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BARRIERS AND FACILITORS OF HEALTHCARE USE AMONG PEOPLE WHO
INJECT DRUGS

DISSERTATION

A dissertation submitted in partial fulfillment of the
requirements for the degree of Doctor of Philosophy in the
College of Nursing
at the University of Kentucky

By

C. Brooke Kuns-Adkins
Lexington, Kentucky

Director: Dr. Terry Lennie, Professor of Nursing
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2019

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ABSTRACT OF DISSERTATION

BARRIERS AND FACILITORS OF HEALTHCARE USE AMONG PEOPLE WHO INJECT DRUGS

Hepatitis C Virus (HCV) is an infection that can have grave consequences when left untreated. Hepatitis C can be easily eradicated with direct acting antiviral therapy. People who inject drugs (PWID) and inmates are among those with the highest incidence of HCV. However, cure rates among this population remains low. This is, in part, related to an interruption in the HCV care cascade such that only 30% of PWID are linked to care and only 8% of those receive treatment. Inadequate screening and failure to be linked to HCV care remain the largest impediments to treatment success. There is limited research on barriers and facilitators to primary care, where screening may take place, and linkage to HCV care among PWID. Few studies have evaluated vulnerable populations such as those living in rural communities or inmates.

The purpose of this dissertation was to develop a broader understanding of barriers and facilitators to healthcare utilization among PWID at the primary care and specialist levels (linkage to care). Three manuscripts addressed important gaps in knowledge. The first was a review of the literature to describe the state of science on linkage to care among PWID. All but one reviewed study recruited from countries with universal healthcare, urban areas, and opioid substitution facilities. The review of the literature revealed that little is known about the barriers/facilitators to linkage to HCV care faced by rural-dwelling PWID from countries without universal healthcare.

The second manuscript is a study to determine whether predictors of linkage to care identified in urban-dwelling PWID from countries with universal healthcare predicted seeking HCV care among PWID living in rural Appalachia. Data were obtained from a subsample of 63 HCV positive PWID who recently used opioids, were between the ages of 18-35 years, and lived in one of five rural counties in Kentucky. Logistic regression revealed that recent injection drug use was the only predictor of seeking HCV care. However, remote use of opioid substitution therapy and no transportation issues approached clinical significance.

Although not evaluated in our second manuscript, seeing a primary care provider (PCP) is associated with an increased likelihood of being linked to care and higher rates of screening/diagnosis. Among rural dwelling PWID, there are subpopulations that may face unique barriers to linkage to care. One sub-population that may be particularly

vulnerable are female PWID who are incarcerated. Therefore, the purpose of the third study was to determine predictors of primary care use using data from 302 female inmates from rural Appalachia with a history of injecting drugs. Age, insurance issues, and health problems that interfere with responsibilities were predictors of PCP use.

In this dissertation, I have addressed important gaps in the literature by determining barriers and facilitators to seeking HCV care and primary care use among PWID from rural Kentucky. Additional studies are needed using a larger sample of rural PWID to confirm our findings. In addition, further studies should evaluate system and provider level barriers to linkage to care and PCP use among rural PWID.

KEYWORDS: Linkage to care, hepatitis C, primary care use, predictors, people who inject drugs, rural

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BARRIERS AND FACILITORS OF HEALTHCARE USE AMONG PEOPLE WHO
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CHAPTER 1. INTRODUCTION

1.1 An overview of hepatitis C virus

Hepatitis C virus (HCV), a blood-borne viral infection, is a national health concern with high prevalence and incidence rates. There are approximately 2.4 million persons living with chronic HCV in the United States (U.S.).¹ In 2016, an estimated 41,200 new acute cases of hepatitis C were diagnosed.² Injection drug use remains the leading cause of HCV in the U.S. with an estimated 53% of people who inject drugs (PWID) infected with HCV.³ Thus, examining ways to improve injection drug use treatment can enhance our understanding of ways to curb the high rates of HCV in the U.S.

Left untreated, HCV can have serious consequences including porphyria, glomerular nephritis, cryoglobulinemia, cirrhosis, hepatocellular carcinoma, and subsequent death.⁴ In 2007 alone, there were 15,106 deaths related to HCV, surpassing deaths associated with human immunodeficiency virus (HIV) in the U.S.^{3,6} Up to one fifth of persons with chronic HCV infection develop cirrhosis, making HCV the principal reason for liver transplantation in the U.S.^{3,5} The morbidity and mortality rates due to untreated chronic HCV infection are expected to climb over the next few decades, resulting in 1.76 million persons developing cirrhosis, 1 million dying of HCV-related complications, and 400,000 developing hepatocellular carcinoma.⁷ An estimated 1-5% of persons with chronic HCV will die from cirrhosis or hepatocellular carcinoma.³ HCV-related morbidity and mortality can be prevented with prompt curative treatment, yet less than 10% of persons with chronic HCV infections receive treatment. Therefore, it is crucial to address barriers and optimize access to evidence-based treatments among those with HCV infections.^{6,8}

1.2 Hepatitis C virus care cascade

The cascade of care, or care continuum, is a framework originally designed for persons with HIV, but has been also applied to persons with HCV.⁸⁻¹⁰ While there is no universal consensus on definition,⁸ the World Health Organization defines the HCV care continuum as progression through screening/diagnosis, treatment, cure, to chronic post-treatment care as needed.¹¹ At least seven stages have been identified: (1) being infected with HCV; (2) screening for HCV antibody and being made aware of infection status; (3) accessing specialty care; (4) receiving confirmatory HCV RNA test; (5) undergoing fibrosis assessment; (6) being prescribed HCV treatment; and (7) achieving a sustained virologic response (SVR) or cure.⁴ An eighth stage has been proposed- prevention of reinfection in high-risk groups after being cured.¹² Alternatively, the Infectious Disease Society of America and the American Association for the Study of Liver Diseases use a simplified framework of three major time points: screening, linkage-to-care, and treatment uptake.¹³ Based on this simplified framework, screening is the process by which at risk persons are identified and tested for HCV antibodies followed by confirmatory testing with nucleic acid test (i.e. HCV RNA), when appropriate;¹³ linkage-to-care is the process by which patients are evaluated by a practitioner who can manage and treat HCV infection; and treatment uptake is the process of receiving HCV treatment.¹³⁻¹⁴

Although PWID are at the highest risk for contracting HCV, they are the least likely to be cured. An examination of a cross-sectional surveillance system of 2,222 PWID in Australia found that 89% had received HCV antibody testing in their lifetime of which 57% tested positive.⁴ Nearly half of those who tested positive for HCV antibodies, completed a HCV RNA test (confirmation testing).⁴ Of those completing testing, 76%

had detectable HCV RNA, but, unfortunately, only 31% were linked-to-care an HCV specialist.⁴ Among those linked to care, 8% received treatment, and 3% achieved a cure.⁴ Hence, despite the availability of highly effective antiviral therapy, cure rates remain low among PWID; which, in part, may be attributed to a breakdown in progression through the HCV care cascade.

Fundamentally, appropriate screening, diagnosis (being made aware of having HCV), and referral to a healthcare specialist are necessary for successful treatment. Primary care providers (PCP's), are well positioned to screen, diagnose, and refer patients to a HCV specialist. In fact, people who follow with a PCP are nearly four times as likely to be assessed by a HCV specialist (linked to care).¹⁵ Unfortunately, PWID underutilize primary care services; this is more pronounced in rural communities.^{3, 6}

Underutilization of PCP services is an important factor which compromises proper care for PWID. Even less is known about barriers/facilitators to PCP use among rural-dwelling PWID. Moreover, to my knowledge, there are no published reviews of the literature or meta-analysis on linkage to HCV care among PWID. Most research on linkage to care among PWID has been conducted in urban areas and in countries with universal healthcare. Therefore, the purpose of this dissertation was to develop a broader understanding of the barriers and facilitators to healthcare utilization among rural-dwelling PWID at the primary care level (screening) and at the specialist level (linkage to care).

The subsequent chapters of this dissertation represent the foundation of my program of research. First, a review of the literature was performed to establish the state of science on barriers and facilitators to linkage to HCV care among PWID. In all but one

of the studies, participants were recruited from urban areas and in countries with universal healthcare. Subsequently, a secondary data analysis was conducted to determine if barriers/facilitators to seeking HCV care in rural-dwelling PWID in the US were similar to those among urban-dwelling PWID from countries with universal healthcare. Finally, because primary care use is a crucial first step to being screened and referred to a HCV specialist, we conducted a secondary data analysis to determine predictors of primary care use among rural-dwelling PWID.

1.3 Summary of subsequent chapters

Chapter Two is a review of the literature to determine barriers and facilitators associated with linkage to HCV care among PWID. PubMed, Ovid, CINAHL, MEDLINE, and PsychINFO were searched using the following terms: access, HCV care continuum, HCV care cascade, barriers, facilitators, factors, injection drug use, linkage-to-care, treatment evaluation, and hepatitis C. Given the limited research on this topic, no time constraint on publication date was imposed. Twenty-three of the 134 articles identified during the initial searches met inclusion criteria and were reviewed. Articles were excluded if the majority of the sample was not PWID or the majority were co-infected with HIV. Seven articles met selection criteria. In all but one reviewed study, participants were from large urban cities, in countries with universal health care, and from addiction clinics. Little is known about factors associated with linkage to care in rural-dwelling PWID who likely have less access to care and fewer resources.

Chapter Three is a secondary data analysis of PWID living in rural Appalachia. The purpose of the study was to determine whether factors identified in urban populations predicted seeking HCV care among PWID living in rural Appalachia. In the

parent study, data were collected using an online survey from 249 people who use drugs, aged 18-35 years, who reported living in one of five rural counties in Appalachian Kentucky, and using opioids in the last 30 days. We described the progression through the HCV care cascade for the 115 participants that reported a history of injecting drugs. Sixty-three of those PWID, reported testing positive for HCV antibodies. Logistic regression was run using data from these 63 participants, to determine if child caregiver status, recent injection drug use, transportation issues, homelessness, and the absence of criminal issues were predictors of linkage to care (operationally defined as self-report of seeking treatment for HCV).

Seeing a PCP is associated with a lower risk of infection and an increased likelihood of being screened and linked to HCV care.¹⁵⁻¹⁷ Therefore, we examined existing literature to determine what is known about barriers/facilitators of PCP use among PWID and found that little is known about this topic. Furthermore, to our knowledge, none of the published studies had an exclusive sample of rural dwelling or incarcerated PWID. Therefore, Chapter Four is a secondary data analysis to determine predictors of PCP use among incarcerated female PWID living in rural Appalachia. Data were selected from the 302 participants who reported a history of injecting drugs from a larger randomized control trial. Anderson's Behavioral Model of Health Services Use was used as a framework to identify independent predictors of PCP use from predisposing factors, potential enabling factors, and healthcare needs. Multivariate logistic regression analyses, using data from the 302 PWID, were used to determine predictors of primary care use.

