completion depending on the location of where homeless adults reside. In particular, those living in shelters were less likely to complete 3HP than homeless adults who resided in the street or lived temporarily with family. Given that the team frequented at least 10 different agencies, it is plausible that some sites were more restrictive and did not want participants to have program interference as compared to other sites. Indeed, some participants could not leave facilities for extended periods due to the varying program requirements making it more difficult for the RN/CHW team to deliver LTBI.

It is important to bear in mind the possible limitations of these findings include a single-arm study, which was compared to historical control in a large, urban city. Importantly, a sizeable majority of the potential participants screened failed to return for test results. This could be a critical biasing factor in interpreting the results of the study. In addition, the sample size was small, and because the study was underpowered, we were unable to detect improvements in mental health symptoms or drug use that might exist and be associated with treatment completion. Further, as these results were conducted in a small 54-block radius in Los Angeles (Skid Row), these results cannot be generalized to rural homeless or other populations. Future research necessitates conducting a large randomized controlled trial.

Taken together, these results demonstrate a successful RN/CHW team that successfully attained nearly a 92% 3HP treatment completion rate among homeless adults. Despite the challenges of current substance mental health issues and unstable housing, most homeless adults completed 3HP treatment. This most likely resulted from the compassion, support, and dedication the CHW offered to the PEH, depending on the need presented. Given the high levels of 3HP treatment completion and program engagement, an RN/CHW program

may be an effective intervention delivery model that specifically meets homeless adults' health and social service needs.

Despite these promising results, unanswered questions remain, and these findings raise intriguing questions. Given our findings that men were less likely to complete 3HP treatment than women, should the intervention be gender-sensitive, tailored, and adapted differently for them? Secondly, given that younger homeless adults were less likely to complete 3HP treatment, should interventions be tailored differently for homeless adults who are younger than or older than 50 years of age? How can the LTBI continuum of care approach (e.g., screening, diagnosis, linkage to treatment and care), utilizing an RN/CHW team improve LTBI treatment completion, and health and social services referrals translated into a community-based setting? A final consideration, as this study was ending as COVID-19 began, how can an RN/CHW team deliver 3HP with similar medication adherence results? Should telehealth be used to oversee the program? Overall, these questions need future investigation with larger sample sizes using a two-arm design to further assess and examine these research questions.

Conclusions

As LTBI disproportionately affects PEH, we proposed the first-ever study to assess the effect of an RN/CHW program on completion of 3HP among homeless adults. Our findings have resulted in a treatment completion rate of 91.8%. Importantly, neither drug use, depression, nor anxiety was associated with 3HP treatment completion (all $p > .05$). Findings lead the way for more robust clinical trials.

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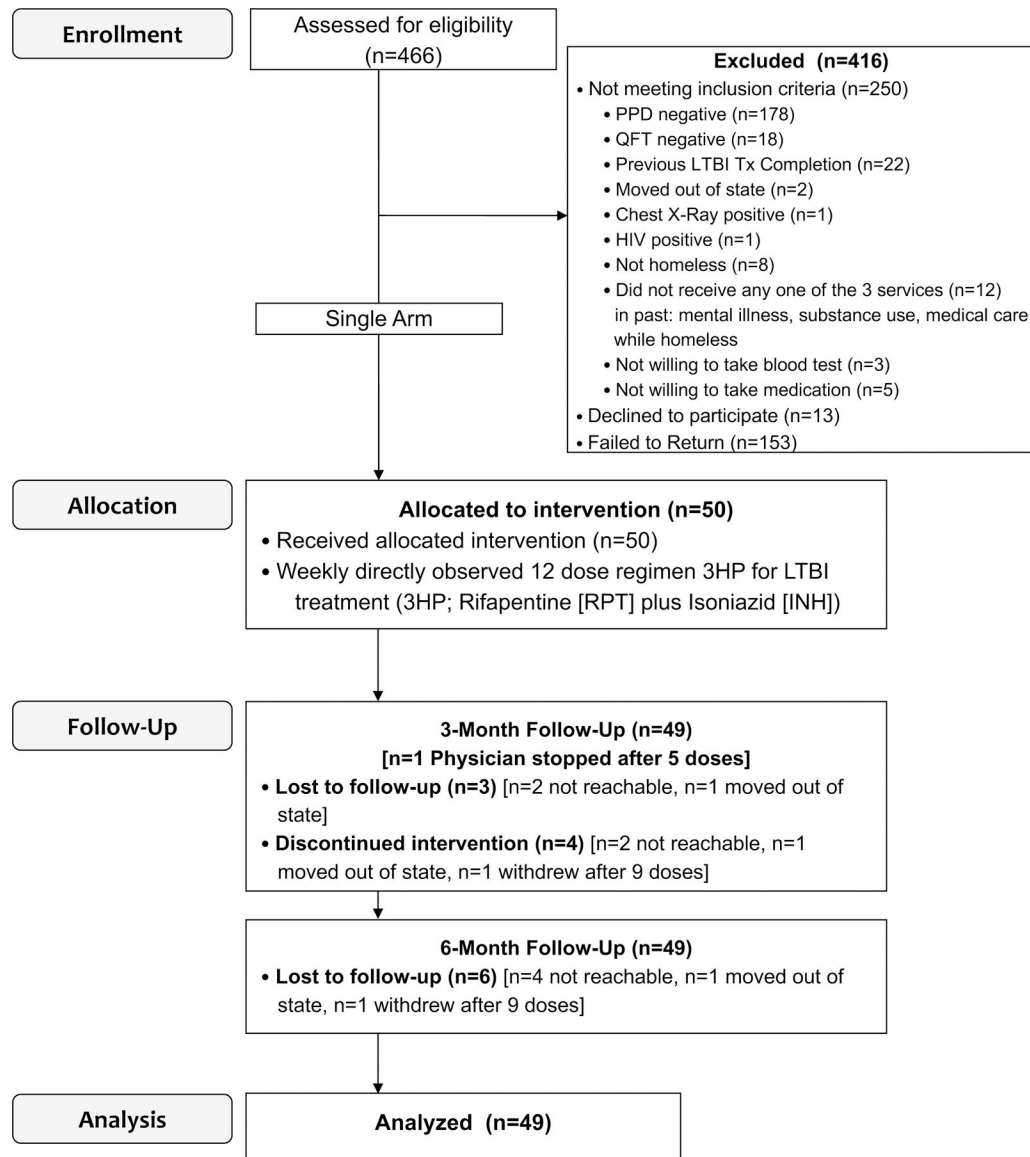
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Figures 1.
CONSORT Flow Diagram

