RISK BEHAVIOURS ASSOCIATED WITH HEPATITIS C INFECTION AMONG PERSONS WHO INJECT DRUGS IN PRINCE GEORGE, BRITISH COLUMBIA

by

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THESIS SUBMITTED IN PARTIAL FULFILLMENT OF
THE REQUIREMENTS FOR THE DEGREE OF
MASTER OF SCIENCE
IN
COMMUNITY HEALTH SCIENCES

UNIVERSITY OF NORTHERN BRITISH COLUMBIA

June 2017

Abstract

Persons who inject drugs (PWIDs) are at high-risk of hepatitis C virus (HCV) infection due to blood-to-blood contact when sharing injection equipment (World Health Organization, 2014). To investigate this health concern, the current thesis research obtained the 2008 and 2012 Prince George I-Track survey datasets from the Public Health Agency of Canada (2012). Multivariate logistic regression analyses were conducted to determine risk behaviours and characteristics associated with HCV infection among PWIDs living in Prince George, British Columbia (BC).

Two independent variables were significantly associated with HCV infection among Prince George PWIDs: injecting for more than two years, Adjusted Odds Ratio (AOR) 7.87, $p < .001$, 95% CI [3.60, 17.18], and injecting alone (versus with others), AOR 2.49, $p = .004$, 95% CI [1.35, 4.59]. The study results provide health practitioners with a highly sensitive (94.1%) predictive tool to identify PWIDs in Prince George, BC who are most likely to be infected with HCV.

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List of Abbreviations

AHR	adjusted hazard ratio
AOR	adjusted odds ratio
ARR	adjusted risk ratio
ARYS	At-Risk Youth Survey
CI	confidence interval
CHC	chronic hepatitis C
DAA	direct-acting anti-viral agent
DTES	downtown east side
DV	dependent variable
HCV	hepatitis C virus
HIV	human immunodeficiency virus
IDU	injection drug use
IV	independent variable
NEP	needle exchange program
OR	odds ratio
PO	prescription opioid
PWID	person(s) who inject drugs
RR	risk ratio
SE	standard error
VIDUS	Vancouver Injection Drug Users Survey

Glossary

Back-loading – drawing up a drug into one syringe and then dividing the drug equally between two separate syringes (Harm Reduction Coalition [HRC], 2011)

Cooker – container used for mixing and heating a drug (HRC, 2011).

Filter – small cotton ball (preferably sterile) that is placed in dissolved drug to remove particles prior to injection (HRC, 2011).

Speedballs – a combination of cocaine and opiate that is injected simultaneously (Centre for Addiction and Mental Health [CAMH], 2012).

Shooting gallery – a place used for drug injection (HRC, 2011).

Swabs – 70% isopropyl alcohol wipes used to clean skin prior to injection (HRC, 2011).

Tourniquets - a strip of elastic tied around the arm to raise veins for injection (HRC, 2011).

Water – sterile or unsterile liquid required to dissolve drugs prior to injection (HRC, 2011).

Washes – large amounts of residue from prescription opioids that remain on injection equipment and are rinsed with water and re-injected (Roy et al., 2012).

Acknowledgement

I would like to express sincere gratitude to everyone who supported me to write this research thesis. First of all, to Dr. Russ Callaghan for his expertise, patience, and support while I worked to complete my thesis and maintain my nursing career. Secondly, to the Centre for Addictions Research of British Columbia, Northern Health, the University of Northern British Columbia, and the British Columbia Nurses Union for generously providing me with financial funding. Thirdly, to Dr. Wagner, Dr. Hamour, and all of the graduate course instructors at the University of Northern British Columbia for constructive feedback and guidance to develop my research and writing skills at a graduate level. And finally, to my friends, family, and co-workers for asking me about my thesis research and encouraging me to complete it to the best of my abilities.

CHAPTER 1: Introduction

Persons who inject drugs (PWIDs) are at high-risk of hepatitis C virus (HCV) infection due to blood-to-blood contact when sharing injection equipment (World Health Organization [WHO], 2014). The worldwide prevalence of HCV among PWID populations is estimated at 67%, or approximately 10 million persons (WHO, 2014). In 2013, the global burden of disease from HCV infections attributable to injection drug use (IDU) was estimated to be 7.5 million disability adjusted life-years (DALYs): a four-fold increase since 1990 (Degenhardt et al., 2016). Although regions in Asia jointly account for an estimated 50% of the IDU-attributable global burden of HCV disease, it is estimated that high-income North America (Canada and the United States) accounts for the second largest proportion (11%) of IDU-attributable HCV disease burden (Degenhardt et al., 2016).

In Canada, approximately 225,000 Canadians are chronically infected with HCV, and it is estimated that 60-89% of these cases are current or former PWIDs (Degenhardt et al., 2016; Myers, Shah, Burak, Cooper, & Feld, 2015). Despite the high burden of HCV disease among PWIDs living in Canada, extremely low rates of HCV treatment have occurred (Degenhardt et al., 2016). Recent advancements in orally-administered direct-acting anti-viral agents (DAAs) are yielding HCV infection cure rates of more than 90% within 8-24 weeks of treatment (Pawlotsky, Feld, Zeuzem, & Hoofnagle, 2015). Therefore, enhanced screening and timely provision of DAAs to PWIDs infected with HCV has the potential to greatly reduce the financial, social, and personal costs of chronic infection.

Using the 2008 and 2012 Prince George I-Track survey data, the current thesis research investigates the risk behaviours and characteristics associated with HCV infection among PWIDs living in Prince George, BC. Identifying significantly associated risk behaviours and characteristics will assist health practitioners to identify HCV positive

PWIDs for screening, monitoring and treatment of chronic HCV (CHC) infections; and to identify HCV negative PWIDs for ongoing harm reduction interventions.

Context of the Current Study

The I-Track research project is a behavioural and biological surveillance system monitoring the prevalence of human immunodeficiency virus (HIV), HCV, and associated risk behaviours among PWIDs in Canada (Public Health Agency of Canada [PHAC], 2014). The system was developed as part of the Federal Initiative to Address HIV/AIDS and funding was provided by the PHAC, regional health authorities, and local community agencies (PHAC, 2014). A detailed description of the I-Track research methodology and I-Track survey is presented in Supplement One.

Several research studies preceded the selection of Prince George as an I-Track sentinel site. The Vancouver Injection Drug Users Study (VIDUS) (Miller et al., 2002; Patrick et al., 2001), the At-Risk Youth Survey (ARYS) (Miller et al., 2009; Wood et al., 2006), the Cedar Project (Craib et al., 2009; Jongbloed et al., 2015; Mehrabadi et al., 2008, Miller et al., 2009), as well as research conducted by Callaghan et al. (2003; 2007; 2008) identified high HCV prevalence and multiple risk behaviours among PWIDs in Vancouver and/or Prince George, BC. Rachlis et al. (2008) also evaluated the risks of HCV transmission due to increased mobility of PWIDs between Vancouver and outlying communities such as Prince George, BC. A review of these studies will establish the context for the selection of Prince George as an I-Track sentinel site, as well as the current thesis research.

Vancouver Injection Drug Users Survey

In response to an alarming HIV outbreak in Vancouver, BC, the VIDUS open prospective cohort study was initiated in 1996 (Patrick et al., 2001). Eligible PWIDs resided in Vancouver, reported injecting drugs in the month prior to enrollment, and were older than

13 years (Miller et al., 2002). Baseline and semi-annual questionnaires were administered by trained interviewers, and venous blood samples were collected and tested for HIV and HCV antibodies (Miller et al., 2002). Among the 1,345 eligible participants, HCV prevalence at enrollment was 81.6%, 95% Confidence Interval (CI) [79.6%, 83.6%], and the overall HCV incidence density between 1996 and 1999 was 29.1 per 100 person-years, 95% CI [22.3, 37.3] (Patrick et al., 2001). Of particular interest was the association between age, number of years injecting, and HCV serostatus (positive or negative blood test result). HCV positive participants were older (median age 35 vs. 25 years) and had been injecting longer (median 14 vs. 3 years) than HCV negative participants (Patrick et al. 2001). The VIDUS research clearly indicated "extreme pressure toward HCV transmission among seronegative [PWIDs]" and highlighted significant differences in characteristics and risk behaviours of HCV positive and HCV negative PWIDs (Patrick et al., 2001, p. 894).

Subsequently, Miller et al. (2002) utilized the VIDUS cohort data to explore risk behaviours, HCV prevalence, and HCV incidence among younger PWIDs. Of the 232 participants aged 13 to 24 years, 46% (n = 107) were HCV positive at initial enrollment (Miller et al., 2002). Additionally, 49% of the youth participants who were HCV negative at enrollment seroconverted during the initial five-year study period for an estimated incidence rate of 37.3 per 100 person-years (Miller et al., 2002). Significant risk behaviours associated with HCV seroconversion included daily cocaine use, Risk Ratio (RR) 3.04, 95% CI [1.20, 7.70]; having a partner who uses injection drugs, RR 2.48, 95% CI [1.08, 5.66]; and requiring help injecting, RR 2.48, 95% CI [1.08, 5.66] (Miller et al., 2002). The VIDUS research highlighted a narrow window of opportunity for HCV prevention among young PWIDs and warranted further investigation of the risk behaviours and characteristics associated with HCV infection.

At-Risk Youth Survey (ARYS)

Evolving from the VIDUS research, the At-Risk Youth Survey (ARYS) was implemented to examine risk behaviours and characteristics associated with injection initiation among street-involved youth living in Vancouver (Wood et al., 2006). Using an open prospective cohort design, enrollment began in October 2005 with baseline interviewer-administered questionnaires and venous blood samples collected and tested for HIV and HCV antibodies (Wood et al., 2006). Eligibility requirements were 1) ages 14 to 26 years, and 2) use of drugs other than marijuana in past 30 days (Wood et al., 2006). Follow-up questionnaires and venous blood tests were conducted semi-annually to monitor HCV incidence, transition to IDU, and associated risk behaviours (Wood et al., 2006).

Miller et al. (2009) found ARYS participants who were HCV positive (13%) were older in age ($p = .035$), engaged in sex trade ($p = .027$), reported childhood sexual abuse ($p = .040$), and reported ever injecting drugs ($p < .001$). Similar to the VIDUS findings, among ARYS participants who reported IDU, the number of years injecting was significantly associated with HCV infection, Adjusted Odds Ratio (AOR) 1.23 per year increase, 95% CI [1.11, 1.37] (Miller et al., 2009). Additionally, injecting crystal meth at least once per day, AOR 3.10, 95% CI [1.25, 7.70], and injecting heroin at least once per day, AOR 8.56, 95% CI [3.64, 20.13] were significantly associated with HCV infection (Miller et al., 2009). The ARYS results indicated IDU among young PWIDs was high-risk for HCV seroconversion.

The Cedar Project

Concurrent with the ARYS research, the Cedar Project prospective cohort study began recruiting self-identified Aboriginal youth aged 14 to 30 years living in Vancouver, BC or Prince George, BC (Mehrabadi et al., 2008). Eligible participants reported smoking illegal drugs in previous week or injecting illegal drugs within the previous month

(Mehrabadi et al., 2008). Similar to the VIDUS and ARYS studies, participants completed interviewer-administered questionnaires and provided venous blood samples to be tested for HCV and HIV antibodies (Mehrabadi et al., 2008). The purpose of the Cedar Project was to compare socio-demographics, drug use patterns, injection practices, sexual experiences, lifetime and historical trauma, and HIV and HCV prevalence between young Aboriginals living in two urban centres in BC (Mehrabadi et al., 2008). As a resource-based town located in northern BC and with approximately 10% of the population self-identified as Aboriginal, Prince George was considered ideal to recruit a target population of 300 young Aboriginal participants (Mehrabadi et al., 2008).

HCV prevalence among Cedar Project PWIDs was 62.4% and 57.1% in the Prince George and Vancouver cohorts respectively (Craib et al., 2009). The incidence of HCV exposure during the first two years of study was 12.9 per 100 person-years in Prince George vs. 7.5 in Vancouver (Craib et al., 2009). Despite higher HCV prevalence and incidence in the Prince George cohort, the differences were not statistically significant (p =.370) (Craib et al., 2009). However, Aboriginal female PWIDs were significantly more likely to be HCV positive, AOR 1.9, p = .012, 95% CI [1.1, 3.4]; as were those reporting opiate injection, AOR 2.7, p = .033, 95% CI [1.0, 7.4]; reusing syringes, AOR 2.4, p < .001, 95% CI [1.3, 4.4]; at least one parent attended residential school, AOR 1.9, p = .038, 95% CI [1.1, 3.4]; and duration of IDU, AOR 1.4 per year, p < .001, 95% CI [1.3, 1.5] (Craib et al., 2009). The Cedar Project results expanded on previous evidence from the VIDUS and ARYS studies, and identified multiple risk behaviours and characteristics specific to HCV among young Aboriginal PWIDs.

The Cedar Project findings also demonstrated that 1) HCV had spread to areas outside of the downtown east side (DTES) of Vancouver, 2) associated risk behaviours and

characteristics were changing, and 3) Aboriginal PWIDs living in rural areas were especially vulnerable to HCV infection (Craib et al., 2009). As a result, the Northern BC Aboriginal HIV/AIDS Task Force (now named the Northern BC First Nations HIV/AIDs Coalition) was established. Sixty Chiefs from Aboriginal communities across northern BC mandated the task force to develop a comprehensive strategy to strengthen Aboriginal individuals and communities to combat HIV/AIDs and HCV (Carrier Sekani Family Services, 2016). Consequently, the task force became a primary stakeholder in the 2008 and 2012 Prince George I-Track surveys.

Prince George Inpatient Detox Research

Several retrospective medical chart reviews of inpatients admitted to the Prince George detoxification centre also occurred concurrently with the VIDUS and ARYS and Cedar Project research. A three-year medical chart review conducted by Callaghan and Cunningham (2002) compared intravenous and non-intravenous cocaine drug users admitted to the Prince George detox centre between 1999 and 2002. The review identified higher rates of residential instability, unemployment, Aboriginal ethnicity, problematic opiate use, HCV and HIV infections, and cirrhotic liver disease among intravenous cocaine users as compared to non-intravenous users (Callaghan & Cunningham, 2002). In particular, Aboriginal PWIDs self-reported daily cocaine use, residential instability, and high prevalence of HCV infection (Callaghan & Cunningham, 2002). The combination of these risk behaviours revealed the potential for HCV transmission to outlying Aboriginal communities throughout northern BC.

Subsequently, Callaghan, Tavares, and Taylor (2007) investigated the residential instability of Aboriginal PWID detox inpatients between on-reserve and off-reserve locations. Aboriginal PWIDs who had been admitted at least twice to the detox centre from 1999 to 2005 were examined for place-of-residency transitions (Callaghan et al., 2007). Of

the Aboriginal PWIDs with two admissions, 26%, 95% CI [21%, 31%], who had been living off-reserve at first admission had moved to on-reserve by second admission (Callaghan et al., 2007). Conversely, of those living on-reserve at first admission, 96%, 95% CI [88%, 100%], had moved off-reserve by the second admission (Callaghan et al., 2007). Additionally, 46% of the Aboriginal PWIDS included in the study had self-reported being HCV positive (Callaghan et al., 2007). The results demonstrated significant mobility between on-reserve and off-reserve locations, and reiterated the potential for HCV transmission to PWIDs in outlying communities.

Prevalence of HCV in Northern BC

Between 1998 and 2007, the reportable disease statistics from the BC Centre for Disease Control (BCCDC) reported an overall provincial decrease in annual HCV incidence (BCCDC, 2008). However, declining provincial HCV incidence rates did not reflect the persistently high HCV incidence rates within the Northern Health (NH) region of northern BC. With an estimated population of 300,000, the NH region encompasses almost two-thirds of BC (600,000 square kilometers) and includes all populations living north of Quesnel and west of Valemount (NH, 2016). As shown in Figure 1, the NH region has had persistently high HCV incidence rates as compared to national rates since 2003 (BCCDC, 2015).

High HCV incidence rates within the NH region may have reflected increased HCV testing due to an overall increased awareness of HCV prevalence (BCCDC, 2008). Moreover, the specific mode of transmission for HCV incident cases was not captured by the BCCDC epidemiological data and the incident cases may not have represented incident cases among PWIDs (BCCDC, 2008). However, the BCCDC estimated that 54% -70% of all incident HCV cases were related to IDU (BCCDC, 2013). Combined with the primary research findings, the HCV incidence rates reported within the NH region provided further evidence

that PWIDs in northern BC were particularly vulnerable to HCV infections.

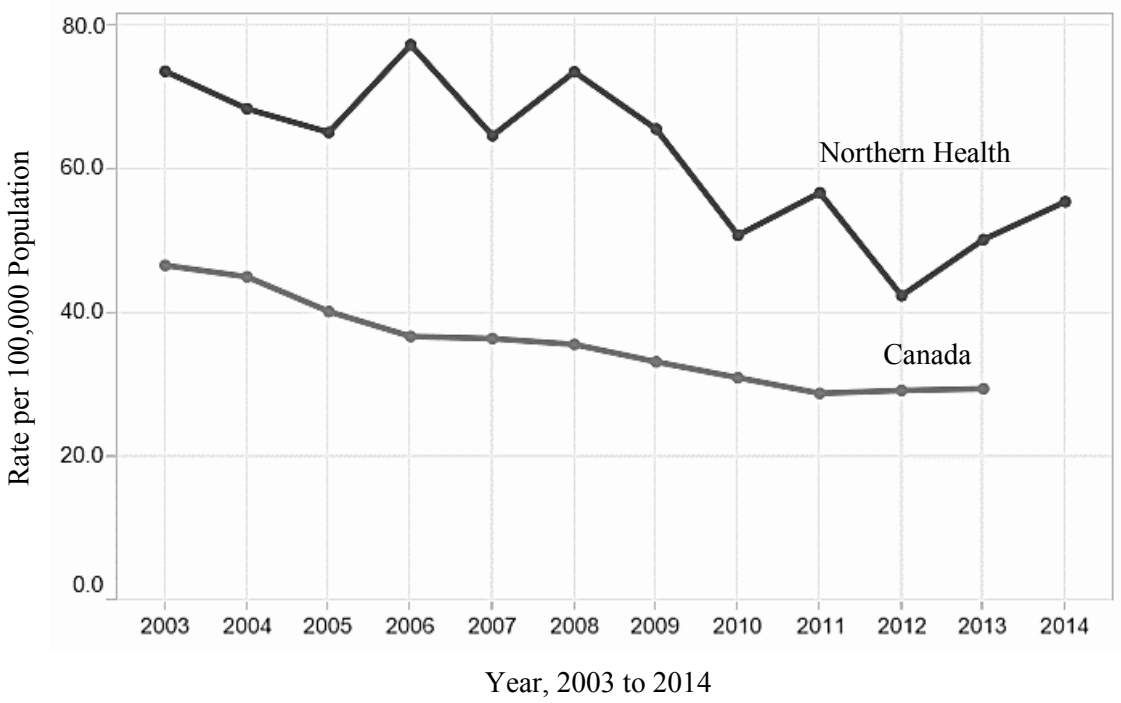

Figure 1. A comparison of the NH region and Canadian annual HCV incidence rates per 100,000 population, 2003-2014 (BCCDC, 2015).

Summary of the Study Context

As outlined above, multiple studies establish the context for the selection of Prince George as an I-Track sentinel site, as well as the current thesis research. The VIDUS and ARYS studies identified multiple risk behaviours associated with HCV infections among PWIDs living in Vancouver, BC. The Cedar Project focused on risk behaviours and characteristics associated with HCV infections among Aboriginal youth in both Vancouver and Prince George. Additionally, the Prince George inpatient detox research identified multiple HCV risk behaviours and characteristics within PWIDs in Prince George and highlighted the residential mobility of Aboriginal PWIDs to smaller communities within northern BC. High annual HCV incidence rates within the NH region warranted the selection

of Prince George as an I-Track sentinel site, as well as further research of HCV prevalence among high-risk PWID populations living in northern BC.

Study Purpose

The purpose of the current thesis research is to investigate the risk behaviours and characteristics associated with HCV infection among PWIDs who participated in the Prince George I-Track surveys. The research findings will provide evidence-based information to guide public health interventions focused on HCV, and will promote improved health and wellness for high-risk PWIDs living in northern BC.

Research Question

What are the risk behaviours and characteristics associated with HCV infection among the PWIDs who participated in the Prince George I-Track surveys?

CHAPTER 2: Literature Review

A review of the literature was conducted to identify risk behaviours and characteristics associated with HCV among PWIDs that had been investigated by previous research. Chapter Two will outline the literature search strategy, describe the selection criteria for relevant research articles, and present a critical narrative review of the research evidence. The results of the review will guide the selection of risk behaviours and characteristics to be included in the statistical analyses of the current thesis research.

Literature Search Strategy

Using the EBSCO search engine, a search for relevant research was conducted within four on-line databases: CINAHL complete, Academic Search Complete, MedLINE, and PsycINFO. Grey literature was also located using search engines on the WHO (www.who.int), the PHAC (http://www.phac-aspc.gc.ca), and the BCCDC (www.bccdc.ca) websites. All searches included subject headings and keywords of ["HCV" OR "hepatitis c" OR "hep c" OR "hepatitis c virus"] AND ["IV drug use*" OR "IDU*" OR "intravenous drug use*" OR "IVDU*" OR "persons who inject drug*" OR "PWID*"] AND ["risk factor*" OR "risk behavio*"].

Selection of Relevant Research Articles

The large number of search results were then limited to 1) English language and 2) the publication period of 2010 to 2016. The publication period was selected based on significant advancements in HCV virology that occurred in 2010. During that year, the ability to replicate HCV in a laboratory setting rapidly expanded the knowledge of HCV infectivity and transmission, and has greatly influenced all HCV research conducted since 2010 (Paintsil, He, Peters, Lindenbach, & Heimer, 2010; Ray, Bailey, & Thomas, 2013). The search results with these filters applied rendered 1,192 hits.

Research articles that were not peer-reviewed and all duplicates were also removed resulting in 419 articles. Manual browsing of abstracts was conducted and all research studies conducted in developing countries were removed. It was felt that research conducted in developed countries would share similar socio-economic, political, and health care infrastructures with the study sample of the current thesis research, thus minimizing confounding factors unique to PWID populations in developing countries.

Manual browsing also identified and removed research articles predominantly focused on HIV. The tendency for HCV infections to be lumped in with HIV research is problematic because the pathogenicity, modes of transmission, and natural history of the two viruses are quite different. A detailed description of the natural history of HCV is provided in Supplement Two. Differences in virology result in differences in associated risks: an important distinction often overlooked in HIV-focused research. Multiple studies mentioned HCV in the title or abstract, but focused the analyses on HIV. These studies were excluded from the review due to the lack of attention to HCV-specific risk behaviours and characteristics that differ from HIV.

Additionally, HCV research studies that primarily focused on sub-groups of PWIDs were removed from the search results. Such studies had selection criteria that differed from the current thesis research. For instance, several studies focused exclusively on incarcerated PWIDs; or male PWIDs who have sex with men; or PWIDs who had become re-infected with HCV; or PWIDs co-infected with HIV. Arguably, these sub-groups of PWIDs may have different risk behaviours (e.g., tattooing, sexual transmission, immune-suppression) from the community-based sample of PWIDs who participated in the Prince George I-Track surveys. Therefore, research studies that focused on specific sub-groups of PWIDs were excluded.

The manual browsing and filtering process resulted in thirty-eight relevant research articles. The reference list of each research article was then scanned for articles that appeared relevant to the current thesis research or were repeatedly referenced. The scanning process resulted in a further twenty-nine research articles which were then filtered using the same aforementioned process. Ten research articles were deemed relevant, resulting in forty-eight relevant articles to be included in the literature review. Studies that contributed to the context of the current thesis research (Chapter One) were also included in the literature review.

Risk Behaviours and Characteristics

Several risk behaviours associated with HCV infection among PWIDs were repeatedly investigated in the relevant research. Sharing injection equipment; number of injection years; drug of choice; injection partners and sexual partners; female gender; Aboriginal status, and unstable housing were commonly included in multivariate analyses throughout the literature. Each of these risk behaviours and characteristics were also suspected to be relevant within the current thesis research. Two further risk behaviours considered to be relevant that were not as prevalent in the literature were involvement in sex trade and residential mobility. The following narrative critically reviews the related research of risk behaviours and characteristics associated with HCV infection among PWIDs.

Sharing Injection Equipment

PWIDs are especially vulnerable to HCV transmission via blood-to-blood contact with HCV-infected blood. The prolonged environmental viability of HCV (Paintsil et al., 2010; 2014), the potential for HCV reservoirs on multiple pieces of injection equipment (Doerrbecker et al., 2011; 2013; Hagan et al., 2011; Thibault, Bara, Nefau, & Duplessy-Garson, 2011), and ubiquitous sharing behaviours among PWIDs (Kim, Jim, McFarland, & Raymond, 2015; Palmanteer et al., 2010; 2013; Pouget, Hagan, & Des Jarlais, 2011; Strike et

al., 2010) all contribute to high rates of HCV transmission. A review of the related research strongly suggests sharing injection equipment is the premier risk factor associated with HCV infection among PWIDs.

Contaminated injection equipment. Multiple laboratory studies have indicated the prolonged viability of HCV within needles and syringes. Cardinal research conducted by Paintsil et al. (2010) claimed HCV viability in syringes was dependent on syringe type, time, and temperature. They found that HCV remained viable in high-void syringes (residual volume = 32 μL) at various temperatures for up to nine weeks. Low-void syringes (residual volume = 2μL) maintained viable HCV for up to seven days at various temperatures (Paintsil et al., 2010). Although laboratory results may not be generalizable to the natural injection environment, the Paintsil et al. (2010) findings suggested prolonged HCV viability and increased risk for transmission among PWIDs when sharing syringes.

Further research conducted by Doerrbecker et al. (2011) investigated the stability of HCV on cookers commonly shared between PWIDs. After applying a constant heat source to an HCV-contaminated cooker for 85-90 seconds, they found HCV infectivity was compromised at ~50º C and was undetectable by 65-70º C. Concurrently, observational research conducted by Hagan et al. (2011) in multiple shooting galleries found only 12% of PWIDs heated cookers for >45 seconds, while almost 50% of those observed heated cookers for <15 seconds. The laboratory setting of the Doerrbecker et al. (2011) study may not simulate the natural injection environment, while the Hagan et al. (2011) study was strictly observational with much potential for confounding factors. However, the combined findings strongly suggest the risk for HCV transmission among PWIDs when sharing cookers contaminated with infected blood.