Chapter Five is a synthesis of the results from Chapters 2, 3, and 4 in reference to how they contribute to the state of science on healthcare utilization among rural PWID.

CHAPTER 2. BARRIERS AND FACILITATORS TO LINKAGE TO CARE: A REVIEW OF THE LITERATURE

Abstract

BACKGROUND: Hepatitis C virus (HCV), a blood-borne viral infection, disproportionately affects people who inject drugs (PWID). However, PWID are the least likely to receive HCV treatment due to difficulty navigating the HCV care continuum.

PURPOSE: Conduct a review of literature to describe the state of science on barriers and facilitators associated with linkage-to-care among PWID. **METHOD:** PubMed, Ovid, CINAHL, MEDLINE and PsychINFO searches using the following terms: HCV care continuum, HCV care cascade, barriers, facilitators, factors, injection drug use, linkage-to-care, and hepatitis C. **RESULTS:** Seven articles met selection criteria. Barriers to linkage-to-care at the patient-level included ongoing substance use, limited knowledge or understanding to make an informed decision, competing priorities, and symptoms. Provider-level facilitators included clinical manifestations (i.e. elevated liver enzymes and diagnosis of cirrhosis) and a trusting patient-provider relationship. Distance traveled, lack of transportation, forgetting appointments, and early appointment times were system-level barriers to linkage-to-care. Barriers and facilitators are most frequently assessed in urban-dwelling PWID. Little is known about barriers faced by their rural counterparts. **DISCUSSION:** Future research should be dedicated to exploring the barriers and facilitators faced by rural-dwelling PWID from countries without universal healthcare.

2.1 Introduction

Hepatitis C virus (HCV) disproportionately affects persons who inject drugs (PWID) with an estimated 30% of PWID between 18-30 years old infected with chronic HCV.¹ HCV infection can easily be eradicated with treatment success rates approaching 100%.² In spite of advancements in antiviral therapy, the percentage of PWID who are cured remains low.^{3,4}

Successful treatment requires progression through a three step HCV care cascade: (1) screening, (2) linkage-to-care and (3) treatment uptake.⁴ Screening is the process of testing at risk persons for HCV antibodies and nucleic acid test (when appropriate) and then making him/her aware of their status.⁴ Linkage-to-care is the process of being evaluated by a HCV specialist and treatment uptake is the process of taking prescribed treatment.⁴ However, successful treatment is rarely achieved, as most people are lost along the care cascade. In a large cross-sectional study of PWID, an estimated 31% of those with an active infection were linked to care, 8% were treated, and 3% were cured.³ The largest dropout occurred between diagnosis and linkage-to-care with a nearly 70% attrition rate occurring after screening and diagnosis.³

PWID are disproportionately burdened with complex social, medical, and psychiatric co-morbidities that generate difficulties navigating the HCV care continuum.⁵ A better understanding of factors that affect linkage to care is needed to improve cure rates. Therefore, the purpose of this review was to describe the state of the science regarding barriers and facilitators to linkage to HCV care among PWID.

2.2 Methods

2.2.1 Search Strategy and Selection Criteria

PubMed, Ovid, CINAHL, MEDLINE and PsychINFO databases were searched using a combination of the following search terms: access, HCV care continuum, HCV care cascade, barriers, facilitators, factors, injection drug use, linkage-to-care, treatment evaluation, and hepatitis C. No time constraint was enforced given the limited available literature. Article reference lists were examined for additional relevant studies. Articles were included if they were from peer-review journal articles, published in English, and examined barriers/facilitators to linkage-to-care. Articles were excluded if less than half of the sample were not injection drug users and if all participants were co-infected with human immunodeficiency virus (HIV).

The initial search yielded 134 articles. The titles of all 134 articles were reviewed for relevance. A total of 106 articles were either duplicates or did not evaluate linkage-to-care. The abstracts of the remaining 28 were reviewed. Five additional studies were eliminated because they did not include barriers/facilitators to linkage-to-care. Among the remaining 23 articles, 17 were eliminated because the majority of the population did not have a history of injection drug use, or the sample was almost exclusively co-infected with HIV. Six articles met inclusion and exclusion criteria. Review of reference lists yielded one additional study. No meta-analyses on linkage to HCV care among PWID

2.2.2 Data Extraction

Components of the study of interest were extracted and organized in a chart (see Table 1). Barriers and facilitators were categorized according to three levels- patient, provider and healthcare system. Patient-level barriers are related to patient characteristics

such as race, education or socioeconomic status. Provider-level barriers included a healthcare provider's knowledge, bedside manner or experience with a specific population and/or condition. System-level barriers are those that occur because of the infrastructure or design of the healthcare system. For example, the distance between one's home and the nearest doctor's office. Some barriers and facilitators could be conceived as fitting multiple levels. In these cases, the level was determined based on a consensus among authors.

Barriers and facilitators were further grouped under themes. At the patient level they were grouped under: drug use, patient symptoms, HCV knowledge, fear, and social factors. At the provider level they were grouped under: clinical findings and patient-provider relationship. At the system-level, barriers and facilitators were grouped together as there were not enough variations to develop themes. Variables that were not predictors of linkage-to-care were not included in the results.

2.2.3 Quality Assessment

Quantitative studies were assessed for bias using the Scottish Intercollegiate Guidelines Network (SIGN) (Table 2).⁶ The SIGN is used to rank the quality of studies as high, acceptable or low using a 10-item checklist with the following domains: subject selection, methodology, confounding variables, and statistical analysis.⁶ SIGN is recommended for critiquing cohort studies.⁶ Qualitative studies were assessed for bias using the Critical Appraisal Skills Programme (CASP) Check List (Table 3).⁷ The CASP is a 10 question check list that evaluates the rigor of methodology, validity of the results, and the value of the study findings on the local community.⁷ There are no scoring systems for the SIGN or CASP.⁶⁻⁷ All seven articles were assessed by two independent

readers and disagreement was resolved with a third reader. Overall, bias was relatively low (Tables 2 and 3).

2.3 Results

Two studies were qualitative,⁸⁻⁹ four were quantitative (two cross-sectional and two cohort studies)¹⁰⁻¹³ and one was mixed methods.¹³ Four studies were conducted in Australia,^{8,10-11, 14} two in Ireland^{9, 13} and one in Greece.¹² In all seven studies, patients were recruited from addiction-based clinics or community service facilities. Only two studies were conducted after direct acting antiviral therapy became standard of care.^{12, 13}

2.3.1 Patient Level

2.3.1.1 Drug Use

On-going and recent drug use emerged as a barrier to linkage-to-care in four of the seven reviewed articles.^{9-10, 13, 14} Continued substance abuse including injection drug use and alcohol use were associated with poor attendance to consultation with a HCV specialist.^{13, 9} In a cross-sectional study, participants who were receiving Opioid Substitution Treatment (OST) or reported injecting drugs in the last 6 months were less likely to report having been evaluated by a HCV specialist.¹⁴ Conversely, persons who had not injected drugs in the last six months were more likely to attend specialty consultation.¹⁰ None of the authors suggested reasons for why ongoing drug use was a barrier. Potential reasons could include lack of referral, which is a provider-level barrier or persons who have recent or ongoing drug use may not be willing/able to prioritize HCV treatment, which is a patient-level barrier. Persons with recent drug use may also

believe that they must be sober for a specified amount of time prior to being treatment eligible and, therefore, do not attend their consultation visit—also a patient-level barrier.

2.3.1.2 Lack of Symptoms

HCV infection is often asymptomatic. Being asymptomatic or the perception of being physically well, is associated with low rates of engagement with treatment services.^{8-9, 11} Participants in a qualitative study reported that being asymptomatic or feeling well was a reason for not seeking care while a decline in physical health or presence of symptoms attributed to HCV was a motivator for seeking care.⁹ In contrast, participants with HCV-related symptoms were more likely to have seen a HCV specialist.¹¹ While it was not possible to determine if this was attributed to provider referral or an individual seeking treatment, it is clear that the presence or absence of symptoms was an important factor in treatment engagement.

2.3.1.3 HCV Knowledge

HCV-related knowledge was noted to be a facilitator in three of the seven articles.^{8-9, 14} Greater HCV knowledge (transmission, treatment options) and an understanding of the potential severity of untreated HCV were associated with a higher likelihood of being linked-to-care.^{8-9, 14} In contrast, a lack of knowledge about the diagnosis, the required workup, and treatment options emerged as barriers to seeking care.⁹

2.3.1.4 Fear

Fear also served as both a patient-level barrier and facilitator. Specifically, fears regarding side-effects of treatment, having a liver biopsy, the inefficacy of treatment, and

self-injecting PEGylated Interferon were barriers.^{8-9, 13} Surprisingly, one of these studies¹³ was conducted after DAA therapy which is known for fewer side effects. In addition, persons who reported hearing positive accounts from those who received HCV treatment (and therefore had less fear) were more likely to receive HCV care.⁸⁻⁹ Persons who witnessed friends become ill, require liver transplant or die related to HCV were more likely to be engaged in specialty care.⁸⁻⁹ Thus, patients' specific fears can either increase or decrease the likelihood of seeing a HCV specialist.

2.3.1.5 Social Factors

Social factors were identified as barriers to linkage-to-care in four of the studies.^{8-9, 11, 13} In an observational cohort study in which participants were asked to complete a six-item questionnaire on social functioning (financial problems, conflict with partner, spouse, relatives or employer, and living with drug users), lower social functioning scores were associated with lower likelihood of attending scheduled consultation with a HCV specialist.¹¹ Additional competing identified social factors included pending court cases (i.e. custodial sentencing), employment obligations, poor financial status, and responsibilities for children.^{8-9, 11, 13} PWID have complex social circumstances which influence their ability to be linked to care.

2.3.2 Provider Level

Provider-level barriers and facilitators to linkage-to-care were addressed in less than half of the reviewed studies. Two major themes were identified as important: clinical findings and provider-patient relationships.

2.3.2.1 Clinical Findings

Clinical findings included findings from laboratory values or diagnostic imaging. In the reviewed studies, participants with elevated liver enzymes or a prior diagnosis of cirrhosis were more likely to attend initial consultation appointment as compared to participants without such complications.^{10, 14} However, it cannot be ascertained if these persons were more likely to be referred to a specialist by a provider based on their findings/assessment or if the patients were more likely to attend referral since they were aware of this information.

2.3.2.2 Patient-provider Relationship

In a qualitative study, participants were asked to identify factors that facilitate or inhibit linkage-to-care.⁹ Participants emphasized the importance of having continuity of care.⁹ Seeing the same provider created a comfortable environment which in turn supported their engagement in care.⁹ Another important facilitator was believing that the provider was genuinely concerned about their well-being.⁹ Participants also identified having trust and confidence in their provider as an important influential factor.⁹ Specifically, participants needed to be confident that their provider had adequate knowledge about hepatitis C.⁹ Conversely, participants who felt that their provider was impersonal or distant, were less likely to engage in HCV care.⁹ Lastly, participants reported feeling stigmatized as a barrier to seeking care.⁹ If the participant felt that their drug use caused inequitable treatment by their provider, they were less likely to seek

HCV care.⁹ Verbal and non-verbal communication from providers has the ability to facilitate or impede linkage-to-care.