Table 1

Characteristics of People Experiencing Homelessness on 3HP Treatment (N = 50)

Characteristic		N (%)
Age	<50	15 (30)
	50–59	16 (32)
	60+	19 (38)
Gender	Male	37 (74)
	Female	13 (26)
Race/Ethnicity	Latino	21 (42)
	Black	23 (46)
	Other	6 (12)
Country of Birth	Non-US	18 (36)
	US	32 (64)
Housing History	Own Apt/Family/ Friend	7 (14)
	Shelter	32 (64)
	Street	11 (22)
General Health Score	Less favorable perception of Health	18 (36)
	Favorable Perception of Health	14 (28)
	More favorable perception of Health	18 (36)
Drug Use Category	No Disorder	32 (64)
	Mild/Moderate	11(22)
	Severe	7 (14)
Problematic Alcohol Use		15 (30)

Note. 3HP = 12-dose treatment of rifapentine (RPT) plus isoniazid (INH); US = United States; Apt = apartment.

Table 2

3HP Treatment Completion by Participant Characteristics (N = 49)

Variable	3HP LTBI Treatment Completion	
	n/N	% (95% Confidence Interval)
All Participants	45/49	91.8 [80.8, 96.8]
Age	<50	10/14
	50–59	16/16
	60+	19/19
Gender	Male	32/36
	Female	13/13
Race/Ethnicity	Latino	19/21
	Black	21/22
	Other	5/6
Country of Birth	Non-US	17/18
	US	28/31
Housing History	Own Apt/Family/Friend	7/7
	Shelter	27/31
	Street	11/11
General Health Score	Less Favorable	17/18
	Favorable	14/14
	More Favorable	14/17

Note. 3HP = 12-dose treatment of rifapentine (RPT) plus isoniazid (INH); n/N = number of subjects completing 3HP treatment/total number of subjects within the category; US = United States; Apt = apartment.

Table 3

Baseline Findings of 3HP Treatment Completion by Substance Use and Mental Health (N=49)

Variable		3HP Treatment Completion	
		n/N	% [95% CI]
Drug Use Category	No disorder	28/31	90.3 [75.1, 96.7]
	Mild/moderate	10/11	90.9 [62.3, 99.5]
	Severe	7/7	100 [64.6, 100]
Alcohol Use	No	31/34	91.2 [77.0, 97]
	Yes	14/15	93.3 [70.2, 99.7]
Drug treatment motivation	Low	38/42	90.5 [77.9, 96.2]
	High	7/7	100 [64.6, 100]
Social Support	Low	13/14	92.9 [68.5, 99.6]
	Moderate	17/19	89.5 [68.6, 97.1]
	High	15/16	93.8 [71.7, 99.7]
Depression	No	27/29	93.1 [78, 98.1]
	Yes	18/20	90 [69.9, 97.2]
Anxiety	None	22/25	88 [70, 95.8]
	Mild	15/16	93.8 [71.7, 99.7]
	Moderate/Severe	8/8	100 [67.6, 100]

Note. 3HP = 12-dose treatment of rifapentine (RPT) plus isoniazid (INH); n/N = number of subjects completing 3HP treatment/total number of subjects within the category.

Table 4

Change in Mental Health and Substance Use Measures Over 3 and 6 Months Compared to Baseline (N = 49)

Variable	3 Month		6 Month	
	b	p	b	p
Depression	-0.31	.719	0.43	.626
Anxiety	-2.13	.007	-1.38	.093
TCU Score ^a	-0.24	.603	-0.12	.805
	OR [95% CI]	p	OR [95% CI]	p
Alcohol Use	0.83 [0.39, 1.79]	.642	0.49 [0.18, 1.34]	.165

Note. TCU = Texas Christian University; OR = odds ratio.

^aTCU Score ranges from 0 to 11 corresponding to the number of substance use-related symptoms reported by the participant.

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