Doerrbecker et al. (2013) investigated the survival of HCV in water containers and injection filters. In a laboratory setting, room temperature water with high concentrations of HCV (500 μL) maintained infectivity for more than twenty-one days, and low concentrations (8 - 40 μL) remained infective for four days (Doerrbecker et al., 2013). Additionally, they found injection filters consistently harboured infectious HCV (10% of the initial viral load) when stored in foil wrappers for 24-48hrs; a common practice among PWIDs. The Doerrbecker et al. (2013) findings strongly suggest prolonged viability of HCV and potential risk of HCV transmission among PWIDs when sharing contaminated water and filters.

Thibault, Bara, Nefau, and Duplessy-Garson (2011) found high rates of infective HCV detection in pools of used alcohol swabs. By analyzing used injection equipment collected from HCV-positive PWIDs, they found blood macroscopically visible on most swabs, and levels of HCV RNA were 10-fold higher than in used syringes. Subsequent laboratory research found swabs needed at least 50% alcohol concentration and one minute of exposure time to render HCV undetectable (Doerrbecker et al., 2013). Paintsil et al. (2014) also found that decreasing alcohol concentrations (70% to 7%) became progressively ineffective as an antiseptic when applied to HCV contaminated surfaces. The research indicates inadequate antiseptic exposure time and/or inadequate antiseptic concentrations increase the risk for HCV transmission when sharing swabs.

A review of the related research strongly suggests that the sharing of any injection equipment, not just needles and syringes, among PWIDs potentially increases risk for HCV transmission due to prolonged environmental viability. Arguably, the studies were conducted in laboratory settings, and may not reflect the natural injection environment. However, the prolonged environmental viability of HCV demonstrates the potential for all injection drug

equipment to be effective vectors for HCV transmission when contaminated and shared among PWIDs.

Prevalence of sharing injection equipment. Sharing needles/syringes has been repeatedly identified as the premier risk behaviour associated with HCV infections among PWIDs. Meta-analyses conducted by Palmanteer et al. (2013) reviewed sixteen cross-sectional and four longitudinal studies to estimate pooled association between needle/syringe sharing and HCV prevalence/incidence. Results of their meta-analyses estimated sharing needles/syringes was significantly associated with HCV infection, Odds Ratio (OR) 3.34, $p <$ .001, 95% CI [2.42, 4.62]. Differences between classification of sharing behaviours, study designs, and sample populations create limitations within meta-analyses studies (Palmanteer et al., 2013). However, the Palmanteer et al. (2013) meta-analyses strongly suggest prevalent sharing behaviours within PWID populations are significantly associated with HCV infections.

Interestingly, the Palmanteer et al. (2013) meta-analyses also highlighted HCV prevalence of 82% among PWIDs who reported they had never shared needles/syringes. The researchers surmised that the HCV infections were most likely due to ubiquitous sharing of injection drug equipment, such as cookers, water, and filters. Such suggestions are supported by meta-analyses conducted by Pouget, Hagan, and Des Jarlais (2011). Using twenty-one eligible studies, they estimated the population-attributable risk percentages of sharing behaviours associated with HCV infection. Among those exposed to HCV through syringe sharing, Pouget et al. (2011) estimated that 25% of HCV seroconversions could be prevented by eliminating syringe sharing behaviours. Moreover, they estimated 43% of PWIDs sharing cookers, 42% of those sharing filters, and 37% of those sharing water could avoid HCV seroconversion by eliminating their sharing practices. Similar to the Palmanteer et al. (2013)

research, the Pouget et al. (2011) meta-analyses results are limited due to differences between study methodologies. However, their study highlights the potential risk for HCV transmission among PWIDs who share any injection equipment.

Of the articles identified in the literature search, two primary research studies focused specifically on the prevalence of sharing behaviours within sample PWID populations. Cross-sectional research conducted by Strike et al. (2010) found 36% of PWID participants living in London, Ontario reported they shared needles, 45% shared cookers, 39% shared water, and 29% shared filters in the previous 6 months. Those who self-reported as HCV positive (53.1%) also reported distributing used cookers (56.1%), water (54.3%), and filters (59.5%) for re-use by other PWIDs (Strike et al., 2010). Although generalizability is limited, and selection, recall, and social desirability biases may have influenced the results, self-reported sharing of injection drug equipment within the sample PWID population was prevalent.

More recently, Kim, Jin, McFarland, and Raymond (2015) found significant decreases in reported needle sharing during their longitudinal cohort study of PWIDs living in San Francisco, California. Participants reported decreased receptive needle sharing from 25.5%, 95% CI [19.7, 32.0] to 14%, $p < .001$, 95% CI [8.6, 20.4]; decreased receptive cooker sharing from 46.5%, 95% CI [39.1, 54.1] to 37.9%, $p = .003$, 95% CI [31.8, 44.1]; and decreased receptive water sharing from 38.3%, 95% CI [31.0, 46.0] to 25.5%, $p < .001$, 95% CI [20.3, 31.3] (Kim et al., 2015). Reports of distributive sharing decreased, but such reports may be limited by social desirability bias (Kim et al., 2015). Although the longitudinal cohort study identifies decreasing trends of self-reported sharing behaviours, the overall receptive sharing of injection equipment among PWIDs remains prevalent.

Summary of sharing injection equipment. A review of the research supports the claim that sharing of injection equipment is the premier risk behaviour associated with HCV infections among PWIDs. The prolonged environmental viability of HCV greatly contributes to the risk of transmission when sharing any injection equipment among PWIDs. The high prevalence of HCV within PWID populations, as well as ubiquitous sharing behaviours contribute to the high-risk for HCV transmission. The research evidence demonstrates that sharing injection equipment is a premier risk factor for HCV infection among PWIDs and will be included in the bivariate and multivariate analyses of the current thesis research.

Number of Injection Years

Multiple studies in the relevant literature have investigated the number of injection years as a risk factor for HCV infections among PWIDs. Longitudinal studies have identified increasing HCV incidence rates for PWIDs as duration of drug injection increases (Roy, Boudreau & Boivin, 2009; Spittal et al., 2012). Additionally, cross-sectional studies have found significant associations between number of injection years and HCV infections (Craib et al., 2009; Garfein et al., 2012; Havens et al., 2013; Miller et al., 2009; PHAC, 2010). A review of the related research strongly suggests the number of injection years is an important risk behaviour significantly associated with HCV infections among PWIDs.

Number of years to seroconversion. Longitudinal cohort studies provide temporal data to estimate incidence of HCV infection among PWIDs. Roy, Boudreau, and Boivin (2009) used prospective cohort data from young street-involved PWIDs in Montreal to estimate that 55% of HCV negative participants seroconverted within four years of injection initiation. They also found the median length of time to HCV infection was 3.3 years, and estimates of HCV incidence dropped significantly after the first four years of injection (p = .002). Arguably, the study participants were aged 14 to 23 years and maturational bias may

limit the generalizability of the results. For instance, an older cohort of injection initiates may engage in different risk behaviours resulting in different rates of HCV incidence from first injection. However, the Roy et al. (2009) findings indicate the first four years of injection are high-risk for HCV infection among young PWIDs.

The Cedar Project estimated hazard ratios between the number of years injecting and HCV infection (Spittal et al., 2012). Using prospective cohort data of young Aboriginal participants who were HCV negative, they estimated that those who had been injecting for less than two years experienced HCV seroconversion at more than four times the rate of those who had injected more than five years, Adjusted Hazard Ratio (AHR) 4.14, $p < .001$, 95% CI [1.91, 8.94]. Additionally, the HCV incidence density of those reporting injecting drugs for two years or less was 26.3 per 100 person-years (Spittal et al., 2012). Survivorship bias may have caused under-estimations by excluding the highest risk participants who were (already) HCV positive at baseline, and attrition bias may have skewed results due to missing data from non-returners. However, the Spittal et al. (2012) research suggests high incidence of HCV infection among young Aboriginal PWIDs during the initial two years of IDU.

Multiple cross-sectional studies suggest the number of injection years is significantly associated with HCV infections among PWIDs. The national I-Track, Phase 1 survey reported young street-involved PWIDs aged 20 to 24 years were five times more likely to be HCV positive than those aged 15 to 19 years, OR 5.2, $p < .001$, 95% CI [2.7, 9.9] (PHAC, 2010). Similarly, the national Enhanced Street-Involved Youth Survey [E-SYS] found street-involved PWIDs aged 20 to 24 years were four times more likely to be HCV positive than younger PWIDs, OR 4.0, $p < .001$, 95% CI [2.9, 5.5] (PHAC, 2010). In both studies, young PWIDs in the older age group were significantly more likely to be HCV positive.

Similarly, cross-sectional data from the ARYS and Cedar Project studies indicate the number of injection years is significantly associated with HCV infection among young PWIDs. At baseline, young PWIDs in the ARYS study were 1.23 times more likely to be HCV positive per year of IDU, AOR 1.23, 95% CI [1.11, 1.37] (Miller, Kerr, Fischer, Zhang, & Wood, 2009). The Cedar Project also found young Aboriginal PWIDs were 1.4 times more likely to be HCV positive per year of IDU, AOR 1.4, 95% CI [1.3, 1.5] (Craib et al., 2009). Both observational studies suggest the number of injection years is a significant risk factor associated with HCV among young PWIDs.

Among adult PWIDs, significant associations between number of years injecting and HCV infection have also been identified. Cross-sectional research conducted by Garfein et al. (2012) found the risk of HCV among adult PWIDs increased by almost three times per year of injecting, AOR 2.82, $p < .001$, 95% CI [2.06, 3.84]. Similar observational research by Havens et al. (2013) found rural Appalachian PWIDs injecting who had been injecting for more than five years were three times more likely to be HCV positive, AOR 3.08, $p < .001$, 95% CI [1.67, 5.66]. The cross-sectional studies strongly suggest the number of injection years is significantly associated with HCV infection among several PWID samples.

Summary of number of injection years. A review of both longitudinal and cross-sectional research indicates the number of injection years is a significant risk behaviour associated with HCV infection among PWIDs. Unfortunately, differences in study methods and categorization of injection years (e.g., range of ages vs. per year of injection) make it difficult to further synthesize the evidence. Thus, the current thesis research estimates the greatest risk for HCV seroconversion occurs within the first two years of injection, and the independent variable IV_INJECTION_YEARS will be categorized accordingly.

Drug of Choice

Drug of choice refers to the type of drug that each individual PWID prefers to inject. Cocaine, amphetamine, heroin, and prescription opioids (POs) are the most common drugs reported to be injected by PWIDs. The amphetamine category in the current thesis research includes crystal meth and methamphetamine. Heroin and POs such as morphine, hydromorphone, fentanyl, methadone, oxycodone, and codeine are all classified as opiates. Each of these injection drugs of choice have been found to be significantly associated with HCV infections among PWIDs in the related research.

Confounding considerations. Although the related research has investigated the drug of choice as the risk factor associated with HCV, the injection behaviours that coincide with each drug may be underlying confounders. For example, cocaine injection is typically associated with a bingeing pattern of drug use with multiple injections occurring over relatively short periods of time (hours/days) (De, Jolly, Cox, & Boivin, 2006). It is not the cocaine use per se, but the increased frequency of injections that greatly increase the chance of exposure to blood-borne pathogens such as HCV. Therefore, frequency of injection would be the true associated risk behaviour.

Conversely, opiate injections typically occur two to three times daily over longer periods of time (weeks/months/years). The longer duration of injection may increase the chance of being exposed to HCV infection. However, opiate injection behaviours often involve multiple “washes” to get the entire amount of drug injected (Roy et al., 2012, p. 249). Therefore, sharing “washes” may be the true risk behaviour associated with HCV infections rather than drug of choice. Although drug of choice may be confounded by underlying injection behaviours, the related research investigates drug of choice and the current thesis research will do so also.

Cocaine injection. Two longitudinal cohort studies in the literature review have investigated cocaine injection as a risk factor for HCV seroconversion among PWIDs. Using prospective cohort data of HCV negative PWIDs living in Montreal, Bruneau et al. (2012) found cocaine injectors were three times more likely to become HCV infected than those not injecting cocaine, AHR 3.00, $p < .05$, 95% CI [1.44, 6.24]. As previously noted, longitudinal cohort analyses are susceptible to underestimations due to survivorship bias when PWIDs at highest risk are excluded because they are already infected with HCV at baseline. Attrition bias may also lead to underestimations and systematic errors when participants enrolled in the study are lost to follow-up at subsequent meetings. Bruneau et al. (2012) acknowledge such limitations in their study design. Despite underestimations, their findings strongly identify cocaine injection as a significantly associated risk behaviour for HCV infection among PWIDs.

Similarly, Grebely et al. (2014) used VIDUS longitudinal data from 1996 to 2012 to estimate hazard ratios of cocaine injection associated with HCV seroconversion. Within the large sample population of PWIDs who were HCV negative at baseline, cocaine injection was significantly associated with HCV seroconversion, AHR 1.77, $p < .05$, 95% CI [1.20, 2.61] (Grebely et al., 2014). Once again, the results may be underestimated due to attrition or survivorship bias. However, the research results indicate cocaine injection is a significant risk behaviour associated with HCV seroconversion even among the lowest risk PWIDs.

Cocaine injection has also been associated with HCV infections among PWIDs in cross-sectional research. Roux, Fugon, Jones, and Comer (2013) found cocaine injectors in their study to be more than eight times more likely to be HCV positive than non-injection cocaine users, AOR 8.52, $p < .001$, 95% CI [2.58, 28.21]. However, they did not compare cocaine injection with other injection drugs, and their small sample population limited

generalizability. Concurrently, Havens et al. (2013) found rural Appalachian cocaine injectors were more than twice as likely to be HCV positive than other PWIDs, AOR 2.13, $p < .001$, 95% CI [1.31, 3.45]. They also identified cocaine injectors reported significantly more years of injecting drugs than PO injectors, AOR 4.85, $p < .001$, 95% CI [2.70, 8.71]. With biases and limitations in mind, the cross-sectional study findings suggest cocaine injection is significantly associated with HCV infection among PWIDs.

Methamphetamine injection. Research by Miller, Kerr, Fischer, Zhang, and Wood (2009) used baseline data from the ARYS cohort study to investigate methamphetamine as a risk behaviour associated with HCV infection among young PWIDs. Those who reported methamphetamine injection at least once per day were more than three times more likely to be HCV positive, AOR 3.10, 95% CI [1.25, 7.70] (Miller et al., 2009). Particularly concerning, almost half of the young PWIDs in the Miller et al. (2009) study reported injecting methamphetamine on a daily basis, thus increasing their risk for HCV infection. Moreover, research conducted by Werb et al. (2013) identified methamphetamine use was independently associated with the initiation of IDU among street-involved youth, AHR 1.93, 95% CI [1.31, 2.85].

Grebely et al. (2014) also identified increased reports of methamphetamine injection in their study using VIDUS cohort data from 1996-2012. Prior to 2006, methamphetamine injection was not reported by HCV negative participants, whereas 35% of HCV negative participants reported injecting methamphetamine between 2006 and 2012 (Grebely et al., 2014). Those that reported methamphetamine injection during this time had 2.5-fold greater risk of HCV seroconversion, AHR 2.53, $p < .05$, 95% CI [1.11, 5.73]. However, associations between methamphetamine injection and HCV infection may be specific to PWIDs living in the DTES of Vancouver.

Opiate injection. Several studies in the related research have found heroin injection to be significantly associated with HCV infection. The Roux et al. (2013) study identified PWIDs who injected heroin were more than three times more likely to be HCV infected than non-injection heroin users, AOR 3.49, $p = .040$, 95% CI [1.09, 11.18]. Miller et al. (2009) found ARYS participants who reported injecting heroin more than once per day were greater than eight times more likely to be HCV positive, AOR 8.56, 95% CI [3.64, 20.13]. Additionally, PWIDs in the VIDUS study who were HCV negative at baseline and reported injecting heroin were found to have 1.5-fold greater risk of HCV seroconversion, AHR 1.57, $p < .05$, 95% CI [1.05, 2.35] (Grebely et al., 2014). Although the odds/hazards are greatly varied between studies, the related research repeatedly indicates PWIDs who inject heroin are at increased risk for HCV infection.

Differences between heroin injection versus PO injection, and associated risks for HCV infection are also identified in the related research. Havens et al. (2013) found PWIDs injecting POs were more than twice as likely to be HCV infected than those who were injecting just heroin, AOR 2.22, $p < .05$, 95% CI [1.13, 4.35]. Zibbell, Hart-Malloy, Barry, Fan, and Flannigan (2014) found similar risk associations between PO use and HCV infection. Notably, PWIDs reporting PO injection were more than five times more likely to be HCV positive than PWIDs who did not inject POs, AOR 5.53, $p < .05$, 95% CI [1.92, 15.91] (Zibbell et al., 2014). Similarly, Bruneau et al. (2012) investigated HCV infections among PWIDs who reported injecting both heroin and POs, as well as those who reported using POs exclusively. For those reporting only injecting POs in the previous 6 months, the risk of HCV seroconversion was almost three times greater than those who had injected both heroin and POs, AHR 2.88, $p < .05$, 95% CI [1.52, 5.45] (Bruneau et al., 2012). Although

both heroin and POs are opiates, the research suggests that each drug type has different injection practices resulting in different risk behaviours associated with HCV infection.

Research conducted by Roy et al. (2011) in downtown Montreal has identified multiple risk behaviours associated specifically with the injection of POs among PWIDs. Although POs are readily available, dose-reliable, and easy to divide, the small doses and methods of manufacturing (e.g., time-release beads) require more frequent injections (Roy et al., 2011). Furthermore, Roy et al. (2012) describe how PO injection preparation leaves large quantities of residue in the syringe, requiring multiple "washes" to get the full effect of the drug (p. 249). They further explain that injecting POs also requires a lot of water to dissolve, thus requiring multiple injections, as well as multiple uses of cotton filters and cookers. Surprisingly, Roy et al. (2012) report that most PWIDs in their study did not realize "doing a wash" with someone else's used equipment was high-risk sharing behaviour (p. 249).

Other related research further explains important characteristics of PO injection that may contribute to the increased risk for HCV infection. Havens et al. (2013) found PO injectors were almost seven times more likely to share syringes, OR 6.87, $p < .01$, 95% CI [1.61, 29.4]; and almost eight times more likely to share other injection equipment, OR 7.66, $p < .01$, 95% CI [2.34, 25.1]. Additionally, Zibbell (2015) explains that PO injectors may be at significantly higher risk for HCV due to "abuse-deterrent formulations" that cause POs to not dissolve, but clump when prepared for injection (Zibbell, 2015, p. 7). According to Zibbell (2015), this process may actually contribute to the risk for HCV infection because "people attempt to circumvent the diversion formulations, resulting in more opportunities for HCV contamination on drug preparation equipment" (p. 7). Therefore, the frequency of injection, multiple pieces of shared equipment, and the lack of awareness of potential risks of

sharing all contribute to PO injection being significantly associated with HCV infections among PWIDs.

Summary of drug of choice. The research suggests cocaine, amphetamine, and opiate injection are all significant risk behaviours associated with HCV infection among PWIDs. Additionally, there is mounting evidence that injecting POs is particularly high-risk for sharing used injection equipment and HCV transmission. Drug of choice may be a proxy for underlying injection behaviours such as frequency of injection and sharing of injection equipment. However, to remain congruent with the related research, drug of choice will be investigated in the multivariate analyses of the current thesis research.

Injection Drug Partners

Research focussed on long-term injection drug partnerships, as well as sexual injection partnerships have found both to be associated with HCV infection among PWIDs. Research has also identified PWIDs who are involved in sex trade relationships are particularly vulnerable to HCV infections. A review of the related research indicates injection drug partnerships are a significant risk factor associated with HCV infection among PWIDs.

Non-sexual injection partners. High-risk sharing behaviours between opiate injection partners have been evidenced in the related research. Hahn, Evans, Davidson, Lum, and Page (2010) claim receptive sharing of injection equipment is almost twice as likely to occur among long-term opiate injection partners than among non-opiate injection partners. Their research identified the longer opiate injection partners have been acquainted, the greater the risk for sharing injection equipment, OR 1.77, $p < .05$, 95% CI [2.40, 5.64]. Moreover, opiate injection partners who resided together shared a significantly higher risk of sharing injection equipment, OR 3.29, $p < .05$, 95% CI [1.68, 6.41] (Hahn et al., 2010).

Therefore, research suggests the risk for sharing equipment greatly increases as injection drug partnerships mature, leading to increased risk for HCV infection.

Obviously, the length of an injection partner relationship and associated risk for HCV infection is particularly concerning among sero-discordant PWIDs. A longitudinal study conducted by Morris et al. (2014) found an HCV incidence rate of 23.8 per 100 person-years among sero-discordant injection partners. Sero-discordant injection partners who had co-habited for ≥ 28 days were almost five times more likely to share syringes, Adjusted Risk Ratio (ARR) 4.90, $p < .05$, 95% CI [1.01, 24.30]; and greater than eight times more likely to share other injection equipment, ARR 8.62, $p < .05$, 95% CI [2.40, 31.30] (Morris et al., 2014). Despite the small sample size and broad CIs, the research indicates PWIDs who are in sero-discordant injection partnerships are at increased risk for HCV sero-conversion the longer they are involved with an HCV-infected partner.

Sexual injection partners. When considering HCV transmission within sexual partnerships, it is important to remember that "sexual partners of people infected with HCV may become infected, although the risk is very low in heterosexual couples" (WHO, 2014, p. 16). Christian, Hopenhayn, Christian, McIntosh, and Koch (2010) describe HCV infections as "inefficiently transmitted" via sexual behaviours, and conclude that transmission between sexual partners must then occur as a result of high-risk injection behaviours (p. 125). A systematic review conducted by Tohme and Holmberg (2010) concluded "the real risk for sexual transmission [of HCV] …is unprotected sex between HIV-infected partners, particularly HIV positive MSM [men who have sex with men]" (p. 1502). Notably, the sub-population of male PWIDs who are HIV positive and are sexually involved with other men are high-risk for HCV transmission via sexual contact. However, among all other PWIDs the

premier risk behaviour for HCV transmission within sexual injection partnerships continues to be sharing injection equipment, not sexual transmission.

PWIDs who are both injection partners and sexual partners have been repeatedly found to be at increased risk for HCV infection compared with non-intimate injection partners. According to Morris et al. (2014), injection partners who are co-habiting and are sexually involved are at significant risk for receptive syringe sharing, ARR 5.45, $p < .05$, 95% CI [1.72, 17.18]; and receptive cooker use, ARR 7.40, $p < .05$, 95% CI [1.95, 28.04]. Similarly, research conducted by Evans, Morris, Yu, Page, and Hahn (2014) found PWIDs involved in HCV sero-discordant sexual relationships reported receptive syringe sharing (15%), receptive cooker sharing (28%) and receptive syringe backloading (56%).

Receptive sharing between sexual injection partners highlights unique vulnerabilities within the context of intimate relationships. As evidenced by Wagner, Bloom, Hathazi, Sanders, and Lankenau (2013), female PWIDs are especially vulnerable in intimate injection drug relationships. After multiple interviews, they found female PWIDs reported a lack of control over drug preparation and injection processes; most often to their male sexual partners. Further research indicates gender and age differences contribute to early injection initiation when young high-risk females become sexually involved with older, male PWIDs (Roy, Boivin, & Leclerc, 2011). As postulated by Hahn et al. (2010), partnership age differences and partnership gender may contribute to inequities within sexual injection partnerships, leaving young female PWIDs particularly vulnerable to receptive sharing and HCV infection.

Involvement in sex work. Defined as exchanging sex for money, drugs, shelter or other commodities, PWIDs involved with sex trade work are particularly vulnerable to HCV infections (Shannon et al., 2010). The ARYS longitudinal cohort research identified both

male and female youth who transitioned to survival sex work were at significantly higher risk for HCV infection than those not involved in survival sex work, AHR 2.30, $p < .05$, 95% CI [1.27, 4.15] (Chettiar, Shannon, Wood, Zhang, & Kerr, 2010). Similarly, female Aboriginal participants in the Cedar Project who reported sex trade involvement were almost twice as likely to be HCV positive than those not involved in sex work, OR 1.76, $p = .031$, 95% CI [1.05, 2.95] (Mehrabadi et al., 2008). In both of these studies, it remains unclear if survival sex work preceded the high-risk injection practices and HCV infection, or whether the high-risk injection practices and HCV infection preceded sex work involvement.

Research conducted by Shannon et al. (2010) suggests receptive syringe sharing is a significant risk behaviour among sex trade workers, AOR 1.8, $p < .05$, 95% CI [1.00, 3.24]. Similarly, Mehrabadi et al. (2008) found Aboriginal female sex workers reported much higher risk of lending, OR 3.02, $p = .01$, 95% CI [1.33, 6.89], and borrowing used needles, OR 2.06, $p = .029$, 95% CI [1.07, 3.94], than those not involved in sex work. Multiple sexual injection partners, as well as multiple socio-economic inequities result in extreme vulnerability for sharing injection equipment and HCV infection among PWIDs involved in sex work.

Summary of injection partners. A review of the related research suggests injection partners are significantly associated with HCV infection because of high-risk sharing behaviours, not sexual transmission. The risk for sharing injection equipment with injection partners is associated with the length of injection relationship, sexual injection partnerships, and involvement in sex work. As such, the current research thesis will investigate injection partners as a risk behaviour associated with HCV infection.

Female Gender

Throughout the related research, female gender has repeatedly been investigated as a characteristic associated with HCV infection among PWIDs. Multiple studies indicate female PWIDs are significantly more likely to be HCV positive than their male PWID counterparts (Craib et al., 2009; Cullen et al., 2015; Iversen et al., 2010; Mehrabadi et al., 2008; PHAC, 2010; Roy et al., 2012). To explain the gender-based difference in HCV infections among PWIDs, the literature suggests female PWIDs experience injection initiation at a younger age, are more susceptible to receptive sharing within injection relationships, and are more often involved with survival sex work. Although female PWIDs report fewer years of IDU, gender-based vulnerabilities may increase their risk for HCV infection.

Gender and injection initiation. Initiation into IDU greatly increases the risk for HCV transmission among PWIDs due to the increased risk of blood-to-blood contact. Prospective cohort data collected from street-youth in Montreal found young females and males were initiated into IDU at similar rates: 7.0 per 100 person-years, 95% CI [5.2, 9.4], vs. 5.9 per 100 person-years, 95% CI [4.7, 7.2], respectively (Roy et al., 2011). Multivariate analyses revealed young females were at significantly higher risk to initiate injection when they were homeless in the previous six months, AHR 2.49, 95% CI [1.21, 5.15], and were socializing with others who inject drugs, AHR 4.46, 95% CI [2.39, 8.33] (Roy et al., 2011). Conversely, significant risk factors for male injection initiation included; homelessness prior to age 16, AHR 1.68, 95% CI [1.04, 2.71], and incest or rape prior to age 14, AHR 1.98, 95% CI [1.18, 3.3]. The Roy et al. (2011) findings indicate gender-based differences in risk factors for injection initiation, and suggest young homeless females experience injection initiation within networks of experienced PWIDs, potentially increasing exposure to HCV infections.