2.3.3 System Level

System-level barriers/facilitators to linkage-to-care were identified in three studies.^{9, 12-13} In a qualitative study, participants identified forgetting appointment dates/times which they attributed to the length of time between making the appointment and the actual appointment date, and a lack of appointment reminders as barriers to attending consultation appointment.⁹ Other barriers included lack of transportation, long distance to nearest HCV specialist, and appointment times early in the day.¹²⁻¹³

2.4 State of the Science

There are several limitations with the reviewed literature and gaps in the knowledge. First, there is an overall lack of knowledge about barriers and facilitators of linkage to care among PWID with HCV. There were only seven studies that met inclusion criteria with nearly 40% being qualitative data. Most of the quantitative studies were cross-sectional. Only one study examined longitudinal data over 2-5 years.¹⁰ Barriers to linkage to care at one time point may not predict linkage to care over the years to come; barriers and facilitators may evolve over time. Moreover, provider- and system-level barriers were only reported in three articles. It is unlikely that all provider- and system-level barriers have been identified.

The results of these studies have limited generalizability as the majority (all but one)⁸ recruited participants from urban cities, countries with universal healthcare, and community health centers, needle exchange programs or from addiction treatment

facilities. These participants likely have better access to resources and system-level engagement than PWID who reside in rural areas, countries with a multi-payer healthcare system, and third-world countries, or are not engaged in addiction treatment. Predictors of being evaluated by PCP for HCV among rural-dwelling PWID were reported in only study in the United States.¹¹ These findings suggest similarities in predictors of seeing a PCP for hepatitis C infection as urban populations.¹¹ However, further research is needed to confirm the generalizability of such findings to rural populations.

The recruitment sites for three studies employed staff with the intent of increasing engagement in HCV specific services.^{10-11, 13} In one study specifically, all participants who failed to attend their specialty appointment were given another appointment and offered additional support aimed at increasing linkage to care.¹⁰ Participants in the other two studies were recruited from facilities that offered on-site hepatitis C treatment facilities.^{11, 13} This is not standard of practice in most clinics in the U.S., which also limits generalizability.

Barriers related to fear of side effects treatment and knowledge may be less relevant. Only two studies were conducted after direct-acting antiviral (DAA) therapy became standard of care.^{12, 13} Interferon-based therapy was notorious for debilitating side-effects and low cure rates whereas DAA therapy is known for fewer side effects and higher efficacy.² It is likely that fear of side effects, concerns about efficacy, and being aware of others negative treatment experiences are less significant today. Likewise, DAA therapy has been widely advertised, which provided public education about treatment and HCV. Therefore, a lack of knowledge about treatment availability may also be less significant. However, to our knowledge this has not been formerly evaluated.

Lastly, linkage to care was operationally defined differently in each study. Definitions ranged from objective measures such as documented referral and attendance to specialist consultation¹⁰⁻¹¹ or engagement in treatment services¹³ to self-report measures such as “have you ever gone to see a specialist about your HCV?”⁹ Refer to Table 1 for more details. This variation could explain differences in the barriers/facilitators found in each study and limits comparisons across studies.

2.5 Conclusion

Little is known about the barriers and facilitators to linkage to care among PWID. In particular with respect to vulnerable populations such as those living in rural environments and in countries without universal healthcare. Future research should focus on filling the above identified gaps in knowledge and advancing the state of the science. Specifically, longitudinal data that focuses on vulnerable populations with high rates of infections such as those residing in rural areas and former/current inmates. Ideally, a large observational study should be conducted following rural PWID that test positive for HCV antibodies in their natural environment (not recruited only from addiction clinics or community resource facilities) over several years to determine predictors of linkage to care. In addition, future research should focus on provider- and system-level barriers as this is likely more pronounced in rural communities. More current research is also needed in the new DAA treatment era to determine if fear of side effects or the ineffectiveness of treatment is still relevant. Lastly, future studies should attempt to obtain more objective predictor variables as opposed to relying on self-report measures and consistency should be used in how linkage to care is defined. In the interim, caution should be used in

generalizing these findings to rural-dwelling PWID from countries without universal healthcare.

Table 2.1 Barriers and Facilitators to Linkage to Hepatitis C Care among People Who Inject Drugs

Author (Date)	Design	Location (Facility, Country)	Sample	Linkage-to- Care Operational Definition	Barriers and Facilitators
Fortier, E. (2015)	Observational cohort	Nine clinics: four OST, two private OST clinics, two community health centers and one Aboriginal community-controlled health organization Australia	415 former/current injection drug users	Referred to a specialist and attended their appointment	Barriers: 1. Lower social functioning (six-item questionnaire: money problems, conflict with partner/spouse, relatives or employer, living with people who use)
Islam, M. (2012)	Prospective Cohort	Redfern Harm Minimization Clinic- a needle syringe program Australia	212 injection drug users classified as > 6 months or < 6 months	Uptake of referral/attended appointment	Facilitators: 1. Elevated liver enzymes 2. No recent injection drug use
Treloar, C. (2013)	Qualitative	Three OST clinics (inner city private clinic, outer metropolitan public clinic and regional city public clinic) and one community center within a large rural town; Onsite HCV clinic Australia	57 clients with history of injection drug use	Engaged with treatment services	Barriers: 1. Perception that they were physically well/had no symptoms related to HCV 2. Concern about side effects and efficacy of treatment 3. Competing Priorities: pending court cases, interference with employment 4. Fear of sharing of information between HCV clinic and OST clinic Facilitators: 1. Witnessing friends becoming ill, requiring liver transplant or dying related to HCV. 2. Positive accounts from others who sought treatment-related services 3. Awareness of HCV potential severity

Table 2.1 (Continued)

<p>Swan, D. (2010)</p>	<p>Qualitative</p>	<p>Two addiction clinics, a community drop-in center, a general practice, two hepatology clinics, and an infectious disease clinic</p> <p>Ireland</p>	<p>36 current and former injection drug users</p>	<p>Not defined</p>	<p>Barriers:</p> <ol style="list-style-type: none"> 1. Employment obligations 2. Lack of HCV education investigations, treatment 3. Continued substance use 4. Lack of reminders-forgot appointments 5. Lack of opportunity 6. Fear of liver biopsy, self-injection 9. Concerns about side effects 10. Ineffective treatment options 11. Responsibility of children <p>Facilitators:</p> <ol style="list-style-type: none"> 1. Good relationships with health care providers 2. Awareness of potential health implications 3. Seeing others visibly ill or dying due to HCV 4. Presence of symptoms 5. Seeing peers/family complete treatment
<p>Souliotis, K. (2017)</p>	<p>Cross-sectional study</p>	<p>Primary services, health vans, community services, day-care centers</p> <p>Greece</p>	<p>101 with history of injection drug use</p>	<p>Access to HCV care</p>	<p>Barriers:</p> <ol style="list-style-type: none"> 1. Financial burden of health services 2. Deteriorated health status 3. Lack of transportation
<p>Grebely, J. (2011)</p>	<p>Cross-sectional study</p>	<p>Hepatitis C Council and Hemophilia Foundation Australia mailing lists, from OST clinics, pharmacies that dispense methadone and needle and syringe programs</p> <p>Australia</p>	<p>634 substance abusers, mix of injection (83%) and non-injection (17%)</p>	<p>“Have you ever gone to see a specialist about your hepatitis C?”</p>	<p>Barriers:</p> <ol style="list-style-type: none"> 1. Recent injection drug use (< 6 months). 2. HCV-related/ attributed symptoms 3. Cirrhosis 4. Receiving opiate therapy <p>Facilitators:</p> <ol style="list-style-type: none"> 1. Greater HCV knowledge 2. Previously diagnosed with cirrhosis 3. Greater HCV symptoms score 4. Not receiving OST
<p>Crowley, D. (2017)</p>	<p>Cross-sectional/ Mixed-method</p>	<p>OST facility</p> <p>Ireland</p>	<p>68 former injection drug users</p>	<p>Barriers to attendance of initial HCV clinic appointment</p>	<p>Barriers:</p> <ol style="list-style-type: none"> 1. On-going drug and alcohol use 2. On-going injecting drug use 3. Custodial sentencing 4. Fear around invasive HCV treatment and interventions 5. Attendance to early appointments 6. Lengthy distance from clinic 7. Chaotic personal and family lifestyles/family responsibilities.

HCV = Hepatitis C Virus; OST = Opioid Substitution Treatment

Table 2.2: Scottish Intercollegiate Guidelines Network Cohort Check List

	Fortier	Islam	Souliotis	Grebely
The study addresses an appropriate and clearly focused question.	Yes	Yes	Yes	Yes
The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Yes	Yes	Yes	Yes
The study indicates how many of the people asked to take part did so in each of the groups being studied.	No	No	Yes	Yes
The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	N/A	N/A	N/A	N/A
What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?	Unable to determine	Unable to determine	Unable to determine	Unable to determine
Comparison is made between full participants and those lost to follow up, by exposure status.	No	No	No	No
The outcomes are clearly defined.	Yes	Yes	Yes	Yes
The assessment of outcome is made blind to exposure status. (If the study is retrospective this may not be applicable).	Unable to determine	N/A	N/A	Unable to determine
Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome.	N/A	N/A	N/A	N/A

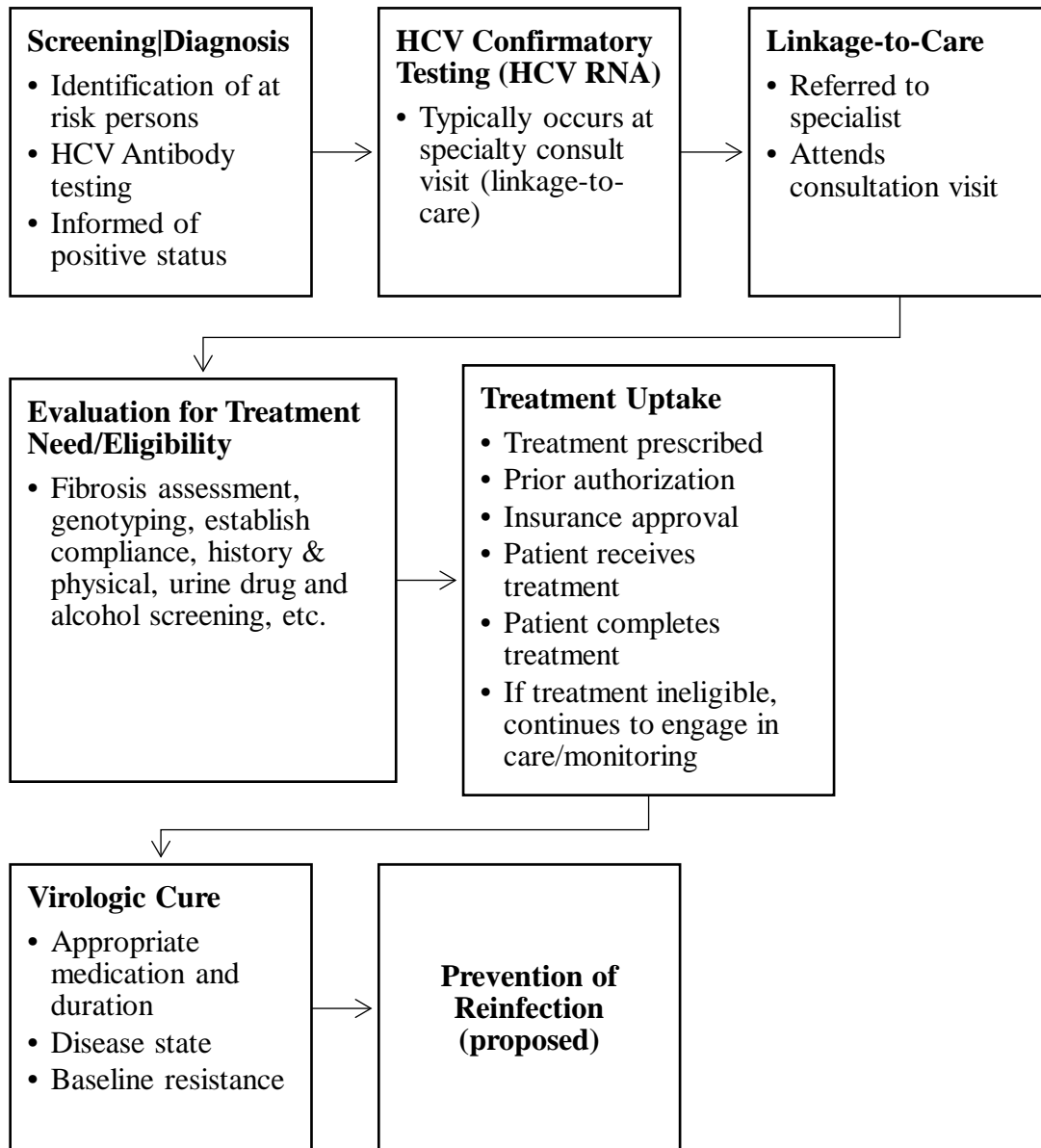
Table 2.2 (Continued)

The method of assessment of exposure is reliable.	Yes	Yes	Yes	Yes
Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable.	No	No	Yes	No
Exposure level or prognostic factor is assessed more than once.	No	No	No	No
The main potential confounders are identified and taken into account in the design and analysis.	Unable to determine	Unable to determine	No	Unable to determine
Have confidence intervals been provided?	Yes	Yes	No	Yes
How well was the study done to minimize the risk of bias or confounding?	Acceptable	Acceptable	Acceptable	Acceptable
Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?	Yes	Yes	Yes	Yes

Table 2.3 Critical Appraisal Skills Programme Check List

	Treloar	Swan	Crowley
Was there a clear statement of aims of the research?	Yes	Yes	Yes
Is a qualitative methodology appropriate?	Yes	Yes	Yes
Was the research design appropriate to address the aims of the research?	Yes	Yes	Yes
Was the recruitment strategy appropriate to the aims of the research?	Yes	Yes	Yes
Was the data collected in a way that addressed the research issue?	Yes	Yes	Yes
Has the relationship between researcher and participants been adequately considered?	No	No	Yes
Have ethical issues been taken into consideration?	Yes	Yes	Yes
Was the data analysis sufficiently rigorous?	Yes	Yes	No
Is there a clear statement of findings?	Yes	Yes	No
How valuable is the research?	Very valuable	Very valuable	Valuable

Figure 2.1 Progression Through the Hepatitis C Care Cascade



CHAPTER 3. PREDICTORS OF SEEKING HEPATITIS C CARE AMONG PEOPLE WHO INJECT DRUGS LIVING IN RURAL KENTUCKY

Abstract

Background: An estimated 3% of persons who inject drugs (PWID) with hepatitis C virus (HCV) will progress through the care cascade and be cured. This is due, in part, to challenges in being linked to HCV care. Several barriers to linkage to HCV care among PWID have been identified, but there are limited studies in rural inhabitants.

Purpose: To determine whether the factors associated with linkage to care in urban areas predict seeking HCV care among PWID with HCV in rural Kentucky. **Methods:** Data were collected through an online survey of 115 PWID between 18-35 years old living in one of five rural counties. Logistic regression was used to identify predictors of seeking HCV care. **Results:** A majority (83%) reported being screened for HCV of which approximately 66% reported testing positive. Of those testing positive, 60% reported seeking treatment, 8% reported receiving treatment, and 3% reported being cured. The PWID with self-reported HCV (n=63) in our sample were predominately Caucasian (98%) and male (62%). Participants who did not self-report recent injection drug were 88% less likely to have sought HCV care (OR 0.12, $p = 0.049$). Recent opioid substitution therapy and transportation issues were important but non-significant factors (OR 5.002, $p = 0.097$; OR 3.169, $p = 0.089$, respectively); recent criminal history, homelessness, and being a caregiver were not predictors. **Conclusion:** The number of PWID who progressed through HCV care cascade was similar to other studies. Remote drug use placed people at an increased risk for not seeking HCV care. Additional research is needed to confirm these findings due to the small sample size.

3.1 Introduction

Hepatitis C virus (HCV) disproportionately affects persons who inject drugs (PWID) with an estimated 30% of PWID between 18-30 years old infected with chronic HCV.¹ HCV infection can easily be eradicated with treatment success rates approaching 100%.² In spite of advancements in antiviral therapy, the percentage of PWID who are cured remains low.^{3,4} Thus, it is crucial to enhance engagement in healthcare services among PWID.

Successful treatment requires progression through a three step HCV care cascade: (1) screening, (2) linkage-to-care and (3) treatment uptake.⁴ Screening is the process whereby persons are tested for HCV antibodies and nucleic acid test (when appropriate) and made aware of his/her status.⁴ Linkage-to-care is the process by which people with HCV are evaluated by a practitioner experienced in the management and treatment of HCV (i.e. a hepatitis C specialist).⁴ Treatment uptake is the process of receiving treatment.⁴ However, successful treatment is rarely achieved, as most people are lost along the cascade of care. For example, in a large cross-sectional study of PWID, 89% were screened at least once in their lifetime with over half (57%) testing positive.³ An estimated 31% of those with an active infection were linked to care, 8% received treatment, and 3% were cured.³ The largest dropout occurred between diagnosis and linkage-to-care with a nearly 30% attrition rate occurring after diagnosis.³ Hence, it is essential to examine barriers to receiving treatment among PWID.

Several barriers to linkage to HCV care have been identified at the patient level including on-going/recent drug use, being asymptomatic, and poor HCV knowledge. As an example, on-going or recent drug use is an important hindrance to being linked to HCV care.^{5-7, 11} Participants who reported receiving Opioid Substitution Treatment (OST)

or injecting drugs in the last 6 months were less likely to report being evaluated by a HCV specialist.⁵ In contrast, participants who had not injected drugs in the last six months were more likely to be linked to care.^{6-7, 11} Moreover, being asymptomatic can also be a barrier to linkage-to-care. Participants in a qualitative study reported not having symptoms or feeling well as reasons for not seeking care.⁷ Others reported seeking HCV care when they experienced a decline in their physical health or developed symptoms, which they attributed to HCV.⁷ In addition, Hepatitis C virus knowledge can be a facilitator to HCV care. Patients who understand the potential severe consequences of remaining untreated are more likely to seek care.⁷⁻⁸ In contrast, a lack of knowledge about the diagnosis, the required workup, where to get treatment, and treatment availability can be deterrents to seeking care.⁷

Moreover, additional patient barriers include fears and social circumstances. In previous studies, fear of treatment-related side-effects, liver biopsy, perceived low treatment efficacy, and/or having to self-inject medications were reported as barriers.⁷⁻⁸ In contrast, fear may serve as a motivator such that patients who witness friends becoming ill, requiring liver transplants or dying from HCV, report seeking HCV care.^{7,8} Additionally, several social circumstances may pose significant barriers to HCV care among PWID. In an observational cohort study, participants were asked to complete a six-item questionnaire on social functioning (financial problems, conflict with partner, spouse, relatives or employer, and living with drug users).¹² Lower social functioning scores were associated with lower likelihood of attending a scheduled consultation with HCV specialist.¹² Other identified competing priorities included legal issues (i.e.

custodial sentencing), employment obligations, family responsibilities, poor financial status, and chaotic lifestyles.¹⁰⁻¹¹

In addition to patient-level barriers, several system-level barriers exist in the literature. Participants in a qualitative study identified forgetting appointment dates/times, which they attributed to the extended length of time between making the appointment and the appointment date compounded by the lack of appointment reminders as barriers to attending their consultation appointment.⁷ Other barriers were lack of transportation, distance to nearest HCV specialist, and appointment times early in the day.¹⁰⁻¹¹ It is important to examine such system level barriers to understand ways to mitigate their detrimental impact on HCV care among PWID.

Clinical findings and provider-patient relationships are important facilitators to linkage to care. Elevated liver enzymes and/or a prior diagnosis of cirrhosis were associated with higher likelihood of attending initial consultation appointment.^{5,6} In a qualitative study, continuity of care, believing the provider was genuinely concerned about their well-being, and having trust and confidence in their provider were identified as important facilitators.⁷ Participants who felt that their provider was distant or felt stigmatized were less likely to seek care.⁷ Interactions with and responses of providers can have a meaningful impact on linkage-to-care.

3.2 Purpose and Specific Aims

Given the challenges that exist in enhancing care for PWID with HCV, it is important to further explore ways to improve their access to care. The majority of existing studies were conducted in urban areas and in countries with universal healthcare and/or from opioid substitution facilities. However, less is known about the barriers and

facilitators to linkage to HCV care among PWID who live in rural areas without universal healthcare where health disparities are greater. Thus, the purpose of this study was to describe progression through HCV care cascade and determine barriers and predictors of linkage to HCV care among rural PWID. The specific aims were to (1) determine differences in sociodemographic variables between those who did or did not seek HCV care; (2) describe progression through the HCV care cascade; (3) describe self-reported reasons for not seeking HCV care; and (4) determine which factors associated with linkage to HCV care in urban areas predict seeking HCV care in rural residents who inject drugs.

3.3 Methods

3.3.1 Sample and Setting

The present study was a secondary analysis of data from a study to determine the utility of an online survey (about substance misuse and related risk behaviors) to screen and enroll a rural community of people who use drugs (PWUD). Initial participants were recruited via advertisements at community cookouts, use of flyers, and local study staff from outreach facilities. Additional PWUD were recruited using respondent-driving sampling. All participants were required to complete an online screening survey to confirm eligibility. Inclusion criteria were: self-reported use of opioids (prescription opioids, heroin, buprenorphine, methadone, and synthetic opioids) in the last thirty days to get high; living in one of five rural counties in Appalachia Kentucky; and between 18-35 years of age. Eligibility was confirmed using date of birth to determine age and an online screening tool to assess opioid use and local community knowledge, respectively.