Hadland et al. (2012) further investigated the phenomenon of injection initiation among young PWIDs. Using prospective cohort data, they found youth aged 14 to 26 years who had experienced childhood sexual abuse were almost three times more likely to initiate IDU than those who had not been abused, AHR 2.71, $p = .003$, 95% CI [1.42, 5.30]. Additionally, female gender was not significantly associated with injection initiation, but a significantly larger proportion of females reported childhood sexual abuse than males (58% vs. 42%, $p < .001$) (Hadland et al., 2012). Although the results imply there may be multiple factors influencing injection initiation, the Hadland et al. (2012) study suggests childhood sexual abuse is significantly associated with IDU and more research is needed to identify possible gender-based differences.

Gender-based power imbalances. Power imbalances within social networks may explain why female PWIDs are more vulnerable to HCV infection. Roy et al. (2011) questioned why female PWIDs most often reported being initiated into IDU by romantic partners. They theorized that injection initiation reflects socially embedded gender inequities resulting in a lack of power and control for females within sexual partnerships. After injection initiation, the lack of power and control over drug supply and injection practices results in female PWIDs being vulnerable to receptive sharing, or being "second on the needle" (Craib et al., 2009, p. e225).

Iversen et al. (2010) claim that within the context of intimate relationships, receptive sharing can imply trust, commitment, and intimacy, thus leading to increased risk for HCV. They further surmise that refusing to share equipment might be perceived as a lack of trust, and lead to abusive consequences for female PWIDs. Thus, power imbalances within sexual injection partnerships may strongly influence injection behaviours where female PWIDs are at increased risk for receptive sharing and HCV infection.

Power imbalances were also explored by Scheidell et al. (2015) when they investigated female PWIDs' ability to plan for safe injection. Their research findings reported female PWIDs had adequate planning abilities for safe injection, were well-prepared with sterile injection equipment, and demonstrated safe injection knowledge. However, the Scheidell et al. (2015) study identified female PWIDs remained at high-risk for receptive needle sharing and HCV infection. They postulate that "gendered power dynamics may limit women's ability to negotiate harm reduction strategies if male partners control the drug supply and injection equipment" (p. 35). Therefore, the research infers high-risk sharing behaviours and increased risk for HCV infection among female PWIDs are embedded within complex power imbalances within injection relationships.

Receptive sharing of injection equipment. The related research consistently demonstrates that female PWIDs may be particularly vulnerable to receptive sharing practices due to age, gender, and socioeconomic inequities. For example, female PWIDs participating in the Edmonton I-Track survey were younger ($p = .002$), more likely to inject with their sex partners ($p = .002$), more likely to share needles ($p < .001$), and more likely to be paid for sex ($p < .001$) than their male counterparts (Plitt et al., 2010). Similarly, Hahn et al. (2010) found female PWIDs injecting with male sexual partners were almost twice as likely to report receptive needle sharing, OR 1.73, $p < .05$, 95% CI [1.03, 2.90].

Research conducted by Iversen et al. (2010) found females who had been injecting for four years or less were particularly vulnerable to receptive needle sharing ($p < .001$), receptive equipment sharing ($p = .004$), and being injected by someone else ($p < .001$). In their large cross-sectional study, reports of receptive sharing decreased for female PWIDs as the duration of injection years increased, suggesting a change in sharing behaviours with age.

However, other confounding factors, as well as social desirability bias and recall bias may have influenced the results.

Involvement in the sex trade. Both female and male PWIDs involved in sex-trade work are at very high-risk for injection initiation and HCV infections. For instance, Miller et al. (2011) found that young Aboriginals involved in sex trade work were almost four times more likely to transition to IDU that those not involved, AHR 3.94, $p < .001$, 95% CI [1.45, 10.71]. Moreover, the related research repeatedly indicates female PWIDs are particularly vulnerable to involvement in sex work. For instance, Aboriginal female participants in the Prince George cohort of the Cedar Project research were almost twenty-five times more likely than males to have ever been paid for sex, OR 24.3, $p < .05$, 95% CI [11.6, 50.8] (Mehrabadi et al., 2008). Chettiar et al. (2010) also found female street involved youth were three times more likely to be involved in survival sex work than males, AOR 3.02, $p < .05$, 95% CI [1.66, 5.46]. The over-representation of female PWIDs in sex work supports the proposed theory that age, gender, and socioeconomic inequities greatly influence female PWIDs' abilities to maintain control over their bodies and their injection practices, resulting in high-risk sharing behaviours and HCV infection.

Summary of female gender. The related research strongly suggests that gender-based differences in injection initiation, sexual injection partnerships, and sex trade involvement are complex vulnerabilities facing female PWIDs. Each of these risk behaviours has been associated with HCV infection among female PWIDs in various studies, and highlights the prevalence of gender-based receptive sharing practices. As a result, the current thesis research will investigate gender as a risk factor associated with HCV infection among the Prince George I-Track PWIDs.

Aboriginal Status

HCV infection among Aboriginals has been deemed a "broken spirit" disease due to multiple associated risk behaviours embedded in historical and personal trauma (Rempel & Uhanova, 2012, p. 3912). A meta-analyses of HCV prevalence and incidence within racial/ethnic groups from different national territories was conducted by Lelutui-Weinberger et al. (2009). They found Aboriginals in Australia and Canada were twice as likely as their "white" counterparts to be HCV positive, OR 2.04, $p < .05$, 95% CI [1.48, 2.82]. In Canada, a national surveillance report also found HCV incidence among Aboriginals was almost five times the rate of non-Aboriginals, 203 per 100,000 population vs. 36 per 100,000 population respectively (PHAC, 2010). A review of the related research strongly suggests Aboriginal PWIDs are particularly vulnerable to risk behaviours associated with HCV infection.

Aboriginal PWIDs. According to national HCV surveillance research, Aboriginals are clearly overrepresented within the PWID population (PHAC, 2010). Among incident cases of HCV infections, the prevalence of IDU is significantly higher among Aboriginals than in the non-Aboriginal population, 67.3% vs. 53.6%, $p < .001$ (PHAC, 2010). Street-involved Aboriginal youth are also over-represented within PWID populations, contributing to high prevalence of HCV infection among Aboriginal youth (7.4%) as compared with other ethnicities (2.8%), $p < .05$ (PHAC, 2010). The obvious over-representation of Aboriginal ethnicity within PWID populations suggests multiple, complex socio-economic factors.

Researchers postulate that IDU and subsequent HCV infection among Aboriginals directly stem from intergenerational effects of residential school (Craib et al., 2009; Spittal et al., 2012). Inarguably, the residential school legacy has resulted in devastating historical and personal trauma, and widespread socio-economic inequities for Aboriginals across Canada (Craib et al., 2009). As stated by Craib et al. (2009), "drug use is just one way that people

deal with the complex effects of poverty, despair, discrimination, loss of language and traditional territories, erosion of culture" (p. e225). Socio-cultural inequities greatly contribute to the over-representation of Aboriginals involved in high-risk behaviour such as IDU, and result in particular vulnerability to blood-borne infections such as HCV.

Aboriginal injection initiation. Unfortunately, Aboriginal youth and Aboriginal females appear to be most vulnerable to the intergenerational effects of historical and collective trauma. For example, national surveillance research found Aboriginal PWIDs are initiated into IDU at an earlier age than non-Aboriginal PWIDs, and more than one fifth of young Aboriginal PWIDs (21.9%) reported initiating injection before age 16 years (PHAC, 2010). Compared with other ethnicities, early injection initiation was significantly more prevalent ($p = .004$) among young Aboriginals (PHAC, 2010). As discussed previously in this chapter, early injection initiation is a risk factor for HCV infection and may be due to power and control imbalances that exist between injection partners, leaving the younger, female partner more vulnerable to receptive sharing.

The Cedar Project research has specifically looked at HCV infections among drug-using Aboriginal youth in Prince George and Vancouver, BC (Craib et al., 2009; Mehrabadi et al., 2008; Miller et al., 2011; Spittal et al., 2012). Using prospective cohort data, incidence of HCV seroconversions among young Aboriginal PWIDs was estimated to be 26.3 incident cases per 100 person-years within the first two years of injection initiation (Spittal et al., 2012). According to Miller et al. (2011), injection initiation was significantly associated with sex work, AHR 3.94, $p < .001$, 95% CI [1.45, 10.71]. Further analyses of the cross-sectional baseline data indicated female gender, AOR 2.44, $p < .001$, 95% CI [1.48, 4.01]; and history of incarceration, AOR 2.95, $p < .001$, 95% CI [1.92, 4.54], were also significantly associated with injection initiation (Miller et al., 2011). The Cedar Project research highlights the risk

behaviours associated with injection initiation and subsequent HCV infections among vulnerable young Aboriginal PWIDs.

Aboriginal PWIDs and sharing behaviours. Aboriginal PWIDs have also been found to be at higher risk for sharing injection equipment than non-Aboriginal PWIDs (PHAC, 2010). National surveillance research found Aboriginal PWIDs who were HCV positive were more likely to borrow needles than those who were HCV negative, OR 1.6, p = .047, 95% CI [1.0, 2.7] (PHAC, 2010). However, young Aboriginal PWIDs were two times more likely to borrow used injection equipment than non-Aboriginal PWIDs, OR 2.1, p = .030, 95% CI [1.1, 4.1] (PHAC, 2010). Participants in the Cedar Project were more than twice as likely to be HCV positive when reporting equipment sharing, AOR 2.56, $p < .001$, 95% CI [1.47, 4.49] (Spittal et al., 2012). The related research indicates Aboriginal PWIDs report prevalent sharing behaviours resulting in increased risk for HCV transmission.

The related research proposes reasons for why high-risk sharing behaviours are prevalent among Aboriginal PWIDs. Miller et al. (2009) surmise that historical and sexual traumas lead young Aboriginal people "to experiment with injection drugs to numb feelings of shame and isolation" (p. 1152). Moreover, early intervention and harm reduction strategies are not tailored to the needs of high-risk Aboriginal youth who have been subjected to "racialized care", and harbour "generations of mistrust of both provincial and federal authorities" (Spittal et al., 2012, p. 8). Lelutui-Weinberger et al. (2009) also suggest health disparities such as "unequal access to resources…. result in uneven disease distribution" (p. 3). They theorize that Aboriginals are predisposed to risky behaviours due to "individual, community, or social conditions of disadvantage", which manifest as "reduced access to healthcare, services, and prevention" (p. 3). The related research suggests there are multiple,

complex historical and persistent inequities facing Aboriginal PWIDs that result in increased risk-taking behaviours and HCV infections.

Aboriginal female PWIDs. As noted previously, female PWIDs are particularly vulnerable to multiple risk behaviours associated with HCV infection. However, the related research indicates Aboriginal females are even more vulnerable. A large cross-sectional study of PWIDs conducted in Australia found Aboriginal female PWIDs who had been injecting for four or less years were almost twice as likely to be HCV positive than non-Aboriginal female PWIDs, AOR 1.71, $p = .005$, 95% CI [1.18, 2.48] (Iversen et al., 2010). Young Aboriginal female PWIDs participating in the Cedar Project were also almost twice as likely to be HCV positive than their Aboriginal male counterparts, AOR 1.9, $p = .012$, 95% CI [1.1, 3.4] (Craib et al., 2009). The research indicates Aboriginal female PWIDs are at greater risk for HCV than both non-Aboriginal female PWIDs, and Aboriginal male PWIDs.

As stated by Spittal et al. (2012), "impoverished Aboriginal women involved in sex work and concomitant illicit drug use continue to be exposed to alarming levels of drug related harm, infectious disease, and violent predation" (p. 8). They found Aboriginal female PWIDs involved in sex trade work were significantly more likely to be HCV positive than those not involved, AHR 1.59, $p = .030$, 95% CI [1.05, 2.42]. Moreover, a higher proportion of Aboriginal female PWIDs living in Prince George reported sex-trade involvement than Aboriginal female PWIDs living in Vancouver (56%) suggesting greater inequities facing young Aboriginal females in northern BC (Mehrabadi et al., 2008).

Summary of Aboriginal status. Research strongly suggests Aboriginal PWIDs are particularly vulnerable to high-risk behaviours for HCV infections. Associated risk behaviours of early injection initiation and sharing injection equipment are significantly more prevalent among young Aboriginal PWIDs than non-Aboriginals. The related research also

indicates female Aboriginal PWIDs are particularly vulnerable to IDU, early injection initiation, sex trade work, and HCV infections. As stated by Rempel and Uhanova (2012), "the face of the indigenous HCV infected individual is becoming increasingly female and younger compared with non-indigenous counterparts" (p. 3912). The current thesis research will explore both Aboriginal status and Aboriginal females as characteristics associated with HCV among the Prince George I-Track participants.

Unstable Housing

The related research investigates unstable housing as a potential risk factor associated with HCV infections among PWIDs. Unstable housing includes living in multiple residences, living in shelters, and/or living on the street. Only one study in the literature review found unstable housing to be associated with HCV infection, AHR 1.61, $p < .05$, 95% CI [1.10, 2.36] (Grebely et al., 2014). However, unstable housing has been associated with a history of abuse, Aboriginal status, and an increased risk for sharing injection equipment when injecting in public places. Thus, the research suggests unstable housing is an important consideration for risks associated with HCV infections among PWIDs.

History of abuse and unstable housing. The related research indicates young PWIDs who lack stable housing are more vulnerable to abuse and violence. For instance, Rachlis et al. (2009) found homeless youth were more likely to report a history of physical abuse, OR 1.49, $p = .035$, 95% CI [1.03, 2.16]; or to have been a victim of violence, AOR 1.57, $p = .020$, 95% CI [1.07, 2.30]. The Cedar Project also found the most transient young Aboriginal PWIDs (lived in more than six places in previous six months) were significantly more likely to report having been sexually assaulted, AOR 2.48, $p = .008$, 95% CI [1.26, 4.86] (Jongbloed et al., 2015). The cross-sectional results are unable to determine if history of abuse leads to unstable housing, or unstable housing leads to increased abuse. However, a

history of abuse has been associated with unstable housing, as well as early injection initiation and survival sex work; all of which are also risk behaviours associated with HCV infection among PWIDs.

Aboriginals and unstable housing. In the Cedar Project research, young Aboriginal drug users reported experiencing unstable housing more often in Prince George than in Vancouver (Jongbloed et al., 2015). In fact, the researchers found 90% of the Prince George participants reported living in two or more places, while almost 20% reported having lived in more than six different places in the previous six months. Jongbloed et al. (2015) propose that unstable housing is a result of a lack of affordable housing, as well as frequent visits to outlying communities and reserves. Furthermore, they claim housing instability among Aboriginals is directly associated with the "historic dispossession of traditional territories and forced displacement from community structures" (p. 125). The research suggests young Aboriginals are particularly vulnerable to unstable housing, and such instability leads to high-risk injection behaviours of sharing injection equipment, injection initiation, and survival sex work. Consequently, Aboriginal PWIDs are particularly vulnerable to HCV infection.

Injection in public places. Two studies in the related research found injecting in public places as a risk behaviour associated with unstable housing. Rachlis et al. (2009) found PWIDs who had unstable housing were more than twice as likely to inject drugs in public places, AOR 2.32, $p < .001$, 95% CI [1.43, 3.78]. Jongbloed et al. (2015) also found unstable housing was significantly associated with public injection, AOR 2.87, $p < .001$, 95% CI [1.65, 5.00]. The researchers claim that public injection increases the risk for sharing injection equipment due to rushed injection practices and fear of interruption (e.g., police presence) (Rachlis et al., 2009). Therefore, the research suggests unstable housing increases risk for HCV infection among PWIDs due to increased risk for sharing injection equipment.

Other risk behaviours and unstable housing. Two other risk behaviours significantly associated with HCV infections have also been found to be associated with unstable housing. For instance, the Cedar Project found survival sex work was significantly associated with unstable housing among young Aboriginal females, AOR 3.52, $p < .001$, 95% CI [2.06, 6.05] (Jongbloed et al., 2015). Additionally, Feng et al. (2013) found injection initiation to be significantly associated with unstable housing, AHR 1.80, $p = .014$, 95% CI [1.13, 2.87]. Although unstable housing may not be directly associated with HCV infections among PWIDs, these studies suggest it is an important risk behaviour to consider due to significant associations with sex work and injection initiation.

Summary of unstable housing. A review of related research indicates unstable housing is significantly associated with history of abuse, Aboriginal status, and injecting in public places. Although only one study has identified unstable housing as a risk behaviour significantly associated with HCV infections among PWIDs, several studies have identified multiple common risk behaviours associated with both HCV infections and unstable housing. As a result, unstable housing will be investigated in the current thesis research.

Residential Mobility

Residential mobility has been considered in the related research as a potential risk behaviour associated with HCV infections among PWIDs. Residential mobility may contribute to HCV transmission due to limited harm reduction services in outlying, under-sourced areas, and subsequent increased risk of sharing injection equipment among transient PWIDs. Although the related research does not indicate residential mobility as a risk factor directly associated with HCV infection among PWIDs, the potential for HCV transmission to outlying, under-sourced areas due to sharing injection equipment must be considered.

Travel to outlying areas. As described by Rachlis et al. (2008), when IDU and residential mobility overlap, highly mobile individuals can potentially spread HCV from areas of high prevalence to areas of low prevalence. Their study investigated risk behaviours of VIDUS participants when they travelled from the DTES to outlying areas. Interestingly, the study found alcohol use was the only significant risk behaviour reported, AOR 1.25, p = .011, 95% CI [1.05, 1.48]; and migration out of the DTES appeared to have protective effects on high-risk injection behaviours (Rachlis et al., 2008). In fact, the Rachlis et al. (2008) study suggests that PWIDs migrate to outlying communities to escape heavy drug use and high-risk behaviours. However, such results must be viewed with caution because attrition bias may have excluded the most transient and highest-risk PWIDs from the study conclusions.

Montgomery et al. (2012) also investigated risk behaviours of highly-mobile young PWIDs in their cross-sectional study. Their findings indicated PWIDs reported high-risk sharing behaviours when injecting drugs in urban centres with populations greater than 500,000, AOR 7.05, $p < .01$, 95% CI [2.25, 22.06]. An increased number of travelling partners, AOR 2.77, $p < .01$, 95% CI [1.46, 5.27], and alcohol use, AOR 3.03, $p < .01$, 95% CI [1.32, 6.97], were also significantly associated with the risk of sharing equipment among travelling PWIDs (Montgomery et al., 2012). Capturing data from transient PWIDs is very difficult due to selection bias, but the Montgomery et al. (2012) study indicates riskier injection behaviours occur in larger urban centres, and suggests the risk of HCV transmission into smaller, outlying areas may be unfounded. However, such findings must be viewed with caution due to attrition and selection bias, and further research is warranted.

Travel to Aboriginal communities. Callaghan et al. (2007) identified significant mobility between on-reserve and off-reserve settings reported by Aboriginal PWIDs admitted to the Prince George detox unit. Their review of medical charts found 26% of inpatient

Aboriginal PWIDs reported moving to on-reserve settings between admissions, whereas 96% of Aboriginal PWIDs had transitioned to living off-reserve. The demonstrated transience is concerning because 46% of the participants self-reported as HCV positive, indicating potential risk for transmission among PWIDs moving between urban and rural communities (Callaghan et al., 2007).

Similarly, Jongbloed et al. (2015) found young Aboriginal participants in the Prince George cohort of the Cedar Project who were highly transient were significantly more likely to report visiting a reserve in the previous six months ($p < .001$), and significantly more likely to be HCV positive ($p = .015$). Although the Prince George cohort reported transient behaviours, the researchers propose that frequent visits to reserves may actually serve as a protective factor due to stronger ties with family and home community (Jongbloed et al., 2015). However, reported transience of Aboriginal PWIDs between on-reserve and off-reserve locations still suggests potential risk for HCV transmission to outlying communities.

Summary of residential mobility. Residential mobility has been considered as a potential risk factor for HCV transmission among PWIDs to outlying areas. Two research studies found high-risk injection behaviours were reported to occur less often when PWIDs travelled to smaller communities, and two other studies reported high residential mobility among Aboriginal PWIDs. Although the latter studies did not specifically investigate risk behaviours associated with transience, they highlight the potential transmission of HCV among Aboriginal PWIDs travelling to smaller, rural communities. Due to the high prevalence of HCV infection within the Prince George I-Track sample, the large proportion of Aboriginal participants, and frequent reports of travel to/from locations outside of Prince George, residential mobility will be considered as a risk factor associated with HCV infection among PWIDs in the current thesis research.

History of Incarceration

During the literature search, multiple research studies were excluded from the final literature review because they focused exclusively on sub-populations of incarcerated PWIDs. However, several studies included in the literature review did investigate incarceration as a risk factor associated with HCV within general PWID populations. Indeed, the research findings strongly suggest a history of incarceration is significantly associated with HCV infection among PWIDs (Bruneau et al., 2012; Cullen et al., 2015; Hahn et al., 2012; Iversen et al., 2010; Palmanteer et al., 2013). Despite repeated indications that incarceration is a significant risk factor associated with HCV infections among PWIDs, limitations within the Prince George I-Track survey dataset do not allow for it to be included in the analyses of the current thesis research.

Summary of the Literature Review

A review of the related research has highlighted multiple risk behaviours and characteristics associated with HCV infections within PWID populations. As presented in Figure 2, the premier risk behaviour associated with HCV infection among PWIDs is sharing injection equipment. Multiple risk behaviours and characteristics have been found to be associated with sharing injection equipment; namely, injection years, drug of choice, injection partners, female gender, Aboriginal ethnicity, unstable housing, and residential mobility. With the exception of history of incarceration, all of these risk behaviours and characteristics will be investigated in the current thesis research.

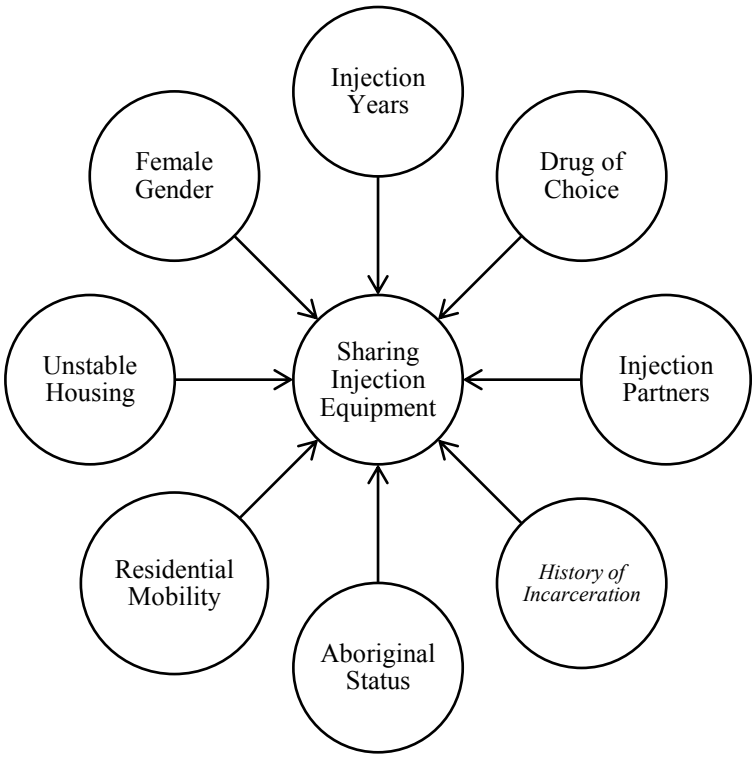

Figure 2. Diagram of risk behaviours and characteristics associated with HCV infection.

Limitations in the Related Research

The literature review process highlights several limitations in the related research. First of all, the literature search found an overwhelming number of primary research studies, but very few meta-analyses and systematic reviews of risk behaviours and characteristics associated with HCV among PWIDs. This is somewhat surprising considering the vast amount of research that has been conducted within PWID populations. Unfortunately, the multitude of small-scale studies with differing selection criteria and differing research methods does not allow risk behaviours and characteristics associated with HCV among PWIDs to be easily synthesized.

Secondly, the studies included in the literature review, as well as the current thesis research all rely on serum HCV antibody test results to determine prevalence of HCV infection. However, serum HCV antibody tests only identify PWIDs who have been exposed

to HCV, not those who actually have acute or chronic infections (WHO, 2014). Due to spontaneous clearance, 15% to 45% of incident cases are able to overcome the HCV infection with an effective host immune response, but will still test positive for HCV antibodies (BCCDC, 2013; WHO, 2014). Therefore, analyses involving HCV prevalence based on serum antibody tests are prone to over-estimations, and results must be considered with caution. A detailed explanation of HCV virology is provided in Supplement Two.

Finally, engaging PWIDs in research studies is very challenging due to social stigma and marginalization of the study population. As a result, the most appropriate quantitative research methods are observational cross-sectional and/or longitudinal cohort studies. Limitations in cross-sectional studies include the inability to determine causation or temporal change (Lavrakas, 2008). Longitudinal studies are also unable to determine causation, and they are particularly reliant on participants' return for follow-up interviews (Lavrakas, 2008). However, implementing experimental methods would be impossible without ethical ramifications. Therefore, limitations of cross-sectional and longitudinal study methods of the related research must be accepted and considered when reviewing results.

Multiple limitations inherent to observational research may have influenced the validity of the research findings. For instance, each of the primary studies relied on convenience sampling at locations where PWIDs would be easily recruited (e.g., NEPs) resulting in a non-probability sample population (Lavrakas, 2008). Moreover, each study implemented some form of interviewer-administered survey tool reliant on self-reporting of behaviours and are subject to recall bias and social desirability bias (Lavrakas, 2008). Interviewer-administered questionnaires may also create bias whereby participants' responses are affected by facial expressions, tone of voice, and body language of the

interviewer (Lavrakas, 2008). The potential for such biases must be considered as a limitation of the study designs and results in the related research.

Specific to longitudinal studies, when participants do not return for follow-up interviews the research results are subject to attrition bias (Lavrakas, 2008). Moreover, if follow-up interviews are conducted a long time after baseline interviews, maturational bias may be confounding the observed changes (Lavrakas, 2008). Survivorship bias also influences longitudinal studies by disregarding the highest-risk individuals who presented with the outcome of interest at baseline, thus excluding them from incidence calculations. (Lavrakas, 2008). Despite these limitation, observational cross-sectional and longitudinal research remain the most effective, efficient, economically feasible, and ethical study designs for engaging vulnerable PWID populations.

Gaps in the Related Research

The majority of studies in the related research have been focused on PWID populations living in large metropolitan centres. Exceptions include the Prince George cohort of the Cedar Project research (Craib et al., 2009; Mehrabadi et al., 2008; Miller et al., 2009; Spittal et al., 2012); northern sentinel sites in the I-Track survey including Saskatoon, Thunder Bay, Sudbury, and Prince George (PHAC, 2014); and studies conducted in the rural Appalachian region of Kentucky (Christian et al., 2010; Havens et al., 2013). In an attempt to address the paucity of HCV research outside of large metropolitan centres, the current thesis research will explore risk behaviours and characteristics associated with HCV among PWIDs living in the northern, non-metropolitan location of Prince George, BC.