A total of 249 participants met inclusion criteria and were enrolled between August 2017 to July 2018. Among the 115 PWID participants who reported a prior history of injection drug use, 63 reported screening positive for HCV in their lifetime and were included in the data analysis (Figure 1).

3.3.2 Measures

3.3.2.1 Sought HCV Care

The primary outcome was linkage to HCV care defined as the process of being evaluated by a practitioner experienced in the management and treatment of HCV (i.e. a hepatitis C specialist).⁴ For this study, we operationally defined linkage-to-care as responding ‘yes’ to the question: “have you ever sought treatment for your hepatitis C infection?”

3.3.2.2 Predictor Variables

Predictor variables chosen based on literature review were: (1) child caregiver status: “Are you the primary caregiver for any children” (yes); (2) recent injection drug use: “I have not injected in the past 6 months” (yes); (3) transportation issues: “In the past 6 months, have you been unable to do something that you needed to do because you did not have a way to get there?” (yes) (4) homelessness: “In the past 6 months, have you been homeless at any time?” defined as living on the street, or in a car, park, abandoned building, or shelter; (yes) and (5) criminal issues: “Check all that apply: in the past six months have you been in jail, prison, probation, parole, had a warrant out for your arrest or none of the above” (at least one checked).

3.3.3 Ethics

Institutional Review Board approval was obtained at both study sites. All data were protected by a Federal Certificate of Confidentiality. Participants were provided the links to the screening survey, informed consent, and the main survey were posted on the study's website hosted by WordPress. Those who completed the screening survey and met inclusion criteria, were directed to sign the informed consent prior to completing the survey. De-identified data were kept in a safe location.

3.3.4 Procedures

Those who met inclusion/exclusion criteria were asked to complete the online survey that assessed rural risk environments; drug use patterns; human immunodeficiency virus (HIV) and HCV risks; the risk and occurrence of overdose; and use of at-home HIV testing. In addition to the standard survey questions, the participants who reported not seeking HCV care were asked to select (all that apply) from a list of predetermined reasons and/or fill-in-the-blank for additional reasons they had not sought care.

3.3.5 Data Analyses

Data were analyzed using SPSS Statistics 25. Specific Aim 1 was addressed by between groups comparisons using Chi Square. Descriptive statistics were calculated (means and standard deviations or frequency and percentages depending on level of measurement) to address Specific Aims 2 and 3. Univariate logistic regression were conducted to address Specific Aim 4 in which the following independent variables were entered in one step: (1) child caregiver status (2) recent injection drug use (3)

transportation issues (4) homelessness and (5) criminal issues. There was no multicollinearity identified among variables. Alpha was set *a priori* at 0.05

3.4 Results

3.4.1 Sample Characteristics

The majority of the 63 HCV positive participants were Caucasian (98.4%), male (63.5%), and unemployed (66.7%). Almost 42% reported their highest level of education as a high school diploma or General Education Development (GED). There were no significant differences in gender, race, education, or employment status between participants who reported seeking HCV care and those who did not seek care.

3.4.2 Progression through the HCV Care Cascade

A total of 115 participants reported a lifetime history of injection drug use. As depicted in Figure 1, 83% of PWID reported being screened for HCV in their lifetime. Of those, 65% reported testing positive with 60% of those reporting seeking HCV care. However, only 8% of those who sought care reported receiving treatment and only 3% were cured.

3.4.3 Self-Reported Barriers to Not Seeking Care

Self-reported barriers are listed in Table 2. The most frequently selected barrier was could not afford care (25%) followed closely by not knowing where to go (22.2%) and not having insurance coverage (19.44%). Other barriers in decreasing order of frequency were not worried about HCV (13.89%), did not know treatment was available (11.11%), transportation problems (8.33%), and being worried about treatment side

effects (5.56%). Ten participants provided self-generated barriers as follows: recent or ongoing drug use (11.11%), worried the doctor would not treat them (5.56%), being incarcerated (2.78%), being worried about side effects (2.78%), being worried it would be a waste of time (2.78%), and being recently diagnosed (2.78%). These reasons were not included in our analysis, as we did not have corresponding data for those who sought HCV care.

3.4.4 Predictors of Seeking Hepatitis C Care

People who self-reported they did not inject drugs in the last six months were 88% less likely to report seeking HCV care (OR 0.12, 95% CI 0.015-0.994, $p=0.049$). Self-reported use of Opioid Substitution Therapy (i.e. methadone or Suboxone) in the last six months and not being able to do something in the last six months due to not having transportation (transportation issues) approached statistical significance (OR 5.002, 0.748-33.446, $p = 0.097$; OR 3.169, 0.839-11.974, $p = 0.089$, respectively). Self-report of criminal issues, homelessness, and being the primary caregiver of a child in the last six months were not significant predictors of seeking HCV care.

3.5 Discussion

Progression through the HCV care cascade in our study was similar to the findings of an Australian study in which a comparable percentage of PWID were screened for HCV in their lifetime.³ However, only half as many PWID with HCV in their sample were linked to HCV care compared to our study. This is surprising because in contrast to the U.S., Australia has universal healthcare. We expected that fewer participants would be linked to care in the U.S because of costs associated with a

multiplayer healthcare system. It is possible that the difference between studies may be based on how we operationally defined linkage to care (have you ever sought treatment for HCV). In the Australian study, linkage to care was objectively measured as attendance to an HCV specialist. In contrast, we measured linkage to care as self-report of seeking care and therefore our findings are more vulnerable to self-report bias.

Alternatively, our participants may have understood ‘sought treatment for HCV’ to mean seeing their PCP rather than seeing a HCV specialist. Despite differences in linkage to care rates in our study and the Australian study, there was a similarly low percentage of participants who received treatment and were cured. This suggests that a greater percentage of those linked to care in rural US did not receive treatment. This could be due to a difference in treatment eligibility between Australia and our sample or it could be that our sample faces more barriers to treatment uptake.

Inconsistent with results from urban-dwelling populations,^{5-6, 11} recent injection drug use was a predictor of being linked to care. Our findings are interesting. Even though only six participants reported recent injection drug use, recent injection drug use predicted seeking HCV care. One reason for this difference could be the wording of the question; participants were asked to select all that apply with no recent injection drug use defined as, “I have not injected drugs in the last 6 months.” Perhaps they were confused by this statement. Moreover, perhaps our study differs from the total rural-dwelling PWID population in that they have better resources which allow them to be linked to care despite recent drug use. Using Suboxone or methadone therapy have also been identified as a barrier to linkage to care in prior studies⁵⁻⁶ and approached significance in our study.

This difference may be due to our smaller sample size. Future studies with more robust samples should further explore this relationship.

Consistent with our predictions and similar to a prior study,⁷ a large portion of participants in our study reported not knowing there was treatment for HCV and/or not knowing where to get treatment as barriers to seeking care. This is not surprising as PWID residing in rural Kentucky may often need to cross county lines to receive HCV-specialty care. This further illustrates the importance of providing education about treatment availability/accessibility to all PWID.

Fear of side-effects was commonly reported as a barrier in prior studies.⁷⁻⁸ One reason it was not common in our study may be related to the time of data collection. In prior studies, data were collected when PEGylated interferon (well-known for its severe side effects) was frequently used, while our data were collected in the era of direct acting antiviral therapy, which has fewer side effects.

Not surprisingly, social circumstances such as legal issues, homelessness, and family responsibilities have been reported as barriers to linkage to care elsewhere.¹⁰⁻¹² One possible reason why our findings differed is that our sample size was rather small. It could also be that other non-measured social circumstances have a greater influence on linkage-to-care in people living in rural areas. Thus, future qualitative studies may be warranted to examine social circumstances that influence linkage to care among rural PWID.

Because transportation was named a barrier to HCV treatment among urban-dwelling PWID,¹⁰ we expected transportation to be a significant barrier. Rural areas may have fewer if any modes of public transportation and residents usually have with limited

access to reliable vehicles and/or gas money. However, transportation issues were not a significant predictor of seeking HCV care in our study, although it did approach significance and was self-reported as a reason for not seeking care by a few participants. It is possible that with a larger sample it would be a predictor for rural residents.

Cost or financial burden was only reported in one prior study as a barrier to linkage to care.¹⁰ Cost and lack of insurance accounted for a large percentage of participants who did not seek care in our study. Not surprising, this is most likely due to prior studies being conducted in a country with universal healthcare versus a country with a multi-payer healthcare system.^{5-8, 10-12} Hence, practitioners should make an effort to help PWID navigate the costs associated with healthcare.

3.5.1 Limitations

This study is among the first to provide data about barriers to seeking HCV care among rural inhabitants in the U.S, a country without universal healthcare. However, a few limitations are noted. First, our study may be underpowered due to our small sample size. Second, our study was a secondary data analysis and is therefore limited to the data collected. Therefore, we were not able to determine if factors that were important in existing literature such as fear of treatment side-effects and invasiveness, HCV-knowledge, and being a/symptomatic are predictors of linkage to care in this population. In addition, we were not able to assess any provider-level barriers. It is possible that variables not measured in our study are important predictors of linkage-to-care in this population. Third, participants were asked to take part in a very lengthy survey. Longer web-based surveys are associated with lower completion rates.¹³ Moreover, answers to

questions towards the end of the survey are answered at a faster rate and in a more uniform manner which brings to question the quality of responses.¹³

Fourth, participants were required to have functional literacy and basic computer skills to complete the required online survey. It is reported that an estimated 30% of the Appalachian population are functionally illiterate¹⁴ and internet access is limited.¹⁵

Caution should be used in extending these findings to those with limited literacy and/or no internet access. Lastly, as with most behavioral studies, our variables were self-report measures and subject to social desirability and recall-bias. To minimize social-desirability, participants were made aware that their data would be kept confidential and de-identified during the consenting process. In addition, surveys were self-administered which has clearly demonstrated a reduction in social desirability bias.¹⁶

3.6 Conclusions

Our findings suggest that barriers and facilitators associated with linkage-to-care of rural inhabitants with limited access to health care are similar to barriers and facilitators in urban areas and in countries with universal health care. Additional research is needed to confirm these findings using a larger sample as well as provider-level and system-level barriers to HCV care. Findings from these studies can then guide interventions aimed at increasing linkage-to-care, treatment uptake, and ultimately increasing cure rates in rural communities.

Table 3.1 A comparison of sociodemographic variables of rural participants who did and did not self-report seeking hepatitis C virus care

	Total sample n= 63	Never sought HCV care n= 36	Sought HCV care n= 25	<i>P</i>
Gender				0.17
Male	40 (63.5)	27 (67.5)	13 (32.5)	
Female	23 (36.5)	11 (50)	12 (50)	
Race*				
Caucasian	62 (98.4)	37 (97.3)	25 (100)	
African American	1 (1.6)	1 (2.6)	0 (0)	
Education				0.94
Less than high school	21 (32.8)	12 (57.1)	9 (42.9)	
High school/GED	26 (42.9)	16 (42.1)	10 (40)	
Some college or technical school	15 (323.8)	8 (21.1)	6 (24)	
Employment				0.48
Employed	21 (33.3)	13 (32.2)	8 (32)	
Unemployed	42 (66.7)	25 (65.8)	17 (68)	

*Chi square not run due to small sample size. Values are n (%).
 GED = General Education Development. HCV = Hepatitis C Virus.

Table 3.2 Self-reported reasons for not seeking HCV care among rural residents who inject drugs

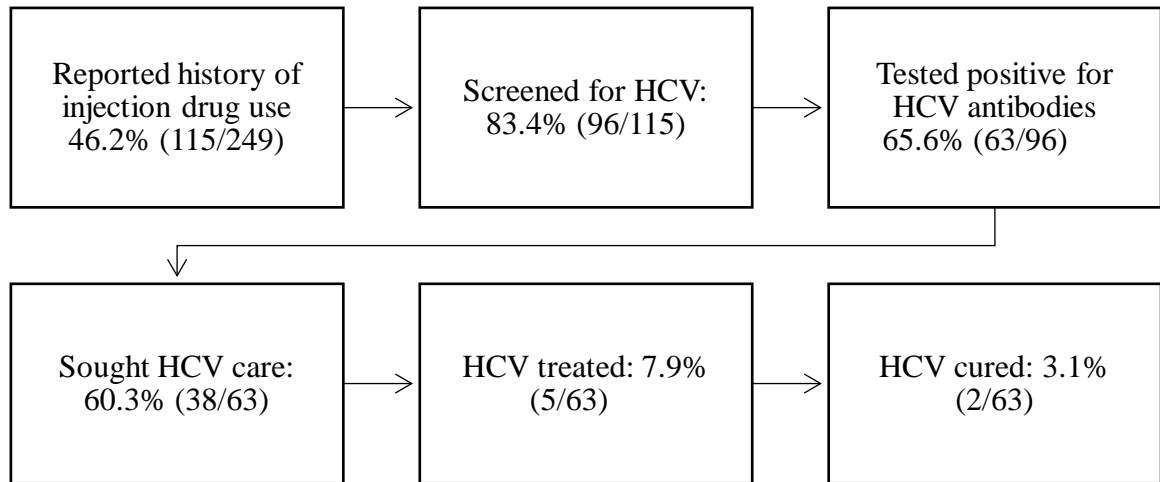
Reasons	Number of participants*
	n (%)
Could not afford it	9 (25)
Did not know where to go	8 (22.2)
Did not have insurance coverage	7 (19.4)
Not worried about HCV	5 (13.9)
Recent drug use	4 (11.1)
Did not know treatment was available	4 (11.1)
Worried about side effects	3 (8.3)
Did not have transportation	3 (8.3)
Worried MD would not treat them	2 (5.6)
Incarcerated	1 (2.8)
Worried it would be a waste of time	1 (2.8)
Recently diagnosed	1 (2.8)

HCV = Hepatitis C Virus; MD = Medical Doctor *options are not mutually exclusive.

Table 3.3 Predictors of Seeking Hepatitis C Virus Care among Rural Residents Who Inject Drugs (n= 63)

	Odds Ratio (95% CI)	P-value
Primary caregiver of a child	0.803 (0.167-3.854)	0.784
No recent injection drug use	0.121 (0.015-0.994)	0.049
Had recent suboxone or methadone use	5.002 (0.748-33.446)	0.097
Had transportation issues	3.169 (0.839-11.974)	0.089
Had recent criminal issues	0.763 (0.229-2.54)	0.659
Was recently homeless	0.934 (0.261-3.346)	0.916

Figure 3.1 Progression Through the Hepatitis C Virus Care Cascade among Rural-dwelling People Who Inject Drugs



CHAPTER 4. PREDICTORS OF PRIMARY CARE USE AMONG FEMALE INMATES WHO INJECT DRUGS LIVING IN RURAL APPALACHIA

Abstract

Hepatitis C virus (HCV) infection is a growing epidemic with highest prevalence among people who inject drugs (PWID) especially those in rural Appalachia and inmates. To receive HCV treatment, one must be screened and referred to a HCV specialist. Primary care providers (PCPs) are ideally situated to provide these services. However, PWID are at an increased risk for contracting HCV but are less likely to access PCPs. Factors associated with accessing a PCP include being female and employed while low socioeconomic status, daily injection drug use, illegal income, and chronic homelessness have been identified as barriers. Few studies have evaluated vulnerable subpopulations of PWID such as those living in rural communities or inmates

PURPOSE: To identify predictors of PCP use among incarcerated female PWID living in rural Appalachia.

METHODS: This was a secondary analysis of data from 302 incarcerated female PWID from a larger randomized control trial. Multivariate logistic regression was used to determine predictors of primary care use.

RESULTS: The majority (55%) of the sample had less than a high school education, were single (35.7%) and were unemployed (74.5%) with an average age of 32 (+/-7.92) years. Age (OR 1.05, CI 1.01-1.09, $p = 0.01$) and reporting a lack of insurance as a barrier to seeking healthcare (OR 1.95, CI 1.12-3.4, $p = 0.02$) were significant predictors of PCP use.

CONCLUSIONS: Knowing that younger, rural-dwelling female inmates with a history of injecting drugs are more likely to not use PCP services- clinicians should use opportunities such as emergency departments, jails, prisons, urgent treatment centers, and addiction clinics to screen and refer to specialist.

4.1 Introduction

People who inject drugs (PWID) are at the highest risk for contracting HCV, a blood-borne viral infection affecting 2.4 million people in the United States.¹ As the opioid crisis continues to grow, so do acute cases of hepatitis C virus (HCV) infection. In fact, acute cases of HCV infection have been on the rise since 2004, coinciding with the opioid epidemic and increasing rates of injection drug use.² A recent analysis of several national data bases indicates a steady rise in HCV cases across the nation, with the largest seen east of the Mississippi River.³ This is even more pronounced in Appalachian states (Tennessee, West Virginia, Virginia, Kentucky) where the incidence of acute HCV infections increased by 45% from 2006-2012 among people less than 30 years old with approximately 75% reporting injection drug use as their primary risk factor.³

Naturally, inmates are another at-risk group since a history of drug use is common among inmates.²³ In fact, incarcerated persons have 2-10 times higher prevalence of HCV infections than the general population with an estimated 29% of incarcerated persons in North America testing positive for HCV antibodies (indicating prior exposure to the virus).⁴ This is more pronounced among female inmates. Forty to fifty percent of female inmates have chronic HCV infections; that is a 20 times higher rate of infection than the general population.⁶ In addition, a staggering 33% of Americans infected with HCV will enter into a correctional facility each year.²⁸

Rates of infection are highest among rural female inmates with a history of injecting drugs however cure rates remain low. This low cure rate is owed to a not being screened/diagnosed and/or linked to care.⁷ Primary care providers (PCP) are ideally

situated to facilitate progression through the HCV care cascade. In fact, visiting a PCP is associated with lower risk of HCV infection, increased likelihood of being screened, increased awareness of HCV status, and increased likelihood of being linked to a specialist.⁸⁻¹⁰ However, PWID, often underutilize PCP services.⁹ This is even more pronounced in female inmates.^{5, 11} An estimated one third of PWID reported visiting a PCP within the last month.¹³⁻¹⁴ However, only one third of female inmates reported seeing a PCP when acutely ill in the last year¹¹ and only half who reported a chronic illness saw a PCP in the 12 months prior to incarceration.¹²

Upon release many inmates return to a community with limited access to healthcare (i.e. rural areas) and endure disruptions in treatment for mental health, medical conditions, medications, and substance use disorders.²⁴⁻²⁷ Moreover, most inmates lack health insurance upon release and if they had Medicaid benefits prior to incarceration, those benefits have since been terminated leaving them in a vulnerable position.²⁸ Therefore, rural female inmates represent a vulnerable, unreached group of PWID that are at an increased risk for contracting HCV but unlikely to receive the appropriate medical care and needed follow-through.

4.1.1 Primary Care Utilization among People Who Inject Drugs

Factors associated with a significantly higher likelihood of seeing a PCP within the last month include: being female, employed, living with children, and recent contact with social/welfare worker.¹⁴ Low socioeconomic status (monthly income less than \$400), daily injection drug use, illegal or semi-illegal income, and chronic homelessness were associated with a lower likelihood of a recent PCP visit.¹³⁻¹⁴

PWID self-reported barriers to healthcare access include the burden of appointments, lack of transportation, negative staff attitudes, and fear of receiving bad news pertaining to their health.¹⁵ The impact of these barriers on accessing healthcare appeared to be contingent on the attitudes of healthcare professionals, the circumstances and needs of the PWID, the availability of alternative services, and the frequency of needed care.¹⁵ Self-reported facilitators of healthcare utilization included trust in physician, presence of health insurance, supportive relationships (e.g., familial), personal circumstances/life events (e.g., becoming a parent), and the individual's state of mind (i.e., feeling motivated and positive).¹⁶⁻¹⁷

4.1.2 Anderson's Behavioral Model of Health Services Use

Utilization of healthcare services is a complex interaction between individual, environmental, and healthcare characteristics.¹⁸ Andersen developed the *Behavioral Model of Health Services Use* (Figure 1) to explain this dynamic relationship.¹⁸ Andersen proposed use of health services was a result of the interaction of predisposing factors, potential enabling resources, and need or current level of illness.¹⁸ Predisposing factors are comprised of demographics, social structure, and health beliefs.¹⁸ Demographics include age, gender, and ethnicity whereas social structure includes educational level and social class.¹⁸ Health beliefs are values, attitudes, or knowledge about health and health services that may influence perceived need and use of health services.¹⁸ Enabling resources, include personal, family, and community factors that facilitate the use of health services such as income, health insurance status, and distance traveled.¹⁸ Need is divided into perceived and evaluated where perceived need is one's perception of his/her own general health and functional state.¹⁸ Evaluated need is defined as professional

assessment of one's health status and the need for health care.¹⁸ Anderson's model will serve as the framework for this study.

4.2 Specific Aims

The specific aims were (1) to identify independent predictors of primary care use (defined as having one healthcare facility usually attended prior to incarceration) from predisposing factors (age, marital status, highest educational achievement, employment status, worried about health in the past 12 months, perceived chance of getting HCV), potential enabling factors (insurance coverage, total family 6 month income, too far to go), and healthcare needs (health problems interfered with responsibilities, perceived health); and (2) to determine whether primary care use is a predictor of positive HCV antibody.