CHAPTER 3: Research Methods

The purpose of this chapter is to describe the research methods used to investigate the risk behaviours and characteristics associated with HCV among the Prince George I-Track participants. After outlining the harm reduction theoretical framework, a detailed description of the categorical variables to be included in the statistical analyses is presented, followed by a description of the analytic plan. By the end of Chapter Three, the reader will understand the methods used to investigate the research question: What are the risk behaviours and characteristics associated with HCV infection among the PWIDs who participated in the Prince George I-Track surveys?

Harm Reduction Framework

The current thesis research is grounded in a harm reduction conceptual framework. Harm reduction is defined as "any policy or program designed to reduce drug-related harm without requiring the cessation of drug-use" (Erickson et al., 2002, p. 1). Harm reduction policies and programs accept the fact that mind-altering substances will inevitably be used in society, and advocate for drug users' dignity and individual rights regardless of his/her choice to use substances (Riley & O'Hare, 2000). Moreover, harm reduction interventions focus primarily on the harms resulting from drug use, not the extent of the drug user's addiction (Riley & O'Hare, 2000). However, harm reduction interventions also consider the effect of drug-related problems and associated harms beyond the needs of individual users to include the interests of the community and society (Riley & O'Hare, 2000).

A harm reduction framework can be difficult to translate into effective health care practices, especially with prevalent societal judgments and stigma placed on persons with addictions. Unfortunately, it is often falsely criticized as enabling drug use. But evidence shows it actually engages individuals in the first step toward cessation (Riley & O'Hare,

2002). Harm reduction is compatible with the pursuit of abstinence, but requires intervention programs and health care workers to remain neutral when an individual is not ready to abstain (Riley & O'Hare, 2002). Furthermore, harm reduction interventions require ongoing advocacy against discriminatory drug and policing policies, and awareness of entrenched social inequities such as unstable housing and poverty that can severely interfere with an individual's ability to escape the cycle of addiction (Riley & O'Hare, 2002). The current thesis research is grounded in a harm reduction framework, and the results of the investigation will contribute to the development of harm reduction services for PWID populations in northern BC.

Research Ethics Approval

The national I-Track research project was approved by the National Research Ethics Board of Health Canada, the Northern Health Research Review Committee, and the Research Ethics Board at the Centre for Addiction and Mental Health in Toronto (PHAC, 2013). The current thesis research proposal to utilize the Prince George I-Track survey data was approved by the University of Northern British Columbia Research Ethics Board in April 2014 (Appendix A). All ethics approvals followed the Tri-Council Policy Statement for Ethical Conduct for Research Involving Humans (CIHR, 2010).

Obtaining the Data

As part of the initial data-sharing agreement among the local partners, written consent to use the Prince George I-Track survey data for the current thesis research was obtained from Carrier Sekani Family Services, Northern Health, and the Northern BC First Nations HIV/AIDS Coalition (Appendix B). The local stakeholders agreed that access to study data would be granted if all parties gave their consent. They also agreed that future disclosure of study results would require approval from all stakeholders. In January 2014, permission to

use the Prince George I-Track data was confirmed (E. Palmantier, personal communication, January 23, 2014).

Data Preparation

The raw data of the Prince George I-Track surveys was provided by PHAC in a digital spreadsheet format. The digital spreadsheet was compatible with IBM SPSS Statistics 23.0 software and this software was used for all data preparation and analyses. Using SPSS Statistics 23.0 software, cleaning the data, filtering incomplete and duplicate cases, and merging and re-coding of variables was conducted. The data preparation process for all variables investigated in the current thesis research will be described in this section.

I-Track All-phases Dataset

The Prince George I-Track all-phases dataset contains 307 subjects and 700 variables representing all possible responses to each question asked in the 2008 and 2012 I-Track surveys. Responses to several questions in the Phase 2 and Phase 3 questionnaires were entered in the all-phases dataset as separate variables due to differences in wording or response codes. In order to conduct further analyses, these variables were re-coded and merged together to integrate the all-phases data into uniform categorical variables. Integrating the data from both I-Track survey phases maximizes the sample size and improves the statistical power of data analyses.

The All-phases Codebook

The All-phases Codebook is a reference guide for the coding sequences of responses to each I-Track survey question and is specific to each sentinel site (PHAC, 2014). The Prince George All-phases Codebook numerically lists the I-Track core questions, site specific questions, and all responses in a user-friendly manner. When working with the Prince George I-Track dataset, the variable names and numeric codes listed in the spreadsheet are easily

cross-referenced in the All-phases Codebook to the original survey question and answer key. As such, the All-phases Codebook was an invaluable resource throughout the data preparation process.

Cleaning the Data

Cleaning the data involved 1) becoming familiar with the All-phases Codebook, 2) reviewing the numbers entered into variable data columns, and 3) scanning for missing values and outliers within each variable. Cleaning the data is a very important process because simple problems in the primary data can introduce significant bias and error into the advanced data analyses (Field, 2013). Therefore, the first step in data preparation was to use the All-phases Codebook to identify and address missing values and outliers.

Missing values. Missing values were not found in the dataset because the interviews had been conducted using computerized questionnaires whereby the interviewer could not advance to the next question unless a numeric response was entered by the interviewer (PHAC, 2012). Therefore, there were no literal instances of missing data, but occasional responses of “not stated", don't know" and "refused" were recorded. In order to avoid small cell sizes, these responses were considered uncertain and were filtered out of the advanced analyses. It is strongly recommended that all cell sizes in bivariate analyses have at least five cases because test statistics used in advanced analyses are greatly affected by errors if cell sizes are too small or empty (Field, 2013; Hilbe, 2009, Hosmer & Lemeshow, 2000; Tabachnick & Fidell, 2013).

Outliers. Creating frequency tables of variables in SPSS allowed for outliers in the data to be identified. Outliers are values that are very different or unusual compared to the rest of the values in the variable data. Outliers introduce bias into data results and are described as “any data point > 3*IQR (Interquartile range)” within a variable (Field, 2013).

Therefore, in order for the concept of "outlier" to have any meaning a distance between values must be defined. In the current thesis research, all variables were formatted into binary, ordinal, or nominal categories and distances between values were not possible. Thus, there were no outliers in the categorical variables which may have introduced significant bias into the advanced analyses.

Filtering Incomplete and Duplicate Cases

The next step in data preparation was to identify incomplete survey data and duplicate cases. Participants included in the sample needed to meet certain eligibility requirements to be included in the current thesis research; namely, a valid DBS sample tested for HCV, and a complete set of responses to the survey questions. To avoid deleting data from the original dataset, a filter variable (FV) was created to allow for the selection of participants from the Prince George I-Track sample who were eligible for further analyses in the current thesis research. The FV was applied prior to any statistical analyses.

Incomplete surveys and invalid DBS samples. There were two participants who refused to answer any of the survey questions beyond a few initial questions. Although these participants provided valid DBS samples for HCV testing, they were excluded from the current thesis sample due to missing data for all independent variables. Similarly, eleven participants answered the interview questions, but did not provide valid DBS samples. These cases were also excluded from the current thesis sample because they had missing values for the dependent variable (DV_HCV). Therefore, a total of thirteen participants were excluded from the sample and the statistical analyses of the current thesis research.

Duplicate participants. At the beginning of the I-Track interview, each participant provided three initials and a date of birth. Using a computer-generated encryption software, these letters and numbers were converted into an encrypted label named *encrypt_id* to protect

the identity of the participant (PHAC, 2012). The encryption process ensured that all personal information remained anonymous and confidential throughout the research project (PHAC, 2012). The *encrypt_id* variable also allowed for participant characteristics and risk behaviours to be linked with their HCV test results (PHAC, 2012).

Using the *encrypt_id* variable, twenty-three duplicate participants (same initials and same date of birth) were identified between surveys. Including duplicate participants would violate assumptions of independence and introduce significant error into advanced analyses (Field, 2013). Therefore, a new variable *ENCRYPT_ID* was created in which the duplicates from the Phase 2 dataset were removed. The removal of duplicates from Phase 2 ensured the most recent information from returning participants was included in the analyses. The removal of duplicates also explains the difference in number of eligible participants between surveys (Phase 2: $n = 129$, Phase 3: $n = 143$).

As described previously, there were thirteen invalid DBS samples and/or incomplete questionnaires that were excluded from the sample population. A further twenty-three duplicate participants were removed from the Phase 2 dataset, for a total of thirty-six invalid participants. However, one of the participants was a duplicate and had also produced an invalid DBS in Phase 3. Therefore, a total of thirty-five participants with invalid DBS samples or questionnaires, and/or duplicate data needed to be excluded from the original sample population prior to further analyses. The final sample included 272 participants.

Creating a filter variable. A FV was required to select only the participants eligible for further analyses in the current thesis research. First of all, a new *HCV_VALID* variable was created by re-coding all invalid DBS samples and/or incomplete questionnaires with a value of "0", and all valid DBS samples and complete questionnaires with value of "1". Secondly, a new variable *ENCRYPT _ID_VALID* was also re-coded from the original

ENCRYPT_ID variable with all duplicates being coded as "0" and all non-duplicates coded as "1". Finally, a variable *ELIGIBLE_PARTICIPANTS* was computed by combining all cases with "1" values in the *ENCRYPT_ID_VALID* and *HCV_VALID* variables. The *FV_ELIGIBLE_PARTICIPANTS* variable was then applied as a filter prior to any further data analyses. All further description, analyses, and discussion of the current thesis research is based on the filtered sample population of 272 eligible participants.

Re-coding and Merging of Variables

The final step in data preparation was to merge and re-code the dependent and independent variables to be used in the analyses. I-Track survey questions that had different response codes between phases were re-coded and merged into new variables that shared the same answer key. All new variables that were created for the current thesis research were displayed in capital letters in the all-phases data file in order to easily distinguish between the original raw variables and the new created variables. Once re-coded and merged, the new variables contained the integrated all-phases data suitable for further analyses. A detailed description of the re-coding and merging process, as well as confirming variable frequencies ensures replicability and reliability of the results of the current thesis research.

Dependent variable (DV) – HCV status. The dependent variable *DV_HCV_VALID* represents each DBS test result and has a binary outcome of 0 = HCV negative, or 1 = HCV positive. The proportion of HCV negative participants was 30.1% (n = 82), and HCV positive participants was 69.9% (n = 190). The dependent variable *DV_HCV_VALID* will be used in all statistical analyses in the current thesis research.

Independent variable (IV) – Sharing injection equipment. As noted in the literature review, receptive sharing behaviours have been repeatedly associated with HCV infection among PWIDs (Kim et al., 2015; Palmanteer et al., 2013; Pouget et al., 2011; Strike

et al., 2010). Two questions in both phases of the I-Track survey ask participants about receptive sharing behaviours: “In the past 6 months, when you injected drugs, did you use NEEDLES and/or SYRINGES that had already been used by someone else including your sex partner?” and “In the past 6 months, when you injected drugs, did you use water, filters, cookers/spoons, tourniquets\ties, swabs, and/or acidifiers that had already been used by someone else?” (PHAC, 2012). The associated variables *borrow_needles* and *any_borrow_equip* were merged to create the *IV_RECEPTIVE_SHARING* variable. Of the participants who answered the questions, 69.5% (n = 187) denied receptive sharing, and 30.5% (n = 82) reported receptive sharing in the 6 months prior to the survey. Three participants provided uncertain responses and were not included in further analyses.

IV – Injection years. The literature review repeatedly indicated injection years were significantly associated with HCV infection among PWIDs (Craib et al., 2009; Garfein et al., 2012; Havens et al., 2013; Miller et al., 2009; PHAC, 2010; Roy et al., 2009; Spittal et al., 2012). Consistent between both phases, the questions “How old are you now?” and “How old were you the first time you injected for non-medicinal purposes?” were asked. The responses were coded as two continuous variables: *age* and *age_injt* (PHAC, 2012). A new continuous variable *INJECTION_CAREER* was computed by subtracting the *age_injt* from the *age* variable. The new variable had a normal distribution with no identified outliers.

The *INJECTION_CAREER* continuous variable was then re-coded into a categorical variable named *IV_INJECTION_YEARS*. The new variable contained two categories: less than or equal to 2 years of injecting, and more than 2 years of injecting. These two categories were generalized from the related research that had the first two years of IDU as particularly high-risk for HCV infections among PWIDs (Havens et al., 2013; Roy et al., 2009; Spittal et al., 2012). The *IV_INJECTION_YEARS* categorical variable identified 14.9% (n = 40) of

participants had been injecting for less than or equal to two years, 85.1% (*n* = 228) had been injecting for more than two years. Four participants had provided uncertain responses and were excluded from further analyses.

IV - Drug of choice. The related research investigated cocaine, amphetamine, opiates, and POs injection as risk behaviours associated with HCV infections among PWIDs (Bruneau et al., 2012; Grebely et al., 2014; Havens et al., 2013; Miller et al., 2009; Roux et al., 2013; Zibbell et al., 2014). Accordingly, the variable *IV_DRUG_OF_CHOICE3* was created from the variable *most_drug,* which was associated with the question "In the past 6 months, which [drug] did you inject most often?" (PHAC, 2012). Drug types were re-coded into categories of 1) cocaine/crack; 2) opiates (heroin, prescribed methadone, non-prescribed methadone, prescribed morphine, non-prescribed morphine, Diluadid, Oxycontin/Oxycodone, Fentanyl, Hydromorph-Contin, Demerol, and Suboxone); 3) amphetamine; and 4) other (three reported speedballs and one reported Benzodiazepines).

Of all I-Track participants, 58.1% (*n* = 155) reported injecting cocaine most often, 37.8% (*n* = 101) reported injecting opiates, 4.1% (*n* = 11) reported injecting amphetamine, and 1.4% (*n* = 4) reported injecting other substances in the six months prior to the survey. Due to small cell size, the fourth category was excluded from further analyses. Three participants also provided uncertain responses and were excluded from further analyses.

The small cell size (*n* = 11) of the amphetamine category required careful assessment during further analyses because small cell sizes can result in unstable multivariate LR models and unreliable results (Field, 2013; Hilbe, 2009). In anticipation of this category being statistically problematic, an IV_DRUG_OF_CHOICE2 variable was created by combining the cocaine/crack and amphetamine categories into a new category labeled stimulants. The

two-category variable resulted in 62.6% (*n* = 166) of participants reporting stimulant use, and 37.4% (*n* = 99) reporting opiate use most often in the six months prior to the I-Track survey.

IV - Injection partners. Injection partners were identified as a risk factor associated with HCV among PWIDs in the related literature (Christian et al., 2010; Evans et al., 2014; Hahn et al., 2010; Morris et al., 2013; Roy et al., 2011; Wagner et al., 2013). The I-Track survey question pertaining to injection partners was "In the past 6 months, with whom did you inject most often?" and coincided with the variable *most_drug_partner* (PHAC, 2012). However, the original variable had several categories with less than five responses and needed to be re-coded into *IV_INJECTION_PARTNERS*. The new variable contained two categories: 1) inject with others, and 2) inject alone. Of all I-Track participants, 57.4% (*n* = 155) reported injecting with others, while 42.6% (*n* = 115) reported injecting alone. Two participants gave uncertain responses and were not included in further analyses.

IV - Sex trade. Involvement in the sex trade has been identified in the related research as a risk factor associated with HCV among PWIDs (Chettiar et al., 2010; Mehrabadi et al., 2008; Miller et al., 2011; Roy et al., 2011; Shannon et al., 2010). Both phases of the I-Track survey asked the questions: "In the past 6 months, did you have vaginal, oral, or anal sex with a CLIENT female sex partner?" and "In the past 6 months, did you have vaginal, oral, or anal sex with a CLIENT male sex partner?" (PHAC, 2012). The associated variables in the original dataset were *f_client_sextype* and *m_client_sextype*, and these were merged into a new variable named *IV_SEX_TRADE*. Of the participants who provided responses, 74.1% (*n* = 197) reported no involvement in the sex trade, and 25.9% (*n* = 69) reported they were involved in the sex trade within the previous six months. Six participants provided uncertain responses and were not included in further analyses.

IV – Gender. Female gender has been repeatedly identified in the related research as significantly associated with HCV among PWIDs (Craib et al., 2009; Cullen et al., 2015; Hadland et al., 2012; Hahn et al., 2010; Iversen et al., 2010; Mehrabadi et al, 2008; PHAC, 2010; Plitt et al., 2010; Roy et al., 2011; Scheidell et al., 2015). The *IV_SEX_GENDER* variable was created by re-coding and combining the data from the Phase 2 *sex_birth* variable and the Phase 3 *gender* variable. The Phase 2 questionnaire asked "What was your sex at birth?" and offered only the answers of "Female" or “Male". The Phase 3 questionnaire asked the same question, but with a third option of "Other". The question "Which gender do you most identify with?" was also asked in the Phase 3 survey. Three participants responded that they were born "Other", but self-identified with female gender. It was decided that leaving these three participants in their own category would jeopardize anonymity and confidentiality. However, the question of whether to exclude the three transgendered participants from the *IV_SEX_GENDER* variable remained.

Gender identity is defined as "one's sense of oneself as male, female or transgender" and "is a process of self-identity as chosen by the individual" (American Psychological Association, 2011, p. 4). Clinical guidelines developed by the American Psychological Association (2011) strongly advocate that transgendered individuals are extremely marginalized and misunderstood, and must be treated carefully when involved in research. Furthermore, human rights policy enforces "integration and full participation" of transgendered persons because "segregation or exclusion is less dignified and unacceptable" (Ontario Human Rights Commission, 2014, p. 25). Clearly, including or excluding these participants from further analyses was a challenging dilemma.

Including the three transgendered participants as female could introduce behaviours and characteristics that are significantly different from other female PWID participants, thus

influencing the statistical associations of the *IV_SEX_GENDER* variable. However, exclusion of these participants would be unethical and discriminatory. As a result, the three participants were re-coded as female and included in the *IV_SEX_GENDER* variable because 1) this was their self-identified gender, 2) they identify with behaviours similar to other females, and 3) excluding them would reinforce deeply entrenched social discrimination. The decision resulted in the *IV_SEX_GENDER* variable with two categories: 50.7% (*n* = 138) female participants, and 49.3% (*n* = 134) male participants.

IV - Aboriginal status. Several studies in the related research identified Aboriginal status as a risk factor associated with HCV infection within the PWID population (Craib et al., 2009; Iversen et al., 2010; Lelutui-Weinberger et al., 2009; Mehrabadi et al., 2008; Miller et al., 2011; PHAC, 2010; Spittal et al., 2012). The question, “Are you an Aboriginal person?" was asked in both phases of the Prince George I-Track survey. The variable maintained its original label of *aboriginal*, and no further re-coding was required prior to analyses. Aboriginal status was clearly defined in the interview as Métis, First Nations, Aboriginal, Inuit, and non-status Indians and participants self-identified as one of two options: "Aboriginal", or “non_Aboriginal" (PHAC, 2012). Of the eligible participants, 65.3% (*n* = 177) self-identified as Aboriginal, and 34.7% (*n* = 94) as non-Aboriginal. One participant’s response was uncertain and was excluded from further analyses.

IV - Housing. Several studies in the related research considered unstable housing as a potential risk factor for HCV infection among PWIDs (Feng et al., 2013; Grebely et al., 2015; Jongbloed et al., 2015; Rachlis et al., 2009). All participants in the I-Track surveys were asked the question “In the past 6 months, what types of places have you lived in?” (PHAC, 2012). The participant provided “Yes” or “No” answers to a list of fourteen housing types read by the interviewer. These included: own apartment, friend’s place, hospital,

hotel/motel room, jail or prison, parent's house, other relative's house, psychiatric institute, recovery house or detox, rooming or boarding house, shelter/hostel, transition house/halfway house, and public place (street, park, squats, washroom, stairwell) (PHAC, 2012). To create the variable *IV_HOUSING*, the number of places lived was computed by totalling the number of "Yes" answers for all housing variables.

The Cedar Project research attempted to define unstable housing as "low transience = living in one place", "moderate transience = living in two to five places", and "high transience = living in more than six places" in previous 6 months (Jongbloed et al., 2015, p. 127). However, such categorization with the Prince George I-Track data resulted in small cell sizes and compromised the validity of further analyses. Therefore, the total responses were re-coded into the categories 1) one place in past 6 months, and 2) two or more places in past 6 months. Both categories have adequate cell size for further analyses with 37.5% (n = 102) of participants living in one place, and 62.5% (n = 170) living in two or more places within Prince George in the six months prior to the I-Track survey.

IV - Residential mobility. Residential mobility has also been investigated as a risk factor associated with HCV among PWIDs in the related research (Callaghan et al., 2007; Jongbloed et al., 2015; Montgomery et al., 2012; Rachlis et al., 2008). The I-Track survey participants were asked "Have you lived in more than one city or community in the past 6 months?" and the corresponding variable in the dataset was *residence_6months* (PHAC, 2012) There were two possible responses to this question: "No" or "Yes - at least one other city or community". All participants responded to this question, and 69.5% (n = 189) reported they had not lived anywhere else, whereas 30.5% (n = 83) reported they had lived in at least one other city or community in the previous six months.

IV – Travel to DTES. Another I-Track survey question that captures the residential mobility of the Prince George I-Track participants is "In the past 6 months, have you travelled to or lived in the Downtown Eastside of Vancouver (DTES)?" (PHAC, 2012). As identified in the literature review, travel to and from the DTES to outlying areas such as Prince George was suspected to be associated with transmission of HCV infection into rural PWID populations (Jongbloed et al., 2015; Mehrabadi et al., 2008; Rachlis et al., 2008). The variable for this question in Phase 2 was *pg_travel_eastvanc*, and Phase 3 was *pg_eastside*. The Phase 2 and Phase 3 variables were merged into a new variable *IV_TRAVEL_EASTVAN*. All participants responded to the question with 88.6% (n = 241) reporting no travel to the DTES, and 11.4% (n = 31) reporting travel to the DTES in the previous six months.

Summary of Data Preparation

The previous section has described the process of preparing the I-Track data for further statistical analyses in the current thesis research. Cleaning the data ensured missing values were identified and addressed within the dataset. Creating an FV ensured duplicate participants, and those with incomplete questionnaires or invalid DBS samples were excluded from further analyses. The final sample population of 272 participants was confirmed during the diligent data preparation process.

The selection of IVs was guided by the related research. Variables were merged and re-coded to establish categories that would be meaningful within the current thesis research and consistent with the larger body of literature. Frequencies of each variable were assessed for adequate cell sizes (greater than five cases), and uncertain responses were filtered out of further analyses. The data preparation process confirmed one DV (*DV_HCV_VALID*), and ten IVs to be including in analyses (*IV_RECEPTIVE_SHARING; IV_aboriginal; IV_INJECTION_YEARS; IV_DRUG_OF_CHOICE (2* and *3); IV_INJECTION_PARTNERS;*

IV_SEX_TRADE; IV_SEX_GENDER; IV_HOUSING; IV_residence_6months; and *IV_TRAVEL_EASTVAN).*

Analytic Plan

The analytic plan outlines how the data were analyzed to answer the current thesis research question: What are the risk behaviours and characteristics associated with HCV among PWIDs in Prince George, BC? The statistical method of multivariate logistic regression (LR) was selected to generate ORs of associations between the DV and ten IVs, and to predict probabilities of group membership of HCV status (yes/no). Building the LR model required several steps that are described in the remainder of Chapter Three.

First of all, bivariate analyses, its assumptions, and the appropriate test statistics will be explained. Secondly, the use of multivariate LR, its assumptions, and appropriate test statistics will be discussed and the model building process outlined. Selection of IVs to be included in the model will be based on the related research findings, as well as clinical expertise. Thirdly, assessing the fit of the best LR model will be described. Finally, methods for interpreting the results of the multivariate LR will be presented. The results of each step outlined in the analytic plan are presented in Chapter Four.

Bivariate Analyses

The study of the statistical relationship between two variables is referred to as bivariate analyses (Tabachnick & Fidell, 2013). When analyzing relationships between two discrete categorical variables, 2 x 2 contingency tables are created and the chi-square (χ^2) test of independence is used to evaluate the bivariate relationship (Tabachnick & Fidell, 2013). As outlined in the data preparation process, all variables investigated in the current thesis research are discrete and categorical. Therefore, χ^2 analyses were conducted to assess the statistical relationship between the DV and each IV of interest in the study.

The χ^2 statistical test. The χ^2 statistical test is based on differences between expected frequencies that are generated by the null hypothesis, and observed frequencies within the data (Tabachnick & Fidell, 2013). If the observed frequencies are similar to the expected frequencies, the χ^2 test result is small, the null hypothesis is retained, and the variables are deemed independent (Tabachnick & Fidell, 2013). However, if observed and expected frequencies are sufficiently different, the χ^2 test result is large, the null hypothesis is rejected, and the variables are considered to be related (Tabachnick & Fidell, 2013). The χ^2 test statistic was used to determine the statistical relationship between the DV and each IV in the current thesis research.

For the purposes of the current research, if the calculated significance for the χ^2 test statistic was $p < .10$, the null hypothesis of no relationship between variables was rejected. In other words, the relationship between the DV and IV was accepted as statistically significant and was selected for multivariate analyses. According to Hilbe (2009), the use $p < .250$ is acceptable unless other standards are expected within a body of research. Conservative *p*-values result in fewer variables and is preferable for small sample sizes (Hilbe, 2009). The related research used $p < .10$ in bivariate analyses, and this standard was maintained in the current research also.

Assumptions of χ^2 analyses. There are two important assumptions pertaining to χ^2 analyses of categorical data: independence and expected frequencies (Field, 2013). First of all, the use of χ^2 analyses requires that the assumption of independence is maintained (Field, 2013; Tabachnick & Fidell, 2013). This means that each case (person, item, or entity) can be counted in only one cell of the χ^2 table. If the same entity is present in more than one cell, the assumption of independence is violated and the χ^2 analyses is not valid (Field, 2013).

Applying the FV to the Prince George I-Track data resulted in the removal of duplicate cases, and maintained the assumption of independence.

Secondly, χ^2 analyses of two categorical variables with two categories each (2 x 2 contingency tables) requires the expected frequency of cases in all cells to be greater than five (Field, 2013; Hilbe, 2009; Hosmer & Lemeshow, 2000; Tabachnick & Fidell, 2013). Similarly, in χ^2 analyses of two categorical variables with more than two categories, all expected frequencies in each cell must be greater than one, and no more than 20% of all cells can have less than five cases (Field, 2013; Tabachnick & Fidell, 2013). If the cell sizes are too small, the assumption of expected frequencies is violated and the test power is drastically reduced (Field, 2013; Tabachnick & Fidell, 2013). During the data preparation process, the frequency of cases within each category of each variable was greater than five. However, some cell sizes decreased substantially during χ^2 analyses and were collapsed into broader categories or were removed from further multivariate analyses.