4.3 Methods

4.3.1 Design, Setting, and Participants

This was a secondary analysis of data from 384 participants in a randomized clinical trial (NIH/NIDA 1R01-DA033866) to determine changes in high-risk behaviors and health service utilization in response to traditional education versus motivational interviewing. Data were collected from drug-using rural women from county jails who were at high-risk for HIV and HCV. Inclusion criteria were: 1) National Institute on Drug Abuse-modified Alcohol, Smoking and Substance Involvement Screening Test score of four or greater (moderate to high drug use); 2) engagement in at least one sex risk behavior in the past three months; 3) willingness to participate in brief intervention sessions; 4) incarceration period between two weeks to three months; and 5) reported a

prior history of injection drug use. Participants were excluded if they had a documented mental illness or cognitive impairment.

4.3.2 Procedures

The parent study was approved by the Institutional Review Board and a Federal Certificate of Confidentiality was obtained. Participants were enrolled in the larger study trial and completed baseline interviews before being randomly assigned to one of two conditions- HIV Education or Motivation Interviewing. Only baseline data were used for this secondary analysis.

4.3.3 Measures

The primary outcome for this secondary analysis was PCP use. PCP use falls under the umbrella of healthcare utilization- defined as the description of the use of services by persons for prevention, maintenance or cure of health problems, and for overall well-being.¹⁹ Self-report measures of health care use (e.g. hospital and office visits) have moderate to high agreement with administrative health care claims, especially pertaining to office visits.²⁰ Agreement between the two are highest when evaluated via internet-surveys.²¹ We therefore, operationally defined primary care use as participants' self-report of having a clinic/health center/doctor's office/other facility that they usually attended prior to incarceration.

4.3.3.1 Predisposing Factors

The predictor variables for this secondary analysis were based on Andersen's Model of Health Care Use and on review of the literature (Figures 1 and 2).¹⁸ Age (in years) was the only demographic variable measured. All participants were Caucasian females;

therefore, ethnicity and gender were not included. Social structure was operationally defined as highest level of education (less than high school, high school, or some higher education) and employment status (employed/unemployed). Health beliefs were measured as being worried about health in the past 12 months (yes) and perceived chance of getting HCV (less than 50%).

4.3.3.2 Enabling Factors

For this analysis, we used income, health insurance status, and travel distance as enabling factors. Income was measured based on total income 6 months prior to incarceration in U.S dollars, health insurance status was measured as “was no health insurance a barrier to seeking needed healthcare services?” (yes), and travel distance was measured as “was it too far to go a barrier to seeking needed healthcare services?” (yes).

4.3.3.3 Perceived Need

Perceived need was measured as “have health problems kept you from meeting responsibilities at work, school or home?” (yes) and perceived health in last 12 months (fair to poor).

4.3.3.4 Hepatitis C Virus Antibody Testing

Hepatitis C Virus antibody testing was performed using OraQUICK *ADVANCE*® Rapid HCV Antibody Test kits, which have demonstrated sensitivity (95.5-100%) and specificity (99.2-100%) similar to current laboratory-based EIA (gold standard).²¹

4.3.4 Statistical Analyses

Data were analyzed using SPSS 25.0 with an alpha set at 0.05. Independent *t* tests were calculated for continuous variables and Chi square for categorical variables to compare those who reported primary care use with those who did not. Multivariate logistic regression was run to address Specific Aim 1 in which the following independent variables were forced entered in one step: (1) age, (2) highest level of education, (3) employment status, (4) being worried about one's health, (5) perceived chance of getting HCV, (6) six-month income, (7) insurance status, (8) travel distance, (9) perceived need, (10) perceived health. Univariate logistic regression was run to address Specific Aim 2; determine whether HCV antibody status predicts being in the group that reported use of a PCP prior to incarceration.

No assumptions were violated in either logistic regression model. The assumption of a linear relationship between age and income and the logit transformation of the dependent variable (having one healthcare facility that they usually visited) was tested and found to not be violated. There was no multicollinearity or significant outliers/influential points.

4.3.5 Results

Our analysis included a total of 302 PWID (Table 1). All participants were Caucasian females. The majority (55%) had not graduated high school, were single (35.7%), and were unemployed (74.5%). On average, our sample was approximately 32(+/- 7.4) years of age and had a total average income of \$9,222.05 (+/- 20,855.41) six months prior to incarceration. A majority (58%) of our sample reported using primary care services

prior to incarceration. Those who reported PCP use were significantly older (33 +/- 7.9 vs. 30 +/-6.4 years, $p = 0.01$).

Our multivariate logistic regression model is presented in Table 2. The model was significant ($p = 0.01$). Age was the only predisposing factor to predict primary care use. Participants were 5% more likely to use healthcare for each additional year of age (OR 1.05, CI 1.01-1.09, $p = 0.01$). Income as a continuous variable was highly variable and therefore not included in the regression model. Interestingly, participants who reported that a lack of insurance was not a barrier to healthcare were 95% more likely to engage in primary care services (OR 1.95, CI 1.12-3.4, $p = 0.02$). The remaining enabling factors were not predictors of primary care use. Reporting health problems that interfered with responsibilities was a significant need factor. Those who reported having health problems that interfered with other responsibilities in the last 12 months were about 40% more likely to have engaged in primary care services (OR 0.60, CI 0.33-1.07, $p = 0.08$).

Results from our univariate logistic regression model are presented in Table 3. HCV antibody status (positive versus negative) was not a predictor of primary care use.

4.4 Discussion

In alignment with Anderson's Model, we found that age and lack of insurance were barriers to PCP use. A lack of insurance as a barrier to accessing needed healthcare was the single most important predictor of not seeing a PCP. This is alarming in a group of women who will upon release face limited access to healthcare services, lack of or suspension of health insurance and disruption in continuity of healthcare.²⁴⁻²⁸

Inconsistent with his model, employment status, marital status, chance of getting HCV, being worried about one's health, health issues that interfere with one's

responsibilities, distance traveled, and perceived health were not predictors of primary care use. One reason for this difference, could be that this vulnerable population faces numerous barriers to care and this model did not account for the additive effects of multiple barriers.

Contrary to prior studies among PWID¹³⁻¹⁴, employment status was not a predictor of primary care use. This difference may be due to the majority of our sample being unemployed and therefore employed females were underrepresented in our sample.

In prior studies, transportation issues were a barrier to healthcare utilization¹⁵ however, we found that distance traveled was not a significant barrier. This could be related to how we measured this barrier. We operationalized transportation issues as, ‘is distance a barrier to healthcare use’. Perhaps lack of a reliable vehicle or gas money rather than distanced traveled contributed to difficulty with transportation. Or perhaps, they were incarcerated at the time of needed healthcare services and transportation alone was not the hindering factor. Moreover, asking our participants to be introspective and determine if distance is a barrier may produce different results as opposed to evaluating associations between distance traveled and PCP use.

4.4.1 Limitations

Our study has some limitations that warrant consideration. First, we used an indirect measure of primary care use rather than administrative healthcare claims. There is considerable data that supports the reliability of self-report measures of healthcare use. However, there are numerous ways to ask patients about use of primary care services. Depending on how this is operationalized, it could render different findings. Because this was a secondary analysis, we were not able to examine an exhaustive list of

barriers/facilitators. Therefore, it is possible that other factors are influential in PCP use. While our sample size of 302, was acceptable, our sample size restricted the number of predictor variables we could use in our model. Last, are data were primarily self-report measures. Self-report measures are vulnerable to social desirability bias in which the participants may answer in the most favorable way. Self-report measures are also susceptible to recall bias.

4.5 Conclusions

Our findings suggest only two predictors of PCP use among this vulnerable population. Additional research is needed to find other predictors of PCP use among rural-dwelling female inmates with a history of injecting drugs. Special attention should be given to examining provider level barriers as well as the additive effects of multiple potential barriers in this population.

In the meantime, our findings can be applied at the clinical and policy level. PWID can be very transient (frequently relocating, changing phone numbers, etc.) but while incarcerated they remain in a fixed location and therefore are an ideal target for interventions. Specifically, jail staff could offer information about Medicaid eligibility after release. This responsibility extends beyond jail staff to healthcare personnel who should provide at-risk individuals (i.e. those who are underinsured or uninsured and young PWID) with information on local facilities that offer sliding-scale/income-based payment plans. Clinicians should also use alternative contacts such as emergency departments, jails, prisons, urgent treatment centers, and addiction clinics to screen for HCV and refer to specialists. On a policy level, greater access to affordable insurance is a clear necessity to increase PCP use among female PWID inmates.

Table 4.1 Comparison of socio-demographic variables of people who inject drugs and used primary care services with those who did not

	Total (n=302)	No regular healthcare facility, n=127	Regular healthcare facility, n=175	P-Value
Age (Years)	31.6+/-7.5	29.9+/-6.4	32.9+/-7.9	0.01
Total income in 6 months before incarceration	9222 ± 20855	8268 ± 17026	9908 ± 23249	0.48
Highest level of education				0.37
Less than high school	154(50.1)	70(55)	84(48)	
Completed high school	88(29.14)	36(28.3)	52(29.7)	
Some higher education	60(19.9)	21(16.5)	39(22.3)	
Marital Status:				0.01
Married	95(31.5)	37(29.1)	58(33.1)	
Single	108(35.8)	57(44.9)	51(29.2)	
Separated, widowed, divorced	99(32.7)	33(25.6)	66(37.8)	
Employment Status:				0.32
Employed	63(20.9)	23(18.1)	40(22.9)	
Unemployed	239(79.1)	104(81.9)	135(77.1)	

Table 4.2 Predictors of Primary Care use among Female Inmates with a History of Injecting Drugs Living in Rural Appalachia

	Odds Ratio	95% Confidence Intervals	P value
Omnibus model $X^2 = 36.998$, df 13, $p < 0.001$			
Age (Years)	1.05	1.01-1.09	0.01
Employment status 6 months			
Unemployed		Reference	
Employed	1.8	0.95-3.41	0.07
Highest level of education			
Some higher Education		Reference	
High School	0.62	0.31-1.22	0.16
Less than high School	0.81	0.39-1.67	0.56
Marital status			
Separated, divorced, widowed		Reference	
Not Married	0.99	0.52-1.87	0.97
Married	0.59	0.32-1.11	0.11
Perceived chances of getting Hepatitis C			
High (75-100%)		Reference	
Small to Moderate (0- 50%)	0.8	0.47-1.35	0.40
Worried about health/behaviors during past 12 months			
Yes		Reference	
No	0.636	0.35-1.17	0.15

Table 4.2 (Continued)

No insurance coverage a barrier seeking needed health care services

Yes		Reference	
No	1.95	1.12-3.4	0.02

Distance a barrier to seeking needed health care services

Yes		Reference	
No	1.09	0.61-1.97	0.77

Had health problems that prevented meeting responsibilities at work, school or home during past 12 months

Yes		Reference	
No	0.596	0.33-1.07	0.08

Perceived health in last 12 months

Good to Excellent		Reference	
Poor to Fair	0.64	0.35-1.17	0.15

Table 4.3 Hepatitis C antibody status as a predictor of primary care use (n= 277)

	Odds ratio	95% confidence intervals	P value
Hepatitis C antibody status			
Positive	Reference		
Negative	1.320	0.791-2.203	0.288