Summary of bivariate analyses. Upon completion of the χ^2 analyses, significant relationships ($p < .10$) between the DV and each of the IVs were identified. If cells did not have five cases, the categories of the IV were re-considered, collapsed into broader categories, or removed from the multivariate analyses. The final selection of variables for multivariate analyses was not limited to statistical significance, but remained grounded in clinical knowledge of risk behaviours and characteristics associated with HCV among PWIDs (Field, 2013; Hilbe, 2009).

Multivariate Analyses

The relationships between a DV and multiple IVs can be statistically analyzed using multivariate LR analyses (Tabachnick & Fidell, 2013). Multivariate LR is very popular in health science research because it allows the prediction of binary disease outcomes such as

"disease" or "no disease", and emphasizes the probability of each outcome for each case (Tabachnick & Fidell, 2013). Moreover, multivariate LR provides flexibility in analyses because it does not require IVs to be normally distributed, nor to be linearly related to the DV, nor of equal variance within each group (Tabachnick & Fidell, 2013). The current thesis research used multivariate LR to investigate the relationship between the DV and multivariate IVs, to estimate ORs, and to predict probabilities of HCV infections among PWIDs who participated in the Prince George I-Track surveys.

Multivariate LR. Multivariate LR involves a discrete DV that is either binary or dichotomous, as well as multiple IVs that are discrete, dichotomous, continuous, or a mixture of all three (Tabachnick & Fidell, 2013). While linear regression estimates the value of *Y* from known values of one IV (X_1) or several IVs (*X*s), multivariate LR estimates the *probability* of *Y* occurring based on known values of IVs (*X*s) (Field, 2013). Using logarithmic transformations, the non-linear relationships in categorical data can be expressed in a linear manner (Field, 2013).

Known as the *logit*, the natural ($\log_e$) of the odds (ln[odds]) is the link function that linearizes the relationship of the categorical DV to multiple IVs (Hilbe, 2009). Using the *logit*, the goal of multivariate LR is "to find the best linear combination of [IVs] that maximizes the likelihood of obtaining the observed [DV] frequencies" (Tabachnick & Fidell, 2013, p. 440). Multivariate LR was used in the current thesis research to compare various predictor models estimated from the observed Prince George I-Track data, to select the model with the best fit, and to interpret the results of the final LR model.

Assumptions and issues of multivariate LR. There are several important assumptions and issues that must be considered when using multivariate LR. Similar to χ^2 bivariate analyses, the assumption of independence must be maintained, namely; every case

(person, item, entity) in each cell must be different and unrelated (Field, 2013; Tabachnick & Fidell, 2013). If the same case is present in more than one cell, the independence assumption is violated and causes over-dispersion (Field, 2013). Over-dispersion results in very small standard errors (*SE*s), overly large test statistic results, and narrow confidence intervals (CIs) which appear very significant, but are actually incorrect (Field, 2013). The dispersion parameter (ϕ) is calculated using the χ^2 goodness-of-fit statistic, and is concerning if the ratio is near or greater than two (Field, 2013). In the current thesis research, over-dispersion was not a concern because the FV removed all duplicate cases from the study sample.

Secondly, incomplete information causes significant errors in the statistical results of multivariate LR (Field, 2013). Within the categories of IVs, if too many cells are empty, or if more than 20% of cells have less than five cases, extremely large parameter estimates and *SE*s will result (Field, 2013; Hilbe, 2009; Tabachnick & Fidell, 2013). During the χ^2 analyses, cells that were empty or had very few cases were identified. As recommended by Tabachnick and Fidell (2013), categories with few cases within an IV were collapsed, or the IV was excluded from further multivariate LR analyses.

Another multivariate LR concern is "over-fitting" and occurs when the DV is perfectly predicted by one of the IVs in the model (Hosmer & Lemeshow, 2000, p. 92). When this occurs, largely over-estimated β coefficients and *SE*s will be observed, and predicted probabilities will be only zero or 1.0 (Hosmer & Lemeshow, 2000). The most likely cause of over-fitting is when there are too many IVs and too few cases resulting in small cell sizes and instability in the multivariate LR model. One solution to over-fitting proposed by Tabachnick and Fidell (2013) is to collect more data, while another solution would be to reduce the number of IVs in the multivariate LR model.

Hosmer and Lemeshow (2000) suggest using the "rule of ten" to avoid problems of over-fitting within multivariate LR models. The "rule of ten" refers to the maximum number of events per parameter (variable) in the LR model, and is calculated with the equation "$p + 1 \leq \min (n_1, n_0)/10$ parameters" (Hosmer & Lemeshow, 2000, p. 347). According to Hosmer and Lemeshow (2000), the rule of ten is considered "a simple solution to a complex problem ...and should only be used as a guideline for parameter selection in an LR model" (p. 347). When applying the events per parameter equation to the current thesis research, the result is approximately nine parameters [(272 + 1) (.35) / 10 = 9.55]. Therefore, when building the multivariate LR model, nine parameters (variables) were used as a guideline.

Three other issues common in multivariate LR models include; linearity of the logit, outliers in the solution, and multicollinearity (Tabachnick & Fidell, 2013). Linearity of the logit is an assumption that there is a linear relationship between all continuous IVs and the *logit* of the DV within the multivariate LR model (Field, 2013). Although important, the current thesis research had no continuous IVs, so further explanation of this assumption is irrelevant.

Outliers in the solution refer to "outlier" cases that are very poorly predicted by the LR model and show a high probability for belonging to another category (Tabachnick & Fidell, 2013). Outliers are found when examining the residuals of the IVs, and the model is considered to be a poor fit if there are too many (Tabachnick & Fidell, 2013). The current thesis research generated a summary of residual statistics using the SPSS statistics software, and the residuals were inspected for unusual cases (Field, 2013).

Multicollinearity refers to the biasing effect of collinearity of two or more IVs (Field, 2013). Tabachnick and Fidell (2013) recommend using multiway frequency analyses to detect multicollinearity issues, whereas Hosmer and Lemeshow (2000) and Field (2013)

recommend using linear regression methods for collinearity analyses. These methods were not investigated in the current thesis research because there were no indications of multicollinearity; such as "aberrantly large estimated standard errors" or "evidence of degradation in the fit" of the model (Hosmer & Lemeshow, 2000, p. 141).

Selection of IVs for LR model. Regardless of the statistical significance of relationships found between the DV and IVs in χ^2 bivariate analyses, the selection of IVs for multivariate LR modeling was grounded in the theoretical and clinical knowledge of the disease of study (Tabachnick & Fidell, 2013). Therefore, variables that lacked statistical significance ($p > .10$) in the bivariate analyses were still included in the multivariate analyses. Despite the "rule of ten" recommending the number be limited to nine, ten IVs were included in the multivariate LR model because there were no obvious reasons for exclusion. Reasons for exclusion of IVs were small cell sizes in categories that could not be collapsed, evidence of over-fitting, and/or evidence of multicollinearity. All ten IVs were supported as clinically relevant in the related research.

Interaction terms. Sometimes an interaction between two IVs is significantly associated with the DV and can be assessed in an LR model as an interaction term (Field, 2013). The literature review in the current thesis research repeatedly highlighted Aboriginal female PWIDs as being particularly high-risk for HCV infection. Therefore, an appropriate interaction term to include in the multivariate LR model would be: *IV_aboriginal* x *IV_SEX_GENDER.* The interaction term would identify if the combined effect of Aboriginal *and* female characteristics was significantly associated with HCV infection among PWIDs. In order to be valid, the inclusion of an interaction term requires that the original IVs also be maintained in the multivariate LR model regardless of overall effect (Field, 2013). Therefore,

in addition to the ten original IVs, the interaction term *IV_aboriginal* x *IV_SEX_GENDER* was included in the model.

Multivariate LR Model Building

Once the ten IVs had been assessed using χ^2 bivariate analyses, all variables (regardless of statistical significance) and one interaction variable were included in the multivariate LR model using sequential forced entry methods (Field, 2013; Tabachnick & Fidell, 2013). In this approach, all IVs and the DV were initially introduced into the full model. A new model was then constructed with only the IVs that had statistically significant Wald tests ($p < .05$) and Exp (β) with 95% CIs that did not cross 1.0 (Field, 2013).

The full model was then compared with the new model using the Omnibus Test of Model Coefficient. Using the deviance calculation (*-2LL*) of each model, this test statistic identifies if the full model shows improvement of fit over the new model (Field, 2013). The difference between the deviance of each model is treated as a χ^2 value and is assigned a p-value based on the χ^2 distribution table. If the fit of the full model shows no significant improvement ($p > .05$), the new model is accepted as the best model (Field, 2013).

Assessing the fit of the best model. Once selected, the overall fit of the best model was confirmed using the Hosmer and Lemeshow (2000) goodness of fit (GOF) test. Standardized residuals were analysed using Cooks distance, DF Betas, and leverage values. SEs of the coefficient, and the 95% CIs of the Exp (β) were also reviewed. A re-sampling procedure called bootstrapping was used to test the reliability of the 95% CIs of the best model. Each of these assessment methods confirmed a well-fitted model.

Hosmer and Lemeshow goodness of fit (GOF) test. The GOF test uses decile tables of probability values to compare actual observed counts in the data with fitted or expected counts in the model, and theoretically these counts should be close (Hilbe, 2009). Based on a

χ^2 distribution, a well-fitted model has a low GOF statistic with a *p*-value greater than .05 (Hilbe, 2009). However, Hosmer and Lemeshow (2000) strongly recommend that residual outliers be analyzed before accepting a model as well-fitted based on the GOF statistic.

Residual outliers. Examining standardized residuals isolates points where the model fits poorly, as well as points that greatly influence the model (Field, 2013). Standardized residuals are calculated by SPSS when the LR model is constructed. No more that 5% of residuals should be greater than +/- 1.96 and no more than 1% should be greater than +/- 2.58 (Field, 2013). Cases above 3.0 are also concerning, and must be inspected (Field, 2013).

Any residuals with a Cooks distance and/or DF Beta value greater than 1.0 greatly influence the fit of the model (Field, 2013). Leverage values must be between zero and 1.0, and should lie close to the expected leverage value (Field, 2013). Expected leverage is calculated by (k + 1)/N where k is the number of predictors and N is the sample size (Filed, 2013). Values greater than two to three times larger than the expected leverage are overly influential on model fit (Field, 2013). The residuals of the best model were carefully examined to ensure a well-fitted model.

Standard errors and 95% CIs of Exp (β). As stated previously, large SEs indicate a violation of the assumptions of multivariate LR, such as over-fitting, missing data, and multicollinearity (Field, 2013). Therefore, large *SE*s require careful inspection, adjustment, and possible removal of problematic IVs from the model. Additionally, if the 95% CIs of Exp (β) included the value of 1.0, the variable was removed from the model because it indicated an ambiguous relationship between the IV and DV (Field, 2013).

Bootstrapping. Bootstrapping is a statistical process whereby multivariate small samples (at least 1,000) are randomly taken from the data, and a parameter of interest is estimated from each sample (Field, 2013). Each bootstrap sample is returned to the original

sample before the next random sample is selected (Field, 2013). Standard deviations are estimated and 95% CIs for the β coefficients are estimated (Field, 2013). Large discrepancies between the *SE*s of the original model and the bootstrapped model, as well as CIs that cross zero indicate a poorly fit model. Due to the small dataset, a bootstrap of 1,000 samples was implemented and assessed in the multivariate analyses.

Interpreting the results of the best model. Multivariate LR models are used to predict the category of the DV (e.g., HCV positive and HCV negative) to which an individual case belongs (Tabachnick & Fidell, 2013). Once the best model is established and an acceptable fit confirmed, the results of the best model can be interpreted in several ways. The current thesis research interpreted the ORs for HCV exposure, and estimated predictive probabilities from the multivariate LR model.

Odds ratios (ORs). ORs are an important method of interpreting multivariate LR modeling. The OR is defined as "the change in odds of being in one of the categories of outcome when the value of the predictor increases by one unit" (Tabachnick & Fidell, 2013, p. 463). An OR greater than 1.0 indicates an increase in the odds of having the outcome of study (HCV positive). Conversely, an OR less than 1.0 indicates reduced odds of having the outcome. The equation for calculating ORs is: OR = (a/b) / (c/d) = a*d / b*c (Tabachnick & Fidell, 2013, p. 464). The ORs were displayed in output tables as Exp (β) values along with 95% CIs for each independent variable entered into the LR model.

Classification of predicted outcomes. The classification table, classification matrix, and a receiver operating characteristic (ROC) curve will be used to interpret predicted probability ($\hat{Y}_i$) values. To understand classification and ROC curves, the concepts of sensitivity and specificity must be defined (Hilbe, 2009). The sensitivity of a test refers to the probability of testing positive and actually having the disease, whereas the specificity of a

test refers to the probability of testing negative and actually not having the disease (Hilbe, 2009). The point where sensitivity and specificity are the closest in a classification table is the optimal cut-off for the percentage of correct classifications (Hilbe, 2009).

ROC curves utilize predictive probabilities to determine the "model's ability to discriminate between those subjects who experience the outcome of interest versus those who do not" (Hosmer & Lemeshow, 2000, p. 160). A multivariate LR model with no predictive value (very poor fit) has a slope of 1.0, and an ROC of 0.5 (Hilbe, 2009). As the multivariate LR model improves in fit and predictive value, the area under the ROC curve increases (Hilbe, 2009). ROC curve values greater than 0.95 are highly unlikely, and most ROC values range from 0.6 to 0.9 for well-fitted models (Hilbe, 2009). An ROC curve was created and interpreted in the results of the current thesis research.

Probability prediction equation. Multivariate LR modeling results can be expressed in an equation that predicts the probability of each having the disease outcome (DV = 1.0) from a particular combination of scores in the IVs (Tabachnick & Fidell, 2013). As presented in Tabachnick and Fidell (2013), the probability prediction equation is:

$$Prob\ (HCV) = \hat{Y}_i = \frac{e^{(b0 + b1X1i + b2X2i)}}{1 + e^{(b0 + b1X1i + b2X2i)}}$$

(p. 448). The β coefficients calculated by the multivariate LR model were entered into the prediction equation, and HCV probabilities were calculated for each IV category.

Summary of Analytic Plan

The analytic plan has described the analyses methods used in the current thesis research. Bivariate χ^2 methods were used to evaluate relationships between the DV and each IV, and to determine if small cell sizes needed attention. Subsequently, multivariate LR analyses assessed the statistical relationships between the DV and multiple IVs, and a

predictive LR model was created. A classification matrix and ROC curve visually displayed the sensitivity and specificity of the model predictions. Finally, the multivariate LR model provided ORs for each IV, and a prediction equation calculated the probability of new cases being in one of the DV categories. Results of bivariate and multivariate analyses are presented in Chapter Four.

CHAPTER 4: Results

The results of the analytic plan outlined in Chapter Three will be presented in this chapter. First of all, descriptive statistics of the sample population will be presented. Secondly, bivariate analyses of the relationship between the DV and each of the selected IVs will be conducted. Thirdly, the multivariate LR model will be constructed and goodness-of-fit test statistics, an examination of residuals, and bootstrapping will assess the fit. Finally, the ORs, classification table, classification matrix, ROC curve and prediction equations will be interpreted. Discussion of the results are presented in Chapter Five.

Descriptive Statistics

The sample consisted of 272 eligible participants. Within the sample, 50.7% (*n* = 138) were females and 49.3% (*n* = 134) were males. The age of eligible participants ranged from 17 years to 65 years. Overall, the population had an average age of 40 years. HCV prevalence among eligible participants was 69.9% (*n* = 190). Table 1 displays percentages of males and females in each category of the variables to be included in the bivariate analyses.

Table 1

Percentages of male and female participants across categories of study variables

Variable Label (Variable Name)	**Male % (*n*)**	**Female % (*n*)**	**Total % (*n*)**	**Missing % (*n*)**
HCV status (Positive) (DV_HCV_VALID)	32.7 (89)	37.1 (101)	69.9 (190)	0.0 (0)
Aboriginal (Yes) (IV_aboriginal)	24.0 (65)	41.3 (112)	65.3 (177)	0.4 (1)
Number of years injecting (IV_INJECTION_YEARS)				
Two years or less	9.0 (24)	6.0 (16)	14.7 (40)	1.5 (4)
More than two years	41.0 (110)	44.0 (118)	83.8 (228)	

Table 1 (Continued)

Injection partners (IV_INJECTION_PARTNERS)				
Injecting alone	20.0 (54)	22.6 (61)	42.6 (115)	0.7 (2)
Injecting with others	29.3 (79)	28.1 (76)	57.4 (155)	
Unstable housing (Two or more places) (IV_HOUSING)	30.9 (84)	31.6 (86)	62.5 (170)	0.0 (0)
Residential mobility (Yes) (IV_residence6months)	14.3 (39)	16.2 (44)	30.5 (83)	0.0 (0)
Receptive sharing (Yes) (IV_RECEPTIVE_SHARING)	14.1 (38)	16.4 (44)	30.5 (82)	1.1 (3)
Drug of choice* (IV_DRUG_OF_CHOICE2)				
Stimulants	31.1 (83)	31.1 (83)	61.0 (166)	1.9 (5)
Opiates	19.1 (51)	18.7 (50)	37.1 (101)	
Travel to DTES (Yes) (IV_TRAVEL_EASTVAN)	5.1 (14)	6.3 (17)	11.4 (31)	0.0 (0)
Involved in sex trade (Yes) (IV_SEX_TRADE)	2.3 (6)	23.7 (63)	25.9 (69)	2.2 (6)

* Drug of choice will be investigated using the IV_DRUG_OF_CHOICE2 variable. Supplement Three presents the analyses of IV_DRUG_OF_CHOICE3.

Bivariate Analyses

Using χ^2 bivariate analyses, relationships between the DV and each IV were evaluated using 2 x 2 contingency tables. Adequate cell sizes (> 5 cases) were confirmed, and relationships were considered statistically significant if the χ^2 test statistic had a *p*-value of ≤ .10 (Hilbe, 2009). As shown in Table 2, three of the IVs had statistically significant relationships with the DV: number of years injecting (IV_INJECTION_YEARS), injection partners (IV_INJECTION_PARTNERS), and unstable housing (IV_HOUSING). Seven IVs were not statistically significant in the bivariate analyses. According to best practices for multivariate LR model-building, statistically significant *as well as* clinically relevant IVs

should be included in multivariate analyses (Field, 2013; Hilbe, 2009; Hosmer & Lemeshow, 2000; Tabachnick & Fidell, 2013). Therefore, all ten variables were included in the initial multivariate LR model.

Table 2

Results of bivariate analyses using 2 x 2 contingency tables

Variable Label (Variable Name)	**HCV Status** Positive % (*n*)	Negative % (*n*)	**Pearson χ^2**	***p***
Aboriginal status (IV_aboriginal)				
Aboriginal	45.0 (122)	20.3 (55)	.16	.689
Non-Aboriginal	24.7 (67)	10.0 (27)		
Drug of choice (IV_DRUG_OF_CHOICE2)				
Stimulants	42.7 (114)	19.5 (52)	.39	.533
Opiates	27.3 (73)	10.5 (28)		
Gender (IV_SEX_GENDER)				
Male	32.7 (89)	16.5 (45)	1.48	.224
Female	37.1 (101)	13.6 (37)		
Injection partners (IV_INJECTION_PARTNERS)				
Inject alone	33.4 (93)	8.1 (22)	11.27	**.001**
Inject with others	35.6 (96)	21.9 (59)		
Involved in sex trade (IV_SEX_TRADE)				
Yes	17.7 (47)	8.3 (22)	.30	.587
No	53.0 (141)	21.1 (56)		
Number of years injecting (IV_INJECTION_YEARS)				
Two years or less	4.5 (12)	10.4 (28)	39.19	**.000**
More than two years	65.7 (176)	19.4 (52)		
Receptive sharing (IV_RECEPTIVE_SHARING)				
Yes	19.7 (53)	10.8 (29)	1.79	.181
No	50.6 (136)	18.9 (51)		

Table 2 (Continued)

Residential mobility (IV_residence6months)				
Yes	19.5 (53)	11.0 (30)	2.04	.153
No	50.4 (137)	19.1 (52)		
Travel to DTES (IV_TRAVEL_EASTVAN)				
Yes	8.5 (23)	2.9 (8)	.31	.576
No	61.4 (167)	27.2 (74)		
Unstable housing (IV_HOUSING)				
One place	28.7 (78)	8.8 (24)	3.40	.065
Two or more places	41.2 (112)	21.3 (58)		

Multivariate Logistic Regression

To build the logistic regression model, ten IVs were entered into the multivariate LR model with the DV. The interaction variable of IV_SEX_GENDER x IV_aboriginal was also included in the model and is justified by multiple studies in the related research (Craib et al., 2009; Cullen et al., 2015; Hadland et al., 2012; Hahn et al., 2010; Iversen et al., 2010; Mehrabadi et al., 2008; PHAC, 2010; Plitt et al., 2010; Roy et al., 2011; Scheidell et al., 2015). Moreover, female Aboriginal participants were significantly overrepresented in the study sample of the current thesis research ($\chi^2 = 33.05$, $p < .001$).

The results of the initial full model are presented in Table 3. Two IVs had significant Wald statistics ($p < .05$): number of years injecting (IV_INJECTION_YEARS), and injection partners (IV_INJECTION_PARTNERS).

Table 3

Initial full model including ten IVs and one interaction variable

Variable	β	*SE*	Wald	*p*	Exp (β)	95% CI lower, upper
Aboriginal status (IV_aboriginal)	.25	1.06	.06	.813	1.28	.16, 10.16
Aboriginal status x Gender (IV_aboriginal x IV_SEX_GENDER)	-.06	.76	.01	.941	.95	.21, 4.21
Drug of choice (IV_DRUG_OF_CHOICE2)	.10	.33	.10	.756	1.11	.58, 2.12
Gender IV_SEX_GENDER	.66	1.06	.39	.532	1.94	.24, 15.39
Injection partners (IV_INJECTION_PARTNERS)	.87	.34	6.51	**.011**	2.39	1.22, 4.68
Involved in sex trade (IV_SEX_TRADE)	-.46	.43	1.12	.290	.63	.27, 1.48
Number of years injecting (IV_INJECTION_YEARS)	2.16	.43	24.74	**.000**	8.67	3.70, 20.31
Receptive sharing (IV_RECEPTIVE_SHARING)	-.09	.35	.06	.803	.92	.46, 1.81
Residential mobility (IV_residence6months)	-.53	.36	2.24	.135	.59	.30, 1.18
Travel to DTES (IV_TRAVEL_EASTVAN)	.23	.49	.21	.646	1.25	.48, 3.27
Unstable housing (IV_HOUSING)	-.33	.35	.85	.356	.72	.36, 1.44
Constant	-4.75	1.91	5.98	.014	.01	

Table 4 displays the new model that was created including only the two significant variables: number of years injecting (IV_INJECTION_YEARS) and injection partners

(IV_INJECTION PARTNERS). Using sequential logistic regression methods, the fit of the new model was compared with the fit of the full model. As shown in Table 5, the Omnibus Test of Model Coefficients shows the difference between the deviance (*-2LL*) of the full model and the deviance of the new model results in an insignificant χ^2 ($p = .585$). Thus, the new model containing only two variables is a better fit and is accepted as the best model.

Table 4

New model including two significant IVs

Variable	**B**	***SE***	**Wald**	***p***	**Exp (β)**	**95% CI lower, upper**
Injection partners IV_INJECTION_PARTNERS	.87	.33	7.16	.007	2.38	1.26, 4.50
Number of years injecting (IV_INJECTION_YEARS)	2.17	.42	27.18	.000	8.78	3.88, 19.86
Constant	-4.26	.91	21.89	.000	.01	

Table 5

Test statistics comparing the fit of the new model with the initial full model

Test statistic	**New model**	**Full model**
Omnibus Test of Model Coefficients (Block)	$\chi^2 = 40.42$, *df* (2), $p < .001$	$\chi^2 = 7.69$, *df* (9), $p = .565$
-2 Log Likelihood (*-2LL*)	261.11	253.42

After selecting the new model over the full model, multivariate LR was conducted once more to create a final best model of the two significant IVs number of years injecting (IV_INJECTION_YEARS) and injection partners (IV_INJECTION_PARTNERS). The results of the final best model are presented in Table 6. Changes in values in the final best

model as compared with the previous models are due to an increased number of selected cases. The initial full model had twenty cases with missing observations that were removed from the analyses resulting in 252 selected cases. The final best model had only six cases removed due to missing observations resulting in 266 cases selected for the LR analyses.

Table 6

Final best model including two significant IVs

Variable	**β**	***SE***	**Wald**	***p***	**Exp (β)**	**95% CI lower, upper**
Number of years injecting (IV_INJECTION_YEARS)	2.06	.40	26.75	.000	7.87	3.60, 17.18
Injection Partners IV_INJECTION_PARTNERS	.91	.31	8.52	.004	2.49	1.35, 4.59
Constant	-4.17	.87	23.25	.000	.02	

Assessing the Fit of the Best Model

The final best model had an insignificant Hosmer and Lemeshow GOF test result of $\chi^2 = .37$, $p = .832$ indicating a well-fit model. The dispersion parameter is calculated as χ^2 (.37) / *df* (2) = .185. The value was not greater than one and over-dispersion was not a concern. Over-dispersion indicates a violation in the assumption of independence where the same cases are represented in more than one category and would be indicated by very small *SE*s, overly large test statistic results, and narrow confidence intervals (CIs) which appear very significant, but are actually incorrect (Field, 2013). Not surprisingly, over-dispersion is not a concern because the filter variable (FV_ELIGIBLE_PARTICIPANTS) removed all duplicate cases from the sample population.

Residual outliers. A case-wise listing of standardized *z*-score residuals showed no outliers greater than two standard deviations = +/- 2.58. However, examining the standardized *z*-score residuals indicated fourteen cases (5%) were outside of +/- 1.96. The percentage of standardized *z*-score residuals within this range matches the acceptable limit of 5% (Field, 2013). Upon closer inspection, all fourteen cases reported injecting alone *and* injecting for more than two years: the two risks behaviours significantly associated with HCV infection in the multivariate LR model. However, all fourteen cases were HCV negative and represent PWIDs who have managed to remain uninfected despite high-risk behaviours. These cases represent points where the model fits poorly (Field, 2013).

All Cook's distance values were less than one, and all DF Betas of the constant and the IVs were also less than one. The outer leverage limits were calculated as $3(k + 1) / N = 0.03$. Eleven cases (4%) were found to have leverage values greater than the acceptable outer limit. Closer inspection revealed all cases had reported injecting for less than two years *and* were injecting with others, but were HCV positive. These cases represent PWIDs who reported low-risk behaviours, but had still been infected with HCV. Once again, these cases represent points where the model fits poorly (Field, 2013).

Bootstrapping. A bootstrap was completed and results are presented in Table 7. *SE*s and 95% CIs are not excessively large and do not differ greatly from the best model. The bootstrap results combined with the GOF tests and standardized residuals confirm the best model is well-fitted and acceptable for interpretation.

Table 7

Bootstrap of best model (1,000 samples)

Variable	β	*SE*	*P*	Exp (β)	95% CI lower, upper
Number of years injecting (IV_INJECTION_YEARS)	2.06	.44	.001	7.86	3.68, 20.57
Injection partners (IV_INJECTION_PARTNERS)	.91	.33	.001	2.49	1.37, 4.99
Constant	-1.20	.42	.003	0.30	0.12, 0.63

Interpretation of Multivariate LR Results

Odds Ratios (ORs)

Two ORs can be interpreted from the multivariate LR best model results. First of all, the adjusted odds associated with being HCV positive are almost 7.9 higher for PWIDs who have been injecting for more than two years compared to those injecting for two years of less, AOR 7.87, $p = .001$, 95% CI [3.60, 17.18]. Secondly, the adjusted odds associated with being HCV positive are almost 2.5 higher for PWIDs who inject alone compared to those who are injecting with others, AOR 2.49, $p = .004$, 95% CI [1.35, 4.59].

Notably, the ORs must not be interpreted as risk ratios (RRs) for two reasons. First of all, the I-Track dataset is retrospective and was created by merging single observation points. RRs can only be calculated from prospective data collected from multiple points of observation such as clinical trials or longitudinal cohort studies (Friis & Sellers, 2009). Secondly, although ORs and RRs may approximate when the disease of study is rare, ORs will substantially overestimate or underestimate RRs when the disease is common (Andrade,

2015; Cummings, 2009). Since HCV infection within the PWID study sample was very common (~70%), the ORs in the current thesis research can not be used to approximate RRs.

Classification Table

As shown in Table 8, the number of observed HCV positive lab tests was 187 and the best model correctly predicted 176 cases as HCV positive. Therefore, the sensitivity of HCV true positives is 176/187 = 94.1%. Conversely, the number of observed HCV negative lab tests was 79 and the best model correctly predicted 27 as HCV negative. Therefore, the specificity of HCV true negatives is 27/79 = 34.2%. The overall percentage of correct predictions is calculated as predicted positives + predicted negatives / sample size = 176 + 27 / 266 = 76.3%. The observed prevalence of HCV positive lab results was 187 / 266 = 70.3%, indicating an overall improvement in correct predictions of 6%.

Table 8

Classification table of best model results

Observed		**Predicted**		
		HCV status		**Percentage**
		HCV negative by lab test	HCV positive by lab test	Correct
HCV status	HCV negative by lab test	27	52	34.2
	HCV positive by lab test	11	176	94.1
Overall Percentage				76.3

Classification Matrix

The classification matrix presented in Figure 3 visually displays the predicted probability of group membership (HCV yes/no). HCV positive status is represented by the number one (1), and HCV negative status is represented with zero (0). Each number in the matrix represents ten cases. Cases with a predicted probability of HCV negative status are located to the left of the cut-point of .70, and cases with predicted probability of HCV positive status are located to the right. However, the matrix displays ten true positive cases to the left of the .70 cut-point that have been incorrectly predicted to be HCV negative by the LR model. The matrix also shows there are fifty true negative cases that have been incorrectly classified as positive to the right of the .70 cut-point. The true cases that have been incorrectly predicted represent points where the multivariate LR model fits poorly.

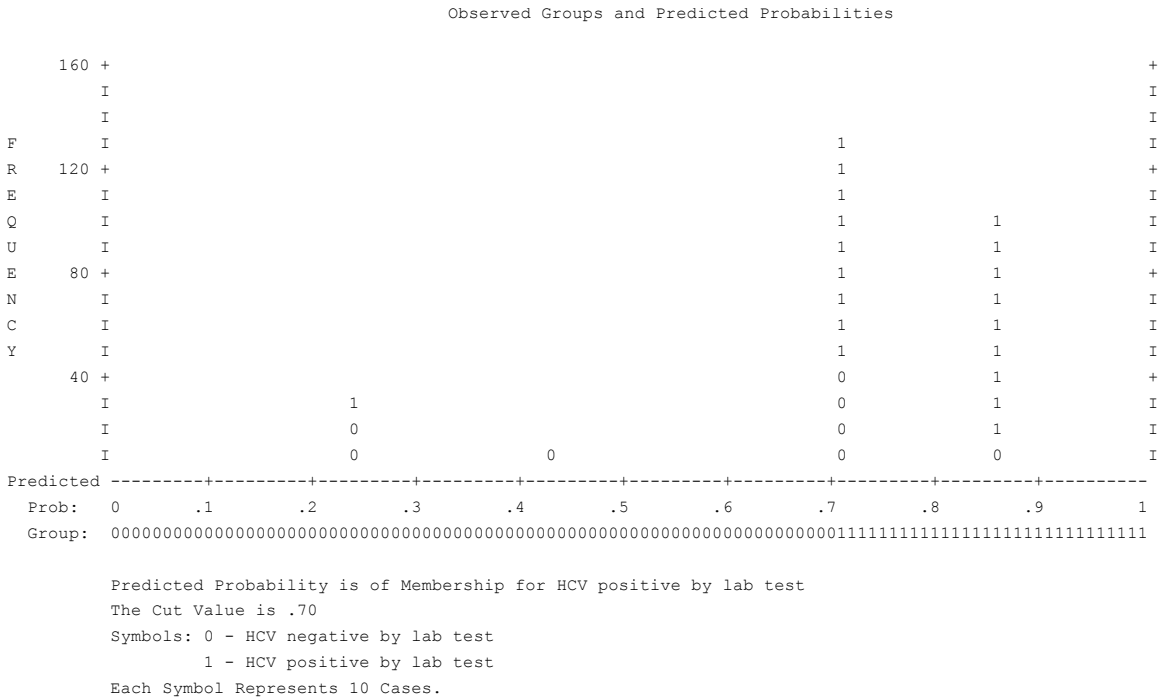

Figure 3. Classification matrix of best model.

ROC Curve

Sensitivity and specificity are demonstrated by the ROC curve displayed in Figure 4. The area under the curve is calculated as .71, p = .001, 95% CI [.65, .78]. As such, the ROC curve indicates the best model is a fair instrument for predictive probability (Field, 2013; Hilbe, 2009). Table 9 display the sensitivity and specificity are maximized at a cut-off probability of .57. At this cut-off point, the sensitivity of the multivariate LR model predicting true positives is 94.1%, whereas the specificity of LR model predicting true negatives is only 34.2%. Therefore, the best model shows high sensitivity to HCV positive cases, but low specificity to HCV negative cases.

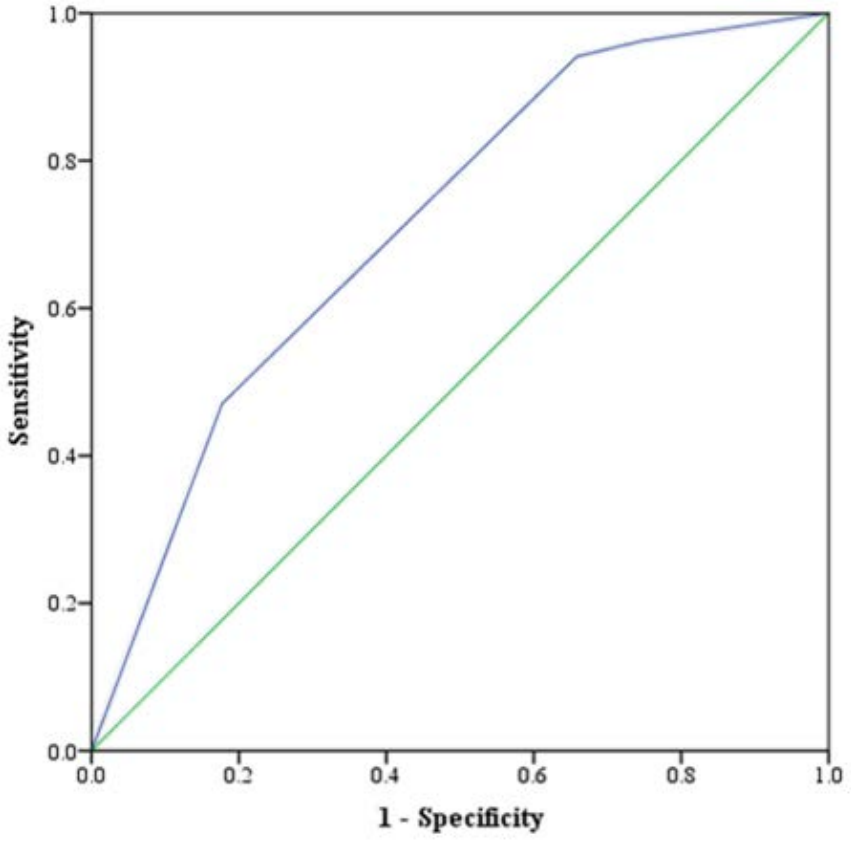

Figure 4. ROC curve of best model.

Table 9

Sensitivity and specificity of the ROC curve

HCV positive if greater than or equal:	**Sensitivity**	**Specificity**
.00	1.00	.00
.33	.96	.25
.57	**.94**	**.34**
.78	.47	.82
1.00	.00	1.00

Prediction Equation

Predicted probability of having the disease outcome (HCV status = 1) is calculated for each category in the IVs using the following equation (Tabachnick & Fidell, 2013, p. 447):

$$Prob\ (HCV) = \hat{Y}_i = \frac{e^{(b0 + b1X1i + b2X2i)}}{1 + e^{(b0 + b1X1i + b2X2i)}}$$

As shown in Table 10, the β coefficients calculated in the multivariate LR model are inserted into the equation to calculate the predicted probabilities (Tabachnick & Fidell, 2013).

Table 10

Predicted probabilities of being HCV positive for each risk behaviour category

Variable	Injects with others (IV_INJECTION_ PARTNERS = 1)	Injects alone (IV_INJECTION_ PARTNERS = 2)
Injecting for two years or less (IV_INJECTION_YEARS = 1)	*Prob (HCV)* = 0.23	*Prob (HCV)* = 0.43
Injecting for more than two years (IV_INJECTION_YEARS = 2)	*Prob (HCV)* = 0.70	*Prob (HCV)* = 0.86

The calculations indicate if a PWID has been injecting for more than two years and reports injecting alone, there is a probability of 0.86 that they will be HCV positive. Conversely, if a PWID has been injecting for less than two years and reports injecting with others, there in only a probability of 0.23 that they will be HCV positive. Calculations for each predicted probability equation are presented in Supplement Three.

Summary of Results

The results of the bivariate and multivariate analyses have been presented in Chapter Four. Bivariate analyses were used to identify the associations between the DV and IVs, and alert the researcher to small cell sizes. Constructing the multivariate LR model required several steps and the fit of the best model was confirmed by several statistical assessments. Once the best model was established, ORs, classification table and matrix, ROC curve, and predicted probabilities were interpreted. The multivariate LR analyses identified two IVs significantly associated with HCV infection: number of years injecting (IV_INJECTION_YEARS) and injection partners (IV_INJECTION_PARTNERS). A discussion of the public health implications of the results is presented in Chapter Five.

CHAPTER 5: Discussion and Conclusion

The fifth and final chapter of the current research thesis will discuss the results of the multivariate LR analyses. First of all, a review of the risk behaviours significantly associated with HCV among the Prince George I-Track participants will be presented. Secondly, public health implications and limitations of the study are identified, and future recommendations proposed. In conclusion, a summation of the study findings and relevance is provided.

Risk Behaviours Associated with HCV

The odds of being HCV positive for PWIDs who reported IDU for more than two years were almost 7.9, OR 7.87, $p < .001$, 95% CI [3.60, 17.18]. The predicted probability of being HCV positive for PWIDs injecting more than two years and injecting with others vs. injecting alone was 0.70 and 0.86, respectively. Thus, the number of years injecting is a very important risk behaviour to consider when exploring HCV infections among PWIDs. These results are consistent with other studies in the related research that have identified number of years injecting to be significantly associated with HCV among PWIDs (Craib et al., 2009; Garfein et al., 2012; Havens et al., 2013; Miller et al., 2009; PHAC, 2010; Roy et al., 2009; Spittal et al., 2012).

The odds of being HCV positive for PWIDs who reported injecting alone were almost 2.5, OR 2.49, $p = .004$, 95% CI [1.35, 4.59]. The predicted probability of being HCV positive for PWIDs injecting alone for more than two years vs. two years or less was 0.43 and 0.23 respectively. Interestingly, studies in the related research did not investigate PWIDs who reported injecting alone, but rather focused on length of injection partnerships and sexual partnerships between PWIDs (Christian et al., 2010; Evans et al., 2014; Hahn et al., 2010; Morris et al., 2013; Roy et al., 2011; Wagner et al., 2013). It is uncertain why HCV positive

PWIDs in the Prince George I-Track survey were significantly more likely to report injecting alone when other studies have not identified this phenomenon.

A possible hypothesis is that PWIDs who are injecting alone are more established in their injection behaviours, and/or are more cognizant of the risks of injecting with others. An awareness of their own HCV positive serostatus may result in injecting alone to avoid putting others at risk. A second hypothesis for the injecting alone phenomenon would be social desirability bias affecting participant responses during the survey interview. The lack of related research on the phenomenon of injecting alone is puzzling, and further research is needed to explore injection behaviours among HCV-positive PWIDs.

In contrast to those PWIDs who reported injecting alone, those who reported injecting with others were much less likely to be HCV positive despite engaging in high-risk behaviours. PWIDs may be injecting with others because they are not established in their injection behaviours (early initiates or sporadic binge users), are unaware of their own HCV serostatus, and/or are unaware of the risks of contracting blood-borne pathogens when injecting with others. Such risk-taking behaviours are undoubtedly influenced by multiple complex psycho-social factors (e.g., low self-esteem, peer pressure, history of trauma/abuse). The results clearly indicate PWIDs who reported injecting with others were significantly more likely to be HCV negative, and are at very high-risk for HCV seroconversion.

Aboriginal Female PWIDs

Aboriginal female PWIDs were significantly overrepresented in the study sample ($\chi^2 = 33.05$, $p < .001$). To explore this overrepresentation, the gender (IV_SEX_GENDER) and Aboriginal status (IV_aboriginal) variables were entered into the multivariate LR model. An interaction variable (IV_SEX_GENDER x IV_aboriginal) was also included to assess the combined effect of gender and Aboriginal status in the model. The multivariate LR analyses

did not find any of these variables to be significantly associated with HCV among the PWID participants. However, several studies in the related research have clearly identified Aboriginal female PWIDs as particularly vulnerable to HCV infections (Craib et al., 2009; Iversen et al., 2010; Mehrabadi et al., 2008; Spittal et al., 2012). Although the current thesis research did not identify Aboriginal status and female gender as a significantly associated characteristics, it is highly suspected that Aboriginal female PWIDS are at very high-risk for HCV infection.

Public Health Implications

Identifying HCV Positive PWIDs

Applying the results of the multivariate LR model to clinical practice greatly improves the prediction of PWIDs who are HCV positive (sensitivity). Public health practitioners can ask PWID patients "How long have you been injecting drugs?" and "Do you inject alone or with others?". If responses are "more than two years" and "injecting alone", they will be able to accurately predict 94.1% of HCV positive PWIDs. As a result, PWIDs predicted to be at high-risk for HCV can be targeted for HCV screening, as well as ongoing harm reduction interventions to reduce the spread of HCV.

The ability for health practitioners to identify HCV positive PWIDs is very important considering recent advances in DAA treatment for those with chronic hepatitis C (CHC) infections. One of the primary recommendations proposed in the Canadian consensus guidelines for the management of CHC states: "To reduce the burden of HCV-related morbidity and mortality in Canada, strategies for case identification, harm reduction, and disease management – including but not limited to antiviral therapy – should be developed and implemented" (Myers et al., 2015, p. 2). The current thesis research has found two risk

behaviours significantly associated with HCV among PWIDs, and the results greatly improve the ability to predict those most likely to be HCV positive.

Identifying HCV Negative PWIDs

Ideally, the multivariate LR model would maximize both sensitivity and specificity for predicting HCV positive and HCV negative PWIDs respectively. However, the results of the multivariate LR model in the current thesis research do not provide a clinically useful prediction model for identifying PWIDs who are HCV negative (specificity = 34%). During the initial development of the thesis project, identifying HCV negative PWIDs who might be at high risk for seroconversion was considered an important goal for harm reduction services and HCV prevention within PWID populations. However, further refinement of the specificity of the multivariate LR model is now considered clinically irrelevant – especially given the transformative changes in HCV treatment at present.

At this time, public health approaches for HCV management in PWID populations are changing dramatically. Ideally, all PWIDs – regardless of likelihood of HCV positive or HCV negative status – should be screened and engaged in HCV treatment. Given that approximately 70% of PWIDs worldwide are HCV positive (and approximately 70% of the Prince George sample were positive) it may be helpful for public health programs to implement a seek-and-treat approach for all PWIDs, regardless of risk factors associated with HCV status. However, despite the potential success of HCV treatment for infected PWIDs, it remains imperative that HCV treatment be combined with ongoing harm reduction services such as NEPs to decrease the risk of transmission. The risk factors associated with HCV infection among PWIDs identified by the current thesis research provide guidance for such public health policies and harm reduction strategies.

Limitations

I-Track Study Design

There are several limitations within the I-Track research project that influence the results of the current research. First of all, the convenience sampling method introduces a selection bias into the data (Lavrakas, 2008). The PWIDs who participated in the I-Track survey were familiar with the Prince George NEP, and felt comfortable going to this location to complete the survey. However, there may be other PWIDs in Prince George who did not complete the survey because 1) they did not know about the survey, 2) did not want to go to the NEP to participate due to stigma or triggers, or 3) were not available to participate (e.g., out of town, in treatment, incarcerated). As a result, the data may not be truly representative of the PWID population, and the generalizability of the current thesis results are limited.

Secondly, interviewer bias may have been introduced into the data due to different interviewers in each phase of the survey. Despite standardized I-Track training, each interviewer would bring their own tone of voice, body language, level of comfort, and previous rapport to the interview (Lavrakas, 2008). Moreover, most of the participants were familiar with the Phase 3 interviewers because they had all been employees at the NEP. All NEP staff are required to teach harm reduction practices to clients whenever possible. For the same staff to ask clients about unsafe injection practices and unsafe sexual behaviours may have affected what participants were willing to disclose; thus, introducing social desirability bias into the results (Lavrakas, 2008).

Current Thesis Research Methods

There are also several limitations in the research methods of the current thesis research. First of all, the data were obtained from the observational, cross-sectional I-Track research survey. As such, the current study is unable to determine causation or temporal

change, and associations between the DV and IVs may be greatly influenced by confounding factors (Lavrakas, 2008). Secondly, the prevalence estimates obtained from the I-Track survey results are only valid for that specific "snapshot" in time. The current thesis research relies heavily on those prevalence point estimates, and may not be representative of the true HCV prevalence among PWIDs in Prince George.

Thirdly, merging the datasets from the 2008 and 2012 I-Track surveys almost doubled the sample size, but small cell sizes remained a limitation during the multivariate LR analyses of the current thesis research. Fourthly, it was assumed that relations between the DV and the IVs remained constant across the 2008 and 2012 I-Track survey cycles. However, there may have been differences between the two survey cycles that were lost when the datasets were merged.

Finally, the HCV antibody test used in the I-Track survey only provides prevalence estimates of lifetime exposure to HCV, and not necessarily active infection. As outlined in Supplement Three, it is broadly estimated that spontaneous clearance of HCV infection occurs in 15% to 45% of those infected (BCCDC, 2013; WHO, 2014). Therefore, the HCV prevalence estimates used in the current research thesis may be somewhat misleading because not all PWIDs who have been exposed to HCV remain infected. Obtaining more accurate HCV prevalence estimates would require HCV RNA tests to confirm active infections (Myers et al., 2012). Notably, all studies in the related research used HCV antibody tests to estimate HCV prevalence and incidence, and such methods may substantially over-estimate the true prevalence and incidence of active HCV infections among PWIDs.

Despite limitations in the I-Track study design and the current research thesis methods, risk behaviours significantly associated with HCV among PWIDs in Prince George

have been identified. Undoubtedly, involving PWIDs in research studies is very challenging due to social stigma and marginalization, and the I-Track survey was able to effectively engage PWIDs using anonymous, observational, cross-sectional methods. As stated in Chapter Two, implementing experimental methods would be impossible without ethical ramifications. Therefore, the current thesis research was able to conduct important research using the survey data, and the results are very relevant to the health and wellness of the Prince George PWID population.

Recommendations

Harm Reduction Interventions

It has been repeatedly evidenced in the related research that sharing of any injection equipment is high-risk for HCV seroconversion among PWIDs (Kim et al., 2015; Palmanteer et al., 2013; Pouget et al., 2011; Strike et al., 2010). Although the current thesis research did not find receptive sharing significantly associated with HCV among the Prince George PWIDs, this risk behaviour for HCV seroconversion may be confounded by the number of injection years and injecting partners. For example, the longer someone engages in IDU the higher the risk for sharing equipment which then leads to HCV infection. Similarly, injecting with others increases the risk for sharing equipment and becoming infected with HCV. Thus, the underlying risk behaviour for HCV infection remains sharing injection equipment.

As repeatedly recommended by the BCCDC (2013) and the WHO (2014), harm reduction strategies must find methods to provide unlimited availability of sterile injection equipment to PWIDs. Additionally, accurate information on the prolonged environmental viability of HCV, the risks of injection practices such as "washes", and suggestions of safer injection overall must be provided (BCCDC, 2013; WHO, 2014). In accordance with these

recommendations, the current thesis research has highlighted the ongoing need for harm reduction services for all PWIDs.

Improvements in HCV Screening

Throughout the related research and current thesis research, HCV prevalence and incidence within PWID populations has been estimated using HCV antibody testing. This method of testing is cost-effective and efficient, but it provides only the prevalence of HCV *exposure*, not active infection. However, it is broadly estimated that 15% to 45% of incident HCV infections are eliminated by spontaneous clearance of the host's immune system (BCCDC, 2013; WHO, 2014). Therefore, all prevalence estimates based on HCV antibody testing must be viewed with caution because they only indicate lifetime exposure to HCV.

Utilizing HCV RNA tests to confirm active HCV infection would establish accurate HCV prevalence estimates and incidence rates, but such tests are very expensive (PHAC, 2009). A less expensive HCV RNA test that accurately identifies active HCV infection (similar to the HIV point-of-care test) would greatly improve the diagnosis of HCV among PWIDs (Pawlotsky et al., 2015). In the meantime, HCV prevention, screening, and treatment among PWIDs will depend on the timely follow-up of HCV RNA testing after a positive HCV antibody test. Such timely follow-up will be dependent on the availability and expertise of pubic health practitioners.

Providing PWIDs with HCV Treatment

Recent advances in HCV treatment have led to cure rates of more than 90% from DAAs (Pawlotsky et al., 2015). Moreover, DAA treatment are proving accessible and sustainable for PWIDs who have previously been excluded due to co-morbidities, risk of liver toxicity, and poor adherence (Pawlotsky et al., 2015). Harm reduction-based treatment programs designed to establish rapport, maintain adherence, and provide medical monitoring

for PWIDs have proven successful for HIV antiviral programs, and similar initiatives may be equally successful with HCV (Pawlotsky et al., 2015). HCV treatment for PWIDS is important because decreasing viral loads through effective treatment programs will reduce HCV incidence and prevalence among PWIDs.

Engaging PWIDs in HCV screening and DAA treatment will also greatly reduce the financial, social, and personal costs of chronic infection (Myers et al., 2015). The financial burden of HCV disease (excluding treatment) in Canada in 2013 was estimated at $52,000 (non-fibrotic stage) per patient to approximately $328,000 (liver transplant) per patient (Myers et al., 2014). Total costs associated with CHC are expected to increase by 60% annually to its peak in 2032 (Myers et al., 2014). Current costs of DAAs are estimated at $1,000 (USD) per pill for an estimated cost of $56,000 to $84,000 for 8 to 12 weeks of uncomplicated treatment (Pawlotsky et al., 2015).

With an estimated 80% of incident cases occurring among PWIDs, the need for prompt HCV screening and treatment interventions is imperative (Degenhardt et al., 2016). As stated in the CASL (2015) guidelines, “increased resources are needed to improve HCV treatment capacity… including the training of expert treaters and the public funding of treatment nurses” (Myers et al., 2015, p. 3). Clearly, the future burden of HCV disease will be dependent on current allocations of resources and funding to treat HCV infected PWIDs and provide harm reduction services to reduce HCV incidence. The current thesis research provides evidence of risk behaviours associated with HCV among PWIDs, and contributes to the identification of HCV positive PWIDs in Prince George.

Rural PWID Populations

As noted in the summary of Chapter Two, the lack of HCV research focused on northern, non-metropolitan populations of PWIDs is a notable gap in the related literature.

Prince George is known as “BC’s Northern Capital” because it is an urban hub for the northern two-thirds of the province. With a population of approximately 80,000, it is far from being a metropolitan centre. However, there are comprehensive health care services available in Prince George, and PWIDs living in the city have access to several harm reduction programs (e.g., daily NEP and evening Outreach services). As a result of the current health care infrastructure in Prince George, developing and implementing an effective HCV screening and treatment program would be feasible, and is clearly warranted by the high prevalence of HCV among PWIDs identified in the current thesis research.

The current thesis research found one-third of PWID participants reported living outside of Prince George in the six months prior to the surveys. However, residential mobility was not found to be a significant risk behaviour associated with HCV in the current thesis research, and unfortunately only Phase 3 of the Prince George I-Track survey inquired specifically about travel to outlying communities, and was not eligible for advanced analyses. Despite these results, it remains strongly suspected that PWIDs living in rural communities throughout northern BC are at high risk for HCV infection due to the high prevalence of HCV among PWIDs, the reported residential mobility, and limited access to harm reduction services in outlying communities.

Previous research studies have also identified increased residential mobility among PWIDs living in outlying communities in northern BC, and have speculated on the high risk for HCV transmission (Callaghan et al., 2007; Jongbloed et al., 2015; Mehrabadi et al., 2008; Rachlis et al., 2008). Additionally, annual epidemiological data collected by the BCCDC indicates the HCV incidence rate in 2015 in the Northwest sub-region was 53.2 per 100,000 population, and the Northeast sub-region was 54.6 per 100,000 population. Both rates are substantially higher than the national incidence rate of 29.4 per 100,000 population (BCCDC,

2016). In light of these research findings and the limited availability of harm reduction services in outlying communities, an HCV screening campaign for PWIDs living throughout northern BC is clearly warranted.