Figure 4.1 Andersen's Behavior Model of Health Services Use

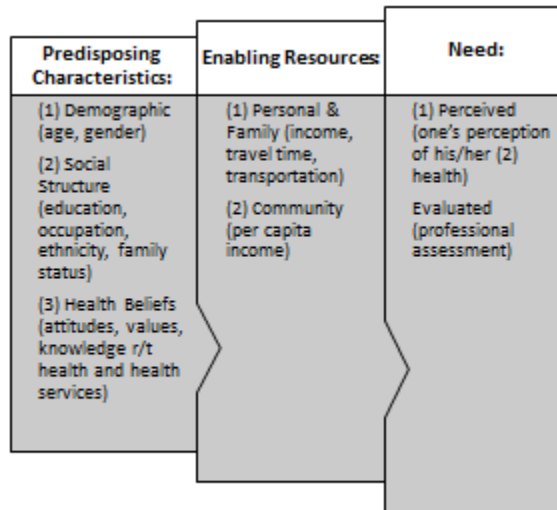


Figure 4.2 Predictor variables included in logistic regression model

Predisposing Characteristics:	Enabling Resources:	Need:
<p>(1) Demographic:</p> <ul style="list-style-type: none"> • Age (Years) • Marital Status <p>(2) Social Structure:</p> <ul style="list-style-type: none"> • Highest Educational Achievement • Employment Status <p>(3) Health Beliefs:</p> <ul style="list-style-type: none"> • "Have You Been Worried About Health In The Past 12 Months (Yes, No)?" • Perceived chance Of Getting HCV 	<p>(1) Personal & Family:</p> <ul style="list-style-type: none"> • "Was No Insurance Coverage A Barrier To Participant In Seeking Needed Health Care ?" • Total Family 6 mo. Income <p>(2) Community:</p> <ul style="list-style-type: none"> • "Was Too Far To Go A Barrier To Participant In Seeking Needed Health Care Services ?" 	<p>(1) Perceived:</p> <ul style="list-style-type: none"> • "During The Past 12 Months Have Health Problems Kept You From Meeting Responsibilities At Work, Home, School?" • Perceived Health In The Last 12 Months (Excellent-good Or Fair-poor) <p>(2) Evaluated: Not Done</p>

CHAPTER 5. CONCLUSIONS

5.1 Background and Purpose

Untreated hepatitis C can have grave consequences.¹ Fortunately, HCV can be cured with direct acting antiviral therapy.² PWID and inmates are among those with the highest incidence of HCV but cure rates in these populations remains low.³⁻⁶ Inadequate screening and linkage to care remain among the largest impediments to successful treatment.²

The purpose of this dissertation was to develop a broader understanding of the barriers and facilitators to healthcare utilization among rural-dwelling People Who Inject Drugs (PWID) at the primary care level, where screening for hepatitis C virus (HCV) may take place and at the specialist level (linkage to care). The following three manuscripts addressed important gaps in knowledge: (1) a review of the literature to describe the state of science on linkage to care among PWID, (2) a cross-sectional study to determine whether predictors of linkage to care identified in urban-dwelling PWID from countries with universal healthcare predicted seeking HCV care among PWID living in rural Appalachia, and (3) a cross-sectional study to determine predictors of primary care provider (PCP) use among female inmates living in rural Appalachia with a history of injecting drugs.

This chapter will summarize the findings of this dissertation with the intention of advancing the state of science on healthcare use (primary care and specialist care) among rural-dwelling PWID. This chapter will also provide recommendations for clinical applications and future research.

5.2 Summary of Findings

Chapter Two is a review of the literature on the current state of science on linkage to HCV care among PWID. We reviewed a total of seven studies, two of which were qualitative, four were quantitative and one was mixed methods. Four studies were conducted in Australia, two in Ireland and one in Greece. In all seven studies, patients were recruited from addiction-based clinics or community service facilities. Only two studies were conducted after direct acting antiviral therapy became standard of care. Barriers to linkage-to-care at the patient-level included: ongoing substance use, limited knowledge about HCV, competing priorities, and being asymptomatic. Distance traveled, lack of transportation, and early appointment times were reported as system-level barriers. Facilitators at the provider-level included elevated liver enzymes, diagnosis of cirrhosis, and a trusting patient-provider relationship.

Chapter Three is a cross-sectional study in which we examine predictors of seeking HCV care among rural-dwelling PWID. Our final analysis included sixty-three HCV positive PWID. Inconsistent with prior studies,⁷⁻⁹ recent injection drug use was a (and the only) predictor of seeking HCV care. Self-reported use of Opioid Substitution Therapy in the last six months and transportation issues seemed to be important but were not statistically significant. Inconsistent with existing literature¹²⁻¹³ self-report of criminal issues, homelessness, and being the primary caregiver of a child in the last six months were not predictors of seeking HCV care. The following were the most commonly self-reported barriers provided by HCV positive PWID who did not seek care: could not afford care (n= 9), did not know where to go (n= 8), no insurance coverage (n = 7), not worried about HCV (n = 5), did not know treatment was available (n = 4), recent or ongoing drug use (n=4), transportation problems (n = 3), and being worried about

treatment side effects (n =3) and are consistent with prior findings.¹⁰⁻¹² Our findings suggest some differences between barriers/facilitators to seeking HCV care among rural and urban dwelling PWID.

Chapter Four is a cross-sectional study to determine predictors of PCP use among rural-dwelling inmates with a history of injecting drugs. Our analysis included a total of 302 participants. Age and no insurance issues were significant predictors of primary care use. Participants were 5% more likely to use healthcare per each additional year of age and participants who reported a lack of insurance was not a barrier to healthcare were 95% more likely to engage in primary care services. Our results suggest that there are differences between rural-dwelling female inmates with a history of injecting drugs compared to their non-incarcerated urban counterparts.

5.3 Impact of Dissertation on the State of Science

This dissertation has advanced the state of science on the predictors of primary care use and linkage to care among vulnerable populations (rural-dwelling, female inmates) by (1) identifying gaps in the literature, (2) describing predictors and self-reported barriers to seeking HCV care among rural-dwelling PWID after the advent of direct acting antiviral therapy, and (3) determining predictors of PCP use among rural-dwelling female inmates with a history of injecting drugs.

Chapter Two revealed several gaps in the literature on predictors of linkage to care. First, there is an overall lack of knowledge about barriers and facilitators of linkage to care among PWID with only seven studies meeting inclusion criteria. Nearly 40% of the reviewed studies were qualitative data and only one study examined longitudinal data⁸ over 2-5 years. Second, findings from existing literature lack generalizability.

Researchers in only one study recruited participants from rural areas ¹¹; all others recruited participants from urban cities and countries with universal healthcare. In addition, participants for all studies were recruited from community health centers, needle exchange programs or addiction treatment facilities, often with onsite HCV treatment available. This demonstrates a lack of real-world data. Third, only two studies ^{9, 12} were conducted after direct-acting antiviral (DAA) therapy became standard of care and therefore, it remains unclear if fear of side effects is still important. Lastly, linkage to care was operationally defined differently in each study and likely attributes to inconsistent findings in the literature.

Chapter Three broadened our understanding of barriers and facilitators to seeking HCV care among PWID by providing insights on barriers/facilitators faced by rural PWID. Specifically, our findings illuminate key differences between urban PWID from countries with universal healthcare in a Pre-DAA era and rural PWID from countries with a multi-payer healthcare system in a post-DAA era. We found three key differences. First, our sample of recent injection drug users were more likely to be linked to care. Second, consistent with our expectations, fear of side-effects related to HCV treatment are much less relevant in the post-DAA era. Lastly, our findings suggest that cost associated with healthcare and lack of insurance are very important barriers for rural PWID in countries without universal healthcare.

Chapter Four represents to our knowledge, the only study to examine predictors of PCP use among rural, female inmates with a history of injecting drugs. The results illustrate the need to improve insurance access to this vulnerable population. In addition, we identified differences between rural and urban dwelling PWID.

5.4 Recommendations for Clinical Practice and Research

We conducted one study to address one of the gaps identified in Chapter 2, but additional research is needed to confirm these findings and expand the existing knowledge base. Specifically, longitudinal data and more real-world data are needed that focus on vulnerable populations with high rates of infections such as those residing in rural areas, jails, prisons, etc. Ideally, a large study should be conducted following rural PWID from time of diagnosis and over several years to determine predictors of linkage to care. More current research is also needed in the new DAA treatment era to determine if fear of side effects or concerns about the ineffectiveness of treatment is still relevant. Lastly, consistency should be used in how linkage to care is defined. In the interim, caution should be used in generalizing these findings to real-world populations.

Findings from Chapter Three suggest that while there are similarities in barriers and facilitators associated with linkage-to-care in rural inhabitants, there are also some key differences. Additional research is needed to confirm these differences using a larger sample size of rural PWID. In addition, future studies should attempt to obtain more objective predictor variables as opposed to relying exclusively on self-report measures. Future research is also needed to determine system-level and provider-level barriers among vulnerable populations such as PWID.

In Chapter Four, we found that younger age and no insurance were barriers to PCP use among female inmates with a history of injection drugs. Knowing this, clinicians should target this vulnerable group and seek out opportunities to screen and refer to specialist. For example, when clinicians encounter young and/or uninsured PWID in an emergency department, jail, prison, urgent treatment center, and/or addiction clinic,

they should offer information about free screening sites or treatment facilities that offer income-based payment plans.

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CHAPTER ONE

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United Clinics of Kentucky

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Advanced Practice Provider

2009 - 11

MedfusionRx

Birmingham, Alabama

Nurse Educator

2009 -11

Eastern State Hospital

Lexington, Kentucky

Nursing Assistant

2004 -07

PUBLICATIONS AND ABSTRACTS

Racho, R. G., Abdelwadoud, M., Brown, J. A., Santos, P. A., **Kuns-Adkins, C. B.**, Rosenau, J., Dela Cruz, A. C. (2017) Treatment Uptake in Hepatitis C virus infected patients in central and eastern Kentucky. *Gastroenterology* 152 (5), s1076.

Santos, P., Racho, R., Abdelwadoud, M., Cooper, M., **Kuns-Adkins, C.B.** (2016) Stage 3-4 Fibrosis does not guarantee access to direct-acting antivirals in patients with state-funded insurance: An analysis of a HCV referral program. *Hepatology*, 63 (1 supp), 406A-406A.

Crittenden, N. E., Buchanan, L. A., Pinkson, C. M., Cave, B., Barve, A., Marsano, L., McClain, C. J., Jones, C. M., Marvin, M. R., Davis, E. G., **Kuns-Adkins, C. B.**, Gedaly, R., Brock, G., Shah, M. B., Rosenau, J., Cave, M. C. (2016) Simeprevir and Sofosbuvir with or without Ribavirin to Treat Recurrent Genotype 1 Hepatitis C Virus Infection After Orthotopic Liver Transplantation. *Liver Transplantation*, 22 (5), 635-643.