Aboriginal PWIDs

According to a study compiled by PHAC (2010), the HCV incidence rate among Aboriginals is almost five times higher compared with other Canadians: 4.34 per 100,000 population vs. 0.90 per 100,000 population respectively. Therefore, not only are Aboriginal PWIDs at increased risk for HCV infections, but the general Aboriginal population is also at increased risk. In response to the stark difference in HCV incidence between Aboriginals and non-Aboriginals, a pilot study similar to the I-Track survey named A-Track was conducted in Regina, Saskatchewan in 2011. HCV prevalence of the general Aboriginal population was 41.6% (n = 434) with significantly more males (46.1%) than females (36.9%) testing positive (PHAC, 2014b). With a large Aboriginal population living in northern BC, an A-Track survey would establish prevalence estimates and identify risk behaviours among Aboriginals vulnerable to HCV infections.

Specific to Aboriginal PWIDs living in Prince George, a task force similar to the HIV AIDS Coalition of the Carrier Sekani Family services (2016) is warranted. Aboriginal leaders and health care stakeholders need to establish a task force mandated to address HCV infections and engage Aboriginal PWIDs in a culturally appropriate manner. A primary focus of the task force would be to engage with Aboriginal female PWIDs and high-risk Aboriginal youth, as these sub-populations have been identified in the related research as particularly vulnerable. Culturally sensitive HCV screening to estimate prevalence, as well as prompt HCV RNA testing and treatment would greatly benefit Aboriginal PWIDs in Prince George.

Attitudes toward HCV

Qualitative research conducted by Rhodes and Treloar (2008) highlighted a common belief among PWIDs that HCV is "no big deal", that "everybody's got it", and that they "will not live long enough to die from HCV" (Rhodes & Taylor, 2008, p. 1594). Unfortunately, dismissive attitudes toward HCV have been inadvertently propagated and perpetuated by public health research and initiatives focusing primarily on the HIV epidemic, while ignoring the long-term effects of HCV infection (Rhodes & Treloar, 2008). As result, HCV health campaigns will need to directly address the entrenched belief systems shared by PWIDs that HCV is ubiquitous and trivial compared to HIV.

In addition to entrenched beliefs normalizing and dismissing HCV, PWIDs have displayed much confusion about HCV transmission and testing (Rhodes & Treloar, 2008; PHAC, 2012). The risk of sharing *any* injection equipment (not just needles and syringes) must be reiterated, and safer injection practices promoted to decrease the risk of HCV infection. Explanations of HCV antibody tests, HCV RNA tests, and the progression of HCV to chronic illness must inform PWIDs of long-term health problems related to the illness. Careful evaluation of HCV education programs tailored, not only to the PWID population, but also to public health practitioners will improve the overall understanding of HCV infections, prevent further transmission, and promote treatment for infected PWIDs.

Conclusion

For almost two decades, research studies have reported unacceptably high HCV prevalence and incidence among PWIDs in Canada. For example, Patrick et al. (2001) reported HCV prevalence among PWID participants in the VIDUS study as 81.6%, 95% CI [79.6%, 83.6%] long ago in 1999. Unfortunately, the extensive harm reduction and prevention efforts tailored to HIV have been ineffective at curbing the spread of HCV within

PWID populations. Although some risk factors are similar between HIV and HCV, the latter is more complicated due to its prolonged environmental viability, asymptomatic hosts, and the ubiquitous sharing of injection equipment (not just needles and syringes) among PWIDs.

The current thesis research investigated the risk behaviours and characteristics associated with HCV infection among PWIDs who participated in the Prince George I-Track surveys. Independent variables of interest included receptive sharing, number of years injecting, injection partners, drug of choice, unstable housing, residential mobility, female gender, travel to DTES, involvement in sex trade, and Aboriginal status. Each of these variables were evidenced in the related research as risk behaviours and characteristics associated with HCV infection. Using multivariate LR analyses, the current research thesis found risk behaviours of injecting for more than two years and injecting alone to be significantly associated with HCV among PWIDs in Prince George.

The results of the current thesis research contribute to knowledge of HCV infections among PWIDs living in Prince George, BC. Although not generalizable to other PWID populations, the results provide evidence to guide the development of HCV prevention, screening and treatment programs tailored to the Prince George PWID populations. It is hoped that the current thesis research will increase awareness and understanding of HCV infections among PWIDs, promote the ongoing provision of accessible harm reduction services to PWIDs, and encourage prompt HCV screening and treatment of infected PWIDs to reduce the financial, social, and personal costs of living with chronic HCV infection.

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Appendix A: UNBC Research Ethics Approval

UNIVERSITY OF NORTHERN BRITISH COLUMBIA

RESEARCH ETHICS BOARD

MEMORANDUM

To: Martha Ridsdale
CC: Russ Callaghan

From: Michael Murphy, Chair
Research Ethics Board

Date: April 3, 2014

Re: **E2014.0314.015.00**
Risk behaviors and characteristics of injection drug users (IDUs) with hepatitis C and HIV infection in Prince George, BC

Thank you for submitting the above-noted application to the UNBC Research Ethics Board (REB). Your application has been reviewed and it has been determined that REB approval is not required.

If you have any questions on the above or require further clarification please feel free to contact Rheanna Robinson in the Office of Research (reb@unbc.ca or 250-960-6735).

Sincerely,

Dr. Michael Murphy
Chair, Research Ethics Board

Appendix B: Consents for Prince George I-Track Data

Russ Callaghan

From: Emma Palmantier <emma@csfs.org>
Sent: Thursday, January 23, 2014 1:54 PM
To: Russ Callaghan
Subject: RE: Merged PG I-Track data sets from 2008-2012

From: Emma Palmantier
January 23, 2014
Yes, I support and provide approval for Martha to access 2008 and 2012 I-Track Prince George data. This will also assist our organization as I am sure she is going to share her report once she is finished. I hear you are unable to attend our quarterly Coalition meeting next week but will be available for introduction. It would be good while the introduction if you could provide update on the I-Track to mention that there was a press release done last month on this.

From: Russ Callaghan [mailto:Russ.Callaghan@unbc.ca]
Sent: Thursday, January 23, 2014 1:25 PM
To: Emma Palmantier
Subject: Merged PG I-Track data sets from 2008-2012

Hello Emma,
I hope you're well. I would like to request your approval for Martha Shoemaker and I to use the 2008 and 2012 merged I-Track Prince George data set. I have requested these data from Jill, but before I or Martha can access them, I need to have approval from the Northern Health Authority and the Coalition and CSFS (see email below from Jill). It'd be great if Martha could analyze these data for her master's degree at UNBC. She is planning to focus on patterns of HCV positive status among people reporting current injection drug use in Prince George. In particular, she is interested in understanding the characteristics of people who are HCV positive. I think this work will be important for us, and I will supervise her in her Master's degree. In order for Martha and I to access the merged 2008 and 2012 Prince George I-Track data, we need your approval (on behalf of the Coalition). Would you support our accessing these data?
Talk to you soon,
Russ

Dr. Russ Callaghan, PhD
Associate Professor
Northern Medical Program
University of Northern British Columbia
3333 University Way
Prince George, British Columbia
V2N 4Z9
E-mail: Russ.Callaghan@unbc.ca
Phone: 250.960.5668

This email was generated using voice-to-text software.

From: Jill Tarasuk [mailto:jill.tarasuk@phac-aspc.gc.ca]
Sent: Thursday, January 23, 2014 11:13 AM
To: Russ Callaghan
Cc: William Osei; nathan@csfs.org; Emma Palmantier; warner@csfs.org
Subject: RE: Merged PG I-Track data sets from 2008-2012

Russ Callaghan

From: Warner Adam <warner@csfs.org>
Sent: Thursday, January 23, 2014 3:01 PM
To: Russ Callaghan
Cc: Martha Shoemaker
Subject: Re: Merged PG I-Track data sets from 2008-2012
Attachments: graycol.gif

Hi Russ

Hope you are well. I have no problems with Martha proceeding with your recommendation.

Cheers,

W

Sent from my iPad

On Jan 23, 2014, at 1:37 PM, "Russ Callaghan" <Russ.Callaghan@unbc.ca<mailto:Russ.Callaghan@unbc.ca>> wrote:

Hello Warner,
I hope you're well. One of my students at UNBC (Martha Shoemaker) would like to undertake a Masters thesis with me, and she would like to study patterns of hepatitis C among people reporting current injection drug use in the Prince George I-Track studies (the 2008 and 2012 interview cycles). Martha wrote the final report of the 2012 Prince George I-Track study, and she has worked at the needle exchange for a number of years. Currently, she is a nurse working at Prince George inpatient alcohol/drug withdrawal management unit. Martha would like to study the patterns of HCV among people reporting current injection drug use in these studies, and she has a particular interest in understanding the characteristics of people who are HCV positive. I think this work as important clinical implications for all people using injection drug use in the Prince George area. As part of the data sharing agreements for the I-Track studies, I wanted to ask you if you would be okay for us to use these data for her master's degree (see the data sharing email from Jill at the Public Health Agency of Canada, below). In order for Martha and I to access the merged 2008 and 2012 Prince George I-Track data, we need your approval (on behalf of CSFS). Would you support our accessing these data?
If you'd like to talk about this in person, be happy to do so.
All the best to you,

Russ

Dr. Russ Callaghan, PhD
Associate Professor
Northern Medical Program
University of Northern British Columbia
3333 University Way
Prince George, British Columbia
V2N 4Z9
E-mail: Russ.Callaghan@unbc.ca<mailto:Russ.Callaghan@unbc.ca>
Phone: 250.960.5668

This email was generated using voice-to-text software.

Russ Callaghan

From: Osei, William <William.Osei@northernhealth.ca>
Sent: Friday, January 24, 2014 3:49 PM
To: 'Warner Adam'; 'Jill Tarasuk'
Cc: teegeen-UBC; 'Emma Palmantier'; Russ Callaghan; MacDonald, Kathy (Prince George PH); Hampe, Tanis
Subject: NH Approval for access to Merged PG I-Track data sets from 2008-2012

Hello:

In consultation with Kathy MacDonald, NH hereby approves the release by PHAC of the data CD to Russ for the purposes described by him in his earlier emails.

As part of the original NH Research Review Committee approvals for I-Track in Prince George, Russ is expected to share a copy of the resultant report with NH which would be posited on its website.

Thanks to all.

William

Dr. William Osei, Medical Health Officer PRINCE GEORGE. BC. Canada Northern Interior HSDA
Ph: 250-565-7461
Fax: 250 565-2144

Northern Health: I'm Proud to Belong.

-----Original Message-----
From: Warner Adam [mailto:warner@csfs.org]
Sent: Friday, January 24, 2014 2:10 PM
To: Jill Tarasuk; Osei, William
Cc: nathan.teegee@alumni.ubc.ca; Emma Palmantier; Russell Callaghan; MacDonald, Kathy (Prince George PH)
Subject: Re: Merged PG I-Track data sets from 2008-2012

Appendix C: Predicted Probability Calculations

1) Predicted probability of HCV positive status of PWIDs who have been injecting for less than two years (1.0) and have been injecting with others (1.0):

$$P(Y) = \frac{e^{(-4.170 + 2.062 * 1.0 + .912 * 1.0)}}{1 + e^{(-4.170 + 2.062 * 1.0 + .912 * 1.0)}} = \frac{e^{(-1.196)}}{1 + e^{(-1.196)}} = \frac{0.302}{1.302} = 0.23$$

2) Predicted probability of HCV positive status of PWIDs who have been injecting for less than two years (1.0) and have been injecting alone (2.0):

$$P(Y) = \frac{e^{(-4.170 + 2.062 * 1.0 + .912 * 2.0)}}{1 + e^{(-4.170 + 2.062 * 1.0 + .912 * 2.0)}} = \frac{e^{(-0.284)}}{1 + e^{(-0.284)}} = \frac{0.752}{1.752} = 0.43$$

3) Predicted probability of HCV positive status of PWIDs who have been injecting for more than two years (2.0) and have been injecting with others (1.0):

$$P(Y) = \frac{e^{(-4.170 + 2.062 * 2.0 + .912 * 1.0)}}{1 + e^{(-4.170 + 2.062 * 2.0 + .912 * 1.0)}} = \frac{e^{(0.866)}}{1 + e^{(0.866)}} = \frac{2.377}{3.377} = 0.70$$

4) Predicted probability of HCV positive status of PWIDs who have been injecting for more than two years (2.0) and have been injecting alone (2.0):

$$P(Y) = \frac{e^{(-4.170 + 2.062 * 2.0 + .912 * 2.0)}}{1 + e^{(-4.170 + 2.062 * 2.0 +. 912 * 2.0)}} = \frac{e^{(1.778)}}{1 + e^{(1.778)}} = \frac{5.918}{6.918} = 0.86$$

Supplement 1: I-Track Research Survey

The I-Track research project monitors the prevalence of HIV, HCV and associated risk behaviours among persons who inject drugs (PWID) in Canada (Public Health Agency of Canada, 2013). The surveillance system was developed as part of the Federal Initiative to Address HIV/AIDS to further the understanding of the HIV epidemic (PHAC, 2013). One of the key components of the Federal Initiative is the development of knowledge from sentinel surveillance programs of vulnerable populations across Canada (PHAC, 2013).

The PHAC Centre for Communicable Diseases and Infection Control developed and implemented the I-Track surveillance system in collaboration with provincial health authorities and community organizations (PHAC, 2013). The primary objectives of the I-Track research are to describe:

- the prevalence of HIV and HCV;
- drug use, injection and sexual behaviours;
- HIV and HCV testing behaviours;
- care and treatment history of HIV and HCV
- core knowledge of HIV-related risk behaviours, modes of transmission, and risk reduction strategies; and
- trends in prevalence and core behavioural measures (PHAC, 2013).

Ongoing behavioural and biological surveillance can serve as an early warning system for the spread of blood-borne infections. Moreover, knowledge gained from the I-Track system helps to inform and evaluate the development of public health policies, programs and interventions such as new prevention technologies and therapies (PHAC, 2013).

Pilot Study

The I-Track pilot phase was conducted in 2002 and 2003 in four sentinel sites: Regina, Sudbury, Toronto and Victoria (Health Canada, 2004). Prior to the pilot project, several centres in Ottawa and Quebec (SurvUDI) had already been conducting studies of PWIDs since 1995. These SurvUDI sites were included in the pilot phase of the I-Track questionnaire and collection of dried blood spot (DBS) specimens (Health Canada, 2004).

The purpose of the pilot study was to assess the feasibility of the proposed methods for conducting behavioural and biological surveillance of PWID populations across Canada (Health Canada, 2004). Research methods included a survey instrument consisting of 35 core questions, additional site-specific questions, and a standardized collection of dried blood spot (DBS) samples. A total of 794 participants were recruited in the sentinel sites, and an extra 297 participated at the selected SurvUDI centres (Health Canada, 2004).

The results of the pilot study revealed high levels of reported needle sharing, high levels of risky sexual activity, and unacceptably high prevalence of HIV (8.1%) and HCV (63.8%) infections within PWID populations (Health Canada, 2004). The pilot study also successfully demonstrated the overall feasibility of national level risk behaviour surveillance and laid the foundation for future phases of the system (Health Canada, 2004).

Phase 1

I-Track Phase 1 was underway by spring of 2003 and was expanded to include seven sentinel sites: Edmonton, Regina, Sudbury, Victoria, Toronto, Winnipeg, and the SurvUDI centres in Ottawa and Quebec (PHAC, 2006). By May 2005, a total of 3,031 participants had completed the survey and provided biological samples for testing of HIV and HCV (PHAC, 2006). Results revealed an increase in both HIV prevalence (13.2%) and HCV prevalence (65.7%). The prevalence of HCV infections between sentinel sites ranged from 61.5% in

Winnipeg to 68.5% in Victoria. As a result of the high prevalence estimates, it was recommended that the surveillance be expanded to include more urban and semi-urban sites to capture local differences between PWID populations (PHAC, 2006).

Phase 2

I-Track Phase 2 occurred between 2005 and 2008, and was expanded once again to include ten sentinel sites across Canada: Victoria, Central and North Vancouver Island, Prince George, Edmonton, Regina, Thunder Bay, Sudbury, Toronto, Kingston and the SurvUDI sites (PHAC, 2013). Results of HIV prevalence (13.2%) remained stable, while HCV prevalence (69.1%) continued to increase (PHAC, 2013). Moreover, the addition of new sentinel sites revealed substantial geographical variations in HCV infections existed between sentinel sites. For instance, the prevalence of HCV among Thunder Bay I-Track participants was 50%, while the prevalence of HCV among Prince George I-Track participants was 76.7% (PHAC, 2013).

Phase 3

I-Track Phase 3 occurred between 2010-2012 in 11 sites: all of those sites previously enlisted, as well as Whitehorse. Overall results revealed a slight decrease in both HIV prevalence (11.2%) and HCV prevalence (68%) from the previous Phase 2 results (PHAC, 2014). In Prince George, the Phase 3 results also showed a 12% decrease from in HCV prevalence from 76.7% in 2008 to 65% (PHAC, 2014). Despite the decrease, both Phase 2 and Phase 3 results identified Prince George I-Track participants as having among the highest prevalence of HCV of all sentinel sites (PHAC, 2014).

I-Track Research Methods

Cross-sectional surveys were conducted at selected sentinel sites during each phase of the I-Track research (PHAC, 2006; 2013; 2014). As noted in the I-Track overview section, each consecutive phase from the Pilot Study to Phase 3 increased in the number of sentinel sites. The target population of the surveillance system included PWIDs over the age of 14, 16 or 17 (varied by province) who voluntarily participated in the survey (PHAC, 2006). The intended research outcomes were point estimates of HIV and HCV serostatus, and reported behavioural risk data (PHAC, 2006).

Sample Size

Venue-based, convenience sampling at needle exchange programs (NEPs) offered a suitable site for recruitment because of high reported rates of NEP use by PWIDs in Canada (Health Canada, 2004; PHAC, 2006). The optimal sample size target was between 150-250 participants per sentinel site. Smaller communities, such as Prince George, were able to obtain the minimum number of participants during each phase of the survey. Length of time to achieve the required sample size varied from 2 weeks to 8 weeks, depending on the venue and the availability of resources (Health Canada, 2004). The recruitment and sampling of I-Track participants in Prince George commenced in mid-May and ended in late June in both survey phases.

Recruitment of Participants

Recruitment strategies were constrained by time, budget and access to populations (Health Canada, 2004). The most popular method for promoting the survey was by word of mouth (PHAC, 2013: PHAC, 2014). This occurred within the PWID population, as well as by staff working at the sentinel site. Staff involved in the needle exchange program promoted the survey to their clients, and directly solicited PWIDs to participate (Health Canada, 2004).

Two weeks prior to the commencement of the Prince George survey, posters and pamphlets were distributed by interviewers to 36 community services frequented by PWIDs. During Phase 3 recruitment, staff members at the needle exchange and the Wellness Van were also given promotional posters and small flyers to hand out to eligible clients. Whether by word of mouth or displayed on posters and pamphlets, the purpose of the survey, the eligibility requirements, and the $20 reimbursement were clearly explained to potential participants (PHAC, 2006).

Eligibility Criteria

All participants were voluntary and fulfilled five eligibility criteria:

- minimum age of consent (14, 16 or 17 years of age depending on province)
- IDU within the past 6 months prior to the interview
- capable of providing informed consent (as determined by site coordinator)
- able to complete the interview in English or French
- had not previously participated in the current phase of the survey (PHAC, 2013)

The site coordinator and/or interviewer determined if the eligibility criteria were adequately met for each participant prior to obtaining verbal consent.

Training of Staff

In Prince George, a site coordinator and 3 interviewers were hired by the Northern BC Aboriginal HIV/AIDS Coalition and Northern Health. The site coordinator and interviewers were trained by the National I-Track co-ordinator and data specialist according to the standardized I-Track procedural guidelines. A three-day training workshop reviewed all aspects of the survey protocol; namely, research ethics, questionnaire administration, routine infection control, dried blood specimen collection technique, awareness of PWID

culture/language, and debriefing (PHAC, 2006). The survey team met for two extra training days to practice survey interviewing, organize details of participant recruitment and screening, and review site-specific safety concerns.

Survey Implementation in Prince George

The Prince George I-Track survey took place at the AIDS Prevention/ Needle Exchange Program in the downtown core. Open interview times were scheduled daily and conveyed to NEP staff. Potential participants were actively solicited by NEP staff and/or the site coordinator when interviews were being conducted. In Phase 2, the site coordinator conducted the initial screening of participants because she was an employee of the NEP and was familiar with the clients. In Phase 3, both the site coordinator and interviewers conducted initial screenings, as they were all employees of the NEP and were familiar with the clients.

Interviews were conducted in private offices in the same building as the NEP. For safety reasons, at least two members of the I-Track team were always on site together. During Phase 2, participants were compensated $20 in cash, whereas in Phase 3 they were reimbursed $20 in gift certificates ($10 increments for McDonalds, Tim Hortons or Mohawk Bucks). All interviews were conducted on a first come, first served basis during the times posted. The site coordinator kept a confidential list of participants' first names and last initial to minimize any duplicates in participation within one survey cycle.

Data Collection

Informed consent. Once eligibility was confirmed and the participant was willing to proceed, the site coordinator or the interviewer reviewed a description of the survey. Participants were asked if they preferred to read the description themselves, or have the survey staff read it to them. The consent informed the candidates of their rights as a research study participant with respect to 1) choosing not to answer any question, 2) ending the

interview at any time, and 3) the fact that their right to service and/or treatment would not be affected by their decision to participate or not (Health Canada, 2004). Verbal consent was obtained after the survey description, ethical approval and consent agreement were reviewed (Health Canada, 2004).

All participants were assessed by the site coordinator or interviewer to be competent to give consent prior to starting the survey. Many clients who were willing to participate were under the influence of drugs and/or alcohol. Anyone who was too intoxicated to participate was kindly encouraged to return at a later time to complete the survey.

Questionnaire. The interviewer-administered I-Track questionnaire collected information on socio-demographic items, characteristics of drug use, injecting and sexual risk behaviours, HIV and Hep C testing and treatment history, use of local health services, and HIV-related knowledge. The Pilot Study and Phase 1 questionnaires were comprised of 45-65 core questions which had been adopted from the SurvUDI and other research involving PWID risk behaviours. The Phase 2 and Phase 3 questionnaires had 49 and 81 core questions respectively. The majority of the questions were step-wise, branching questions with skip patterns to ensure that respondents were only asked questions that applied to their responses. Both Phase 2 and Phase 3 questionnaires were conducted using a laptop computer program designed by the PHAC for interview data collection. Average time for each interview was 20-30 minutes.

Site-specific questions. Each sentinel site was encouraged to add site-specific questions to the core survey questionnaire. The purpose of the site-specific questions was to obtain feedback from PWIDs on local programs and resources (Health Canada, 2004). The Prince George I-Track Phase 2 questionnaire had 14 additional questions, and the Phase 3 questionnaire had 28 (PHAC, 2008; PHAC, 2012). The Prince George site-specific questions

were used to improve relations between PWIDs and the RCMP, to support the expansion of the NEP to include a mobile outreach van, and to determine the need for crack pipes as a harm reduction intervention.

Post-interview debriefing. At the end of the interview, participants were provided with time to ask any questions about the survey. Interviewers also provided harm reduction counselling for safer sex and safer injection practices. It was noted during both surveys that many I-Track participants were interested in formal HIV and HCV testing immediately after the interview. However, a public health nurse was most often not available during the interview times. The Prince George I-Track Phase 3 final report recommended that public health nursing services be provided concurrently with future phases of the survey for participants who were interested in formal HIV and HCV testing after they had completed the interview.

Biological specimen collection. Upon completion of the questionnaire, a biological sample (dried blood sample or oral fluid exudates) was collected and tested for HIV and HCV antibodies. A suitable finger on the non-dominant hand was cleaned with an alcohol swab (PHAC, 2006). A finger prick blood sample was obtained using a Sure-Step micro-lancet. It had been determined in the pilot study that most participants preferred to have the interviewers administer the lancet and to assist with blood extraction (Health Canada, 2004). It was noted that when interviewers assisted with DBS collection by performing the lancing procedure client stress was reduced, the interview time was shortened and the quality of the sample collected was improved (Health Canada, 2004).

A large drop of free-flowing blood was collected onto a cotton-fiber based product designed for the collection of body fluids (Health Canada, 2004). Five 1/2" diameter perforated circles on each specimen collection paper needed to be filled with blood. The

minimum number of circles for adequate testing was three, but most participants were able to provide all five (PHAC, 2007). It was emphasized that the blood needed to drop from the finger, not be dabbed onto the paper to avoid contamination. A bandage was applied after blood collection and routine infection precautions were practiced by all staff (PHAC, 2007).

Filter papers were carefully labelled with a computer-generated encrypted code that corresponded with the code that was on the participant's completed questionnaire (PHAC, 2007). There were no personal identifiers on any questionnaire or DBS collection paper. Each specimen paper was then allowed to dry in a suspended position for at least 3 hours, carefully packaged as per I-Track protocol, and sent to the HIV reference laboratory in Ottawa for testing (Health Canada, 2004).

HCV laboratory testing. The I-Track survey research used DBS specimens to assess HCV serostatus. The decision to use DBS came from a combination of information from the literature and the results of feasibility exercises (e.g., feasibility for M-Track Ontario Lambda survey) (PHAC, 2009). HCV antibody detection, acceptability to participants, cost-effectiveness, and stability for transportation and storage were all important considerations when choosing DBS specimen collection (PHAC, 2009).

All I-Track DBS specimens were tested for HCV antibodies at the National HIV and Retro-virology Laboratories in Ottawa (PHAC, 2009). HCV testing for DBS specimens was conducted using the Ortho Version 3 EIA. Validation testing has concluded that the sensitivity and specificity of the Ortho EIA when used with DBS was measured at 96.6% and 100% respectively (PHAC, 2009). As a result, HCV point estimates obtained through DBS specimens and EIA testing are considered valid and reliable.

Supplement 1: References

British Columbia Centre for Disease Control [BCCDC]. (2013). *Communicable Disease Control Manual.* Vancouver, British Columbia: British Columbia Centre for Disease Control.

Health Canada. (2004). *I-Track: Enhanced surveillance of risk behaviours among injecting drug users in Canada. Pilot survey report. February 2004.* Ottawa, Canada: Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control.

Public Health Agency of Canada [PHAC]. (2006). *I-Track: Enhanced surveillance of risk behaviours among people who inject drugs. Phase 1 report. August 2006.* Ottawa, Canada: Surveillance and Risk Assessment Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada.

Public Health Agency of Canada [PHAC]. (2007). *Procedural guidelines for I-Track training*. Ottawa, Canada: Public Health Agency of Canada.

Public Health Agency of Canada [PHAC]. (2008). *Prince George I-Track phase 2 questionnaire.* Ottawa, Canada: Public Health Agency of Canada.

Public Health Agency of Canada [PHAC]. (2009). *Report on the investigation of the validity of using dried blood spot (DBS) specimens for testing of selected pathogens.* Ottawa, Canada: Public Health Agency of Canada.

Public Health Agency of Canada [PHAC]. (2012). *Prince George I-Track phase 3 questionnaire.* Ottawa, Canada: Public Health Agency of Canada.

Public Health Agency of Canada [PHAC]. (2014a). *I-Track: Enhanced surveillance of HIV, hepatitis C and associated risk behaviours among people who inject drugs in Canada.*

Phase 2 Report. Ottawa, Canada: Centre for Communicable Disease and Infection Control, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada.

Public Health Agency of Canada [PHAC]. (2014b). *Summary of key findings from I-Track Phase 3 (2010-2012).* Ottawa, Canada: Centre for Communicable Diseases and Infection Control, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada.

Supplement 2: Hepatitis C Virus

The hepatitis C virus (HCV) is very unique and complex in its pathogenicity, mode of transmission, environmental viability, and natural history. Persons who inject drugs (PWIDs) are particularly susceptible to the inherent complexities of HCV, and has manifested into very high prevalence of acute and chronic infections within PWID populations. The purpose of Supplement Two is to describe the unique qualities of HCV, outline the transmission and long-term outcome of HCV infection among PWIDs, and review the challenges of providing HCV treatment to the particularly vulnerable PWID population.

HCV Pathogenicity

The HCV genome is classified as genus Hepacivirus within the Flaviviridae family (Irshad, Mankotia, & Irshad, 2013; Ray, Bailey, & Thomas, 2013). Initially known as “non-A non-B hepatitis”, HCV was identified as a unique infectious virus in 1989 (Irshad et al., 2013, p. 7896). As with all RNA viruses, HCV has very poor proofreading abilities and makes frequent replication errors (Ray et al., 2013). Continuous mutations cause HCV to be very heterogeneous with six identified genotypes and 120 identified sub-types or quasi-species (Irshad et al., 2013). Genotype 1a is the most common HCV genotype found among PWIDs in North America and northern Europe (Ray et al., 2013).

HCV has been described as an "infectious enigma" because it is extremely mutable and is able to evade host immunological detection and elimination (Previsani & Lavanchy, 2004). Efforts to develop a vaccine to control the spread of HCV have been impeded by the multiple infectious genotypes and sub-types dispersed worldwide (Irshad et al., 2013; Previsani & Lavanchy, 2004; Ray et al., 2013). Moreover, all HCV genotypes have been extremely evasive in their responsiveness to anti-viral treatments (Previsani & Lavanchy,

2004). The lack of effective vaccine and unsuccessful anti-viral medications have contributed to the rapid spread of HCV among vulnerable populations such as PWIDs.

HCV Transmission

HCV is a blood-borne pathogen transmitted by blood-to-blood contact (BCCDC, 2013; WHO, 2014). Transmission is most often caused by unsafe medical practices, blood transfusions, and injection drug use (BCCDC, 2013; WHO, 2014). High-risk groups include health care workers by accidental needle stick injuries; blood transfusion recipients prior to 1990; and PWIDs by sharing injection equipment (BCCDC, 2013; WHO, 2014). It is estimated that 80% of incident HCV infections occur among PWIDs (PHAC, 2011).

Low risk HCV exposures include: sharing toothbrushes, nail clippers and razors that may have tiny amounts of blood on them; skin piercings caused by tattoos, acupuncture or electrolysis; sexual intercourse; and vertical transmission during childbirth (BCCDC, 2013; WHO, 2014). HCV is not spread by coughing or sneezing; hugging or kissing; sharing cutlery or dishes; swimming in treated pools with open cuts or scrapes; being bitten by insects such as mosquitoes; skin contact with body fluids such as saliva, feces, urine or vomit; or breast-feeding (BCCDC, 2013; WHO, 2014).

The WHO (2014) estimates 80% of acute and chronic infections remain asymptomatic, leaving the host and recipient unaware of the potential for HCV transmission. Those who become symptomatic may experience multiple symptoms, including; fever, nausea, vomiting, abdominal pain, dark urine, loss of appetite, fatigue, grey stool, arthralgia, and jaundice (WHO, 2014). However, with an incubation period ranging from two weeks to six months, transmission can occur well before those infected develop symptoms or undergo HCV serostatus testing (WHO, 2014).

The ability of HCV infections to remain asymptomatic contributes to the high-risk of transmission between unaware PWIDs. Mild flu-like symptoms have been reported during the acute phase, but they resemble other viral infections and often remain ignored (BCCDC, 2013; WHO, 2014). The WHO (2014) strongly recommends that PWIDs presenting with any symptoms be screened for HCV due to the high-risk of infection within this population. Currently, the most accurate method to identify acute infection is by HCV antibody screening followed by viral RNA serology (Chan, 2014).

Prolonged Environmental Viability

Since 2010, the ability to create HCV in cell cultures has allowed for increased understanding of HCV viability on inanimate vectors and surfaces. In laboratory settings, multiple studies have repeatedly demonstrated the ability of HCV to remain infectious despite extended environmental exposure (Doerrbecker et al., 2011; Doerrbecker et al., 2013; Paintsil et al., 2010; Paintsil et al., 2014; Strike et al., 2010; Thibault et al., 2010). Research findings conclude that HCV can be transmitted by sharing contaminated drug injection equipment even after it is exposed to heat, cold, or disuse for prolonged periods of time (Doerrbecker et al., 2013; Paintsil et al., 2010; Paintsil et al., 2014). The prolonged environmental viability of HCV combined with the ubiquitous sharing of injection equipment has greatly contributed to the transmission of HCV among PWIDs.

Natural History of HCV

Acute HCV Infection

The initial six months of HCV infection is considered the acute phase (WHO, 2014). HCV enters the human host through blood-to-blood contact and travels to the liver via the circulatory system (Ray et al., 2013). Once the virus passes into liver cells (hepatocytes), the RNA unwinds and replicates by utilizing the liver's lipoprotein pathways (Ray et al., 2013).

HCV RNA continues to replicate and serum RNA levels become detectable within 2-3 weeks of exposure, whereas serum HCV antibodies are not detectable until 4-10 weeks after exposure (Chan, 2014).

Blood-to-blood exposure to HCV triggers both an innate and adaptive immune response in the susceptible host. The innate immune response involves natural killer (NK) cells that work to rapidly eliminate infected hepatocytes from the liver by cytolysis (Irshad et al., 2013). If the host's NK response is ineffective or compromised, HCV RNA will continue to replicate and invade hepatocytes (Irshad et al., 2013). The adaptive immune response is delayed, but involves cytolytic T-lymphocytes (CTLs) that are antigen-specific and can identify and eliminate HCV-infected hepatocytes (Irshad et al., 2013). The clearance of HCV infection depends on the production and persistence of the host's CTLs (Irshad et al., 2013).

Spontaneous Clearance of HCV

It is broadly estimated that 15% to 45% of incident HCV infections are eliminated by effective host immune responses known as spontaneous clearance (BCCDC, 2013; WHO, 2014). When a host achieves spontaneous clearance, serum HCV antibodies remain detectable, but there is no live HCV RNA in the body (BCCDC, 2013). Several factors have been associated with spontaneous clearance, including; HCV genotype, host genetic factors, female sex, mode of acquisition, clinical symptoms of HCV infection, concurrent immunosuppressive therapy, and HIV co-infection (Maasoumy & Wedemeyer, 2012; Westbrook & Dusheiko, 2014). Therefore, the host immune response, host characteristics, host co-morbidities, and the HCV genotype all influence the spontaneous clearance of acute HCV infection.

HCV Reinfection

Reinfection is defined as "the detection of infection with a strain distinct from the primary strain after spontaneous [clearance] or treatment-induced suppression" (Westbrook, 2014, p. S60). Multiple cohort studies have indicated spontaneous HCV clearance or effective anti-viral treatment do not protect against reinfection (Rapid Response, 2014). Multiple studies have also indicated the incidence of HCV reinfection is similar to the incidence of naïve HCV infection (Rapid Response, 2014). Moreover, broad conclusions suggest that in PWID populations with high HCV prevalence, those under the age of 30 who have received treatment for HCV appear to be at highest risk for re-infection (Rapid Response, 2014). However, more research on HCV reinfection is strongly recommended.

HCV reinfection among PWIDs highlights the controversy surrounding the provision of anti-viral treatment to PWIDs. HCV anti-viral treatments are extremely expensive, and providing PWIDs with the treatment remains ethically challenging due to issues of medication adherence, severe side effects, and the ongoing risk for HCV reinfection with continued injection drug use. Undoubtedly, increased rates of successful anti-viral treatment would decrease viral loads and reduce the incidence and prevalence of HCV infections among PWIDs. However, reinfection rates may offset the benefits of anti-viral treatment if not accompanied by changes in high-risk behaviours such as sharing injection equipment (Westbrook & Dusheiko, 2014). Providing expensive anti-viral treatments to infected PWIDs and the potential for reinfection is ethically challenging and more research is required.

HCV Disease Outcomes

Chronic HCV (CHC) Infection

If detectable levels of HCV RNA remain persistent in the blood beyond six months it is considered to be a chronic infection (WHO, 2014). CHC is confirmed by fluctuating liver

enzymes and detectable HCV RNA serum levels (Chan, 2014). Further blood testing confirms the viral genotype, while other diagnostics assess the degree of liver damage (WHO, 2014). HCV genotype and the extent of liver damage (fibrosis or cirrhosis) are important factors to be considered when developing treatment and management plans (WHO, 2014). CHC infections are not susceptible to spontaneous clearance, and can remain undiagnosed until symptoms of liver disease emerge (Westbrook, 2014).

Over time, the accumulation of necrotic hepatocytes results in fibrotic liver tissue, while the loss of healthy hepatocytes results in de-compensated liver function (Irshad et al., 2013). The gold standard for assessing liver fibrosis is the liver biopsy, but it is costly, invasive, requires expert interpretation, and may cause excessive bleeding or liver damage (Chan, 2014). Less invasive techniques to determine progression of fibrosis include blood tests of albumin levels, platelet count, prothrombin time, and non-invasive sonographic elastography to measure liver stiffness (Ray et al., 2013). These tests do not always confirm cirrhosis, and a liver biopsy may still be required.

During CHC infection, hepatic steatosis, oxidative stress and/or insulin resistance begin to progress concurrently with hepatocyte necrosis (Irshad et al., 2013). HCV-induced steatosis is the accumulation of fat deposits in the liver which also contributes to liver de-compensation over time (Irshad et al., 2013). HCV interferes with the liver's ability to secrete lipids and fatty acids from hepatocytes, and results in lipid accumulations often referred to as "fatty liver" disease (Irshad et al., 2013). Moreover, oxidative stress caused by CHC infection results in significant liver cell damage due to inflammation from the host immune response. As noted by Ray et al. (2013), HCV is not only a very heterogeneous virus, but CHC is also very heterogeneous with variable individual manifestations, variable rates of progression, and variable disease outcomes.

Cirrhosis of the Liver

One of the long-term outcomes of CHC and liver fibrosis is cirrhosis of the liver. Of those who develop CHC, 15-30% will develop liver cirrhosis within 20 years (WHO, 2014), while 41% will develop cirrhosis within 30 years of initial infection (Westbrook, 2014). Liver cirrhosis is "a condition that results from permanent damage or scarring of the liver…[and] leads to a blockage of blood flow that prevents normal metabolic and regulatory processes" (Canadian Liver Foundation, 2015). As cirrhosis progresses, the liver is unable to filter out toxins leading to toxin accumulation and progressive de-compensated liver function (Canadian Liver Foundation, 2015).

Progressive fibrosis and inflammation of the liver also lead to portal hypertension, where blood flow in the liver is restricted and portal venous pressure is greatly increased (Westbrook, 2014). Portal hypertension leads to gastric and esophageal varices in 50% of patients with cirrhosis (Westbrook, 2014). Excessive bleeding from ruptured varices is the second most common cause of death (after hepato-cellular carcinoma) for cirrhotic patients with CHC (Westbrook, 2014).

Hepato-cellular Carcinoma (HCC)

For patients with CHC infection who develop cirrhosis, the risk of progression to HCC is 1-4% per annum (Chan, 2014; Westbrook, 2014). HCC is a cancer that attacks liver cells and grows into multiple malignant tumours throughout the liver (Canadian Liver Foundation, 2015). However, HCC does not develop in CHC infected patients prior to advanced cirrhosis. Multiple studies have shown that providing anti-vial treatment for HCV in patients with cirrhosis results in significant risk reduction for the development of HCC (Westbrook, 2014). Although the risk for HCC is not completely eliminated, the use of HCV

anti-viral treatment shows promising results for reducing the overall burden of disease caused by CHC infection (Westbrook, 2014).

Further Complications

Several other factors have been associated with an increased risk for cirrhosis in those with CHC infection. These include: age at infection, male gender, alcohol consumption, obesity, insulin resistance, Type II diabetes, co-infection with hepatitis B virus or HIV, and immunosuppressive and genetic factors (Chan, 2014; Ray et al., 2013; Westbrook, 2014). Of particular concern to the PWID population are high rates of HIV/HCV co-infection and subsequent disease complications.

Although effective anti-viral treatments exist for HIV and HCV independently, multiple complications arise with concurrent HIV and HCV treatments including hepato-toxicity and cytopenia (Ray et al., 2013). Accelerated progression of HIV disease has been observed in persons co-infected with HIV/HCV, as well as impaired recovery of CD4 cells after anti-retro viral therapy treatments (WHO, 2014). PWIDs co-infected with HIV/HCV have also shown increased progression of cirrhosis, de-compensated liver, and HCC than in those mono-infected with HCV (WHO, 2014).

It is estimated that HIV/HCV co-infection accounts for 93% of cases of HCC (Westbrook, 2014) and co-infection of HIV/HCV has been associated with the development of HCC at a much younger age, and a much more rapid onset (WHO, 2014). In addition to increased HCC incidence among co-infected patients, there is a much poorer prognosis with studies reporting a 10-fold increase in mortality (Westbrook, 2014). Increased prevention and screening efforts, combined with the early treatment of HIV and HCV infections may greatly decrease the long-term outcome of HIV/HCV co-infections within PWID populations.

Recent Advancements in HCV Treatment

Advancements in successful HCV treatment has occurred very rapidly over the past four years. All-oral, single tablet, direct-acting anti-viral agents (DAAs) are now government approved and widely available. With estimated 90% cure rates, DAAs are proving highly effective because they target multiple stages of the HCV lifecycle (Pawlotsky, Feld, Zeuzem, & Hoofnagle, 2015). According to the Canadian Association for the Study of the Liver (CASL) consensus guidelines, HCV genotype 1a (the most common genotype found within North American PWID populations) is successfully treated with sofosbuvir 400mg/ ledipasvir 90mg (SOF/LDV) for eight to twelve weeks depending on HCV RNA levels and/or cirrhosis (Myers, Shah, Burak, Cooper, & Feld, 2015). If contraindicated or ineffective, multiple recommendations of other DAA treatment combinations are provided in the CASL guidelines (Myers et al., 2015).

According to the CASL guidelines, injection drug use is considered to be a "relative contraindication" and the guidelines recommend that "All patients with chronic HCV infection should be considered for antiviral therapy" (Myers et al., 2015, p. 3). However, concerns raised about non-adherence are well justified due to the constant threat of HCV developing resistance to the DAAs. The enigmatic HCV has a large population of related variant viruses known as quasi-species and a high replication rate that results in constant mutations (Myers et al., 2015). However, multiple strategies to overcome HCV resistance to DAAs are advised, including: avoiding DAA monotherapy, avoiding dose reductions due to treatment related side-effects, and maximizing adherence (Myers et al., 2015). Despite skepticism about drug adherence among PWIDs, it is strongly recommended that high-risk populations receive DAA treatment as soon as possible to reduce viral loads and decrease

HCV transmission between hosts, as well as reduce the progression of CHC infections to advanced liver disease (Pawlotsky et al., 2015).

Summary of HCV

As outlined in Supplement Two, the HCV pathogen, mode of transmission, natural history, and disease outcomes display many unique characteristics. First of all, HCV is highly prevalent among PWIDs, and is easily transmitted due to asymptomatic infections and ubiquitous sharing of drug injection equipment. Secondly, spontaneous clearance occurs in 15% to 45% of incident cases, but high rates of reinfection have been evidenced by research. Thirdly, those who are asymptomatic remain unaware of CHC infection until advanced liver fibrosis or cirrhosis has developed. Fourthly, the progression of cirrhosis to decompensated liver disease or HCC is influenced by variations in the host, virus genotype, and the environment. Finally, despite concerns of medication adherence and potential risks of reinfection, DAA treatment among eligible PWIDs must be promptly implemented to decrease the financial, social and personal burden of CHC infections.

Supplement 2: References

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Supplement 3: Drug of Choice (Three Category) Analyses

The multivariate LR analyses that was conducted with the three-category drug of choice variable (IV_DRUG_OF_CHOICE3) will be presented in this supplement. During bivariate analyses, the amphetamine category in the drug of choice variable was found to be significantly associated with HCV infection, $\chi^2 = 14.70$, df (2), $p = .001$. Similarly, studies in the related research had also indicated amphetamine injection as significantly associated with HCV infections among young PWIDS (Grebely et al., 2014; Miller et al., 2009). As a result, the three-category drug of choice variable (IV_DRUG_OF_CHOICE3) was thoroughly examined in the multivariate analyses before it was deemed problematic and replaced with a two-category drug of choice variable (IV_DRUG_OF_CHOICE2).

As shown in Table 11, the bivariate analyses of HCV status (DV_HCV_VALID) and the three-category drug of choice variable (IV_DRUG_OF_CHOICE3) rendered one cell with less than five cases ($n = 2$) in the amphetamine category of HCV positive cases. Multiple statisticians have cautioned that small cell sizes in bivariate analyses *may* become problematic in multivariate analyses, resulting in large SEs and large β coefficients (Field, 2013; Hilbe, 2009; Hosmer & Lemeshow, 2000; Tabachnick & Fidell, 2013). However, due to the clinical relevance of the amphetamine category within the multivariate analyses, it was decided to proceed with multivariate LR modeling and carefully assess the results.

Table 11

Bivariate analyses of IV_DRUG_OF_CHOICE3 and HCV status

Variable Label (Variable Name)	HCV Status (DV_HCV_VALID) Positive % (n)	Negative % (n)	Pearson's χ^2	*p*
Drug of choice (IV_DRUG_OF_CHOICE3)				
Cocaine/ crack	41.9 (112)	16.1 (43)	14.70	.001
Opiates	27.3 (73)	10.5 (28)		
Amphetamine	**0.7 (2)**	3.4 (9)		

Multivariate Logistic Regression

The full multivariate LR model including the three-category drug of choice variable (IV_DRUG_OF_CHOICE3) is presented in Table 12. Three IVs with significant Wald statistics ($p < .05$) are identified: number of years injecting (IV_INJECTION_YEARS), drug of choice: amphetamine (IV_DRUG_OF_CHOICE3), and injection partners (IV_INJECTION_PARTNERS).

Table 12

Full model including ten IVs (IV_DRUG_OF_CHOICE3) and one interaction variable

Variable	B	*SE*	Wald	*p*	Exp (β)	95% CI lower, upper
Number of years injecting (IV_INJECTION_YEARS)	2.16	.45	23.27	**.000**	8.70	3.61, 20.96
Drug of choice: Cocaine (ref) (IV_DRUG_OF_CHOICE3)			10.07	.007		
Drug of choice: Opiates (IV_DRUG_OF_CHOICE3)	-.18	.35	.27	.602	.83	.42, 1.65
Drug of choice: Amphetamine (IV_DRUG_OF_CHOICE3)	-2.84	.89	10.06	**.002**	.06	.01, .34

Table 12 (Continued)

Injection partners (IV_INJECTION_PARTNERS)	.94	.37	6.67	**.010**	2.56	1.25, 5.24
Residential mobility (IV_residence6months)	-.67	.38	3.19	.074	.51	.25, 1.07
Receptive sharing (IV_RECEPTIVE_SHARING)	-.40	.45	.81	.370	.67	.28, 1.60
Unstable housing (IV_HOUSING)	-.32	.37	.75	.387	.725	.35, 1.50
Travel to DTES (IV_TRAVEL_EASTVAN)	.47	.55	.72	.396	1.60	.54, 4.69
Gender (IV_SEX_GENDER)	.66	1.11	.35	.555	1.93	.22, 17.05
Involved in sex trade (IV_SEX_TRADE)	-.16	.46	.12	.729	.85	.34, 2.11
Aboriginal status (IV_aboriginal)	.24	1.11	.05	.832	1.27	.14, 11.20
Aboriginal status x Gender (IV_aboriginal x IV_SEX_GENDER)	-.11	.81	.02	.890	.89	.18, 4.39
Constant	-4.41	1.93	5.20	.023	.01	

As presented in Table 13, the three significant IVs identified in the initial model were then included in a new multivariate LR model. The three categories in the drug of choice variable (IV_DRUG_OF_CHOICE3) did not exhibit overly large β coefficients or *SE*s. Therefore, it was retained in the new model.

Table 13

New model including three significant IVs

Variable	β	*SE*	Wald	*p*	Exp (β)	95% CI lower, upper
Number of years injecting (IV_INJECTION_YEARS)	2.18	.43	26.43	**.000**	8.87	3.86, 20.39
Drug of choice: Cocaine (ref) (IV_DRUG_OF_CHOICE3)			9.12	.010		
Drug of choice: Opiates (IV_DRUG_OF_CHOICE3)	-.06	.33	.03	.859	.94	.50, 1.79
Drug of choice: Amphetamine (IV_DRUG_OF_CHOICE3)	-2.53	.84	9.02	**.003**	.08	.02, .42
Injection partners (IV_INJECTION_PARTNER)	.83	.33	6.24	**.012**	2.30	1.20, 4.43
Constant	-4.09	.93	19.47	.000	.02	

After running the new model with only the significant IVs, a second model was sequentially created by adding in the other seven IVs and one interaction term from the original model. As shown in Table 14, the second model showed no significant improvement in fit when compared with the new model ($p = .386$). Thus, the new model was accepted as the best fit model.

Table 14

Comparing the new model and the full model (Three IVs)

Test statistic	New model	Initial full model
Omnibus Test of Model Coefficients (Block)	$\chi^2 = 52.23$, df (4), $p < .001$	$\chi^2 = 8.70$, df (8), $p = .368$
-2 Log Likelihood	249.30	240.60

Assessing the Fit of the Best Model

The multivariate LR model identified three IVs that significantly contribute to the best fit model. The Hosmer and Lemeshow (2000) GOF test result was $\chi^2 = 0.98$, *df* (4), $p = .912$. The lack of significance of this statistical test indicates a well-fitted model (Hilbe, 2009). Using the Hosmer and Lemeshow GOF test, the dispersion parameter was calculated as GOF $\chi^2 = 0.98$ / *df* (4) = 0.25. As stated by Field (2013), over-dispersion is not present until the dispersion parameter is greater than one, and not problematic until it approaches two (p. 772). Over-dispersion violates the assumption of independence, but is not a concern in the current model.

Residual outliers. A listing of residual outliers identified six cases (4.6%) with residual *z*-scores greater than +/- 1.96 and six cases with residual *z*-scores greater than +/- 2.58. Upon closer inspection, each case reported injecting for more than two years, injecting cocaine or opiates, and injecting alone. However, they all tested HCV negative in the lab test results. As a result, the predicted outcome of HCV positive status based on the behaviours reported by these participants was not observed in reality. However, assessing the residual outliers confirmed that these cases were not problematic, and there was no clear reason for any to be removed from the model.

Further examination confirmed a Cooks Distance of < 1.0 for all residuals (maximum value was 0.49519), and all DF Beta values for the constant and the IVs were also < 1.0. The Leverage statistic was calculated using the equation [(k + 1) / N] where k is the number of IVs and N is the sample size. The expected leverage value was [(3+1 / 261)] = 0.015 and a leverage of [3(3+1) / 261] = 0.046 was used as a cut-off point for assessing influential outliers (Field, 2013). Nineteen cases had leverage values greater than 0.046 ranging from 0.048 to 0.165.

Upon closer inspection, the largest leverage values belonged to nine cases all of whom reported amphetamine as their primary drug of choice. This is concerning because such large leverage values indicate these cases have an excessively large influence on the fit of the model. As recommended by Field (2013), nine cases were removed from the analyses and when the model was run once again, the SEs, Wald statistics, and 95% CIs became extremely large. The three-category drug of choice variable (IV_DRUG_OF_CHOICE3) was clearly problematic.

Bootstrapping. A final test to assess the fit of the model was conducted using the bootstrap function in SPSS. As presented in Table 15, the bootstrapped CIs are excessively large and unacceptable. Clearly, the removal of the three-category drug of choice variable (IV_DRUG_OF_CHOICE3) from the multivariate LR model was warranted, and needed to be replaced by the two-category variable (IV_DRUG_OF_CHOICE2) and re-constructed.

Table 15

Bootstrap of best model (1,000 samples) (Three IVs)

Variable	**β**	***SE***	***P***	**Exp (β)**	**95% CI lower, upper**
Number of years injecting (IV_INJECTION_YEARS)	2.11	.45	.001	8.22	3.68, 22.85
Drug of choice*: Opiates (IV_DRUG_OF_CHOICE3)	-.10	.34	.750	0.91	0.47, 1.82
Drug of choice*: Amphetamine (IV_DRUG_OF_CHOICE3)	-2.50	6.62	.002	0.08	**1.97^{-10}, 0.32**
Injection partners (IV_INJECTION_PARTNERS)	.90	.35	.004	2.45	1.36, 5.27
Constant	-1.05	.45	.007	0.35	0.13, 0.76

*The referent category cocaine/ crack is not listed because bootstrapping does not include referent categories the sampling process.

Summary of Drug of Choice (Three Category) Analyses

Much effort was spent analyzing the three-category drug of choice variable (IV_DRUG_OF_CHOICE3) within the multivariate LR model. Bivariate analyses found the variable strongly associated with HCV ($\chi^2 = 14.70$, $p = .001$). However, when it was included in multivariate LR analyses, the amphetamine category was statistically problematic due to small cell size, and was reluctantly collapsed into a larger stimulants category with cocaine/ crack. Studies in the literature review identified amphetamine (specifically crystal meth) injection as significantly associated with HCV seroconversion; particularly among young PWIDs aged 14 to 26 years who have been injecting for less than two years (Grebely et al., 2014; Miller et al., 2009). Although the current thesis research was unable to conclusively identify injecting amphetamine as a significantly associated risk behaviour due to small sample size, it is suspected that PWIDs injecting these drugs are at very high-risk for HCV infection.